Novel Route to Chiral Polymers involving Biocatalytic Transesterification of *O*-Acryloyl Oximes

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A novel route to chiral poly(acrylates) is established involving biocatalytic transesterification of *O*-acryloyl oximes in organic media.

Polymer synthesis involving biocatalytic steps[1,2] is an attractive route to chiral and stereoregular polymers.[3] Non-aqueous enzyme chemistry which is currently being developed is a valuable tool in macromolecular design. Optically active polymers have found applications as catalysts and reagents for asymmetric synthesis and as chiral absorbents for separation of racemic mixtures.[4,5] Thus far, all synthetic optically active polymers have been prepared by chemical means. Recently, Klibanov *et al.*[6] reported lipase-catalysed condensation between racemic diesters and chiral diols to yield trimers and tetramers. We have reported oxime esters as novel efficient irreversible acyl transfer agents for lipase catalyis in organic media.[7] Our endeavour is to extend the oxime ester methodology to prepare a variety of optically active polymers. We now report the preparation of a chiral acrylate monomer, 2-ethylhexyl acrylate, (+)-2-EHA, by the oxime ester methodology and its polymerization to yield optically active homo- and co-polymers.

We propose the general Scheme 1 for the preparation of chiral polymers having an asymmetric centre in the side chain.

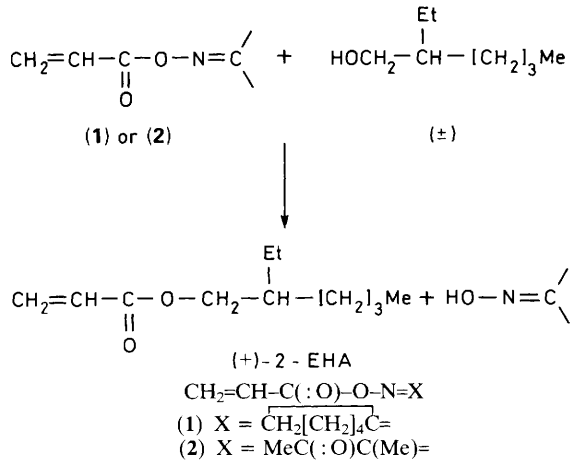
O-Acryloyl oxime + Chiral alcohol $\xrightarrow[\text{Solvent}]{\text{Lipase}}$ Chiral acrylate $\xrightarrow{\text{Polymerization}}$ Chiral polymer

Scheme 1

A typical experimental method for this biocatalytic transesterification is as follows (Scheme 2). Oxime acrylates (**1**) and (**2**) were prepared by the reaction of acryloyl chloride with biacetyl mono-oxime and cyclohexanone oxime respectively.[7] A solution of the *O*-acryloyl oxime (oxime acrylate)† (20 mmol) and racemic 2-ethylhexan-1-ol (20 mmol) in tetrahydrofuran (THF; 20 ml) was stirred at room temperature (35 °C) with porcine pancreatic lipase (PPL; 1 g). The product ester was purified and subjected to free radical polymerization at 80 °C using benzoyl peroxide as initiator. Control polymerizations were carried out with (±)-2-EHA and the physical properties of the polymer samples compared.

Lipase-catalysed tranesterifications are often slow because they are reversible[8]. Our experiments show that reactions involving conventional acrylate esters are even slower. The oxime ester methodology offers the following advantages. (i) They act as irreversible acyl transfer agents analogous to enol esters where the leaving group does not participate in the back reaction. (ii) Oxime acrylates can be prepared by a one-step procedure while enol acrylates are unknown. (iii) Lipase displays an overwhelming preference towards oxime esters over alkyl or enol esters.[7] Our preliminary studies of competitive binding indicate that enzyme–substrate binding is more favourable with oxime esters.[9] Tranesterification data involving conventional acrylates and oxime acrylates are presented in Table 1. Best correlations between hydrophobicity and biocatalytic activity are found using log *P*.[10] Higher rates were observed with hydrophobic solvents such as hexane (log *P* ~3.5) having log *P* >2 while low conversions resulted in solvents such as THF with log *P* <2. However, benzene and chloroform (log *P* ~2.0) did not follow this trend.

Table 2 summarizes the physical properties of chiral homo- and co-polymers of (+)-2-EHA. In optically active acrylates,



Scheme 2. *Conditions*: ~35 °C, lipase, solvent.

Table 1. Transesterification between acrylate esters and 2-ethylhexan-1-ol.[a]

Substrate ester	Solvent	Time /h	% Conversion (+)-2-EHA	$[\alpha]_D^{20}$/° (*c* 5, $CHCl_3$)
Ethyl acrylate	THF	48	6.7	+1.48
n-Butyl acrylate	THF	48	8.9	+1.42
(**1**)	Hexane	48	41.2	+1.1
	Benzene	48	44.2	+1.45
	Chloroform	48	8.7	+1.42
	THF	48	29.4	+1.41
(**2**)	Hexane	7	50.1	+1.13
	Benzene	7	50.0	+1.44
	Chloroform	48	27.4	+1.43
	THF	48	33.8	+1.42

[a] Conditions: lipase (1 g); solvent (20 ml); substrate ester and alcohol (20 mmol each); temp. 35 °C.

Table 2. Polymerization of 2-EHA.[a]

Monomer	% Conversion	M_w	$[\alpha]_D^{20}$/° (*c* 5, $CHCl_3$)	T_g[d] /°C
(±)-2-EHA[b]	56	27 846	0	—
(+)-2-EHA[b]	68	23 898	+3.25	—
(±)-2-EHA + styrene[c]	55	77 360	0	7
(+)-2-EHA + styrene[c]	59	34 879	+0.94	1

[a] Conditions: benzoyl peroxide (1% w/w), benzene, 80 °C, 6 h. [b] 2-EHA (5 mmol). [c] 2-EHA, styrene (10 mmol each). [d] Glass transition temperature.

† The identity of oxime acrylates was established by IR, NMR, and elemental analysis.

there is more space between the backbone of the derived macromolecule and the side chain chiral centres. Also, the ester group imparts a high rotational freedom and the disymmetric perturbation of the main chain occurs only with very bulky chiral side chains.[5] The observed difference in polymerization rates, T_g values, and molecular weights are being investigated from the stereochemical point of view.

Alternatively, the oxime acrylates (**1**) and (**2**) were polymerized first (M_w ~50 000) and lipase-catalysed transesterifications with (±)-2-ethylhexan-1-ol were carried out on the oxime functionalities. Reactions on these macromolecular substrates were incomplete and less selective. Efforts are underway to optimize reaction conditions.

Our work represents a novel enzyme-assisted synthesis of chiral polymers employing oxime acrylates as efficient, irreversible acyl transfer agents.

The authors thank Mr. R. Kelkar and Mrs. J. M. Tilak for analytical assistance and ICI India Ltd. for financial support.

Received, 27th June 1989; Com. 9/02731I

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