^1H and ^{13}C n.m.r. studies of the conformational change in poly(n-butyl isocyanate)

Tetsuo Asakura and Atsuo Nishioka
Department of Polymer Chemistry, Tokyo Institute of Technology, 12-1 Ookayama, 2-Chome, Meguro-ku, Tokyo, Japan
(Received 13 February 1979; revised 7 November 1979)

INTRODUCTION

The unusual properties of poly(n-alkyl isocyanates) in dilute solution have so far been studied by many techniques: intrinsic viscosity, dielectric studies, light scattering, electric dichroism and electric birefringence. These studies lead to the conclusion that this polymer is unusually stiff and has a helical conformation at low molecular weights even though the constituents for hydrogen bonding are absent[1]. A transition to a random coil conformation is observed with increasing molecular weight or with rise in temperature or increasing acidity of the solution environment[1].

In view of the similarity of the repeating unit of poly(n-alkyl isocyanate) with the polypeptide, it is interesting to compare the conformational changes of this polymer with those occurring in polypeptides. A few n.m.r. investigations have been carried out into the conformational behaviour of poly(n-alkyl isocyanate) although ^1H and ^{13}C n.m.r. spectroscopy of synthetic polypeptides has successfully been applied to studies of the helix–coil transitions[2].

Here, the ^1H and ^{13}C n.m.r. spectra of poly(n-butyl isocyanate) (PBIC) were observed in benzene, carbon tetrachloride, pentafluorophenol and deuteriochloroform solutions to clarify: (i) the cause of the chain stiffness; (ii) the interaction of the polymer with the solvent; and (iii) the cause of the conformational changes in solution.

EXPERIMENTAL

Materials

PBIC samples was kindly supplied by Mr. K. Yamamoto and Professor Y. Imamura, University of Tokyo. This sample was prepared according to the method of Shashoua[3] and the molecular weight determined by dilute solution viscosity measurements in benzene was $\sim 10^5$. The molecular weight of this sample is at the discontinuity at which the polymer is thought to be passing from rod to coil behaviour. Since the polymer is polydisperse, it will contain substantial elements of both structures[1].

Benzene (C_6H_6), carbon tetrachloride (CCl_4) and pentafluorophenol (C_6F_5OH) were purchased from the Tokyo Kasei, Co. Ltd. Deuteriochloroform ($CDCl_3$) was purchased from CEA, France.

Method

^1H n.m.r. spectra were measured with a JEOL PS-100 spectrometer operating at 100 MHz. For experiments on the concentration dependence, accumulated spectra were obtained at 100 MHz with a JEOL PFT-100 pulse Fourier transform n.m.r. system (for example, the number of transients accumulated was 7680 for 0.1 w/v% solution). The ^{13}C n.m.r. spectra were also obtained at 25 MHz with a JEOL PFT-100 pulse Fourier transform n.m.r. system. A detailed description of the n.m.r. experimental conditions is given in the text. ^1H and ^{13}C n.m.r. chemical shifts were recorded as δ (ppm) values from an external reference, tetramethylsilane (Me_4Si).

RESULTS AND DISCUSSION

^1H n.m.r. spectra were measured at a series of polymer concentrations (2 to 0.1 w/v%) in $CDCl_3$. Unfortunately, PBIC has no proton directly attached to the backbone chain. We therefore observed the width at half-height of the α-CH_2 proton, $\nu_{1/2,\alpha\text{-}CH_2}$, in the n-butyl side chain to obtain a measure of the chain mobility; this value of $\nu_{1/2,\alpha\text{-}CH_2}$ adequately reflects the mobility in the backbone chain.

The PBIC spectra do not change essentially with a decrease in concentration in the range 2 to 0.1 w/v%. The value of $\nu_{1/2,\alpha\text{-}CH_2}$ also remains constant at 41 Hz. Coles *et al.*[4] have studied the mode of aggregation of poly(n-hexyl isocyanate) in toluene solutions by dielectric relaxation and electric field birefringence methods. They suggested the existence of linear head-to-tail and/or antiparallel side-by-side aggregation over the concentration range 5×10^{-4} to $\sim 10^{-2}$ g/g. Our data suggest that the mobility of the backbone-chain is not affected by such an aggregate of the polymer molecules.

The widths at half-height of the α-CH_2 proton of PBIC were observed as a function of temperature in CCl_4, C_6H_6 and $CDCl_3$ (*Figure 1*). Throughout the temperature range observed $\nu_{1/2,\alpha\text{-}CH_2}$ varies with solvent such that $\nu_{1/2,\alpha\text{-}CH_2}$

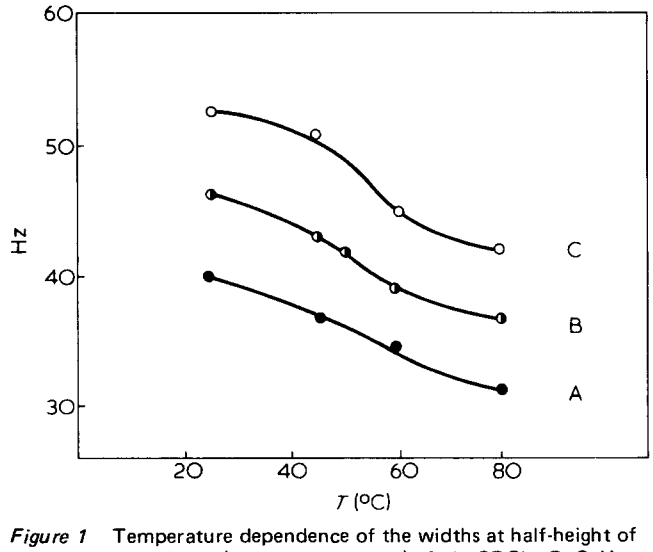

Figure 1 Temperature dependence of the widths at half-height of α-CH_2 protons of poly(n-butyl isocyanate): A, in $CDCl_3$; B, C_6H_6; and C, CCl_4 solutions (sample conc. 2w/v%)

0032–3861/80/050579–04$02.00

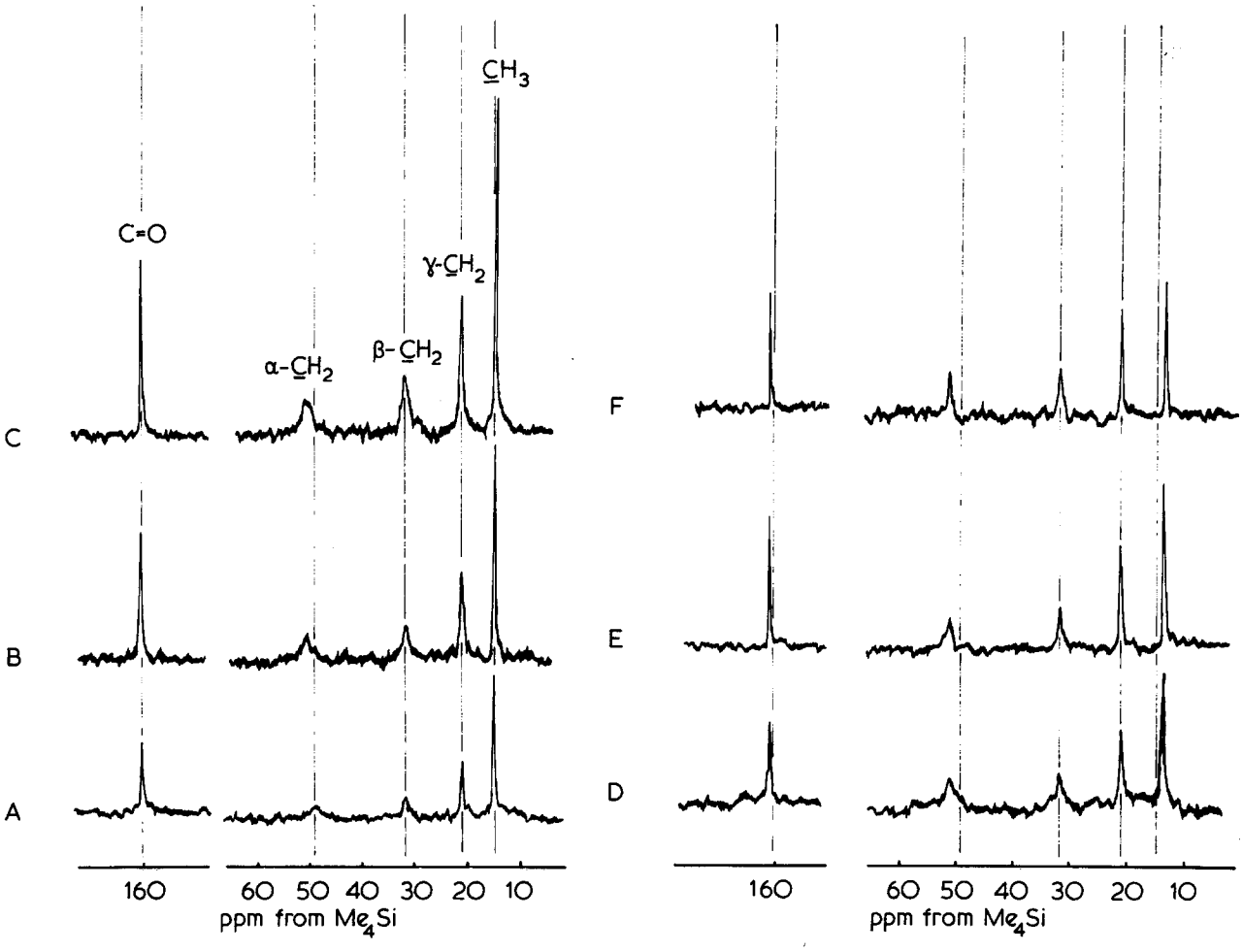

Figure 2 ^{13}C n.m.r. spectra of poly(n-butyl isocyanate) observed in C_6F_5OH–CCl_4 solvent systems. Chemical shifts are present as ppm from TMS. Experimental conditions: sample conc./temp./solvent compositions (volume fraction). (a) 7w/v%/60°C/CCl_4; (b) 10w/v%/25°C/C_6F_5OH (0.06):CCl_4(0.94); (c) 10w/v%/25°C/C_6F_5OH(0.20):CCl_4(0.80); (d) 10w/v%/25°C/C_6F_5OH(0.90):CCl_4(0.10); (e) 20w/v%/60°C/C_6F_5OH (0.90):CCl_4(0.10); (f) 20w/v%/80°C/C_6F_5OH(0.90:CCl_4(0.10)

in $CCl_4 > \nu_{1/2,\alpha\text{-}CH_2}$ in $C_6H_6 > \nu_{1/2,\alpha\text{-}CH_2}$ in $CDCl_3$. This is in agreement with intrinsic viscosity data[5,6] which shows: $[\eta]$ $CCl_4 > [\eta]$ $C_6H_6 > [\eta]$ $CHCl_3$.

Thus the value of $\nu_{1/2,\alpha\text{-}CH_2}$ appears to be a measure of the flexibility and the mobility of the polymer chain. The butyl side chain must shield the highly polar backbone from the solvent. $CDCl_3$ molecules could interact with more amide units in the backbone than could the other solvents, since $CDCl_3$ seems to impart the lowest hydrodynamic volume among these solvents. The interaction of PBIC with $CDCl_3$ will change the C–N bond character slightly along the backbone chain[7] and, as a result, the mobility of the chain will increase.

Moreover, $\nu_{1/2,\alpha\text{-}CH_2}$ decreases with increasing temperature, and this may be considered as the superposition of several effects, such as a decrease in the amount of aggregation, an increase in the mobility of the backbone chain, a decrease of the solution viscosity, etc. Consequently, it seems that the increase in the backbone chain mobility contributes significantly to the temperature dependence of $\nu_{1/2,\alpha\text{-}CH_2}$ since $\nu_{1/2,\alpha\text{-}CH_2}$ is not influenced by aggregation as mentioned above, and the large decreases in $[\eta]$, the mean square dipole moment and dielectric relaxation time of PBIC with increasing temperature have been observed in these solvents[6,8,9].

A strong organic acid such as trifluoroacetic acid has been widely used as a coil solvent for polypeptide[2]. The conformational changes of PBIC induced by this strong acid have also been studied[6]. Although trifluoroacetic acid has a pronounced effect on $[\eta]$ for PBIC solution, it has also been found that PBIC is susceptible to progressive degradation by the acid. We observed ^1H n.m.r. peaks arising from the degradation product, giving peaks different from those for the polymer within 10 min of sample preparation in CCl_4 solution with small amounts of trifluoroacetic acid. Thus trifluoroacetic acid would not be suitable as a coil solvent for PBIC.

Fetters[10] found a reversible non-cooperative conformational change occurring in this polymer in CCl_4 solution when C_6F_5OH was added without simultaneous degradation of the chain. C_6F_5OH was here used as a coil solvent for PBIC. The ^{13}C n.m.r. method was also applied to obtain information on the electronic distribution of the backbone PBIC chain and the detailed interaction of the PBIC with C_6F_5OH molecule.

^{13}C n.m.r. spectra of PBIC are shown in *Figure 2* as a function of C_6F_5OH concentration in C_6F_5OH–CCl_4 solutions. From a comparison of the spectra A–D, the resonance position of the α-^{13}C nucleus is found to shift about 1 ppm to lower field with small amounts of C_6F_5OH (volume fraction 0.067) and do not shift upon further increase in C_6F_5OH concentration. The β-^{13}C and γ-^{13}C peaks do not shift and the C=O peak shifts slightly to lower fields with increasing C_6F_5OH.concentration. Thus, the induced shifts

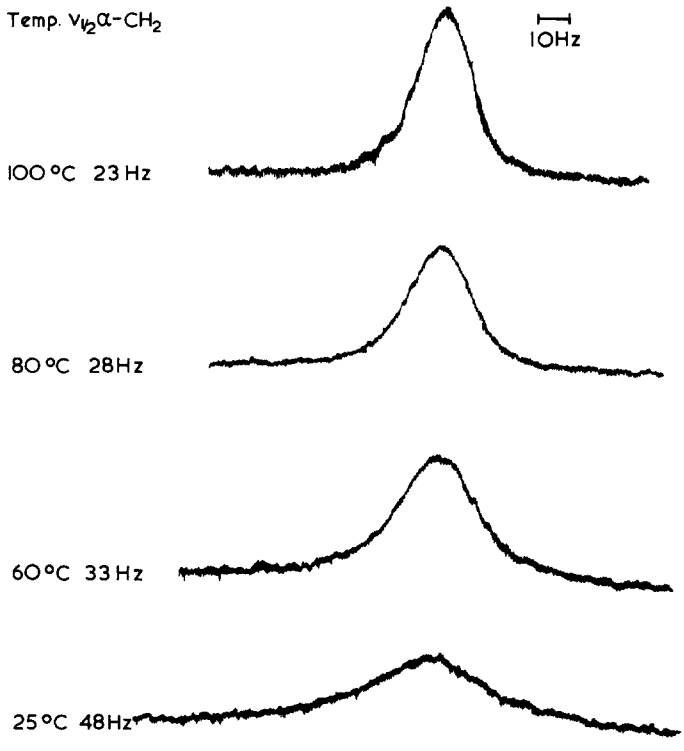

Figure 3 Temperature dependence of ^1H n.m.r. spectra of α-CH_2 protons in poly(n-butyl isocyanate) in C_6F_5OH(0.90):CCl_4 (0.10) (sample conc. 10w/v%)

for PBIC by C_6F_5OH are relatively small compared with those of polypeptides such as poly(γ-benzyl-L-glutamate) or poly(β-benzyl-L-aspartate) by trifluoroacetic acid[2], indicating only a weak interaction between PBIC and C_6F_5OH molecules. As for the upfield shift of the δ-^{13}C peak, this seems to come from the ring current shielding effect due to the C_6F_5OH molecules. Reversals in the PBIC helix have been suggested by Scheraga *et al.*[11] and Tonelli[12] on the basis of conformational energy calculations on these molecules using semiempirical potential energy functions. For such a reversal, part of the helical chain (the C=O groups of PBIC) will be exposed to solvent. C_6F_5OH molecules might form weak hydrogen bonds[13,14] with exposed C=O groups. The OH proton of C_6F_5OH molecule shifts to lower field on addition of small amounts of PBIC and this indicates that the OH proton interacts with PBIC molecules.

The widths of half-height for PBIC in C_6F_5OH–CCl_4 of α-^{13}C=O peaks decrease with increasing C_6F_5OH concentration and become sharper at higher temperatures in C_6F_5OH–CCl_4 (0.9:0.1) as shown in spectra E and F. At 80°C, the widths at half-height of the α-^{13}C peak becomes comparable with that of β-^{13}C peak. Thus the mobility of the backbone chain seems to depend more strongly on temperature than on the degree of acidity in the C_6F_5OH–CCl_4 solutions. This tendency is also observed in the ^1H n.m.r. spectrum of PBIC in C_6F_5OH-CCl_4 solution as shown in *Figure 3*. The value of $\nu_{1,2,\alpha\text{-}CH_2}$ in C_6F_5OH-CCl_4 (0.9:0.1) is smaller than that in CCl_4 solution by only 5 Hz at 25°C. However, the value of $\nu_{1/2,\alpha\text{-}CH_2}$ in C_6F_5OH–CCl_4 (0.9:0.1) decreases markedly by 25 Hz with an increase in temperature from 25° to 100°C.

The temperature dependence of the width at half-height of the β-CH_2 and γ-CH_2 protons of n-butyl side chains in C_6F_5OH–CCl_4 (0.9:0.1) are also shown in *Figure 4*, together with data observed for C_6H_6 solution. The estimated activation energies of these peaks are given in *Table 1*.

In these solvents, we can observe each proton peak of the side chain separately because of the ring current shielding effect. Two important facts can be pointed out. One is that $\nu_{1/2,\alpha\text{-}CH_2}$ depends on temperature more strongly than $\nu_{1/2,\beta\text{-}CH_2}$ and $\nu_{1/2,\gamma\text{-}CH_2}$ in both solutions. This is interesting when discussing the origin of chain stiffness of PBIC. So far two factors have been considered as the origin of the chain stiffness[1,11,15]: (i) a potential barrier to rotation in the amide bond, although this bond deviates significantly from planarity; and (ii) a steric interference of the n-butyl side chain, mainly from α-CH_2 groups and carbonyl groups. Quantitative analysis of the data obtained here is not easy since other factors such as rotation around the C–N and C–C bonds in the side chain, solution viscosity, spin–spin coupling, etc. must be taken into account. However, the increase in internal rotation around the backbone C–N bonds and/or the release of the steric interference of the α-CH_2 group in the side chain and the carbonyl group would cause an increase in the segmental motion of the main chain and an increase in the rotational motion around the main chain axis. These would cause a stronger temperature dependence or larger activation energy for $\nu_{1/2,\alpha\text{-}CH_2}$ in both solutions. Another important fact is that the activation energy of each CH_2 peak in C_6F_5OH–CCl_4 (0.9:0.1) is much larger than that in C_6H_6 solution. This can be explained as follows. The n-butyl side chain must shield the highly polar backbone of PBIC from pentafluorophenol and benzene at room temperature. With increasing temperature, freedom of rotation around the backbone C–N bonds increases, as it does around the C–N and C–C bonds in side chains. As a result, solvent molecules interact more frequently with the polar PBIC backbone. The interaction of PBIC with C_6F_5OH

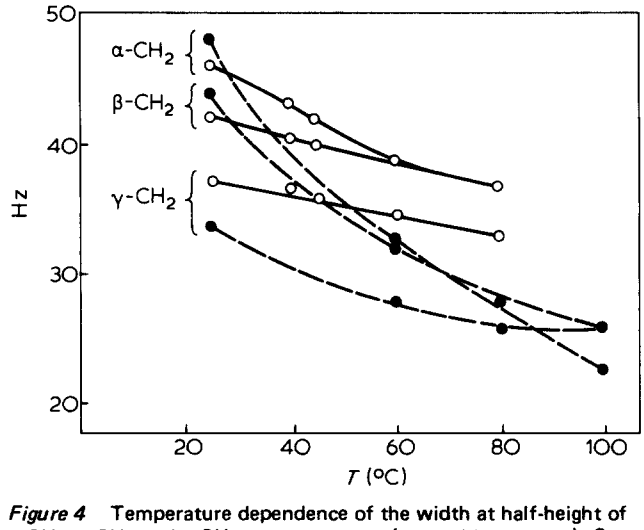

Figure 4 Temperature dependence of the width at half-height of α-CH_2, β-CH_2 and γ-CH_2 protons in poly(n-butyl isocyanate): ●, C_6F_5OH(0.90):CCl_4(0.10); ○, C_6H_6 solution

Table 1 Activation energies for the α-CH_2, β-CH_2 and γ-CH_2 linewidths of the ^1H n.m.r. spectra of poly(n-butyl isocyanate)

Activation energies (kJ mol^{-1}			
α-CH_2	β-CH_2	γ-CH_2	Reference
8.6	6.4	4.1	in C_6F_5OH(0.90):CCl_4 (0.10) solution
3.5	2.0	1.7	in C_6H_6 solution

(a polar solvent) changes the C–N bond character slightly along the backbone chain. This causes additional freedom of backbone rotation in C_6F_5OH–CCl_4 compared with that in benzene.

Finally, it is interesting to compare the helix–coil transition behaviour observed in polypeptides and poly(*N*-methyl alanine) with that observed in PBIC. In the random-coil state of the polypeptide chain, the amide group remains *trans*, although the degree of freedom of the rotation around the backbone N–C^{α} and C^{α}–C bonds increases[16]. For poly(*N*-methyl alanine), the presence of both *trans* and *cis* C–N bonds in the polymer chain converts the polymer into a disordered state in a coil solvent such as trifluoroacetic acid[17]. However, an increase in the degree of freedom around the C–N bonds will cause formation of random coil PBIC.

The ^1H and ^{13}C spin–lattice relaxation times of PBIC would give a more quantitative information on the motions of the main chain and the side chain.

ACKNOWLEDGEMENT

The authors are greatly indebted to Mr K. Yamamoto and Professor Y. Imamura at the Science University of Tokyo for the gift of PBIC sample and their discussion on this study.

REFERENCES

1 Bur, A. J. and Fetters, L. J. *Chem. Rev.* 1976, **76**, 727
2 Bovey, F. A. *J. Polym. Sci. Macromol. Rev.* 1974, **9**, 1
3 Shashoua, V. N. *J. Am. Chem. Soc.* 1959, **81**, 3156; *Ibid.* 1960, **82**, 886
4 Coles, H. J., Gupta, A. K. and Marchal, E. *Macromolecules* 1977, **10**, 182
5 Schneider, N. S., Furusaki, S. and Lenz, R. W. *J. Polym. Sci. (A)* 1965, **3**, 133
6 Berger, M. N. and Tidswell, B. M. *J. Polym. Sci. (C)* 1973, **42**, 1063
7 Goodman, M. and Chen, S. *Macromolecules* 1970, **3**, 398
8 Pierre, J. and Desreux, V. *Polymer* 1974, **15**, 685
9 Pierre, J. and Marchal, E. *J. Polym. Sci. (Polym. Lett. Edn)* 1975, **13**, 11
10 Fetters, L. J. *Polym. Lett.* 1972, **10**, 577
11 Troxell, T. C. and Scheraga, H. A. *Macromolecules* 1971, **4**, 528
12 Tonelli, A. *Macromolecules* 1974, **7**, 628
13 Gramstad, T. and Van Binst, G. *Spectrochim. Acta.* 1966, **22**, 1681
14 Dale, A. J. *Spectrochim. Acta.* 1971, **27A**, 81
15 Ambler, M. R., McIntyre, D. and Fetters, L. J. *Macromolecules,* 1978, **11**, 300
16 Asakura, T., Ando, I. and Nishioka, A. *Makromol. Chem.* 1977, **178**, 1111
17 Goodman, M., Chen, F. and Prince, F. R. *Biopolymers* 1973, **12**, 2549

Synthesis and gelation properties of crosslinked polymers of 4-(*N*-acryloyl-L-phenylalanyl)-morpholine, 4-(*O*-acetyl-*N*-acryloyl-L-tyrosyl)-morpholine and 4-(*N*-acryloyl-L-tyrosyl)-morpholine

M. Buckle, R. Epton and G. Marr

Department of Physical Sciences, The Polytechnic, Wolverhampton WV1 1LY, UK

(Received 3 January 1980)

Polymer networks which are suitable for application as supports for solid (gel) phase peptide synthesis must necessarily undergo gelation (constrained dissolution) in a range of suitable reaction solvents. To date, most polymer-supported peptide syntheses have been effected using supports based on crosslinked polystyrene. These networks have poor gelation properties in solvents of high polarity. Because the latter can be most useful in peptide synthesis, efforts have been made to devise alternative supports able to undergo gelation in such solvents.

Atherton *et al.*[1] and Arshady *et al.*[2] have described the synthesis of alternative supports based on crosslinked poly(*N,N*-dimethylacrylamide) and Smith *et al.*[3] the synthesis of supports based on crosslinked and poly(*N*-acryloylpyrrolidine). Most recently we have described alternative supports based on crosslinked poly(acryloylmorpholine)[4]. All of these matrices compare favourably with those based on polystyrene.

During the course of our work, we have prepared other polymer networks which are able to undergo gelation even more efficiently in the range of reaction solvents most useful in peptide synthesis. Our approach has been to synthesize these networks from suitable single monomers which combine selected polar and non-polar features. Three such networks, derived from amino-acid morpholine amides, are the subject of this report.

EXPERIMENTAL

Synthesis of N-*acryloyl*-L-*phenylalanine*

L-Phenylalanine (165.2 g, 1 mol) was dissolved in 1.5 M aqueous NaOH (1 dm^3) and the solution maintained, stirring mechanically, at 0°C. Acryloyl chloride (181 g, 162.4 cm^3, 2 mol) was added over 1 h while maintaining the pH at 11–11.5 by addition of aqueous 4 M NaOH. The reaction mixture was stirred for a further 1 h and the pH adjusted to 1–1.5 by addition of aqueous 11 M HCl. The resulting precipitate was collected by filtration, washed with distilled water, dried and recrystallized from chloroform/petroleum

0032–3861/80/050582–04$02.00