ELSEVIER

Journal of Molecular Catalysis B: Enzymatic 10 (2000) 551–554

JOURNAL OF MOLECULAR CATALYSIS B: ENZYMATIC

www.elsevier.com/locate/molcatb

Enzymatic synthesis of the acrylic esters: a comparative study

Vilas Athawale *, Narendra Manjrekar

Department of Chemistry, University of Mumbai, Vidyanagari, Bombay 400 098, India

Received 24 December 1999; received in revised form 13 January 2000; accepted 13 January 2000

Abstract

Various acrylic esters were synthesized by *Candida cylindracea* lipase (CCL) catalysed transesterification with different alcohols. A comparative study was carried out using 2,3-butanedione mono-oxime acrylate and vinyl acrylate as acylating agents. The rate of conversion was faster when oxime acrylate was used as acylating agent as compared to vinyl acrylate. Effect of solvents on the rate of conversion was studied and diisopropyl ether (DIPE) was proved to be a better solvent as compared to $CHCl_3$ and THF. The effect of various structural aspects of the substrates on the rate of conversion was studied. Among the linear alcohols studied, ease of conversion was found to be in the order of *n*-octanol > *n*-hexanol > *n*-butanol. Up to 80% conversion was achieved in the case of cyclohexyl methanol.

Keywords: Acylation; Enzymatic synthesis; Lipase; Oxime acrylate; Transesterification

1. Introduction

Acylation reactions using enzymes in organic solvents under nearly anhydrous conditions offer advantages such as better overall yields and the suppression of the undesired side reactions like hydrolysis of labile groups by water [1]. Various activated esters like enol esters [2] and acid anhydrides [3] were used as acyl donors for irreversible enzymatic acylation. However, these methods suffer with some drawbacks, like the generation of the toxic side products thereby inhibiting the formation of the required product. On the contrary, oxime esters have been shown to act as irreversible acylating agents [4], wherein the leaving group, an oxime, owing to its low nucleophilicity suppresses the reversible reaction.

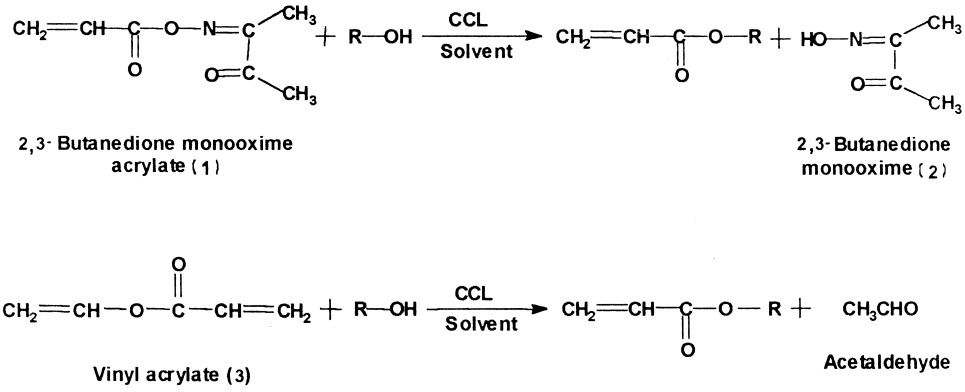
Acrylic monomers are extremely versatile building blocks. In general, they are synthesized by esterification or transesterification processes using chemical catalysts [5,6]. However, the chemical catalysts lead to undesirable side products. Therefore, we thought of using enzyme catalyst to avoid undesirable side products.

In this paper, we report a comparative study in the enzymatic synthesis of acrylate esters of different alcohols using 2,3-butanedione mono-oxime acrylate (**1**) and vinyl acrylate (**3**), as acylating agents and the immobilized lipase from *Candida cylindracea* lipase (CCL) from Sigma, USA (Scheme 1).

* Corresponding author. Tel.: +91-22-652-6091; fax: +91-22-652-8547.

E-mail address: polymerchemistry@yahoo.com (V. Athawale).

1381-1177/00/$ - see front matter
PII: S1381-1177(00)00008-4



Scheme 1.

The rate of conversion was faster when oxime acrylate was used as acylating agent as compared to vinyl acrylate. Various alcohols (Fig. 1) were used to study the effect of the structure of the alcohol on the rate of conversion. Among the linear alcohols studied, ease of conversion was found to be in the order of *n*-octanol > *n*-hexanol > *n*-butanol. In the case of cyclohexyl methanol, highest conversion (80%) was achieved.

2. Experimental

In a typical experiment, alcohol (20 mmol) and acylating agent (20 mmol) were dissolved in 20 ml of diisopropyl ether (DIPE) in a round bottomed flask followed by the addition of CCL (300 mg) with stirring at 200 rpm at 37°C. The progress of reaction was monitored by withdrawing the aliquots of the reaction mixture periodically and analyzing them by gas chromatography (GC). Conditions for GC analysis used are GC Varian Star 3600, Column RSL 200, Temperature Program 100°C/3/30/260, Injector Temperature 300°C, Detector (FID), Temperature 300°C. The absence of any undesired competing chemical acyl transfer reaction was verified in all cases by control experiments in the absence of enzymes. In order to obtain the retention times, all the acrylate monomers used in the present work were also synthesized chemically using triethylamine as a catalyst. In a typical chemical synthesis of acrylates, alcohol and triethylamine (1:1.1 molar ratio) were taken in 5 ml dry dichloromethane and 1.1 mol equivalent of acryloyl chloride was gradually added in 15 min at 0°C and the reaction was continued for 3 h at 30°C.

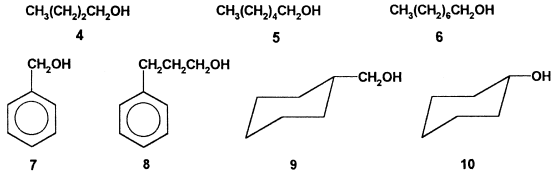


Fig. 1. Various alcohols used in transesterification.

3. Results and discussion

The type of organic solvent used has a profound effect on the reaction kinetics and stability of the enzymes. It is reported that the solvents with $\log P$ values more than two are good solvents, whereas solvents with $\log P$ values less than two show detrimental effects on the enzyme [7]. Various solvents were tested, such as DIPE, $CHCl_3$, and THF to study their effect on the rate of conversion. DIPE proved to be the best solvent of all and was chosen for the other substrates.

The rate of conversion was higher in all the substrates studied when oxime acrylate was used

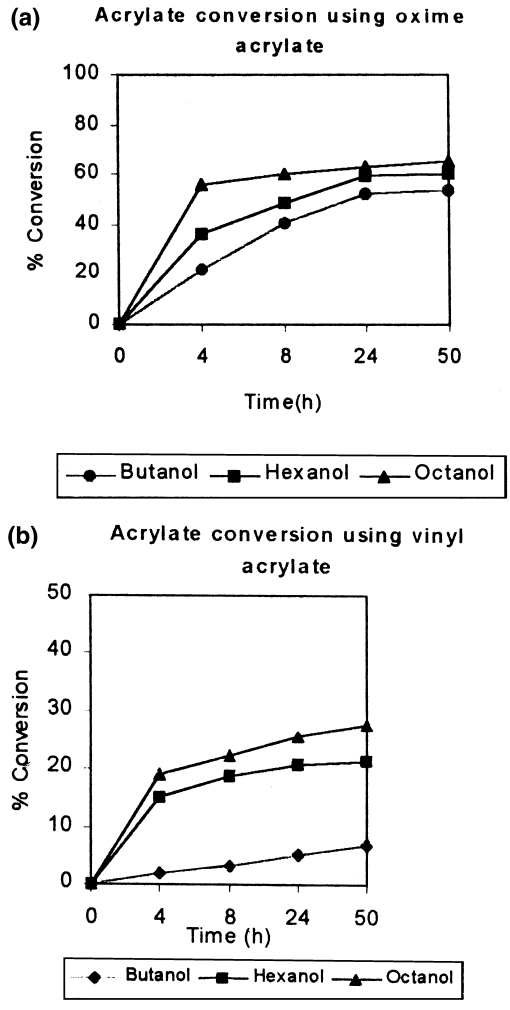


Fig. 2. Lipase catalysed transesterification of (a) oxime acrylate and (b) vinyl acrylate with various alcohols.

as an acylating agent as compared to vinyl acrylate. This must be due to the weak nucleophilicity of oxime (**2**), formed during transesterification, preventing it from taking part in the reversible reaction. Along with this, in the case of vinyl acrylate, the acetaldehyde formed during transesterification must be deactivating the enzyme, leading to low conversion rate. Among the linear chain alcohols studied, ease of conversion was found to be in the order of *n*-octanol (**6**) > *n*-hexanol (**5**) > *n*-butanol (**4**). This can be attributed to the increase in the hydrophobicity of the substrate with the increase in the chain length of the alcohols (Fig. 2a and b).

At this stage, we decided to examine the effect of the ring structure on the rate of conversion of acrylate esters. We therefore examined substrates (**7**) (**8**) (**9**) (**10**) wherein (**7**) and (**8**) have planar aromatic structure, whereas (**9**) and (**10**) have a cyclohexane chair conformation. Substrate (**7**), having a planar aromatic ring, probably does not fit into the enzyme cavity and consequently, low conversion was obtained as against (**9**) having the cyclohexane chair conformation leading to a relatively high conversion (Fig. 3a and b).

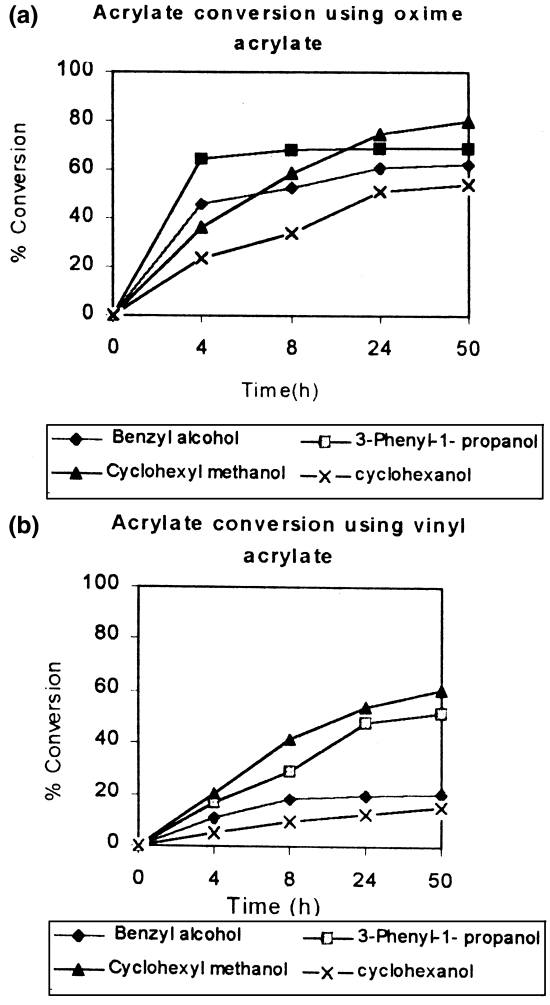


Fig. 3. Lipase catalysed transesterification of (a) oxime acrylate and (b) vinyl acrylate with various alcohols.

The relatively faster rate of the conversion of (**8**) in comparison with (**7**) can be easily ascribed to the presence of two additional $-CH_2$ groups in (**8**), which keep the aromatic ring away from the reactive site, i.e., –OH, thus, making the attack of the enzyme-acylating agent complex, more facile. The less reactivity of (**10**) can be easily traced to its secondary –OH active site.

4. Conclusions

Oxime acrylate proved to be the better acylating agent as compared to vinyl acrylate. Screening of the substrates with various structural aspects showed considerable change in the percentage conversion, which can be utilized to synthesize acrylate esters of alcohols having structural similarities. The results from the present study contribute towards better understanding of the catalytic activity of CCL in the transesterification. This reaction may find application in the preparation of the acrylate esters of more complex alcohols under mild conditions or which require enantio/regioselective esterification.

References

[1] Y. Wang, S. Chen, K. Liu, C. Wong, Tetrahedron Lett. 15 (1989) 1917.
[2] M. Degueil-Castaing, B. De Jeso, S. Drouillard, B. Maillard, Tetrahedron Lett. 28 (1987) 953.
[3] D. Bianchi, P. Cesti, E. Battistel, J. Org. Chem. 53 (1988) 5531.
[4] A. Ghogare, G. Sudesh Kumar, J. Chem. Soc., Chem. Commun. 20 (1989) 1533.
[5] P. Benneville, L. Luskin, H. Sims, J. Org. Chem. 23 (1958) 1355.
[6] F. Merger, H. Hutmacher, W. Schwarz, G. Nestler, M. Szucsanyi, R. Mueller-Mall, US Patent 4,777,265 (Oct. 11, 1988).
[7] A. Leo, C. Hansch, D. Elkins, Chem. Rev. 71 (1971) 525.