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Synthesis and chiro-optical properties of copolymers from *N*-Boc-*O*-methacryloyl-(*S*)-serine benzhydryl ester and methyl methacrylate

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The synthesis of the homopolymer of *N*-Boc-*O*-methacryloyl-(*S*)-serine benzhydryl ester and a series of copolymers with methyl methacrylate by benzoyl peroxide-induced radical polymerisation is reported. All of the polymers are optically active, but both the magnitude and the sign of the specific rotation varies with the composition of the polymers. At low incorporations of the serine-derived monomer, the specific rotation is positive, but a maximum value is reached at approximately 35% serine-derived monomer incorporation. As more serine-derived monomer is incorporated into the polymers, the specific rotation falls and becomes negative at 70% serine-derived monomer incorporation. The molecular weight and molecular weight distributions of the copolymers were determined by GPC. The protecting groups could be removed from the copolymers, giving a class of zwitterionic, chiral polymers some of which are soluble in aqueous solvents.

(Keywords: *N*-Boc-*O*-methacryloyl-(*S*)-serine benzhydryl ester; copolymer; specific rotation)

Introduction

A large amount of work has been published on the preparation of condensation polymers derived from amino acids, usually by the ring-opening polymerisation of Leuch's anhydrides (for examples, see Ref. [1]). However, this type of polymerisation converts the amino and carboxylic acid functionalities present in amino acids into amides. The synthesis of condensation polymers using functional groups present in the sidechains of amino acids has also been reported[2]. In recent publications, we have reported for the first time the synthesis of addition polymers derived from amino acids, in which a polymerisable group has been introduced into the sidechain of the amino acid[3]. This approach has the advantage of retaining the amino and carboxylic 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: solubility in aqueous and highly polar solvents, electrical conductivity, and optical activity since enantiomerically pure amino acids are readily available.

In our previously reported work[3], we have only described the synthesis of polymers derived from serine in which the carboxylic acid functionality has been converted into a methyl ester. We have, however, shown that copolymers derived from such monomers and methyl methacrylate exhibit a non-linear dependence of specific rotation with monomer composition, an effect which seems to be due to asymmetric induction into the polymer backbone. In the present communication, we report the synthesis of homo- and co-polymers derived from a serine unit bearing acid-labile protecting groups on both the amino and carboxylic acid functionalities and methyl methacrylate. The deprotection of the resulting polymers to give for the first time, polymers derived from amino acids, and retaining the amino and carboxylic acid functionalities, is also reported, as is the remarkable non-linear variation of specific rotation with monomer composition observed for the fully protected polymers.

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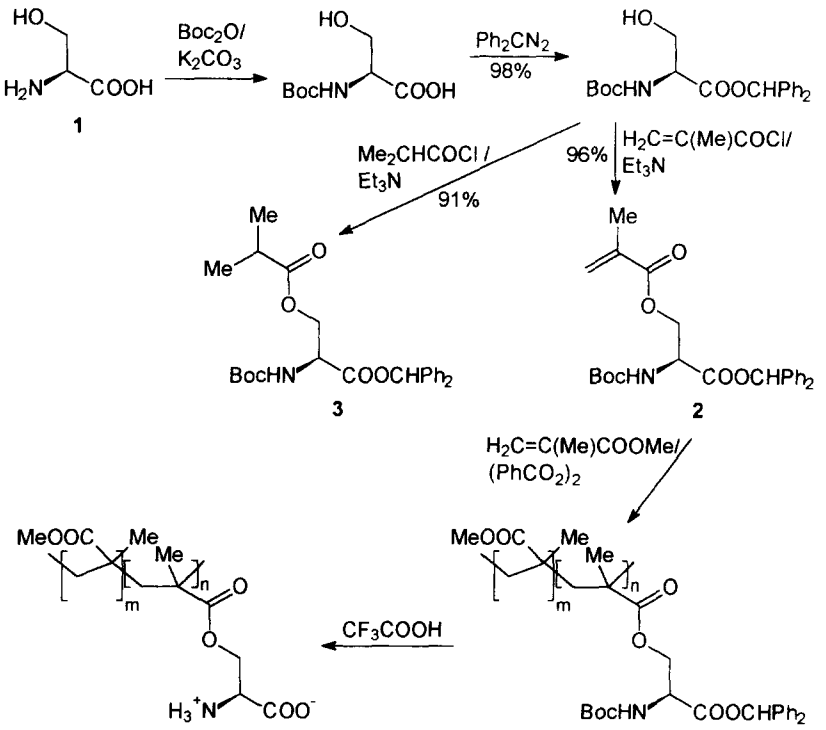
Results and discussion

Based on our previous work, (*S*)-serine **1** was employed as a trifunctional monomer containing three different functional groups. However, an acid-labile benzhydryl ester was employed for protection of the carboxylate functionality rather than the methyl ester previously utilised. The amine-protecting group was also changed from triphenylmethyl to *t*-butyloxycarbonyl (Boc) in order to delineate the effect of the triphenylmethyl group on the structure and properties of the polymers. Thus, the synthesis of monomer **2*** was achieved by reacting (*S*)-serine first with Boc_2O, then with diphenyldiazomethane[4] and finally with methacryloyl chloride as shown in *Scheme 1*.

Monomer **2** was then polymerised and copolymerised with methyl methacrylate using benzoyl peroxide (1 mol.%) as a radical initiator and toluene as the solvent. The polymerisations were carried out at 110°C for 4 h, using as high a concentration of monomers in toluene as possible. The crude polymeric product was dissolved in chloroform, and precipitated by the addition of petrol. Characterisation data for the polymers is given in *Table 1*. The ratio of methyl methacrylate to monomer **2** incorporated into the polymers was determined from the ^1H n.m.r. spectra of the polymers by integration of the peaks due to the methyl ester of methyl methacrylate and the $CHPh_2$ of the benzhydryl ester of monomer **2**. The molecular weight and molecular weight distributions of the polymers was determined by g.p.c. using THF as eluent and polystyrene reference samples. Thus the M_n and M_w values given in *Table 1* are polystyrene equivalent molecular weights rather than true molecular weights. The polydispersities of the polymer samples are

* All new compounds gave satisfactory spectral and analytical data (^1H and ^{13}C n.m.r., [α], IR, low- and high-resolution mass spectra, and for polmers g.p.c.).



Scheme 1

Table 1 Analytical data for polymers derived from monomer **2** and methyl methacrylate

Entry	% **2**[a]	M_n[b]	M_w[b]	M_w/M_n	$[\alpha]_D^{20}$[c]	$[\alpha]_D^{20}$[d]
1	100	12300	45000	3.7	− 7.2	+ 14.9[e]
2	92	11900	91400	7.7	− 5.2	+ 13.2[e]
3	88	15900	160000	10.0	− 5.1	+ 13.0[e]
4	88	7280	15600	2.1	− 4.2	
5	82	10600	42800	4.0	− 2.2	
6	65	3950	8420	2.1	+ 1.5	
7	56	5740	21200	3.7	+ 2.7	
8	36	4690	11300	2.4	+ 3.1	+ 7.5[f]
9	29	5630	12500	2.2	+ 2.8	
10	19	3510	6870	2.0	+ 2.0	
11	16	6910	12500	1.8	+ 1.6	
12	10	21500	171000	8.0	+ 1.0	+ 4.1[f]
13	6	13400	102000	7.6	+ 0.4	+ 3.1[e]

[a]Determined by ^{1}H n.m.r. spectroscopy
[b]Measured by g.p.c. using THF as solvent and polystyrene standards
[c]Specific rotations were measured at a concentration of 1.0 g/100 ml in chloroform
[d]Specific rotation of the deprotected polymer
[e]In a 7:3 DMSO:water mixture at a concentration of 1.0 g/100 ml
[f]In DMSO at a concentration of 1.0 g/100 ml

highly variable (1.8–10), as are the molecular weights, even for polymers containing the same proportion of the monomers (cf. entries 3 and 4 in *Table 1*). The variability of these values is probably at least partly explained by autoacceleration during the polymerisations[5]. It is also possible that hydrogen atom abstraction from the C*H*Ph$_2$ group leading to branched polymers contributes to the high polydispersities. However, the range of polydispersities is the same as that previously reported for monomers derived from serine methyl ester[3], so this does not appear to be a significant reaction. All of the polymers were soluble in chloroform and were optically active (*Table 1*).

A plot of the specific rotation of the copolymers *versus* % monomer **2** incorporation shows a remarkable non-linear effect (*Figure 1*). At low monomer **2** incorporations, the specific rotations are positive, but reach a maximum at *ca.* 35% chiral monomer incorporation. Thereafter, the magnitude of the specific rotation decreases and becomes negative at *ca.* 70% monomer **2** incorporation. Non-linear variations of specific rotation with % chiral monomer in copolymers have previously been reported[3,6,7], however, to our knowledge this is the first time that such a dramatic effect involving a change in the sign of the specific rotation has been observed. The effect is not due to differences in the molecular weight distributions of the polymers, since polymers with the same monomer composition, but very different molecular weight distributions (*Table 1* entries 2 and 3), have comparable specific rotations. Also, entries 4, 6, 8, 9, and 11 in *Table 1* have similar M_n and M_w values and are sufficient to show the non-linear effect.

There are two possible explanations for the non-linear variation of specific rotation; asymmetric induction into the polymer backbone[6,7] or the adoption of a helical conformation with a preferred handedness[8]. The latter situation is

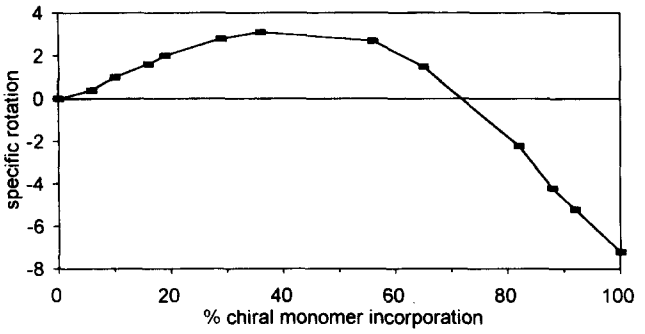


Figure 1 Plot of specific rotation *versus* percentage incorporation of monomer **2**

only encountered with methacrylate derivatives bearing large triphenylmethyl or related substituents. Since no such group is present in monomer **2**, it seemed more likely that the non-linear effect was due to asymmetric induction, as in the case of the related polymers derived from *N*-triphenylmethyl-*O*-methacryloyl-(*S*)-serine methyl ester[3]. This was supported by CD spectra of the copolymers, which showed no evidence of any preferred conformation, and by a variable temperature-specific rotation study (298–323 K) which showed no significant change in the specific rotation as the temperature was increased.

To further investigate the origin of the specific rotation behaviour of the polymers, the corresponding saturated monomer **3** was prepared as shown in *Scheme 1*. It has previously been reported that saturated monomer analogues can act as model compounds for studying the chiro-optical properties of addition polymers[6]. In the present case, the specific rotation of compound **3** was −6.2 (c=1.0, chloroform) which is in excellent agreement with the value of −7.2 (c=1.0, chloroform) recorded for the homopolymer of monomer **2**. Based on these results, we conclude that the non-linear dependence of specific rotation on monomer composition observed in the copolymers of compound **2** is due to asymmetric induction into the polymer backbone. This asymmetric induction results in a positive specific rotation which, at low monomer **2** incorporations, has a higher magnitude than the negative rotation due to the serine unit. However, as the amount of monomer **2** incorporated into the polymers increases, the magnitude of the negative rotation due to the serine units increases and starts to dominate the observed specific rotation, until at very high monomer **2** incorporations the specific rotations of the copolymers tends towards that of model monomer **3**.

Six of the copolymers listed in *Table 1* were fully deprotected by treatment with trifluoroacetic acid for 16 h. That both the benzhydryl and Boc protecting groups had been fully removed by this treatment was readily determined by ^{1}H n.m.r. Unlike the polymers with protecting groups on the functional groups, it was not possible to find a single solvent system in which all of the deprotected polymers were soluble, so it was not possible to investigate the variation of specific rotation with monomer incorporation in this series of polymers. The deprotected homopolymer was water soluble, the copolymers containing >80% of serine-derived monomer were soluble in water/DMSO mixtures, the deprotected copolymers containing 10–40% of serine were soluble in DMSO, whilst the deprotected copolymer containing 6% of serine-derived monomer was soluble in chloroform.

Conclusions

The synthesis of copolymers between *N*-Boc-*O*-methacryloyl-(*S*)-serine benzhydryl ester **2** and methyl methacrylate has been achieved. The copolymers exhibit a pronounced non-linear dependence of both the sign and the magnitude of specific rotation on monomer **2** incorporation, which is due to asymmetric induction into the new stereocentres created along the polymer backbone during the polymerisation. It was also possible to remove the protecting groups from the copolymers, giving a class of polymers containing chiral, zwitterionic pendant groups, some of which are soluble in water or aqueous solvent systems. Our work in this area is continuing, and further results will be reported in due course.

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References

1. Berger, A. and Katchalski, E., *J. Am. Chem. Soc.*, 1951, **73**, 4084; Hardy, P. M., Haylock, J. C. and Rydon, H. N., *J. Chem. Soc., Perkin Trans 1*, 1972, 605; Perly, B., Chachaty, C. and Tsutsumi, A., *J. Am. Chem. Soc.*, 1980, **102**, 1521; Coleman, D., *J. Chem. Soc.*, 1951, 2294; Hanby and Waley, *J. Chem. Soc.*, 1950, 3239; Saudek, V., Stejskal, J., Schmidt, P., Zimmermann, K., Skarda, V., Kratochvil, P., Drobnik, J., *Biopolymers*, 1987, **26**, 705.
2. Kohn, J. and Langer, R., *J. Am. Chem. Soc.*, 1987, **109**, 817; Pulapura, S. and Kohn, J., *Polymer Preprints*, 1990, **31**, 233.
3. Bush, S. M. and North, M., *Polymer* 1996, **37**, 4652; Bush, S. M. and North, M., *Polymer* in press.
4. Kocienski, P. J., *Protecting Groups*. Thieme, Stuttgart, 1994.
5. Billmeyer, F. W., *Textbook of Polymer Science*. Wiley, New York, 1984.
6. Kagawa, K., Oishi, T., Matsusaki, K. and Furimoto, M., *Polymer*, 1995, **36**, 941.
7. Oishi, T. and Fujimoto, M., *J. Polym. Sci. Polym. Chem. Edn.*, 1984, **22**, 2789; Oishi, T., Kagawa, K. and Fujimoto, M., *Macromolecules*, 1993, **26**, 24; Oishi, T., Otsubo, Y. and Fujimoto, M., *Polymer J.*, 1992, **24**, 527; Oishi, T., Okamoto, N. and Fujimoto, M., *J. Macromol. Sci. Chem.*, 1988, **25**, 1039; Oishi, T. and Fujimoto, M., *J. Macromol. Sci. Chem.*, 1992, **29**, 1187; Yamaguchi, H. and Minoura, Y., *J. Polymer Sci: A1*, 1970, **8**, 1467; Binod, B. D., Swaminathan, S. and Pradeep, K. D., *J. Macromol. Sci. Chem.*, 1995, **32**, 227; Oishi, T., Otsubo, Y., Matsusaki, K. and Fujimoto, M., *Polymer*, 1993, **34**, 1504; Oishi, T. and Fujimoto, M., *J. Polym. Sci. Polym. Chem. Edn.*, 1992, **30**, 1821; Oishi, T., Kamori, A. and Fujimoto, M., *J. Macromol. Sci. Chem.*, 1992, **29**, 231; Oishi, T., Kagawa, K. and Fujimoto, M., *Polymer*, 1993, **34**, 2644; Wulff, G. and Dhal, P. K., *Macromolecules*, 1990, **23**, 100.
8. Sanda, F., Takata, T. and Endo, T., *J. Polym. Sci. Polym. Chem. Edn.*, 1995, **33**, 2353; Takei, F., Yanai, K., Onitsuka, K. and Takahashi, S., *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1554; Gao, J. P., Chen, J. P. and Wang, Z. Y., *J. Am. Chem. Soc.*, 1995, **117**, 5377; Okamoto, Y., Nishikawa, M., Nakano, T., Yashima, E. and Hatada, K., *Macromolecules*, 1995, **28**, 5135; Hosoda, M., Schonhausen, U. and Pino, P., *Makromol. Chem.*, 1993, **194**, 223; Chen, C., Ren, C., Zhang, J. and Xi, F., *Macromol. Chem. Phys.*, 1994, **195**, 1177; Okamoto, Y. and Nakano, T., *Chem. Rev.*, 1994, **94**, 349 and references therein.