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PREPARATION OF CARBOXYALKYL ACRYLATE BY LIPASE-CATALYZED REGIOSELECTIVE HYDROLYSIS OF CORRESPONDING METHYL ESTER

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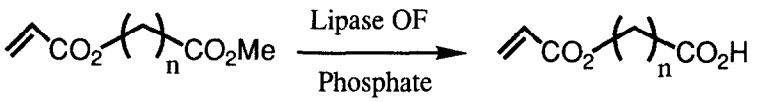
Abstracts: Carboxyalkyl acrylate was synthesized by lipase-catalyzed regioselective hydrolysis of corresponding methyl ester, methoxycarbonylalkyl acrylate, which was conveniently prepared from vinyl acrylate and hydroxyalkanoic acid methyl ester by lipase-catalyzed transesterification in an organic solvent.

Acrylate polymers have been widely used in a large number of important industrial applications[1]. These polymers are normally produced from the lower acrylates such as methyl, ethyl or butyl acrylate. Pendant hydroxyalkyl groups or carboxyalkyl groups, providing sites for further chemical modification or ionic effect, may also be incorporated into the polymers by copolymerization with special acrylates bearing hydroxyalkyl or carboxyalkyl side chaines. A direct chemically catalyzed transesterification method[2] cannot, however, serve as an efficient route for the preparation of these acrylates, since it would yield a complex mixture of unreacted alcohol and partially and fully substituted ester products. Although interesting syntheses of hydroxyalkyl acrylates by enzymatic transesterification have been reported[3], there are no convenient routes to acrylates bearing carboxyalkyl side chains. Chemical hydrolysis of **2**, which includes two ester bonds, is inefficent for preparation of **1** in good yield because of low

regioselectivity. A mixture of **1** and acrylic acid would be obtained. Recently, lipase-catalyzed hydrolysis and transesterification have gained much attention because of their high regio- and stereoselectivities[4]

In this paper, we present a regioselective hydrolysis of methoxycarbonylacrylate **2** by lipase to yield carboxyalkyl acrylate **1**. In addition, following reported procedures[5], a convenient synthesis of **2** by lipase-catalyzed transesterification of hydroxy ester and vinyl acrylate in an organic solvent is reported.

First, several commercially available lipases were surveyed for the hydrolysis of **2a**[6] in phosphate buffer[7]. Lipase OF, a lipase from *Candida cylindracea*, Meito Sangyo Co.,Japan, was found to catalyze the regioselective hydrolysis of **2a** to yield **1a** (74% yield) without any by-product. Other substrates, **2b** and **2c**[6], were also subjected to the same reaction to yield **1b** (84% yield) and **1c** (89% yield) respectively (Scheme 1)



2

a, n=1
b, n=3
c, n=5

1

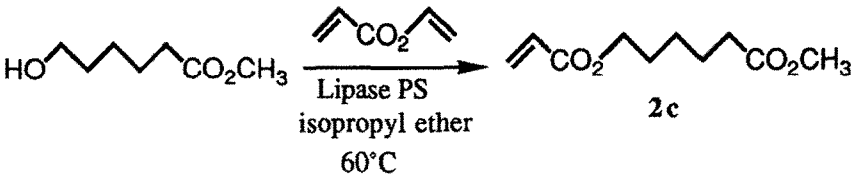
a, n=1
b, n=3
c, n=5

Scheme 1

Among these acrylates, **1c** was especially wanted as a monomer for synthesis of a pressure sensitive adhesive polymer. If a large scale preparation of **1c** were to be performed by this new method (Scheme 1), the current method for preparation of **2c** would need to be improved because of its low yield (55%)[6].

Lipase-catalyzed transesterification[5] was applied to preparation of **2c**. After surveying several commercially available lipases, Lipase PS, a lipase from *Pseudomonas* sp., Amano Pharm.Co., Japan, was found to catalyze the transesterification of vinyl

acrylate and methyl 6-hydroxyhexanoate in isopropyl ether to give **2c** (86% yield)[8].(Scheme 2)



Scheme 2

In conclution, a convenient route for preparation of carboxyalkyl acrylate was established by enzymatic procedure.

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6 Acylations of methyl glycolate with acryloyl chloride in diethyl ether in the usual manner gave **2a** (30%). In similar fashion, methyl 4-hydroxy butanoate and methyl 6-hydroxy hexanoate, which were prepared from 4-butyrolactone and 6-hexanolactone respectively by the established ring opening procedure[9], were converted to **2b** (45%) and **2c** (55%) respectively.

7 **2a-c** (500mg) was suspended in phosphate buffer 0.1M, pH7 (50ml). Lipase OF (50mg) was added to the suspension and the mixture was stirred at room temperature for 10 hr. The mixture was acidifed with 2N HCl and extracted with diethyl ether. The organic phase was washed with brine, dried over magnesium sulfate and concentated *in vacuo*. to give **1a** (74%), **1b** (84%), **1c** (89%) respectively.

8 Methyl 6-hydroxyhexanoate (5g) and vinyl acrylate (4g) were dissolved in isopropyl ether (250ml). Lipase PS (1g) was added to the solution and the mixture was stirred at 60°C for 6 hr. After filtration and concentration, the residue was purified by silica gel column chromatography(hexane/diethyl ether(3/1)) to give **2c** (5.9g, 86%).

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