Tetrahedron Letters,Vol.26,No.30,pp 3623-3624,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

SYNTHESIS OF A NEW AMINO ACID BASED CROSS-LINKER FOR PREPARATION OF SUBSTRATE SELECTIVE ACRYLIC POLYMERS

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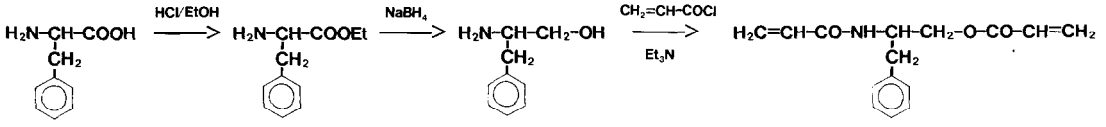
Abstract. The synthesis of N,O-bisacryloyl-L-phenylalaninol is described as well as its application in the preparation of a L-phenylalanine ethyl ester selective acrylic polymer.

In a recent study we have shown that amino acid ester selective polymers can be made by molecular imprinting using ion-pair association of substrate and monomers in the preparation of styrene and acrylic polymers.[1] However, to exploit fully the potential of the imprinting approach it is necessary to utilize various interactions, not merely ionic ones, to preorganize substrate and monomers during polymerization. Thus, there is a need for new monomers possessing different functional groups, and in particular for monomers suitable for the preparation of highly cross-linked macroporous polymers. It appeared to us that an attractive method of preparing polyfunctional monomers would be modification of amino acid derivatives by introducing acrylic groups. In this communication we wish to report on a method of synthesizing an acrylic-functional cross-linker derived from L-phenylalanine. The synthetic route of the chiral monomer is schematically depicted below.



The ester was prepared from L-phenylalanine and ethanol[2] and was subsequently reduced after treatment with sodium borohydride to form L-phenylalaninol.[3] The alcohol (16.6 mmoles) was dissolved in ice-cooled DMF (15 ml) and to this solution equimolar amounts (37 mmoles) of acryloyl chloride and triethylamine were added in portions. The mixture was allowed to react overnight at room temperature and the resulting precipitate was discarded. After a 20-fold dilution with ethyl acetate the solution was extracted with 0.5 M $NaHCO_3$ and 0.5 M citrate. The aqueous phases were discarded, and after evaporation of the organic phase the product was allowed to crystallize in methanol/water (1/10, v/v). The product, N,O-bisacryloyl-L-phenylalaninol, was pure as judged from analysis by NMR, elemental analysis and TLC[4]; m.p. 102 °C, $[\alpha]_D^{22}$ -28.1° (c = 0.43, methanol), yield 20 %. The cross-linker was examined in a polymerization study using acrylic acid as a counter ion of the substrate L-phenylalanine ethyl ester (L-Phe-OEt). The experiments were carried out in much the same manner as those reported earlier to

Table 1. Substrate binding data of phenylalanine based acrylic polymers

Polymer	Polymer specificity (print molecule)	Recovery (% of added print molecule)	$\alpha = K_D/K_L$ [2]
Print polymer	L-Phe-OEt	74 [1]	0.952 ± 0.012 [3]
Reference polymer	-	-	0.983 ± 0.012

1) Recovery of print molecules after extraction of formed polymers with acetonitrile was determined by amino acid analysis of hydrolyzed polymers (6N HCl, 24 hrs at 110 °C). 2) Apparent distribution coefficients for the partitions of D-[^{14}C]- and L-[^{3}H]-Phe-OEt between polymer and solvent. 3) Standard deviations; the error was determined for each binding experiment by counting each sample 8 times for 20 minutes to minimize counting errors.

make imprints of amino acid derivatives in acrylic polymers.[1] Prepared polymers were incubated with a racemic mixture of doubly radiolabelled phenylalanine ethyl ester.[5] The results of the binding experiments, batchwise in acetonitrile, are shown in Table 1. As can be seen, polymers imprinted with L-phenylalanine ethyl ester were chiral, showing preferential L-specificity as postulated in the design of the experiment. In contrast, reference polymers prepared in the absence of substrate during polymerization exhibited hardly any resolving power.

The successful application of a phenylalanine based cross-linker in molecular imprinting in this study suggests that other amino acids derivatized in the same sort of way as described here should be possible to use in radical polymerization processes. Utilization of such cross-linkers might for example allow imprinting of substrates in polyfunctional polymers, preparations of great potential as catalysts and substrate selective adsorbents. In addition, as L-amino acid residues are natural building blocks of enzymes and receptors ultimately forming the basis of nature's enantiomer selectivity, polymerization of such chiral compounds would lead to more natural model systems than those hitherto applied.

Acknowledgement. Part of this study was supported by a grant from the swedish Natural Science Research Council.

References and Notes.

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2. J.P. Greenstein and M. Winitz, In "Chemistry of the Amino Acids", Wiley, New York, p. 925 (1961).

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4. NMR (in $CDCl_3$) δ 2.9 (2H,m,-CH_2-C_6H_5); δ 4.2 (2H,d,J = 4.5 Hz, -OCH_2-); δ 4.5 (1H,m, >CH-); δ 5.6-6.6 (7H,m,CH_2 = CH-CO-NH- and CH_2 = CH-CO-O-); δ 7.3 (5H,m,-C_6H_5). Elemental analysis (C, 68.9 (69.5); H, 6.54 (6.56); N, 5.32 (5.41); O, 19.0 (18.5); calculated values within parenthesis). TLC (R_f 0.73 on silica in $CHCl_3/CH_3OH$, 10/1, v/v).

5. The assay mixture contained 5 μmols each of L-[C-2, C-3, ^{3}H]-phenylalanine ethyl ester (12.7 x 10^{-3} μCi/μmol) and D-phenylalanine [C-1, ^{14}C]-ethyl ester (7.2 x 10^{-3} μCi/μmol), 1 g of dry polymer and 8 ml of dry acetonitrile (incubation for 40 hrs at room temperature).

(Received in UK 5 June 1985)