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Synthesis of homochiral addition polymers derived from *N*-trityl-(*S*)-serine

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The radical induced homo- and copolymerization (with methyl methacrylate) of methyl *N*-trityl-*O*-acryloyl-(*S*)-serine and methyl *N*-trityl-*O*-methacryloyl-(*S*)-serine to give optically active polymers is reported. The resulting polymers are optically active, but show a nonlinear dependence of specific rotation vs. incorporation of chiral monomer. Copyright © 1996 Elsevier Science Ltd.

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The synthesis of condensation polymers derived from amino acids by the ring opening polymerization of Leuch's anhydrides is a well established process for the synthesis of biomimetic polyamides[1]. However, this type of polymerization process destroys the amino and acid functional groups which were present in the amino acid starting materials. Therefore, we have undertaken a project aimed at the synthesis of a different type of polymer derived from amino acids: i.e. the radical induced addition polymerization of amino acid derivatives bearing alkene functionalities in their side chain as outlined in *Scheme 1*[2]. This approach has the advantage of retaining the amine and acid functional groups within the polymer, and as a result of this, the polymers would be expected to possess a number of useful properties including: optical activity, solubility in aqueous and highly polar solvents, electrical conductivity through ion movement, and applications to templated polymers[3]. These properties will also be expected to be pH dependent. In this communication, we report our first results on the synthesis of monomers, polymers and copolymers of the type shown in *Scheme 1*, using serine as the chiral monomer precursor.

(*S*)-Serine **1** was chosen as the starting material, as its three functional groups can be easily differentiated. Thus esterification of (*S*)-serine with methanol/HCl gave the corresponding methyl ester as shown in *Scheme 2*. For amine protection, the triphenylmethyl group was chosen as it is easily removed under a variety of mild conditions and it was anticipated that the steric bulk of this group may confer desirable properties on the final polymers. Hence treatment of (*S*)-serine methyl ester with triphenylmethyl chloride and triethylamine gave the desired derivative[4] with both amine and acid groups protected. Reaction of the doubly protected serine derivative with acryloyl chloride or methacryloyl chloride in the presence of triethylamine gave the desired monomers **2** and **3**†.

Initially, the radical induced copolymerization of monomer **3** with methyl methacrylate was attempted in toluene solution, using AIBN as the radical initiator. However this methodology was found to give polymers with low molecular weights. To increase the molecular weight of the polymers, bulk polymerization effectively using methyl methacrylate as the solvent was undertaken, using benzoyl peroxide as the initiator. As can be seen from the results presented in *Table 1*, this gave polymers with reasonable molecular weights. *Table 1* also shows that there appears to be no correlation between the proportion of monomer **3** incorporated into the polymer, and the molecular weight of the polymer. The polydispersities of the polymers are highly variable, though these are usually in the range of 4–15; values which are typical for polymerizations carried out under conditions where autoacceleration can occur[5]. Consistent with this, a rapid rise in the viscosity of the polymerization mixture was observed soon after polymerization commenced.

In all cases, the ratio of methyl methacrylate to monomer **3** in the polymer was greater than the corresponding ratio in the monomer mix as determined by ^{1}H n.m.r. integration of the two methyl ester signals in the polymers. This analysis was facilitated by the triphenylmethyl group present in monomer **3**, which has a strongly shielding effect[6] on the methyl ester of monomer **3**, shifting its ^{1}H n.m.r. resonance upfield by about 0.5 ppm, compared to the methyl ester of methyl methacrylate. A doubling of the ^{1}H and ^{13}C n.m.r. resonances due to the methyl methacrylate residue peaks was observed in all of the polymerizations, indicating that the polymers are atactic with signals being seen for both syndiotactic and isotactic regions of the polymer chains[7]. All of the polymers derived from monomer **3** were optically active, the specific rotations being given in *Table 1*. However, as shown in *Figure 1*, the specific rotation of the polymers does not vary linearly with the percent-incorporation of chiral monomer. Rather, the specific rotation initially increases rapidly as the percentage of chiral monomer incorporated increases from 0–10%, then the rate of increase of specific rotation slows

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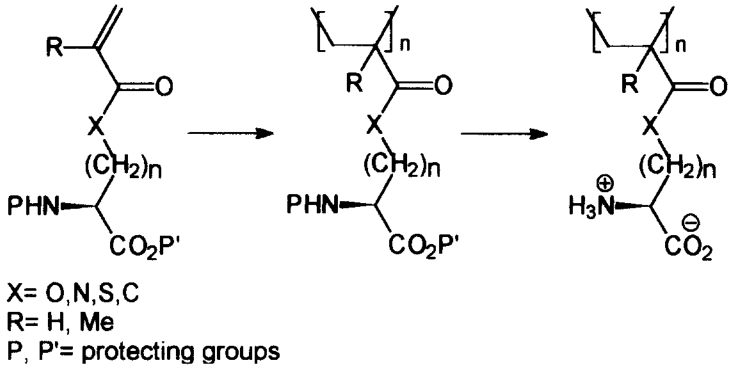
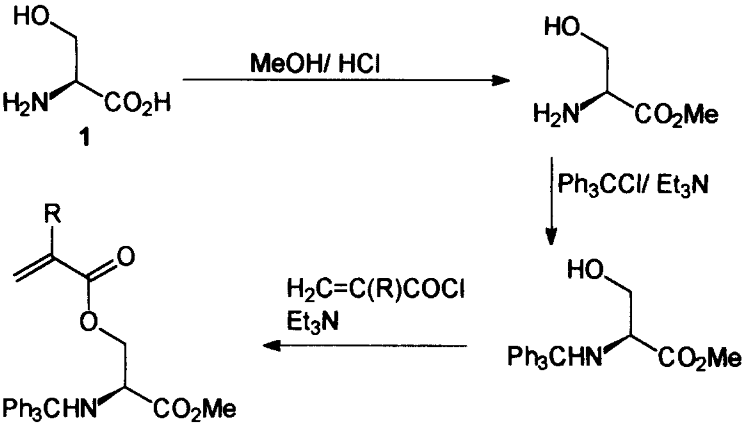
† Monomers **2** and **3** were characterized by ^{1}H and ^{13}C n.m.r., i.r. spectroscopy, mass spectroscopy, elemental analysis, and polarimetry. All polymers were characterized by ^{1}H and ^{13}C n.m.r., gel permeation chromatography, elemental analysis, and polarimetry



Scheme 1



2 R=H, **3** R=Me

Scheme 2

Table 1 Analytical data for polymers derived from monomers **2** and **3**

Monomer	MMA (added)	MMA^a (inc)	M_n^{b}	M_w^{b}	M_w/M_n	$[\alpha]_D^{20}$^{f}
2^c	0	0	4980	20250	4.1	+68.0
2^d	1	2	6330	73550	11.6	+37.7
2^d	2	3	7965	59600	7.5	+32.6
2^d	5	6	3900	46700	12.0	+21.1
2^d	10	21	15350	142500	9.3	+12.9
2^d	15	25	16300	245000	15.0	+9.7
2^d	25	35	18700	113000	6.0	+6.8
2^d	50	98	29400	149000	5.1	+3.0
2^d	100	Not detected	25950	120500	4.8	+1.0
3^c	0	0	16100^e	127500	7.9	+54.1
3^d	1	2	22400^e	299000	13.3	+33.0
3^d	2	3	18400^e	226000	12.3	+28.4
3^d	5	11	14500^e	95550	6.6	+18.0
3^d	10	15	27050	250000	9.2	+14.8
3^d	15	24	20500	122500	6.0	+7.6
3^d	25	37	28200	157000	5.6	+6.2
3^d	50	65	16550	190500	11.5	+3.9
3^d	100	127	29850	177500	6.0	+2.5

MMA = methyl methacrylate

[a] Ratio of MMA to amino acid in polymer determined by ^{1}H n.m.r. of the methyl esters

[b] Measured by g.p.c. using chloroform as eluent and polystyrene standards

[c] Polymerization carried out in toluene using benzoyl peroxide as initiator

[d] Polymerization carried out with no solvent and benzoyl peroxide as initiator

[e] G.p.c. results are calculated on all material in the sample with a molecular weight greater than 1000

[f] All specific rotations were measured at a concentration of 1.0 g/100 ml in chloroform

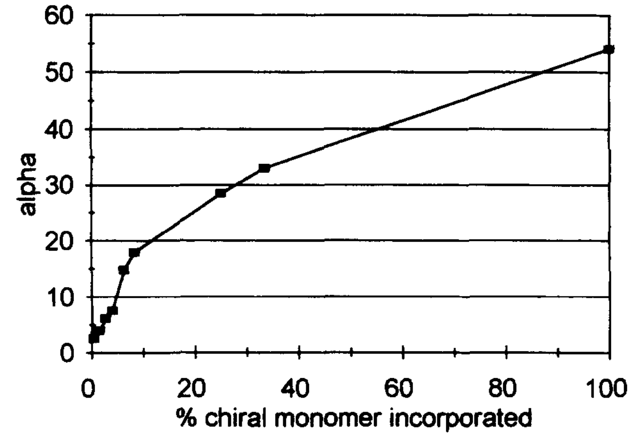


Figure 1 Plot of specific rotation vs. percentage incorporation of monomer **3**

down and continues to rise approximately linearly to 100% incorporation.

There appear to be two possible reasons for this nonlinear dependence of specific rotation to percentage composition of the polymer: asymmetric induction from the enantiomerically pure serine α-centre to the new chiral centres within the polymer backbone which are created during the polymerization; or a change in the conformation of the polymer from random coil to helical, a process which would be essentially complete once the polymer contains about 10% of the chiral monomer. A similar nonlinear variation of specific rotation has been reported for copolymers (radically or anionically initiated) derived from *N*-substituted maleimides and other monomers such as other maleimides[8], styrenes, or methacrylate in which one of the components was enantiomerically pure, with both positive[9] and negative[10] deviations from linearity having been observed, as well as more complex cases in which the specific rotation increases linearly for a period followed by a deviation from linearity[11]. Similar nonlinear effects have also been reported for polymers derived from a chiral styrene unit and a variety of styrene or methacrylate based comonomers[12]. In these cases asymmetric induction into the polymer backbone was reported to be the cause. However, a nonlinear relationship between polymer composition and specific rotation is not always observed, as the radical copolymerization of an enantiomerically pure norbornyl ester of methacrylate with either methyl methacrylate or styrene gave a series of copolymers in which the specific rotation was directly proportional to the percentage of chiral monomer incorporated into the polymer[13].

Sterically hindered esters of methacrylate, such as triphenylmethyl methacrylate, are known to form helically chiral polymers which can be separated into left- and right-handed forms[14], and this could provide the alternative explanation for the nonlinear variation of specific rotation. In these cases no asymmetric induction into the polymer backbone is observed, as removal of the triphenylmethyl esters gives an optically inactive polymer. Rather, the optical activity of the polymer is due solely to its conformation which is maintained by the bulky triphenylmethyl groups. A similar effect has also been observed in the copolymerization of amino acid derived isocyanates[15]. In this case, the specific rotation decreased as the amount of chiral monomer incorporated into the polymer increased. It is not clear which of these two factors is operating in the case of the copolymers incorporating monomer **3**. However, we have observed that the polymers do not exhibit mutarotation, a property which has been observed for other polymethacrylates whose chirality is due to conformational effects[16], and for other helical polymers[15].

To optimize the homopolymerization of monomer **3**, the effect of the monomer concentration in toluene was investigated using benzoyl peroxide as an initiator. The optimum concentration was found to be 3 molar, with lower concentrations producing low molecular weight material and higher concentrations being unsatisfactory due to solubility problems. Under these optimized conditions, a chiral homopolymer with $M_n = 16\,100$ and $M_w = 127\,500$ was obtained (*Table 1*).

Having optimized the polymerization of monomer **3**, the homo- and copolymerization (with methyl methacrylate) of the acrylate derived monomer **2** was also investigated. The results given in *Table 1* and *Figure 2* are very similar to the results obtained using monomer **3**. The molecular weight of the polymer again increases as the proportion of methyl methacrylate in the polymer increases, and the specific rotation again shows a nonlinear effect, initially rising rapidly up to about 10% chiral monomer incorporation, then showing an almost linear increase over the remaining concentration range.

In summary, we have shown that amino acid derived acrylate and methacrylate derivatives can be prepared, and that these compounds are suitable monomers for radical induced addition polymerization and copolymerization reactions. Conditions for the polymerization have been optimized, and the resulting polymers have been shown to be optically active and atactic. The specific rotation of the polymers does not vary linearly with the amount of chiral monomer incorporated into the polymer. The applications of these and related polymers are currently being investigated, and will be reported in due course.

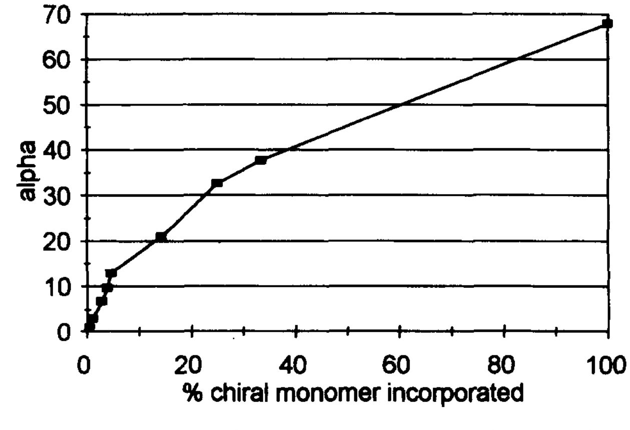


Figure 2 Plot of specific rotation vs. percentage incorporation of monomer **2**

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