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# Copolymerization of peptide derived monomers and methyl methacrylate

A.C. Birchall[a], S.M. Bush[a], M. North[b,*]

[a]*Department of Chemistry, University of Wales, Bangor, Gwynedd LL57 2UW, UK*
[b]*Department of Chemistry, King's College London, Strand, London WC2R 2LS, UK*

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**Abstract**

The copolymerization of a series of peptide derived (meth)acrylate derivatives with methyl methacrylate is reported. The resulting polymers are optically active and display a variety of non-linear dependencies of specific rotation against %-chiral monomer incorporation. The polymers contain acid labile protecting groups that can be removed to generate a second series of polymers, which also show non-linear dependencies of specific rotation against %-chiral monomer incorporation. All of the non-linear effects can be explained by a model based on asymmetric induction from the stereocenters within the peptide, to prochiral centers within the peptide unit and the adjacent methyl methacrylate unit. © 2000 Elsevier Science Ltd. All rights reserved.

*Keywords*: Peptide; Copolymer; Methyl methacrylate

## 1. Introduction

In recent publications, we have reported the radical initiated copolymerization of amino ester derivatives with methyl methacrylate [1–3], for related work on the preparation of condensation polymers utilizing amino acid side-chains see Refs. [4,5]. The solubility of the resulting polymers, could be controlled by the nature or absence of protecting groups on the amine and acid functionalities of the amino acid. The polymers showed a non-linear dependence of specific rotation versus %-chiral monomer incorporation, which suggests that during the polymerization process asymmetric induction is occurring at the newly formed stereocenters.

In this manuscript, the extension of this work to monomers derived from di and tripeptides is reported. In addition to the preparation of polymers with unusual architectures, solubilities and chiro-optical properties, the incorporation of peptides into synthetic polymers may give polymers that are biologically active/biocompatible.

## 2. Monomer syntheses

All of the monomers used in this work employ a serine residue, as a trifunctional amino acid, the alcohol group of which can be converted into a polymerizable acrylate or methacrylate ester. Acid labile protecting groups [6] were used for the monomers, so that these could be removed after polymerization to give polymers derived from unprotected peptides. Thus, the synthesis of the dipeptide monomers is shown in Scheme 1. *N*-Boc-(*S*)-serine [7] was coupled with the *tert*-butyl ester of (*S*)-alanine [8], (*S*)-phenylalanine [9], or (*S*)-proline [10], to give the corresponding dipeptides, which were treated with acryloyl or methacryloyl chloride to give monomers **1**–**6**.

To further extend the range of monomers available, the tripeptide derivatives **7** and **8** were prepared (Scheme 2). Thus, coupling of the known dipeptide derivative *tert*-butyl (*S*)-serinyl-(*S*)-phenylalaninate [11] to *N*-Boc-(*S*)-alanine [12] gave the fully protected tripeptide *tert*-butyl *N*-Boc-(*S*)-alanyl-(*S*)-serinyl-(*S*)-phenylalaninate, which could be reacted with acryloyl or methacryloyl chloride to give monomers **7** and **8**, respectively.

## 3. Polymerization of monomers 1–8

The radical polymerization of monomers **1**–**8** was achieved using benzoyl peroxide as the initiator, in a suitable solvent. Both homopolymers and copolymers with methyl methacrylate were prepared.

Initial studies using monomers **1** and **2** were carried out using toluene as solvent. However, whilst a homopolymer of **1** (**poly-1**) could be obtained in 60% yield in this way, the attempted homopolymerization of monomer **2** was unsuccessful. It was also possible to prepare a series of

* Corresponding author. Tel.: +20-7848-1164; fax: +870-131-3783.
*E-mail address:* michael.north@kcl.ac.uk (M. North).


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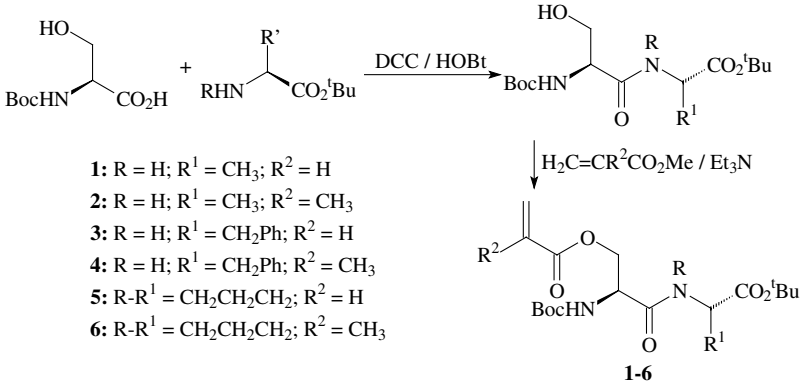


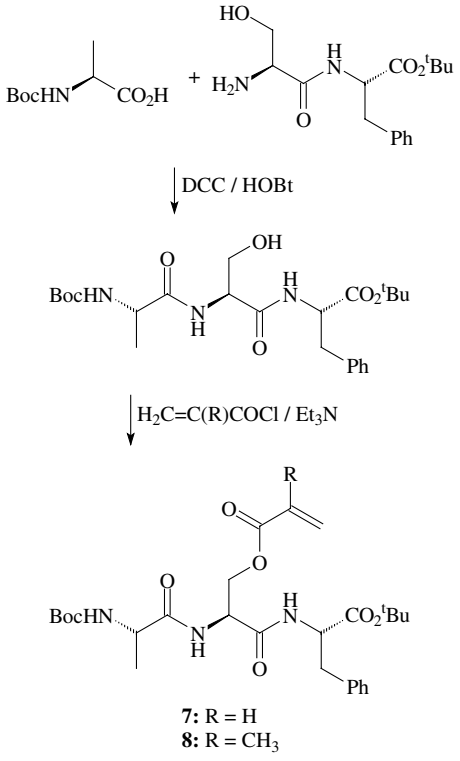

**1:** R = H; $R^1 = CH_3$; $R^2$ = H
**2:** R = H; $R^1 = CH_3$; $R^2 = CH_3$
**3:** R = H; $R^1 = CH_2Ph$; $R^2$ = H
**4:** R = H; $R^1 = CH_2Ph$; $R^2 = CH_3$
**5:** R-$R^1 = CH_2CH_2CH_2$; $R^2$ = H
**6:** R-$R^1 = CH_2CH_2CH_2$; $R^2 = CH_3$

**1-6**

Scheme 1.

copolymers employing varying ratios of monomer **1** and methyl methacrylate (MMA), methyl acrylate, or styrene, however, all of these copolymers were found to be completely insoluble in a range of solvents, thus preventing their characterization. The homopolymerization of both monomers **1** and **2** was successfully achieved by changing the solvent to DMF, giving polymers **poly-1** and **poly-2** in 72% and 82% yields, respectively. The greater solubility of the monomers in this solvent allowed more concentrated solutions to be employed, and it was also possible to prepare a series of copolymers between monomers **1** or **2** and methyl methacrylate (**poly-1-*co*-MMA** and **poly-2-*co*-MMA**), in this way.

Monomers **3**–**6** and the resulting polymers were designed to be more soluble in organic solvents than monomers **1**,**2**, by the incorporation of a large aromatic ring or the removal of an amide NH, respectively. Thus, it was possible to prepare homopolymers (**poly(3–6)**) and copolymers with methyl methacrylate (**poly-(3–6)-*co*-MMA**) from these monomers using toluene as the solvent. Polymerization (and copolymerization with methyl methacrylate) of monomer **7** in toluene was also successful (giving **poly-7** and **poly-7-*co*-MMA**), but the polymerization of monomer **8** gave polymers with relatively low molecular weights, probably because the solubility of monomer **8** in toluene necessitated the use of rather dilute solutions (1.3 M). Consistent with this, changing the solvent to DMF gave homopolymers (**poly-8**) and copolymers with methyl methacrylate (**poly-8-*co*-MMA**) with higher molecular weights, since the polymerizations could be carried out in solutions of higher concentration (4 M).




**7:** R = H
**8:** R = $CH_3$

Scheme 2.

## 4. Polymer characterization

All of the homo and copolymers were characterized by $^1$H NMR, either solution or solid state $^{13}$C NMR, infrared spectroscopy, GPC and specific rotation. Selected characterizing data is given in Tables 1–9. The GPC data in Tables 1–9 shows that the molecular weights and polydispersities of the polymers are highly variable, as is normal for radical polymerizations where the viscosity of the solution is an important factor in the polymerizations [13]. All of the GPC data in this work was referenced to polystyrene samples, so the accuracy of the molecular weight data was checked by a combined GPC-viscosity study using a selection of copolymers derived from monomers **3**–**6**. In each case a similar trend was observed: for copolymers containing small amounts (<10%) of peptide derived monomer, the molecular weight data obtained from GPC-viscosity were approximately double those obtained by referencing to polystyrene; whilst for polymers containing large amounts (>80%) of peptide monomer, the GPC-viscosity suggested that the true molecular weights were three times those determined from polystyrene standards.

Table 1
Data for polymers prepared from monomer **1**

| % Monomer **1** added[a] | % Monomer **1** incorporated[a,b] | $[\alpha]_D^{26}$ ($c = 1$, $CHCl_3$) | $M_n$ (GPC in thf) | $M_w$ (GPC in thf) | $M_w/M_n$ |
|---|---|---|---|---|---|
| 100 | 100 | −2.7 | 71,400 | 989,000 | 13.9 |
| 75 | 75 | −0.7 | 4400 | 16,900 | 3.8 |
| 50 | 45 | 1.4 | 5700 | 29,200 | 5.1 |
| 25 | 12.5 | 1.0 | 5600 | 25,400 | 4.5 |

[a] Remainder is methyl methacrylate.
[b] As determined by $^1H$ NMR.

Table 2
Data for polymers prepared from monomer **2**

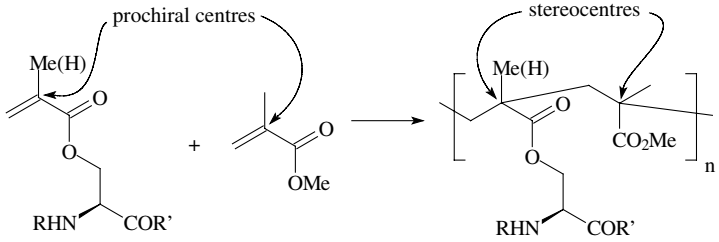
| % Monomer **2** added[a] | % Monomer **2** incorporated[a,b] | $[\alpha]_D^{26}$ ($c = 1$, $CHCl_3$) | $M_n$ (GPC in thf) | $M_w$ (GPC in thf) | $M_w/M_n$ |
|---|---|---|---|---|---|
| 100 | 100 | −1.6 | 6600 | 38,600 | 5.8 |
| 90 | 89 | 0.5 | 11,200 | 165,000 | 14.8 |
| 75 | 68 | 4.4 | 10,300 | 134,000 | 13.0 |
| 60 | 62 | 5.4 | 13,200 | 199,000 | 15.0 |
| 55 | 46 | 6.1 | 5800 | 35,600 | 6.1 |
| 50 | 42 | 6.1 | 8000 | 201,000 | 25.0 |
| 40 | 34 | 6.0 | 4700 | 22,000 | 4.7 |
| 25 | 15 | 5.3 | 7900 | 36,000 | 4.6 |
| 10 | 7 | 4.2 | 10,400 | 35,400 | 3.4 |
| 5 | 3 | 2.2 | 7400 | 22,300 | 3.0 |

[a] Remainder is methyl methacrylate.
[b] As determined by $^1H$ NMR.

The $^1H$ and $^{13}C$ NMR spectra of the copolymers were a superimposition of the peaks expected for homopolymers prepared from monomers **1**–**8** and methyl methacrylate. Integration of suitable peaks in the $^1H$ NMR spectra, allowed the ratio of the monomers incorporated into the polymers to be determined. Tables 1–9 show no significant trend in the amount of monomer **1**–**8** incorporated into the polymers. In some cases (monomers **1** and **2**) this is lower than the amount of monomer added to the polymerization mixture, whilst in other case (monomers **3**,**4**,**7**,**8**) more of the amino acid derived monomer was incorporated than would have been predicted. In all cases however, the deviations from the statistical ratio are relatively small.

The most striking property of the polymers is the variation of specific rotation with %-chiral monomer incorporation into the polymer, for other examples of non-linear variations of specific rotation see Refs. [14–28]. This is emphasized in Figs. 1–8. Polymers derived from monomers **1** and **2** showed similar variations of specific rotation with the percentage of dipeptide in the polymer. As the amount of dipeptide in the polymer increases, the specific rotation initially rises, reaches a maximum at about 40% dipeptide incorporation and then decreases as more dipeptide is incorporated into the polymer. It eventually becomes negative at high (ca. 70% for monomer **1** and ca. 90% for monomer **2**) dipeptide incorporations. This variation cannot be accounted for by differences in the molecular weights and polydispersities of the polymers, since for polymers derived from monomer **2**, the points corresponding to polymers containing 3, 15, 46, and 100% of dipeptide are sufficient to define the curve, and these polymers all have similar molecular weights and polydispersities (Table 2).

During the copolymerization of monomers **1**,**2** with methyl methacrylate, prochiral centers within the monomers are converted into stereocenters as shown in Scheme 3. The




Scheme 3.

Table 3
Data for polymers prepared from monomer **3**

| % Monomer 3 added[a] | % Monomer 3 incorporated[a,b] | $[\alpha]_D^{26}$ ($c = 1$, $CHCl_3$) | $M_n$ (GPC in thf) | $M_w$ (GPC in thf) | $M_w/M_n$ |
|---|---|---|---|---|---|
| 100 | 100 | 37.1 | 4800 | 47,400 | 9.9 |
| 75 | 84 | 30.1 | 9500 | 38,000 | 4.0 |
| 71 | 75 | 26.9 | 3500 | 33,500 | 9.6 |
| 70 | 71 | 25.6 | [c] | [c] | [c] |
| 44 | 54 | 20.7 | 4800 | 47,400 | 9.9 |
| 42 | 53 | 20.4 | 5,300 | 66,400 | 12.5 |
| 21 | 34 | 15.5 | 20,300 | 447,000 | 22.1 |
| 17 | 27 | 13.9 | 20,600 | 552,000 | 26.9 |
| 9 | 14 | 10.0 | 19,000 | 404,000 | 21.3 |
| 5 | 6 | 5.8 | 30,000 | 286,000 | 5.6 |
| 2 | 3 | 3.8 | 21,800 | 100,000 | 4.6 |

[a] Remainder is methyl methacrylate.
[b] As determined by $^1H$ NMR.
[c] Not determined.

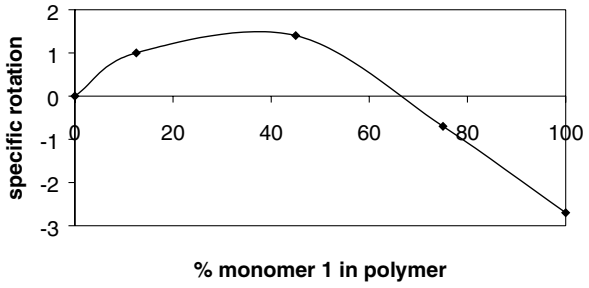



Fig. 1. Variation of specific rotation versus % monomer **1** incorporated into copolymers.

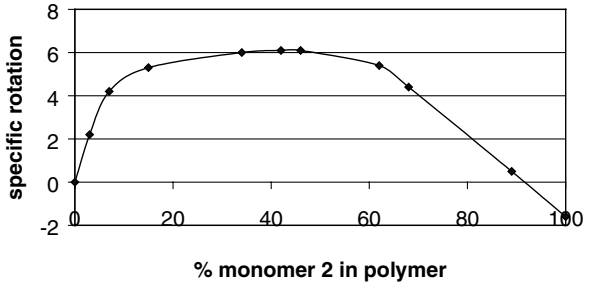



Fig. 2. Variation of specific rotation versus % monomer **2** incorporated into copolymers.

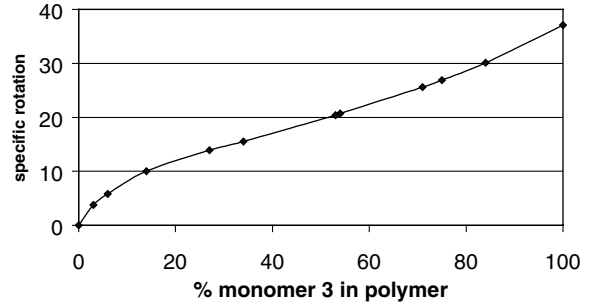



Fig. 3. Variation of specific rotation versus % monomer **3** incorporated into copolymers.

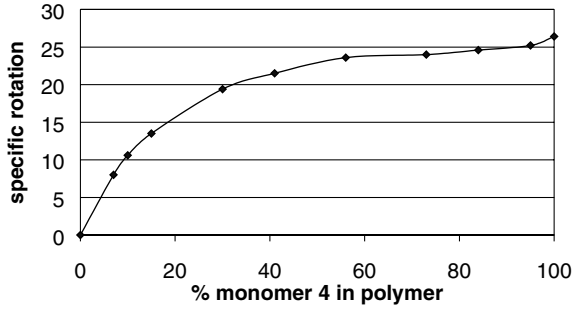



Fig. 4. Variation of specific rotation versus % monomer **4** incorporated into copolymers.

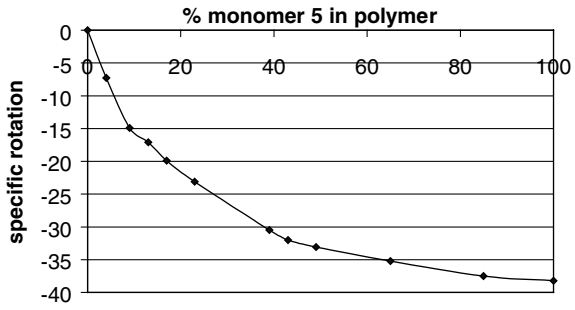



Fig. 5. Variation of specific rotation versus % monomer **5** incorporated into copolymers.

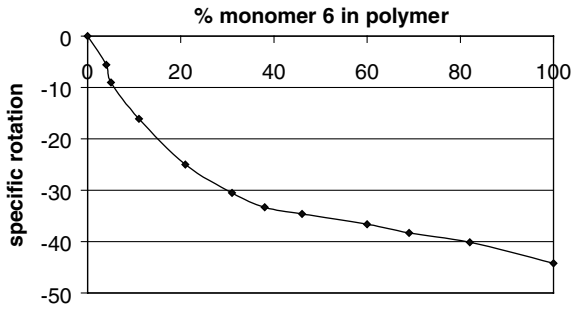



Fig. 6. Variation of specific rotation versus % monomer **6** incorporated into copolymers.

Table 4
Data for polymers prepared from monomer **4**

| % Monomer **4** added[a] | % Monomer **4** incorporated[a,b] | $[\alpha]_D^{27}$ ($c = 1$, $CHCl_3$) | $M_n$ (GPC in thf) | $M_w$ (GPC in thf) | $M_w/M_n$ |
|---|---|---|---|---|---|
| 100 | 100 | 26.4 | 6200 | 20,900 | 3.4 |
| 90 | 95 | 25.2 | 6800 | 40,600 | 6.0 |
| 80 | 84 | 24.6 | 7000 | 38,200 | 5.4 |
| 62 | 73 | 24.0 | 8200 | 39,400 | 4.8 |
| 44 | 56 | 23.6 | 9100 | 33,000 | 3.6 |
| 29 | 41 | 21.5 | 9000 | 73,100 | 8.1 |
| 17 | 30 | 19.4 | 8700 | 34,000 | 3.9 |
| 17 | 15 | 13.5 | 9800 | 33,700 | 3.4 |
| 9 | 10 | 10.6 | 10,100 | 47,200 | 4.7 |
| 5 | 7 | 8.0 | 8700 | 34,000 | 3.9 |

[a] Remainder is methyl methacrylate.
[b] As determined by $^1$H NMR.

specific rotations of the polymers can be explained if:

1. Asymmetric induction from the peptide stereocenters induces the formation of a single stereoisomer at the newly created stereocenter in the dipeptide unit and in the subsequent methyl methacrylate residue. For other examples of non-linear variations of specific rotation see Refs. [14–26].
2. The stereocenters within monomers **1**,**2** induce an anticlockwise rotation of plane polarized light, whilst the newly created stereocenters induce a clockwise rotation.

Table 5
Data for polymers prepared from monomer **5**

| % Monomer **5** added[a] | % Monomer **5** incorporated[a,b] | $[\alpha]_D^{26}$ ($c = 1$, $CHCl_3$) | $M_n$ (GPC in thf) | $M_w$ (GPC in thf) | $M_w/M_n$ |
|---|---|---|---|---|---|
| 100 | 100 | −38.2 | 4200 | 12,600 | 3.0 |
| 85 | 85 | −37.5 | 6700 | 17,000 | 2.5 |
| 65 | 65 | −35.2 | [c] | [c] | [c] |
| 60 | 49 | −33.1 | 10,900 | 149,000 | 13.7 |
| 43 | 43 | −32.0 | 5300 | 40,200 | 7.6 |
| 38 | 39 | −30.5 | 7800 | 32,700 | 4.2 |
| 25 | 23 | −23.1 | 13,700 | 136,000 | 9.9 |
| 21 | 17 | −19.9 | 10,300 | 222,000 | 21.6 |
| 20 | 13 | −17.1 | 10,900 | 209,000 | 19.2 |
| 7 | 9 | −14.9 | 17,700 | 129,000 | 7.3 |
| 4 | 4 | −7.3 | 8900 | 33,900 | 3.8 |

[a] Remainder is methyl methacrylate.
[b] As determined by $^1$H NMR.
[c] Not determined.

Table 6
Data for polymers prepared from monomer **6**

| % Monomer **6** added[a] | % Monomer **6** incorporated[a,b] | $[\alpha]_D^{26}$ ($c = 1$, $CHCl_3$) | $M_n$ (GPC in thf) | $M_w$ (GPC in thf) | $M_w/M_n$ |
|---|---|---|---|---|---|
| 100 | 100 | −44.2 | 2200 | 12,100 | 5.4 |
| 85 | 82 | −40.1 | 6500 | 35,800 | 5.5 |
| 70 | 69 | −38.3 | 9200 | 49,500 | 5.4 |
| 70 | 60 | −36.6 | 7300 | 34,800 | 4.7 |
| 60 | 46 | −34.6 | 9800 | 44,000 | 4.5 |
| 44 | 38 | −33.3 | 5800 | 22,200 | 3.8 |
| 28 | 31 | −30.5 | 9000 | 33,500 | 3.7 |
| 14 | 21 | −25.0 | 11,700 | 132,000 | 11.2 |
| 13 | 11 | −16.1 | 6,400 | 77,200 | 12.0 |
| 7 | 5 | −9.0 | 9,100 | 46,100 | 5.1 |
| 4 | 4 | −5.6 | 12,100 | 45,400 | 3.8 |

[a] Remainder is methyl methacrylate.
[b] As determined by $^1$H NMR.

Table 7
Data for polymers prepared from monomer **7**

| % Monomer **7** added[a] | % Monomer **7** incorporated[a,b] | $[\alpha]_D^{26}$ ($c = 1$, $CHCl_3$) | $M_n$ (GPC in DMF) | $M_w$ (GPC in DMF) | $M_w/M_n$ |
|---|---|---|---|---|---|
| 100 | 100 | 28.7 | 8200 | 20,400 | 2.5 |
| 75 | 96 | 26.8 | 8100 | 20,800 | 2.6 |
| 55 | 75 | 15.5 | 9800 | 25,000 | 2.5 |
| 33 | 52 | 5.5 | 29,500 | 554,000 | 18.8 |
| 24 | 32 | 3.3 | 13,900 | 39,400 | 2.8 |
| 20 | 30 | 3.1 | 19,500 | 69,500 | 3.6 |
| 10 | 12 | 1.5 | 24,100 | 432,000 | 17.9 |
| 5 | 5 | 0.6 | 16,400 | 47,700 | 2.9 |
| 2 | 4 | 0.5 | 17,400 | 49,400 | 2.8 |

[a] Remainder is methyl methacrylate.
[b] As determined by $^1H$ NMR.

Table 8
Data for polymers prepared from monomer **8** in toluene

| % Monomer **8** added[a] | % Monomer **8** incorporated[a,b] | $[\alpha]_D^{26}$ ($c = 1$, $CHCl_3$) | $M_n$ (GPC in DMF) | $M_w$ (GPC in DMF) | $M_w/M_n$ |
|---|---|---|---|---|---|
| 100 | 100 | 22.1 | 1200 | 1300 | 1.2 |
| 75 | 82 | 18.5 | 1000 | 1100 | 1.1 |
| 67 | 77 | 17.9 | 1000 | 1300 | 1.3 |
| 50 | 62 | 15.8 | 1100 | 1300 | 1.2 |
| 33 | 35 | 11.5 | 1600 | 3400 | 2.1 |
| 17 | 20 | 7.1 | 2500 | 8000 | 3.1 |
| 9 | 5 | 0.8 | 5200 | 14,400 | 2.8 |
| 5 | 4 | 0.6 | 1900 | 8700 | 4.7 |

[a] Remainder is methyl methacrylate.
[b] As determined by $^1H$ NMR.

3. The magnitude of the rotation of plane polarized light induced by the newly created stereocenters is greater than that induced by the stereocenters within the dipeptide unit.

In this way, at low incorporations of monomers **1**,**2**, the rotation due to the newly created stereocenters will dominate the observed specific rotation, and the specific rotation will increase as the % of monomers **1**,**2** incorporated into the polymer increases. Once around 50% of monomers **1**,**2** has been incorporated however, all of the backbone stereocenters will be formed as a single stereoisomer, so the rotation of plane polarized light due to the influence of these stereocenters cannot increase further. From this point on, the rotation of plane polarized light induced by the peptide stereocenters becomes increasingly important and the specific rotation decreases, eventually becoming negative.

It is also possible to explain the non-linear variation of specific rotation with polymer composition by invoking the formation of a helical conformation, for examples of linear variations of specific rotation with polymer composition see Refs. [29–36]. However, our previous work [1–3] on amino acid derived polymers has shown no evidence for such a conformation by CD spectroscopy, and the polymers did not

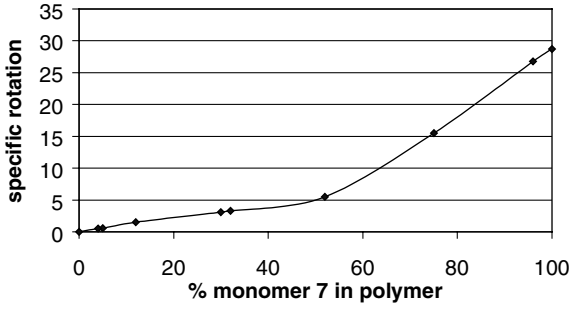



Fig. 7. Variation of specific rotation versus % monomer **7** incorporated into copolymers.

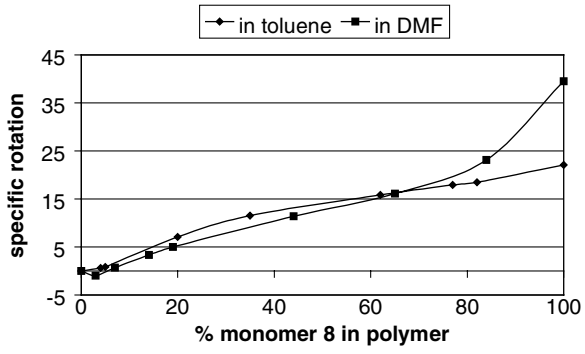



Fig. 8. Variation of specific rotation versus % monomer **8** incorporated into copolymers.

Table 9
Data for polymers prepared from monomer **8** in DMF

| % Monomer **8** added[a] | % Monomer **8** incorporated[a,b] | $[\alpha]_D^{26}$ ($c = 1$, $CHCl_3$) | $M_n$ (GPC in DMF) | $M_w$ (GPC in DMF) | $M_w/M_n$ |
|---|---|---|---|---|---|
| 100 | 100 | 39.5 | 4400 | 86,400 | 19.9 |
| 75 | 84 | 23.1 | 13,600 | 71,000 | 5.2 |
| 65 | 65 | 16.1 | 2000 | 25,300 | 12.4 |
| 50 | 44 | 11.4 | 12,900 | 57,900 | 4.5 |
| 25 | 19 | 5.0 | 9700 | 24,700 | 2.6 |
| 15 | 14 | 3.3 | 4000 | 25,300 | 6.2 |
| 10 | 7 | 0.7 | 10,600 | 35,700 | 3.4 |
| 5 | 3 | −1.0 | 10,800 | 30,000 | 2.8 |

[a] Remainder is methyl methacrylate.
[b] As determined by $^1$H NMR.

exhibit mutarotation or significantly solvent dependent specific rotations. Thus, the asymmetric induction explanation appears to be the more likely of the two possible causes.

Polymers incorporating monomer **3** display a virtually linear dependence of specific rotation on polymer composition (Fig. 3). There are three possible explanations for this:

1. No asymmetric induction occurs during the polymerization.
2. Asymmetric induction occurs to the prochiral center within the peptide unit, but not to subsequent methyl methacrylate units.
3. Asymmetric induction occurs to prochiral centers within the dipeptide and subsequent methyl methacrylate units, but these make a negligible contribution to the overall specific rotation of the polymer.

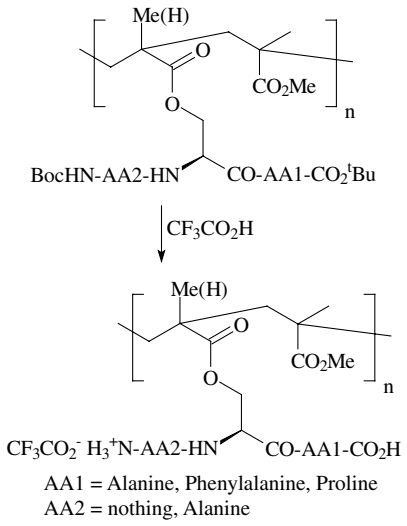
In view of the effects seen with monomers **1**,**2**,**4**–**8**, the first explanation seems unlikely since there is no apparent reason why monomer **3** should behave in a different way from the other monomers. Both explanations 1 and 2 can be ruled out from a study of deprotected polymers derived from monomer **3**, which do show a pronounced non-linear variation of specific rotation (vide infra). Hence, it appears that for this series of copolymers, the rotation of polarized light induced by the stereocenters within the polymer backbone is negligible compared to that due to the stereocenters within the dipeptide.

Monomer **4** shows a pronounced non-linear variation of specific rotation with composition, but unlike monomers **1** and **2**, the gradient of the curve is always positive. This can easily be explained by the same factors discussed for monomers **1**,**2**, except that in this case the newly created stereocenters, and the stereocenters within the dipeptide must both induce a clockwise rotation of plane polarized light. It is notable that as shown in Fig. 4, low monomer **4** incorporations give a pronounced curve, whilst above about 50% incorporation of monomer **4**, a virtually linear relationship is observed. This is again consistent with asymmetric induction occurring to the prochiral centers within the dipeptide unit and to the adjacent methyl methacrylate group, but not to subsequent methyl methacrylate residues. Polymers derived from monomers **5** and **6** show identical behavior to the polymers derived from monomer **4**, except in this case both the stereocenters in the dipeptide and those which are formed during the polymerization induce an anticlockwise rotation of plane polarized light, resulting in negative specific rotations (Figs. 5 and 6).

Polymers obtained from tripeptide derived monomer **7** show a different type of non-linear variation (Fig. 7). In this case, the specific rotation of the polymer increases as the amount of tripeptide in the polymer increases, but less rapidly than expected. This can be explained if the stereocenters in the tripeptide induce a clockwise rotation of plane polarized light, whilst the stereocenters which are created in the polymer backbone induce an anticlockwise rotation, but of lower magnitude than rotation due to the tripeptide stereocenters. Once again, above about 50% incorporation of monomer **7**, the variation of specific rotation with composition is approximately linear, implying that asymmetric induction occurs from a tripeptide to the adjacent methyl methacrylate residue, but not to subsequent residues. Polymers derived from monomer **8** using DMF as the solvent show the same variation of specific rotation with polymer composition as discussed for polymers derived from monomer **7** (Fig. 8). The situation for the polymers obtained from monomer **8** using toluene as solvent is less obvious, there appears to be a small deviation of the same form as seen for polymers derived from monomer **4**, but this may be an artifact due to the very low molecular weights of these polymers.

## 5. Removal of the protecting groups from the polymers

Monomers **1**–**8** were designed to contain only acid labile protecting groups, so that these could be removed from the homo and copolymers by acidolysis [6]. Removal of the protecting groups was expected to significantly alter the solubility properties of the polymers, and it was of interest to see if it would also alter the chiro-optical properties of the polymers. Each of the homo and copolymers derived from monomers **2**–**6**,**8** was thus treated with trifluoroacetic acid to give the corresponding polymers containing unprotected peptides (Scheme 4). $^1$H and $^{13}$C NMR spectroscopy both indicated




Scheme 4.

that complete removal of the Boc and *tert*-butyl protecting groups had occurred as evidenced by the absence of signals due to these groups, in the spectra of the deprotected polymers. The $^{1}H$ NMR spectra also showed that the ratio of peptide to methyl methacrylate in the deprotected polymers was the same as that in the protected polymers, thus showing that no cleavage of the non-*tert*-butyl ester bonds had occurred during the deprotection. No attempt was made to desalt the polymers, so they will have been formed and analyzed as their trifluoroacetate salts. In some cases this was confirmed by $^{13}C$ NMR, which showed two quartets due to the $CF_3CO_2$ group. It was not possible to determine the molecular weight data for the deprotected polymers due to the abnormal elution of the polymers from the GPC columns in DMF. The spectroscopic data however, give no reason to suppose that the molecular weights of the deprotected polymers will be any different from those of the protected polymers, except for a small reduction due to the removal of the protecting groups.

Plots of specific rotation versus percentage monomer **2**–**6**,**8** incorporation are given in Figs. 9–14. There are fewer points on the graphs for the deprotected polymers than for the protected polymers. This is due to two factors: some of the deprotected polymers would not dissolve in the solvent system used for the specific rotations (1:1 DMSO/acetonitrile); and a few of the deprotected polymers dissolved to give solutions whose optical density at the required concentration was too high to allow a specific rotation to be recorded. For the deprotected polymers derived from monomers **1** and **7**, it was not possible to find any solvent system that would dissolve all of the polymers, so these will not be discussed further.

A comparison of Figs. 2 and 9 shows that for polymers derived from monomer **2**, the deprotected polymer series exhibit a different non-linear variation of specific rotation with polymer composition to the protected polymers. The curve for the deprotected polymers resembles the curve for protected polymers derived from monomer **4** (Fig. 4) and can be explained in the same way. The difference between the protected and deprotected polymers derived from monomer **2** thus, seems to be related to a difference in the direction of rotation of plane polarized light due to the stereocenters within the dipeptide unit. This difference may be due to changes in the structure of the polymer around the stereocenters (due to removal of the protecting groups), or to the change in solvent used to analyze the specific rotations, since for solubility reasons the specific rotations shown in Fig. 9 had to be recorded in a 1:1 DMSO/acetonitrile solvent mixture.

Whereas the protected polymers derived from monomer **3** showed only a very small non-linear variation (Fig. 3), the deprotected series of copolymers display a very pronounced non-linear variation (Fig. 10). This is important since it shows that asymmetric induction does occur during the polymerization of monomer **3**, just as for each of the other monomers used in this study. The deprotected polymer series derived from monomer **4** (Fig. 11) show a non-linear variation of specific rotation which contains a maximum at about 40% deprotected monomer **4** incorporation, reminiscent of the curves obtained for the protected polymers obtained from monomers **1** and **2** (Figs. 1 and 2). In this case, however, the specific rotations never become negative even at high incorporations of deprotected monomer **4**, which indicates that the rotation of polarized light due to the stereocenters within deprotected polymer **4** is small (compared to the rotation due to the stereocenters within the polymer backbone) but positive.

The graphs, obtained when the specific rotations of the deprotected polymers obtained from monomers **5** and **6** are plotted against incorporation of the dipeptide (Figs. 12 and 13), show exactly the same trend as the graphs of the corresponding protected polymers (Figs. 5 and 6). This is the only case where the protected and deprotected polymers exhibit the same type of non-linear variation. It is not clear whether this is coincidental, or whether it is related to the fact that monomers **5** and **6** possess a tertiary amide bond whilst all of the other monomers studied in this work contain only secondary amide bonds.

Deprotection of the polymers obtained by the copolymerization of monomer **8** and methyl methacrylate (in DMF) gave the specific rotations shown in Fig. 14. Once again, a non-linear variation similar to that observed for protected polymers derived from monomer **4** and deprotected polymers derived from monomers **2** and **3** was observed.

## 6. Conclusions

Serine containing peptides in which the serine residue bears an acrylate or methacrylate unit attached to its sidechain, undergo radical induced homo and copolymerization with methyl methacrylate. The resulting polymers exhibit a

non-linear variation of specific rotation with polymer composition. The nature of the various non-linear effects that are observed, can be accounted for on the basis of asymmetric induction from the stereocenters in the peptide to the prochiral centers within the peptide and adjacent methyl methacrylate monomer. This appears to be a general phenomenon for polymers prepared from serine containing amino acids and peptides.

## 7. Experimental

General experimental details have been reported elsewhere [1–3].

### 7.1. N-Boc-(S)-Ser-(S)-Ala-O$^t$Bu

To a solution of *N*-Boc-(*S*)-serine [7] (4.2 g, 21 mmol, 1.3 eq.) in glass distilled DMF (50 ml) under an argon atmosphere was added DCC (3.5 g, 16 mmol, 1.0 eq.), HOBt (3.5 g, 26 mmol, 1.6 eq.) and (*S*)-Ala-O$^t$Bu [8] (2.3 g, 16 mmol, 1.0 eq.). The mixture was stirred at room temperature for 48 h after which the solvent was removed in vacuo and EtOAc (25 ml) was added to the brown oil residue. Filtration through Celite removed a white solid and the filtrate was washed with saturated $Na_2CO_3$ (3 × 25 ), water (1 × 25 ml), dilute HCl (2 × 25 ml) and water (2 × 25 ml). The organic layer was dried ($MgSO_4$), filtered and the solvent removed in vacuo to leave a yellow oil; Yield 4.6 g (87%); $[\alpha]_D^{25}$ −9.1 ($c = 1.2$, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3320 (br), 3050 (m), 2980 (s), 1730 (s), and 1660 cm$^{-1}$ (s); $\delta_H$ 1.4 (3H, d $J = 1.7$ Hz, Ala-C$H_3$), 1.45 (9H, s, C(C$H_3$)$_3$), 1.5 (9H, s, C(C$H_3$)$_3$), 3.3 (1H, brs, O*H*), 4.1 (1H, brd $J = 7.1$ Hz, C$H_2$O), 4.2 (1H, br, C$H_2$O), 4.5 (2H, m, 2 × NC*H*), 5.5 (1H, brs, N*H*), 6.9 (1H, brs, N*H*); $\delta_C$ 17.9 (Ala-*C*H$_3$), 27.9 (C(*C*H$_3$)$_3$), 28.2 (C(*C*H$_3$)$_3$), 48.9 (Ala-N*C*H), 55.2 (Ser-N*C*H), 63.0 (*C*H$_2$O), 80.2 (*C*(CH$_3$)$_3$), 82.2 (*C*(CH$_3$)$_3$), 155.9 (N*C*O$_2$), 170.8 (*C*ON), 172.1 (*C*O$_2$); *m*/*z* (Cl) 333 (MH$^+$); Found 333.2026 ($C_{15}H_{29}N_2O_6$ requires 333.2026).

### 7.2. N-Boc-(S)-Ser-(S)-Phe-O$^t$Bu

To a solution of *N*-Boc-(*S*)-serine [7] (7.1 g, 34.4 mmol, 1.3 eq.) in glass distilled DMF (75 ml) was added DCC (5.5 g, 26.4 mmol, 1.0 eq.), HOBt (5.7 g, 42.3 mmol, 1.6 eq.) and (*S*)-Phe-O$^t$Bu [9] (5.9 g, 26.4 mmol, 1.0 eq.). The mixture was stirred at room temperature for 14 h after which the solvent was removed in vacuo and EtOAc (60 ml) was added to the brown oil residue. Filtration through Celite removed a white solid and the filtrate was washed with saturated $Na_2CO_3$ (4 × 25 ml), water (2 × 25 ml), 2 M HCl (2 × 25 ml), and water (2 × 25 ml). The organic layer was dried ($MgSO_4$), filtered and the solvent removed in vacuo to leave a yellow oil. Residual DMF was removed as an azeotrope with $CH_2Cl_2$ (2 × 25 ml) to leave a yellow solid. Yield 10.6 g (98%); m.p. 47°C; $[\alpha]_D^{25}$ −2.2 ($c = 0.8$, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3299 (br), 2977 (m), 1718 (s), 1654 (s), and 1527 cm$^{-1}$ (m); $\delta_H$ 1.39 (9H, s, C(C$H_3$)$_3$), 1.41 (9H, s, C(C$H_3$)$_3$), 3.0 (1H, dd $J = 6.3$, 14.0 Hz, C$H_2$Ph), 3.1 (1H, dd $J = 6.2$, 14.0 Hz, C$H_2$Ph), 3.6 (2H, brm, C$H_2$O + Ser-NC*H*), 3.9 (1H, brd $J = 8.3$ Hz, C$H_2$O), 4.2 (1H, brs, O*H*), 4.7 (1H, q $J = 6.5$ Hz, Phe-NC*H*), 5.5 (1H, brd $J = 5.3$ Hz, Boc-N*H*), 7.1 (1H, brd, $J = 7.6$ Hz, N*H*CO), 7.1–7.3 (5H, m, ArC*H*); $\delta_C$ 27.9 (C(*C*H$_3$)$_3$), 28.2 (C(*C*H$_3$)$_3$), 37.8 (*C*H$_2$Ph), 54.0 (Ser-N*C*H), 55.4 (Phe-N*C*H), 62.8 (*C*H$_2$O), 80.2 (*C*(CH$_3$)$_3$), 82.5 (*C*(CH$_3$)$_3$), 126.9 (Ar*C*H), 128.4 (Ar*C*H), 129.4 (Ar*C*H), 136.1 (Ar *ipso*C), 155.8 (Boc*C*O), 170.4 (*C*ON), 170.9 (*C*O$_2$); *m*/*z* (CI) 409 (MH$^+$); Found 409.2343 ($C_{21}H_{33}N_2O_6$ requires 409.2338).

### 7.3. N-Boc-(S)-Ser-(S)-Pro-O$^t$Bu

To a solution of *N*-Boc-(*S*)-serine [7] (4.6 g, 22.4 mmol, 1.3 eq.) in glass distilled DMF was added DCC (3.6 g, 17.2 mmol, 1.0 eq.), HOBt (3.7 g, 27.5 mmol, 1.6 eq.) and (*S*)-Pro-O$^t$Bu [10]. The mixture was stirred at room temperature for 13.5 h after which the solvent was removed in vacuo and EtOAc (100 ml) was added to the yellow oil residue. Filtration through Celite removed a white solid and the filtrate was washed with saturated $Na_2CO_3$ (2 × 25 ml). The aqueous layer was back extracted with EtOAc (2 × 15 ml) and the combined organic layers were subsequently washed with saturated $Na_2CO_3$ (3 × 25 ml), water (3 × 25 ml), 2 M HCl (2 × 25 ml) and water (2 × 25 ml). The organic layer was dried ($MgSO_4$), filtered and the solvent removed in vacuo to leave a yellow foaming oil. Yield 5.4 g (87%); $[\alpha]_D^{28}$ −4.6 ($c = 0.6$, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3386 (br), 2977 (s), 1719 (s), 1639 (s), and 1500 cm$^{-1}$ (m); $\delta_H$ 1.4 (9H, s, C(C$H_3$)$_3$), 1.45 (9H, s, C(C$H_3$)$_3$), 1.9–2.1 (3H, brm, Pro-γ-C$H_2$ + O*H*), 2.2–2.4 (2H, brm, Pro-β-C$H_2$), 3.7–3.8 (2H, brm, Pro-NC$H_2$), 3.9 (1H, dd $J = 4.6$, 11.3 Hz, C$H_2$O), 4.1 (1H, dd $J = 12.0$, 17.6 Hz, Pro-NC*H*), 4.5 (1H, dd $J = 4.5$, 4.6 Hz, OC$H_2$), 4.6 (1H, brs, Ser-NC*H*), 5.5 (1H, brd $J = 8.3$, Boc-N*H*); $\delta_C$ 24.8 (Pro-γ-*C*H$_2$), 27.9 (C(*C*H$_3$)$_3$), 28.3 (C(*C*H$_3$)$_3$), 29.0 (Pro-β-*C*H$_2$), 47.1 (N*C*H$_2$), 51.4 (Pro-N*C*H), 59.8 (Ser-N*C*H), 64.2 (*C*H$_2$O), 79.8 (*C*(CH$_3$)$_3$), 81.4 (*C*(CH$_3$)$_3$), 155.3 (N*C*O$_2$), 167.5 (*C*O$_2$), 170.6 (N*C*O); *m*/*z* (CI) 359 (MH$^+$); Found 359.2182 ($C_{17}H_{31}N_2O_6$ requires 359.2182).

### 7.4. O-Acryloyl-N-Boc-(S)-Ser-(S)-Ala-O$^t$Bu ***(1)***

To a solution of *N*-Boc-(*S*)-Ser-(*S*)-Ala-O$^t$Bu (1.5 g, 4.5 mmol) in EtOAc (50 ml) cooled with ice was added triethylamine (1.9 ml, 13.5 mmol, 3.0 eq.), then acryloyl chloride (0.6 ml, 6.8 mmol, 1.5 eq.) was added dropwise with a syringe over a period of 1 min. A white precipitate formed immediately upon the addition of the acid chloride. The mixture was stirred in ice for l0 min, then at room temperature for a further 18 h. The reaction mixture was filtered and the filtrate was washed with saturated $Na_2CO_3$ (4 × 30 ml), water (2 × 30 ml), dilute HCl (2 × 30 ml), and finally with water (3 × 20 ml). The organic layer was dried

($MgSO_4$), filtered and the solvent removed in vacuo to leave a white solid, which was washed with petroleum (200 ml). Yield 1.8 g (76%); $[\alpha]_D^{25}$ +19.8 ($c = 1.0$, $CHCl_3$); m.p. 153°C; $\nu_{max}$ ($CHCl_3$) 3389 (m), 3296 (m), 3054 (m), 2982 (s), 1727 (s), and 1682 $cm^{-1}$ (s); $\delta_H$ 1.4 (3H, d $J = 7.1$ Hz, Ala-C$H_3$), 1.5 (18H, s, C(C$H_3$)$_3$), 4.3–4.5 (4H, m, 2 × NC$H$ + C$H_2$O), 5.3 (1H, brd, N$H$), 5.9 (1H, d $J = 10.4$ Hz, =C$H_2$), 6.1 (1H, dd $J = 10.4$, 17.3 Hz, =C$H$), 6.4 (1H, d $J = 17.3$ Hz, =C$H_2$), 6.8 (1H, brd, N$H$); $\delta_C$ 18.5 (Ala-$C$H$_3$), 27.9 (C($C$H$_3$)$_3$), 28.1 (C($C$H$_3$)$_3$), 48.8 (Ala-NCH), 53.6 (Ser-N$C$H), 64.3 ($C$H$_2$O), 80.4 ($C$(CH$_3$)$_3$), 82.1 ($C$(CH$_3$)$_3$), 127.7 (=$C$H), 131.7 (=$C$H$_2$), 155.3 (N$CO_2$$^t$Bu), 165.7 ($CO$), 168.4 ($CO$), and 171.6 ($CO$); *m/z* (Cl) 404 ($M + NH_4^+$), 387 ($MH^+$); Found 387.2131 ($C_{18}H_{31}N_2O_7$ requires 387.2131).

### 7.5. O-Methacryloyl-N-Boc-(S)-Ser-(S)-Ala-O$^t$Bu **(2)**

To a solution of *N*-Boc-(*S*)-Ser-(*S*)-Ala-O$^t$Bu (1.5 g, 4.5 mmol) in EtOAc (50 ml) cooled with ice was added triethylamine (1.9 ml, 13.5 mmol, 3.0 eq.), then methacryloyl chloride (0.7 ml, 6.8 mmol, 1.5 eq.) was added dropwise with a syringe over a period of 1 min. A white precipitate formed immediately upon the addition of the acid chloride. The mixture was stirred with ice for 10 min then at room temperature for a further 18 h. The reaction mixture was filtered and the filtrate was washed with saturated $Na_2CO_3$ (4 × 30 ml), water (2 × 30 ml), dilute HCl (2 × 30 ml), and finally with water (3 × 20 ml). The organic layer was dried ($MgSO_4$), filtered, and the solvent removed in vacuo to leave a yellow oil, which was washed with petroleum (200 ml). Yield 1.4 g (78%); $[\alpha]_D^{25}$ +18.3 ($c = 1.0$, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3415 (m), 3055 (m), 2982 (s), 1722 (s), and 1679 $cm^{-1}$ (s); $\delta_H$ 1.4 (3H, d $J = 7.1$ Hz, Ala-C$H_3$), 1.5 (18H, s, C(C$H_3$)$_3$), 1.9 (3H, s, =CC$H_3$), 4.3–4.5 (4H, m, C$H_2$O + 2 × NC$H$), 5.3 (1H, brs, N$H$), 5.6 (1H, s, $H_2$C=), 6.1 (1H, s, $H_2$C=), 6.8 (1H, brs, N$H$); $\delta_C$ 18.2 ($H_3$CC=), 18.5 (Ala-$C$H$_3$), 27.9 (C($C$H$_3$)$_3$), 29.2 (C($C$H$_3$)$_3$), 48.8 (Ala-N$C$H), 53.6 (Ser-N$C$H), 64.6 (OCH$_2$), 80.4 ($C$(CH$_3$)$_3$), 82.0 ($C$(CH$_3$)$_3$), 126.3 ($H_2C$=), 135.6 (=$C$CH$_3$), 155.3 (N$CO_2$), 166.9 ($CO$), 168.5 ($CO$), 171.9 ($CO$); *m/z* (Cl) 401 ($MH^+$); Found 401.2288 ($C_{19}H_{33}N_2O_7$ requires 401.2288).

### 7.6. O-Acryloyl-N-Boc-(S)-Ser-(S)-Phe-O$^t$Bu **(3)**

To a solution of *N*-Boc-(*S*)-Ser-(*S*)-Phe-O$^t$Bu (0.5 g, 1.2 mmol, 1.0 eq.) in EtOAc (25 ml) cooled with ice, was added triethylamine (0.5 ml, 3.7 mmol, 3.0 eq.). After stirring for 10 min, acryloyl chloride (0.15 ml, 1.9 mmol, 1.5 eq.) was added dropwise via a syringe. Subsequently, the solution was allowed to warm to room temperature and stirred for a further 15 h. The reaction mixture was filtered through Celite to remove a white solid (triethylamine hydrochloride). The filtrate was washed with saturated $Na_2CO_3$ (2 × 25 ml). Subsequently, the aqueous layer was back extracted with EtOAc (2 × 15 ml). The combined organic layers were then washed with saturated $Na_2CO_3$ (4 × 25 ml), water (2 × 20 ml), 2 M HCl (3 × 25 ml) and water (3 × 25 ml). The organic layer was dried ($MgSO_4$) and the solvent removed in vacuo to leave a yellow foaming oil. Flash chromatography, eluting with EtOAc-petroleum (15:85) gave a white solid. Yield 0.5 g (90%); m.p. 72°C; $[\alpha]_D^{25}$ +49.3 ($c = 1.0$, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3418 (br), 2979 (s), 1729 (s), 1661 (s), and 1522 $cm^{-1}$ (s); $\delta_H$ 1.35 (9H, s, C(C$H_3$)$_3$), 1.37 (9H, s, C(C$H_3$)$_3$), 3.1 (2H, d $J = 5.9$ Hz, C$H_2$Ph), 4.3–4.4 (3H, brm, NC$H$ + C$H_2$O), 4.7 (1H, q $J = 6.1$ Hz, Phe-NC$H$), 5.2 (1H, brd $J = 4.6$ Hz, Boc N$H$), 5.8 (1H, d $J = 10.4$ Hz, =C$H_2$), 6.0 (1H, dd $J = 10.4$, 17.2 Hz, =C$H$), 6.4 (1H, d $J = 17.2$ Hz, =C$H_2$), 6.7 (1H, d $J = 7.2$ Hz, N$H$CO), 7.1–7.15 (2H, m, 2 × ArC$H$), 7.2–7.3 (3H, m, 3 × ArC$H$); $\delta_C$ 27.9 (C(C$H_3$)$_3$), 28.2 (C($C$H$_3$)$_3$), 38.0 ($C$H$_2$Ph), 53.6 (NCH), 53.8 (N$C$H), 64.2 ($C$H$_2$O), 80.6 ($C$(CH$_3$)$_3$), 82.5 ($C$(CH$_3$)$_3$), 127.0 (Ar$C$H), 127.6 (=$C$H), 128.4 (Ar$C$H), 129.5 (Ar$C$H), 131.8 (=$C$H$_2$), 136.0 (Ar *ipsoC*), 155.2 (Boc$C$O), 165.7 (NH$C$O), 168.5 ($CO_2$), 170.0 ($CO_2$); *m/z* (CI) 463 ($MH^+$); Found 463.24444 ($C_{24}H_{35}N_2O_7$ requires 463.24443).

### 7.7. O-Methacryloyl-N-Boc-(S)-Ser-(S)-Phe-O$^t$Bu **(4)**

To a solution of *N*-Boc-(*S*)-Ser-(*S*)-Phe-O$^t$Bu (3.8 g, 9.4 mmol, 1.0 eq.) in EtOAc (75 ml) cooled with ice, was added triethylamine (3.9 ml, 28.1 mmol, 3.0 eq.). After stirring at 0°C for 5 min, methacryloyl chloride (1.4 ml, 14.1 mmol, 1.5 eq.) was added dropwise via a syringe. Subsequently, the solution was allowed to warm to room temperature then stirred for a further 17 h. The reaction mixture was filtered to remove a white solid and the filtrate was washed with saturated $Na_2CO_3$ (2 × 25 ml). Subsequently, the aqueous layer was back extracted with EtOAc (2 × 15 ml). The combined organic layers were then washed with saturated $Na_2CO_3$ (4 × 25 ml), water (2 × 25 ml), 2 M HCl (3 × 25 ml), and water (2 × 25 ml). The organic layer was dried ($MgSO_4$) and the solvent removed in vacuo to leave a colorless oil. This was recrystallized from petroleum (20 ml) to give a white solid. Yield 3.8 g (85%); m.p. 56°C; $[\alpha]_D^{25}$ +39.3 ($c = 1.0$, $CHCl_3$); (Found C, 62.7; H, 7.8; N, 5.8. $C_{25}H_{36}N_2O_7$ requires C, 63.0; H, 7.6; N, 5.9%); $\nu_{max}$ ($CHCl_3$) 3407 (br), 2979 (s), 1724 (s), 1656 (s), and 1523 $cm^{-11}$ (s); $\delta_H$ 1.4 (9H, s, C(C$H_3$)$_3$), 1.45 (9H, s, C(C$H_3$)$_3$), 1.9 (3H, s, =CC$H_3$), 3.1 (2H, d $J = 6.2$ Hz, C$H_2$Ph), 4.3 (1H, brm $J = 5.8$, C$H_2$O), 4.4 (2H, brm, Ser-NC$H$ + C$H_2$O), 4.7 (1H, q $J = 6.1$ Hz, Phe-NC$H$), 5.3 (1H, brs, Boc-N$H$), 5.6 (1H, s, =C$H_2$), 6.1 (1H, s, =C$H_2$), 6.6 (1H, brd $J = 7.4$ Hz, N$H$CO), 7.1–7.3 (5H, m, ArC$H$); $\delta_C$ 18.2 (=CC$H_3$), 27.9 (C(C$H_3$)$_3$), 28.2 (C($C$H$_3$)$_3$), 38.1 ($C$H$_2$Ph), 53.8 (2 × NCH), 64.3 ($C$H$_2$O), 82.5 (2 × $C$(CH$_3$)$_3$), 126.5 (=$C$H$_2$), 127.0 (Ar$C$H), 128.4 (Ar$C$H), 129.5 (Ar$C$H), 135.9 (Ar *ipsoC* + =$C$CH$_3$), 156.4 (N$CO_2$), 168.6 (2 × $CO$); *m/z* (CI) 477 ($MH^+$); Found 477.2601 ($C_{25}H_{37}N_2O_7$ requires 477.2601).

### 7.8. O-Acryloyl-N-Boc-(S)-Ser-(S)-Pro-O$^t$Bu **(5)**

To a solution of *N*-Boc-(*S*)-Ser-(*S*)-Pro-O$^t$Bu (**5**) (3.0 g, 8.4 mmol, 1.0 eq.) in EtOAc (40 ml) was added triethylamine (3.5 ml, 25.1 mmol, 3.0 eq.). The solution was cooled to 0°C and acryloyl chloride (1.0 ml, 12.6 mmol, 1.5 eq.) was added dropwise via a syringe. Subsequently, the solution was warmed to room temperature and stirred for a further 20 h. Filtration through Celite removed a white solid. The filtrate was subsequently washed with saturated $Na_2CO_3$ (2 × 25 ml) and the aqueous layer back extracted with EtOAc (2 × 15 ml). The combined organic layers were washed with saturated $Na_2CO_3$ (4 × 25 ml), water (2 × 25 ml), 2 M HCl (3 × 25 ml) and water (2 × 25 ml). Subsequently, the organic layer was dried ($MgSO_4$), filtered and the solvent removed in vacuo to afford a yellow foaming oil. Flash chromatography, eluting with EtOAc:petroleum (3:7) afforded a colorless foaming oil. Yield 3.1 g (89%); $[\alpha]_D^{28}$ −21.4 (c = 0.6, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3404 (br), 3344 (br), 2977 (s), 2933 (s), 1729 (s), 1649 (s), and 1502 cm$^{-1}$ (m); $\delta_H$ 1.31 (9H, s, C(C*H*$_3$)$_3$), 1.33 (9H, s, C(C*H*$_3$)$_3$), 1.8–2.1 (4H, brm, Pro-β-C*H*$_2$ + γ-C*H*$_2$), 3.6–3.7 (2H, brm, Pro-NC*H*$_2$), 4.0 (1H, dd *J* = 8.05, 11.2 Hz, C*H*$_2$O), 4.3 (1H, dd *J* = 4.1, 4.4 Hz, Pro-NC*H*), 4.4 (1H, dd *J* = 4.3, 11.2 Hz, C*H*$_2$O), 4.7 (1H, ddd *J* = 4.2, 8.2, 8.5 Hz, Ser-NC*H*), 5.5 (1H, brd *J* = 8.6, Boc-N*H*), 5.8 (1H, d *J* = 10.3 Hz, =C*H*$_2$), 6.0 (1H, dd *J* = 10.4, 17.3 Hz, =C*H*), 6.3 (1H, d *J* = 17.2 Hz, =C*H*$_2$); $\delta_C$ 24.8 (Pro-γ-*C*H$_2$), 27.9 (C(*C*H$_3$)$_3$), 28.3 (C(*C*H$_3$)$_3$), 29.0 (Pro-β-*C*H$_2$), 47.1 (N*C*H$_2$), 51.4 (Pro-N*C*H), 59.8 (Ser-N*C*H), 64.2 (*C*H$_2$O), 79.8 (*C*(CH$_3$)$_3$), 81.4 (*C*(CH$_3$)$_3$), 128.0 (=*C*H$_2$), 131.4 (=*C*H), 155.3 (N*C*O$_2$), 165.9 (=CH*C*O$_2$), 167.5 (*C*O$_2$), 170.6 (N*C*O); *m/z* (CI) 423 ($MH^+$); Found 413.2288 ($C_{20}H_{33}N_2O_7$ requires 413.2288).

### 7.9. O-Methacryloyl-N-Boc-(S)-Ser-(S)-Pro-O$^t$Bu **(6)**

To a solution of *N*-Boc-(*S*)-Ser-(*S*)-Pro-O$^t$Bu (**5**) (9.0 g, 25.1 mmol, 1.0 eq.) in EtOAc (75 ml), cooled with ice was added triethylamine (10.5 ml, 75.4 mmol, 3.0 eq.). After stirring at 0°C for 5 min, methacryloyl chloride (3.7 ml, 37.7 mmol, 1.5 eq.) was added dropwise via a syringe. Subsequently, the solution was allowed to warm to room temperature then stirred for a further 22 h. The reaction mixture was filtered to remove a white solid and the filtrate was washed with saturated $Na_2CO_3$ (2 × 25 ml). Subsequently, the aqueous layer was back extracted with EtOAc (2 × 15 ml). The combined organic layers were then washed with saturated $Na_2CO_3$ (4 × 25 ml), water (2 × 25 ml), 2 M HCl (3 × 25 ml), and water (2 × 25 ml). The organic layer was dried ($MgSO_4$) and the solvent removed in vacuo to leave a yellow foaming oil. Flash chromatography, eluting with EtOAc:petroleum (2:8) afforded a colorless foaming oil. Yield 3.8 g (81%); $[\alpha]_D^{25}$ −28.4; (Found C, 59.4; H, 7.9; N, 6.2. $C_{21}H_{34}N_2O_7$ requires C, 59.1; H, 8.0; N, 6.6%); $\nu_{max}$ ($CHCl_3$) 3426 (br), 2977 (s), 1736 (s), 1648 (s), and 1508 cm$^{-1}$ (m); $\delta_H$ 1.4 (9H, s, C(C*H*$_3$)$_3$), 1.42 (9H, s, C(C*H*$_3$)$_3$), 1.9 (3H, s, =CC*H*$_3$), 2.0–2.3 (4H, brm, Pro-β-C*H*$_2$ + γ-C*H*$_2$), 3.6–3.8 (2H, brm, Pro-NC*H*$_2$), 4.1 (1H, dd *J* = 8.0, 11.3 Hz, C*H*$_2$O), 4.4 (1H, dd *J* = 4.2, 4.25 Hz, Pro-NC*H*), 4.6 (1H, dd *J* = 4.0, 11.5 Hz, C*H*$_2$O), 4.8 (1H, dd *J* = 4.3, 8.25 Hz, Ser-NC*H*), 5.5 (1H, brd *J* = 10.1, Boc-N*H*), 5.6 (1H, s, =C*H*$_2$), 6.1 (1H, s, =C*H*$_2$); $\delta_C$ 18.2 (=C*C*H$_3$), 24.8 (Pro-γ-*C*H$_2$), 27.9 (C(*C*H$_3$)$_3$), 28.2 (C(*C*H$_3$)$_3$), 28.9 (Pro-β-*C*H$_2$), 47.1 (N*C*H$_2$), 51.4 (Pro-N*C*H), 59.8 (Ser-N*C*H), 64.4 (*C*H$_2$O), 79.7 (*C*(CH$_3$)$_3$), 81.3 (*C*(CH$_3$)$_3$), 126.2 (=*C*H$_2$), 135.8 (=*C*CH$_3$), 155.2 (N*C*O$_2$), 167.2 (*C*O$_2$), 167.4 (*C*O$_2$), 170.5 (N*C*O); *m/z* (CI) 427 ($MH^+$); Found 427.2444 ($C_{21}H_{35}N_2O_7$ requires 477.2444).

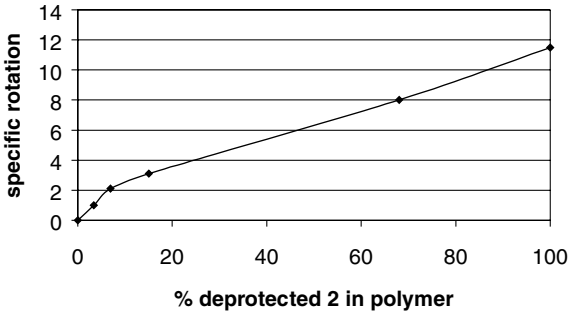



Fig. 9. Variation of specific rotation versus % monomer **2** incorporation for deprotected copolymers.

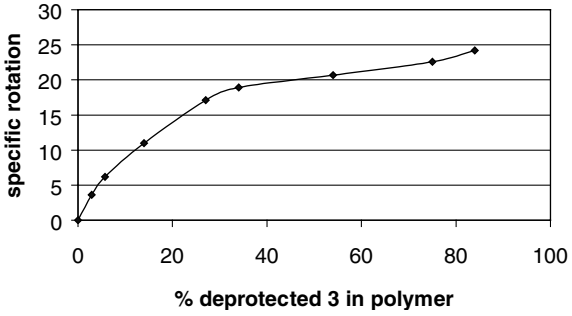



Fig. 10. Variation of specific rotation versus % monomer **3** incorporation for deprotected copolymers.

### 7.10. N-Boc-(S)-Ala-(S)-Ser-(S)-Phe-O$^t$Bu

To a solution of *N*-Boc-(*S*)-alanine (5.5 g, 29.1 mmol, 1.1 eq.) in glass distilled DMF (80 ml) was added DCC (5.5 g, 26.5 mmol, 1.0 eq.), HOBt (4.6 g, 34.4 mmol, 1.3 eq.) and (*S*)-Ser-(*S*)-Phe-O$^t$Bu (8.2 g, 26.5 mmol, 1.0 eq.). The mixture was stirred at room temperature for 18 h after which the solvent was removed in vacuo and EtOAc (70 ml) was added to the yellow oil residue. Filtration through Celite removed a white solid and the filtrate was washed with saturated $Na_2CO_3$ (2 × 25 ml). The aqueous layer was back extracted with EtOAc (2 × 15 ml) and the combined organic layers were subsequently washed with saturated $Na_2CO_3$ (3 × 25 ml), water (3 × 25 ml), 2 M

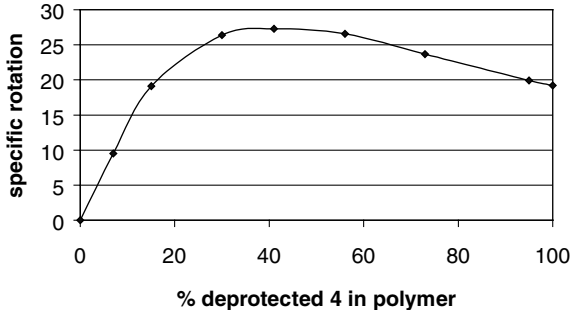



Fig. 11. Variation of specific rotation versus % monomer **4** incorporation for deprotected copolymers.

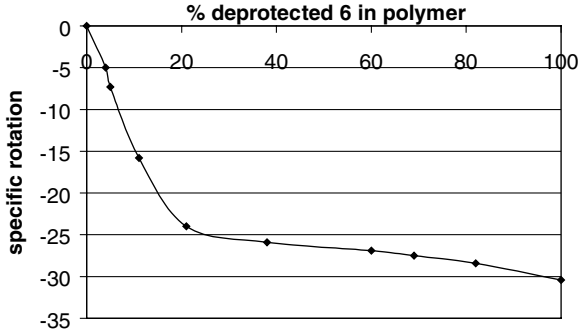



Fig. 13. Variation of specific rotation versus % monomer **6** incorporation for deprotected copolymers.

HCl (2 × 25ml) and water (2 × 25ml). The organic layer was dried ($MgSO_4$), filtered and the solvent removed in vacuo to leave a cream solid. Flash chromatography eluting with EtOAc:petroleum (3:2) afforded a white solid. Yield 11.1 g (88%); m.p. 74°C; $[\alpha]_D^{26}$ −30.0 ($c = 0.6$, $CHCl_3$); (Found C, 59.7; H, 7.5; N, 8.7. $C_{24}H_{37}N_3O_7$ requires C, 60.1; H, 7.8; N, 8.8%); $\nu_{max}$ ($CHCl_3$) 3305 (br), 2979 (s), 2932 (s), 1652 (brs), and 1522 $cm^{-1}$ (brs); $\delta_H$ 1.3 (3H, d $J = 7.1$ Hz, C*H*$_3$), 1.4 (9H, s, C(C*H*$_3$)$_3$), 1.45 (9H, s, C(C*H*$_3$)$_3$), 3.0 (1H, dd $J = 6.5$, 14.0 Hz, C*H*$_2$Ph), 3.1 (1H, dd $J = 6.2$, 14.0 Hz, C*H*$_2$Ph), 3.6–3.8 (2H, brm, O*H* + C*H*$_2$O), 4.0 (1H, brm, C*H*$_2$O), 4.2 (1H, pent. $J = 7.1$ Hz, Ala-NC*H*), 4.5 (1H, t $J = 6.1$ Hz, Ser-NC*H*), 4.7 (1H, q $J = 6.5$ Hz, Phe-NC*H*), 5.3 (1H, d $J = 7.2$ Hz, Boc-N*H*), 7.1–7.3 (7H, m, ArC*H* + 2 × N*H*); $\delta_C$ 18.6 (*C*H$_3$), 27.8 (C(*C*H$_3$)$_3$), 28.3 (C(*C*H$_3$)$_3$), 37.8 (*C*H$_2$Ph), 51.8 (Ala-N*C*H), 54.1 (Phe-N*C*H), 54.5 (Ser-N*C*H), 62.7 (*C*H$_2$O), 79.7 (*C*(CH$_3$)$_3$), 82.2 (*C*(CH$_3$)$_3$), 126.7 (Ar*C*H), 128.2 (Ar*C*H), 129.2 (Ar*C*H), 136.0 (Ar *ipso C*), 155.4 (N*C*O$_2$), 170.0 (NH*C*O), 170.2 (NH*C*O), 170.7 (*C*O$_2$); *m*/*z* (CI) 480 ($MH^+$); Found 480.2706 ($C_{24}H_{37}N_3O_7$ requires 480.2710).

### *7.11. O-Acryloyl-N-Boc-(S)-Ala-(S)-Ser-(S)-Phe-O$^t$Bu* ***(7)***

Triethylamine (2.6 ml, 18.8 mmol, 3.0 eq.) was added to a solution of *N*-Boc-(*S*)-Ala-(*S*)-Ser-(*S*)-Phe-O$^t$Bu (3.0 g, 6.3 mmol, 1.0 eq.) in EtOAc (50 ml). Subsequently, the solution was cooled to 0°C and acryloyl chloride (0.6 ml, 7.8 mmol, 1.3 eq.) was added dropwise via a syringe to the stirring mixture. The mixture was warmed to room temperature and stirred for a further 18 h after which the solvent was removed in vacuo. Filtration through Celite removed a white solid and the filtrate was washed with saturated $Na_2CO_3$ (2 × 25 ml). The aqueous layer was back extracted with EtOAc (2 × 15 ml) and the combined organic layers were subsequently washed with saturated $Na_2CO_3$ (3 × 25 ml), water (3 × 25 ml), 2 M HCl (2 × 25 ml) and water (2 × 25 ml). The organic layer was dried ($MgSO_4$), filtered and the solvent removed in vacuo to leave a white solid. Yield 2.5 g (75%); m.p. 68°C; $[\alpha]_D^{28}$ +6.2 (c = 0.6, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3416 (br), 2978 (s), 1720 (s), 1648 (s), and 1522 $cm^{-1}$ (m); $\delta_H$ 1.3 (3H, d $J = 6.9$ Hz, C*H*$_3$), 1.35 (9H, s, C(C*H*$_3$)$_3$), 1.4 (9H, s, C(C*H*$_3$)$_3$), 3.1 (2H, d $J = 6.1$ Hz, C*H*$_2$Ph), 3.7–4.0 (1H, brm, Ala-NC*H*), 4.3 (1H, dd $J = 5.3$, 11.3 Hz, C*H*$_2$O), 4.5 (1H, dd $J = 5.3$, 11.3 Hz, C*H*$_2$O), 4.7 (1H, q $J = 6.4$ Hz, Phe-NC*H*), 4.8 (1H, q $J = 5.3$ Hz, Ser-NC*H*), 5.2 (1H, d $J = 7.2$ Hz, Boc-N*H*), 5.8 (1H, d $J = 10.4$ Hz, =C*H*$_2$), 6.1 (1H, dd $J = 10.4$, 17.2 Hz, =C*H*), 6.4 (1H, d $J = 17.2$ Hz, =C*H*$_2$), 7.1–7.3 (7H, m, ArC*H* + 2 × N*H*); $\delta_C$ 18.5 (*C*H$_3$), 27.9 (C(*C*H$_3$)$_3$), 28.3 (C(*C*H$_3$)$_3$), 38.0 (*C*H$_2$Ph), 52.0 (Ala-N*C*H), 54.0 (Phe-N*C*H), 54.3 (Ser-N*C*H), 63.8 (*C*H$_2$O), 80.1 (*C*(CH$_3$)$_3$), 82.3 (*C*(CH$_3$)$_3$), 126.9 (Ar*C*H), 127.6 (=*C*H), 128.3 (Ar*C*H),

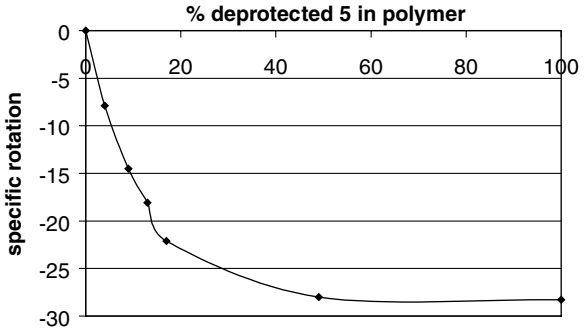



Fig. 12. Variation of specific rotation versus % monomer **5** incorporation for deprotected copolymers.

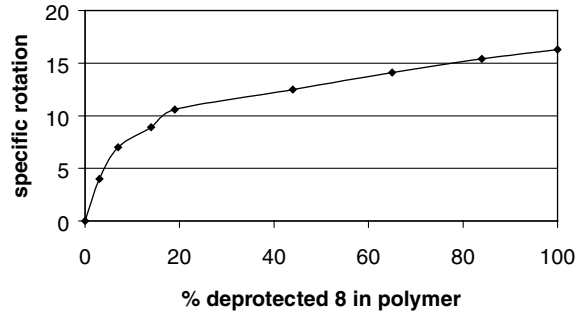



Fig. 14. Variation of specific rotation versus % monomer **8** incorporation for deprotected copolymers.

129.4 (ArCH), 131.7 (=$CH_2$), 136.1 (Ar *ipso C*), 155.5 ($NCO_2$), 170.0 (NHCO), 170.2 (NHCO), 173.0 ($CO_2$), 173.4 ($CO_2$).

### *7.12. O-Methacryloyl-N-Boc-(S)-Ala-(S)-Ser-(S)-Phe-O$^t$Bu **(8)***

Triethylamine (1.6 ml, 11.8 mmol, 3.0 eq.) was added to a solution of *N*-Boc-(*S*)-Ala-(*S*)-Ser-(*S*)-Phe-O$^t$Bu (1.9 g, 3.9 mmol, 1.0 eq.) in EtOAc (50 ml). Subsequently, the solution was cooled to 0°C and methacryloyl chloride (0.5 ml, 5.1 mmol, 1.3 eq.) was added dropwise via a syringe to the stirring mixture. The mixture was warmed to room temperature and stirred for a further 18 h after which the solvent was removed in vacuo. Filtration through Celite removed a white solid and the filtrate was washed with saturated $Na_2CO_3$ (2 × 25 ml). The aqueous layer was back extracted with EtOAc (2 × 15 ml) and the combined organic layers were subsequently washed with saturated $Na_2CO_3$ (3 × 25 ml), water (3 × 25 ml), 2 M HCl (2 × 25 ml) and water (2 × 25 ml). The organic layer was dried ($MgSO_4$), filtered and the solvent removed in vacuo to provide a white solid, which was subsequently recrystallized from petroleum (25 ml) to give a white solid. Yield 2.0 g (91%); m.p. 64°C; $[\alpha]_D^{26}$ +10.0 ($c = 0.6$, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3393 (br), 2979 (s), 2932 (s), 1725 (s), 1647 (s), and 1515 $cm^{-1}$ (m); $\delta_H$ 1.25 (3H, d $J = 7.1$ Hz, C$H_3$), 1.3 (9H, s, C(C$H_3$)$_3$), 1.4 (9H, s, C(C$H_3$)$_3$), 2.0 (3H, s, =CC$H_3$), 3.0 (2H, d $J = 6.2$ Hz, C$H_2$Ph), 4.2 (1H, p $J = 6.6$ Hz, Ala-NC*H*), 4.3 (1H, dd $J = 5.4$, 11.3 Hz, C$H_2$O), 4.4 (1H, dd $J = 5.5$, 11.3 Hz, C$H_2$O), 4.7 (1H, q $J = 6.3$ Hz, Phe-NC*H*), 4.8 (1H, q $J = 5.5$ Hz, Ser-NC*H*), 5.1 (1H, d $J = 7.1$ Hz, Boc-N*H*), 5.6 (1H, s, =C$H_2$), 6.1 (1H, s, =C$H_2$), 7.0 (1H, brd $J = 7.2$ Hz, N*H*CO), 7.1 (1H, brd $J = 7.0$ Hz, N*H*CO), 7.15–7.3 (5H, m, ArC*H*); $\delta_C$ 17.9 (=CC$H_3$), 18.2 (C$H_3$), 27.9 (C(C$H_3$)$_3$), 28.3 (C(C$H_3$)$_3$), 38.0 (C$H_2$Ph), 50.3 (Ala-NCH), 52.2 (Phe-NCH), 53.9 (Ser-NCH), 64.0 (C$H_2$O), 80.3 (C(CH$_3$)$_3$), 82.4 (C(CH$_3$)$_3$), 126.6 (=C$H_2$), 127.0 (ArCH), 128.4 (ArCH), 129.4 (ArCH), 135.5 (Ar *ipso C*), 136.0 (=CCH$_3$), 155.6 ($NCO_2$), 168.1 (NHCO), 169.9 (NHCO), 172.9 ($CO_2$); *m/z* (CI) 548 ($MH^+$); Found 548.2960 ($C_{28}H_{42}N_3O_8$ requires 548.2970).

### *7.13. Homopolymerization of monomers **1**,**3**–**8** in toluene*

To a solution (1–4 M) of monomer **1**,**3**–**8** in toluene, was added benzoyl peroxide (0.01 eq.). The solution was cooled to 273 K and degassed with nitrogen for 30 min. The solution was then heated to reflux under an argon atmosphere for 4 h. The resulting solution was dissolved in chloroform (ca. 5 ml) and poured into petroleum (ca. 100 ml) to give the polymer as a white precipitate.

Data for **poly-1**: Yield 60%; $[\alpha]_D^{26}$ −2.7; $\nu_{max}$ ($CHCl_3$) 3335 (s), 2981 (s), 1729 (s), and 1670 $cm^{-1}$ (s); $\delta_H$ 1.0–1.9 (24H, m, Ala-C$H_3$+2 × C(C$H_3$)$_3$ + C$H$ + C$H_2$), 4.1–4.7 (4H, m, Ala-CH + Ser-NCH + OCH$_2$); $\delta_C$ 18.3 (Ala-C$H_3$), 27.9 (C(C$H_3$)$_3$), 28.3 (C(C$H_3$)$_3$), 38.0 (C$H$), 48.6 (Ala-NC*H*), 53.6 (Ser-NC*H*), 64.3 (OC$H_2$), 79.8 (OC(CH$_3$)$_3$), 81.4 (OC(CH$_3$)$_3$), 168.4 ($CO_2$), 171.7 ($CO_2$); GPC ($CHCl_3$) $M_n$ 9180, $M_w$ 101,150, $M_w/M_n$ 11.0.

Data for **poly-3**: Yield 58%; $[\alpha]_D^{26}$ +37.1 ($c = 0.8$, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3358 (br), 2978 (s), 2932 (s), 1730 (s), 1655 (s), and 1525 $cm^{-1}$ (s); $\delta_H$ 1.2–1.8 (21H, brm, C$H_2$ + C$H$ + 2 × C(C$H_3$)$_3$), 3.0–3.2 (2H, brs, C$H_2$Ph), 4.1–4.4 (3H, brm, Ser-NC$H$ + C$H_2$O), 4.6–4.8 (1H, brs, Phe-NC*H*), 7.1–7.4 (6H, brm, ArC$H$ + CON*H*); $\delta_C$ 27.9 (C(C$H_3$)$_3$), 28.3 (C(C$H_3$)$_3$), 38.2 (C$H_2$Ph), 53.5 (NCH), 53.8 (NCH), 64.5 (C$H_2$O), 79.9 (C(CH$_3$)$_3$), 81.7 (C(CH$_3$)$_3$), 126.8 (ArCH), 128.3 (ArCH), 128.9 (ArCH), 136.3 (Ar *ipsoC*), 155.7 ($NCO_2$), 169.1 (CONH), 170.0 ($CO_2$); GPC (THF) $M_n$ 4780, $M_w$ 47,350, $M_w/M_n$ 9.9.

Data for **poly-4**: Yield 76%; $[\alpha]_D^{26}$ +33.7 ($c = 1.2$, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3331 (br), 3013 (s), 2966 (s), 1725 (s), 1672 (s), and 1514 $cm^{-1}$ (s); $\delta_H$ 1.1–1.6 (23H, brm, C$H_2$ + 2 × C(C$H_3$)$_3$ + C$H_3$), 3.0–3.2 (2H, brd, C$H_2$Ph), 4.1–4.5 (3H, brm, Ser-NC$H$ + C$H_2$O), 4.6–4.8 (1H, brs, Phe-NC*H*), 5.2–5.3 (1H, brs, N*H*CO$_2$), 7.1–7.4 (6H, brm, ArC$H$ + CON*H*); $\delta_C$ 18.2 (C$H_3$), 27.9 (C(C$H_3$)$_3$), 28.2 (C(C$H_3$)$_3$), 38.1 (C$H_2$Ph), 53.5 (NCH), 53.8 (NCH), 64.3 (C$H_2$O), 79.9 (C(CH$_3$)$_3$), 82.5 (C(CH$_3$)$_3$), 127.0 (ArCH), 128.4 (ArCH), 129.6 (ArCH), 136.4 (Ar *ipsoC*), 156.7 ($NCO_2$), 169.1 (CONH), 170.1 ($CO_2$); GPC (THF) $M_n$ 3625, $M_w$ 12,750, $M_w/M_n$ 3.5.

Data for **poly-5**: Yield 94%; $[\alpha]_D^{26}$ −38.2 ($c = 0.7$, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3426 (br), 2977 (s), 2931 (m), 1736 (s), 1648 (s), and 1508 $cm^{-1}$ (m); $\delta_H$ 1.1–1.5 (21H, brm, C$H_2$ + C$H$ + 2 × C(C$H_3$)$_3$), 1.7–2.2 (4H, brm, Pro-β-C$H_2$ + Pro-γ-C$H_2$), 3.7–3.9 (2H, brs, NC$H_2$), 3.9–4.0 (1H, brs, Pro-NC*H*), 4.3–4.4 (2H, brs, C$H_2$O), 4.5–4.9 (2H, brm, Ser-NC$H$ + Boc-N*H*); $\delta_C$ 24.8 (Pro-γ-C$H_2$), 27.9 (C(C$H_3$)$_3$), 28.4 (C(C$H_3$)$_3$), 29.0 (Pro-β-C$H_2$), 47.1 (NC$H_2$), 51.4 (Pro-NCH), 59.8 (Ser-NCH), 64.3 (C$H_2$O), 79.2 (C(CH$_3$)$_3$), 81.2 (C(CH$_3$)$_3$), 156.3 ($NCO_2$), 169.9 (NCO), 170.1 ($CO_2$); GPC (THF) $M_n$ 4160, $M_w$ 12,550, $M_w/M_n$ 3.0.

Data for **poly-6**: Yield 67%; $[\alpha]_D^{26}$ −44.2 ($c = 0.7$, $CHCl_3$); $\nu_{max}$ ($CHCl_3$) 3422 (br), 2978 (s), 1728 (s), and 1650 $cm^{-1}$ (s); $\delta_H$ 1.0–1.6 (23H, brm, C$H_2$ + C$H_3$ + 2 × C(C$H_3$)$_3$), 1.8–2.3 (4H, brm, Pro-β-C$H_2$ + Pro-γ-C$H_2$), 3.4–3.8 (2H, brs, NC$H_2$), 4.2–4.4 (2H, brs, C$H_2$O), 4.5–4.9 (3H, brm, Pro-NC$H$ + Ser-NC$H$ + Boc-N*H*); $\delta_C$ 18.7 (C$H_3$), 24.8 (Pro-γ-C$H_2$), 27.9 (C(C$H_3$)$_3$), 28.3 (C(C$H_3$)$_3$), 29.0 (Pro-β-C$H_2$), 44.5 (CCH$_3$), 47.1 (NC$H_2$), 51.4 (Pro-NCH), 59.8 (Ser-NCH), 64.3 (C$H_2$O), 79.3 (C(CH$_3$)$_3$), 81.0 (C(CH$_3$)$_3$), 156.3 ($NCO_2$), 169.9 (NCO), 170.8 ($CO_2$); GPC (THF) $M_n$ 2225, $M_w$ 12,100, $M_w/M_n$ 5.4.

Data for **poly-7**: Yield 59%; $[\alpha]_D^{26}$ +28.7 ($c = 0.6$, $CHCl_3$); $\nu_{max}$ (KBr) 3307 (br), 2980 (s), 2935 (m), 1738 (s), 1648 (s), and 1522 $cm^{-1}$ (s); $\delta_H$ 0.9–1.6 (24H, brm, C$H$ + C$H_2$ + 2 × C(C$H_3$)$_3$ + C$H_3$), 2.8–3.2 (2H, brs, C$H_2$Ph), 3.4–3.5 (1H, brd, C$H_2$O), 3.8–3.9 (1H, brd, C$H_2$O), 4.0–4.2 (1H, brs, Ala-NC$H$), 4.3–4.4 (1H, brs, Ser-NC$H$), 4.5–4.6 (1H, brq, Phe-NC$H$), 5.1–5.2 (1H,

brd, Boc-N*H*), 6.8–7.2 (7H, brm, ArC*H* + 2 × CON*H*); $\delta_C$ 18.2 (Ala-*C*H$_3$), 20.3 (*C*H$_2$), 27.8 (C(*C*H$_3$)$_3$), 28.2 (C(*C*H$_3$)$_3$), 37.7 (*C*H$_2$Ph), 50.2 (Ala-N*C*H), 54.0 (Phe-N*C*H), 54.2 (Ser-N*C*H), 62.6 (*C*H$_2$O), 80.2 (*C*(CH$_3$)$_3$), 82.5 (*C*(CH$_3$)$_3$), 126.9 (Ar*C*H), 128.4 (Ar*C*H), 129.3 (Ar*C*H), 136.0 (Ar *ipsoC*), 155.5 (N*C*O$_2$), 170.1 (*C*ONH), 170.3 (*C*ONH), 173.2 (*C*O$_2$); GPC (DMF) $M_n$ 8235, $M_w$ 20,350, $M_w/M_n$ 2.5.

Data for **poly-8**: Yield 88%; $[\alpha]_D^{26}$ +22.1 (CHCl$_3$); GPC (DMF) $M_n$ 1150, $M_w$ 1345, $M_w/M_n$ 1.2. GPC (THF) $M_n$ 6945, $M_w$ 23,600, $M_w/M_n$ 3.4. Other data is given for the polymer prepared in DMF.

### 7.14. Homopolymerization of monomers *1*,*2*,*8* in DMF

Monomers **1**,**2**,**8** were added to anhydrous DMF to form a 4 M solution, and benzoyl peroxide (1 mol%) was added. The mixture was degassed with nitrogen for 15 min with cooling at 273 K, and then heated to reflux under a nitrogen atmosphere. Heating was continued for 4 h, after which time the DMF was removed by distillation and the residue was dissolved in chloroform (ca. 5 ml). The resulting solution was added slowly, with stirring to an excess of petroleum (ca. 150 ml). The precipitated white solid was collected by filtration and dried in vacuo for 5 h.

Data for **poly-1**: Yield 72%; $[\alpha]_D^{26}$ −2.7 (CHCl$_3$); $\nu_{max}$ (CHCl$_3$) 3332 (br), 2979 (s), 2934 (s), 1731 (s), 1664 (s), and 1524 cm$^{-1}$ (s); $\delta_H$ 1.0–1.6 (24H, brm, C*H*$_2$ + 2 × C(C*H*$_3$)$_3$ + C*H* + Ala-C*H*$_3$), 4.0–4.6 (4H, brm, C*H*$_2$O + Ala-NC*H* + Ser-NC*H*), 5.3–5.4 (1H, brs, Boc-N*H*), 6.8–6.9 (1H, brd, N*H*CO); $\delta_C$ 18.2 (Ala-*C*H$_3$ + *C*H), 27.9 (C(*C*H$_3$)$_3$), 28.3 (C(*C*H$_3$)$_3$), 48.7 (Ala-N*C*H + *C*CH), 53.6 (Ser-N*C*H), 64.3 (*C*H$_2$O), 79.8 (*C*(CH$_3$)$_3$), 81.3 (*C*(CH$_3$)$_3$), 155.6 (N*C*O$_2$), 168.4 (*C*ONH), 171.5 (*C*O$_2$); GPC (DMF) $M_n$ 71,400, $M_w$ 989,000, $M_w/M_n$ 13.9.

Data for **poly-2**: Yield 82%; $[\alpha]_D^{26}$ −1.6 (CHCl$_3$); $\nu_{max}$ (CHCl$_3$) 3326 (br), 2978 (s), 1734 (s), 1664 (s), and 1523 cm$^{-1}$ (s); $\delta_H$ 0.6–1.9 (26H, brm, C*H*$_2$ + 2 × C(C*H*$_3$)$_3$ + C*H*$_3$ + Ala-C*H*$_3$), 4.0–4.6 (4H, brm, C*H*$_2$O + Ala-NC*H* + Ser-NC*H*); $\delta_C$ 16.4 (*C*H$_2$), 18.6 (Ala-*C*H$_3$ + *C*H$_3$), 27.9 (C(*C*H$_3$)$_3$), 28.4 (C(*C*H$_3$)$_3$), 44.5 (*C*CH$_3$), 44.8 (*C*CH$_3$), 48.8 (Ala-N*C*H), 54.3 (Ser-N*C*H), 64.6 (*C*H$_2$O), 80.1 (*C*(CH$_3$)$_3$), 82.5 (*C*(CH$_3$)$_3$), 155.6 (N*C*O$_2$), 168.1 (*C*ONH), 171.5 (*C*O$_2$); GPC (THF) $M_n$ 6640, $M_w$ 38,600, $M_w/M_n$ 5.8.

Data for **poly-8**: Yield 76%; $[\alpha]_D^{26}$ +39.7 ($c = 1.0$, CHCl$_3$); $\nu_{max}$ (CHCl$_3$) 3299 (br), 2979 (s), 2934 (s), 1729 (s), 1658 (s), and 1522 cm$^{-1}$ (s); $\delta_H$ 0.7–2.5 (26H, brm, C*H*$_2$ + 2 × C(C*H*$_3$)$_3$ + C*H*$_3$ + Ala-C*H*$_3$), 2.7–3.2 (2H, brm, C*H*$_2$Ph), 3.7–4.3 (3H, brm, C*H*$_2$O + Ala-NC*H*), 4.4–4.7 (2H, brm, Ser-NC*H* + Phe-NC*H*), 4.8–5.0 (1H, brs, Boc-N*H*), 6.6–7.3 (7H, brm, ArC*H* + 2 × CON*H*); $\delta_C$ 18.2 (Ala-*C*H$_3$ + *C*H$_3$), 27.9 (C(*C*H$_3$)$_3$), 28.3 (C(*C*H$_3$)$_3$), 38.0 (*C*H$_2$Ph), 44.5 (*C*CH$_3$), 50.3 (Ala-N*C*H), 52.9 (Phe-N*C*H), 54.0 (Ser-N*C*H), 63.8 (*C*H$_2$O), 80.2 (*C*(CH$_3$)$_3$), 82.5 (*C*(CH$_3$)$_3$), 127.0 (Ar*C*H), 128.4 (Ar*C*H), 129.4 (Ar*C*H), 136.1 (Ar *ipsoC*), 155.6 (N*C*O$_2$), 168.1 (*C*ONH), 170.0 (*C*O$_2$), 173.3 (*C*O$_2$); GPC (THF) $M_n$ 4350, $M_w$ 86,350, $M_w/M_n$ 19.9.

### 7.15. Copolymerization of monomers *1*,*2*,*9* with methyl methacrylate in DMF

Monomers **1**,**2**,**9** were suspended in freshly distilled methyl methacrylate and anhydrous DMF to form a 3.0 M solution, then benzoyl peroxide (1 mol%) was added. The mixture was cooled to 273 K and degassed with nitrogen for 15 min and then heated to reflux under a nitrogen atmosphere. Heating was continued for 3 h, or until the polymer had gelled out of solution, after which time the DMF was distilled off, and the crude polymer was dissolved in chloroform (ca. 10 ml). This was added slowly, with stirring, to an excess of petroleum (ca. 125 ml). The precipitated white solid was collected by filtration and dried in vacuo at 298 K for 5 h. The copolymers were characterized by $^1$H NMR, $^{13}$C NMR, GPC, specific rotation and infrared spectroscopy, selected analytical data is given in Tables 1, 2 and 9.

### 7.16. Copolymerization of monomers *3*–*8* with methyl methacrylate in toluene

Monomers **3**–**8** were suspended in freshly distilled methyl methacrylate, and toluene to form a 1.0–3.0 M solution, and benzoyl peroxide (1 mol%) was added. The mixture was cooled to 273 K and degassed with nitrogen for 15 min and then heated to reflux under a nitrogen atmosphere. Heating was continued for 3 h or until the polymer had gelled out of solution, after which time the crude polymer was dissolved in chloroform (ca. 5 ml). The resulting solution was added slowly, with stirring, to an excess of light petroleum (ca. 150 ml). The precipitated white solid was collected by filtration and dried in vacuo at 298 K for 5 h. The copolymers were characterized by $^1$H NMR, $^{13}$C NMR, GPC, specific rotation and infrared spectroscopy, selected analytical data is given in Tables 3–8.

### 7.17. Deprotection of homo and copolymers

The protected polymer (ca. 250 mg) was dissolved in CH$_2$Cl$_2$ (2 ml) and trifluoroacetic acid (2 ml). The solution was stirred at room temperature for 17 h and was then added slowly, with stirring to ether (40 ml). The precipitated white solid was collected by filtration, washed with ether (100 ml) and dried in vacuo at 298 K for 12 h. Analytical data for one polymer in each series is given below:

Data for **deprotected poly-2**: Yield 89%; $[\alpha]_D^{26}$ +11.5 ($c = 0.5$, DMSO:CH$_3$CN, 1:1); $\nu_{max}$ (KBr) 3500 (br), 3333 (br), 3214 (br), 3048 (br), 3003 (s), 2954 (s), 1730 (s), 1702 (s), and 1543 cm$^{-1}$ (m); $\delta_H$ (D$_2$O) 0.4–0.8 (2H, brm, C*H*$_2$), 1.1–1.3 (3H, brm, Ala-C*H*$_3$), 1.5–1.9 (3H, brm, C*H*$_3$), 3.9–4.4 (4H, brm, Ala-NC*H* + C*H*$_2$O + Ser-NC*H*).

Data for **deprotected poly-3-*co*-MMA (84:16)**: Yield 84%; $[\alpha]_D^{28}$ +24.1 ($c = 0.5$, DMSO:CH$_3$CN, 1:1); $\nu_{max}$

(KBr) 3434 (brs), 2946 (s), 1727 (s), 1686 (s), 1638 (m), and 1546 $cm^{-1}$ (w); $\delta_H$ (DMSO-$d_6$) 0.9–1.5 (brm, C$H_2$ + C$H$ + C$H_3$), 2.8–2.9 (brd, C$H_2$Ph), 3.0–3.1 (brd, C$H_2$Ph), 3.4–3.7 (brs, $CO_2CH_3$), 3.9–4.3 (brs, C$H_2$O), 4.4–4.8 (brs, NC$H$ +C$H_2$O), 7.0–7.3 (brm, ArC$H$ + N$H$CO), 8.2–8.5 (brs, N$H_3$), 8.6–9.0 (brs, $CO_2H$); $\delta_C$ (DMSO-$d_6$) 22.2 (*C*$H_2$), 38.6 (*C*$H_2$Ph), 51.8 ($CO_2CH_3$), 54.1 (2 × NC$H$), 64.2 (*C*$H_2$O), 117.1 (q $J = 296$ Hz, *C*$F_3CO_2$), 126.8 (Ar*C*H), 128.4 (Ar*C*H), 129.4 (Ar*C*H), 137.0 (Ar *ipsoC*), 158.5 (q $J = 32$ Hz, $CF_3CO_2$), 167.5 (*C*ONH), 172.1 ($CO_2$), 176.0 ($CO_2$).

Data for **deprotected poly-4**: Yield 97%; $[\alpha]_D^{28}$ +19.2 ($c = 0.5$, DMSO:$CH_3CN$, 1:1); $\nu_{max}$ (KBr) 3434 (br), 3077 (br), 1700 (br), and 1571 $cm^{-1}$ (s); $\delta_H$ (DMSO-$d_6$) 0.6–2.2 (6H, brm, C$H_2$ + C$H_3$), 2.8–2.9 (1H, brd, C$H_2$Ph), 3.0–3.2 (1H, brd, C$H_2$Ph), 3.9–4.3 (3H, brm, NC$H$ + C$H_2$O), 4.4–4.7 (1H, brs, Phe-NC$H$), 7.0–7.4 (6H, brm, ArC$H$ + N$H$CO), 8.2–8.6 (3H, brs, N$H_3$), 8.7–9.1 (1H, brs, $CO_2H$); $\delta_C$ (DMSO-$d_6$) 18.8 (*C*$H_3$), 36.6 (*C*$H_2$Ph), 44.2 (*C*$CH_3$), 51.3 ($CO_2CH_3$), 54.1 (2 × NC$H$), 64.2 (*C*$H_2$O), 116.1 (q $J = 296$ Hz, *C*$F_3CO_2$), 126.7 (Ar*C*H), 128.3 (Ar*C*H), 129.4 (Ar*C*H), 136.9 (Ar *ipsoC*), 158.7 (q $J = 32$ Hz, $CF_3CO_2$), 165.6 (*C*ONH), 172.0 ($CO_2$), 176.0 ($CO_2$).

Data for **deprotected poly-5**: Yield 85%; $[\alpha]_D^{28}$ −28.3 ($c = 0.5$, DMSO:$CH_3CN$, 1:1); $\nu_{max}$ (KBr) 3452 (br), 2997 (s), 2952 (s), 1735 (s), 1719 (s), 1701 (s), 1685 (s), 1676 (s), 1654 (s), 1560 (m), and 1508 $cm^{-1}$ (m); $\delta_H$ (DMSO-$d_6$) 0.5–1.3 (3H, brm, C$H_2$ + C$H$), 1.5–2.4 (4H, brm, Pro-β-C$H_2$ + Pro-γ-C$H_2$), 3.5–3.9 (2H, brm, NC$H_2$), 4.1–4.7 (4H, brm, 2 × NC$H$ + C$H_2$O), 8.0–8.2 (3H, brs, N$H_3$), 8.4–8.8 (1H, brs, $CO_2H$).

Data for **deprotected poly-6**: Yield 83%; $[\alpha]_D^{28}$ −30.4 ($c = 0.5$, DMSO:$CH_3CN$, 1:1); $\nu_{max}$ (KBr) 3452 (br), 2997 (s), 2952 (s), 1735 (s), 1719 (s), 1701 (s), 1685 (s), 1676 (s), 1654 (s), 1560 (m), and 1508 $cm^{-1}$ (m); $\delta_H$ (DMSO-$d_6$) 0.5–1.3 (5H, brm, C$H_2$ + C$H_3$), 1.4–2.4 (4H, brm, Pro-β-C$H_2$ + Pro-γ-C$H_2$), 3.3–3.7 (2H, brm, NC$H_2$), 4.0–4.5 (4H, brm, 2 × NC$H$ + C$H_2$O), 8.0–8.2 (3H, brs, N$H_3$), 8.4–8.8 (1H, brs, $CO_2H$); $\delta_C$ (DMSO-$d_6$) 16.4 (*C*$H_2$), 18.6 (*C*$H_3$), 24.7 (Pro-γ-*C*$H_2$), 28.6 (Pro-β-*C*$H_2$), 44.8 (*C*$CH_3$), 46.8 (N*C*$H_2$), 54.1 (N*C*H), 58.8 (N*C*H), 64.3 (*C*$H_2$O), 173.2 ($CO_2$).

Data for **deprotected poly-8**: Yield 78%; $[\alpha]_D^{28}$ +16.3 ($c = 0.7$, DMSO:$CH_3CN$, 1:1); $\nu_{max}$ (KBr) 3588 (br), 3097 (br), 2954 (s), 1726 (s), 1671 (s), and 1545 $cm^{-1}$ (m); $\delta_H$ (DMSO-$d_6$) 0.5–2.2 (8H, brm, C$H_2$ + C$H_3$ + Ala-C$H_3$), 2.6–2.8 (1H, brdd, C$H_2$Ph), 2.8–3.0 (1H, brdd, C$H_2$Ph), 3.3–4.7 (5H, brm, Ala-NC$H$ + C$H_2$O + Ser-NC$H$ + Phe-NC$H$), 6.6–7.5 (7H, brm, ArC$H$ + 2 × N$H$CO), 7.8–8.2 (3H, brm, N$H_3$), 8.3–8.7 (1H, brs, $CO_2H$); $\delta_C$ (DMSO-$d_6$) 17.2 (*C*$H_3$), 36.7 (*C*$H_2$Ph), 43.9 (*C*$CH_3$), 44.4 (*C*$CH_3$), 48.0 (N*C*H), 53.8 (N*C*H), 54.1 (N*C*H), 64.4 (*C*$H_2$O), 126.5 (Ar*C*H), 128.2 (Ar*C*H), 129.2 (Ar*C*H), 137.2 (Ar *ipsoC*), 169.5 (*C*ONH), 172.6 ($CO_2$).

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