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Nylon-6,6 oligomers : Synthesis, characterization and relevance to the polymer.

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NYLON-6,6 OLIGOMERS:
SYNTHESIS, CHARACTERIZATION &
RELEVANCE TO THE POLYMER

PAUL D. JOHNSON BSc (Hons)

A thesis submitted to Sheffield Hallam
University in partial fulfilment of the
requirements for the degree of
Doctor of Philosophy.

September 1995

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Sheffield Hallam University
in collaboration with ICI Fibres Plc.
(Industrial Supervisor; G.W. FOLLOWS)

ABSTRACT

The primary aim of this work is the investigation of potential routes for the synthesis of selected oligomers of nylon-6.6. and trial syntheses using these routes. Once a general synthetic route to pure oligomers is available it can be applied to the preparation of oligomers of increasing length, while maintaining purity for future characterization studies.

It was soon found that the "nylon intermediates" are not readily amenable to the reaction conditions involved in more conventional syntheses due to solubility, lability etc. Because of this the project rapidly developed into a series of problem solving episodes.

Although the project was intended only to deal with integer oligomers problems concerning the protecting groups arose. A new direction was temporarily taken involving the synthesis of non-integer oligomers. Here the need for selective deprotection was no longer a factor as chain-growth products would have identical end groups.

With no satisfactory method for selective removal of the carbobenzoxy group, the doubling reactions on integer oligomers had to be carried out using unprotected and

N-protected monomers. The presence of these two products in the synthesis of the dimer could obviously lead to over reaction. However in the mixed anhydride reaction the acid end group on the N-protected monomer is activated prior to the addition of the unprotected monomer thus eliminating, or certainly reducing, this potential problem. The scheme was successfully taken up to a D.O.P. of eight although the purity of the octamer was lower than would have been liked.

IR, MS, NMR and GPC were used throughout the synthetic work to determine the purity and identity of each product.

ACKNOWLEDGEMENTS

There are many people to acknowledge in this section for their contributions both great and small.

Firstly I would like to thank Dr Derek Simmonds for his supervision of this project, especially during the more challenging moments, and for all the hard work he has put in. Thanks also to Dr Steve Spells who with Dr Simmonds came up with the original ideas for this project.

My thanks also go to I.C.I. Fibres Plc in Wilton for their help, interest and collaboration in my project in particular for the GPC and DSC analysis. I am particularly grateful to Gordon Follows for his contribution.

I am also grateful to the S.E.R.C. for supplying me with a grant for these studies.

I would like to thank all the staff in the Sheffield Hallam University Chemistry Division, especially those who contributed to this work with their thoughts and ideas. I feel I must single out Kevin Osbourne for his assistance although all the technicians were helpful. Thanks are also due to my fellow students for so often

making the laboratory an enjoyable place in which to work.

Finally, I would especially like to thank Talcs for all her encouragement, patience and support throughout the writing of this thesis.

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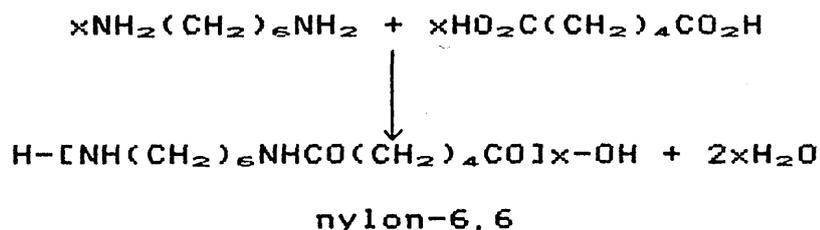
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1. INTRODUCTION

1.1. POLYAMIDES. ^{1,2}

The polyamides were the first truly synthetic fibres to be developed - the inventor being Wallace Carothers while working for the Du Pont Co. research laboratories in Wilmington, Delaware in the early 1930's. His basic and highly successful idea was that equimolar amounts of bifunctional monomers, such as hexamethylenediamine and adipic acid, could lead to very high molecular weight linear polymers if the reaction was forced to a high degree of completion.

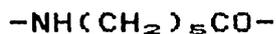
The trade-name adopted by the company for the first commercial member of this family of polymers, 'nylon', has now been accepted as the generic term for synthetic linear polyamides. The first polymer to be called nylon (strictly by the trade-name nylon-6.6) was produced by heating hexamethylenediamine with adipic acid. The product is a linear polymer that is processable. The product is cold drawn after extrusion through spinnerets to orient the molecules parallel to each other so that lateral hydrogen bonding takes place. The resultant nylon fibres are strong and have a characteristic lustre.



A number of polyamides have now been developed for commercial purposes: some are manufactured in massive quantities, while others find less extensive uses. All are referred to as 'nylons' and a nomenclature has been devised to distinguish between the various members of the class. This is based on the total number of carbon atoms in the component, or components, which constitute the repeating unit in the molecular chain of the material. The original 'nylon' has a repeating unit of the following composition;



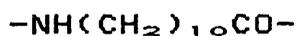
This is made up of two components, as shown above, each of which contains six carbon atoms. This particular material is therefore known as nylon-6.6. Other polyamides which have been developed commercially include nylon-6, developed later in Germany and sold under the trade-name 'Perlon'. It has the one component repeating unit as follows;



Nylon-6.10 has the composition for it's repeating unit of;

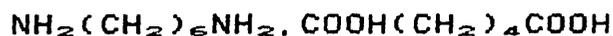


and nylon-11 is made up from a single repeating unit of;

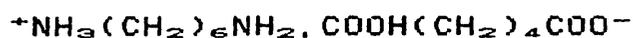


It would be of little value to go into further detail on the properties of these nylons except for nylon-6.6. As our target molecules for synthesis and characterization are oligomers of nylon-6.6 they should be related to the properties and structure of this polymer.

In preparing the polymer the adipic acid and hexamethylenediamine (1,6-hexanediamine) are separately dissolved in methanol. On combination a mixed compound, usually referred to as 'nylon salt', is precipitated. This can be said to have the formula;



although 'salt' implies favourable Zwitterionisation to give;



Use is made of the low solubility of this compound in methanol to separate and purify it.

The purified salt is dissolved in water, with acetic acid being used as a viscosity stabilizer, and the solution is heated in an autoclave under a pressure of 250 lb/in² and a temperature of 220°C. An atmosphere of nitrogen is provided to prevent oxidization of the salt. The temperature is raised subsequently to 270°C then 280°C, the pressure released and the water removed under partial vacuum. Total treatment time is about four hours, during which the nylon salt is converted to nylon polymer with the elimination of water. The molten polymer is extruded, in the form of a ribbon, onto a cooled surface where it solidifies and can be broken up into small pieces or 'chips'.

Fibres are prepared from the polymer by melt-spinning, using an atmosphere of nitrogen to prevent oxidation. The step of first preparing nylon 'chips', which can be re-melted to provide the extrusion syrup is preferred to direct extrusion of the filaments. In this way, prolonged holding of the polymer in the molten state, when changes in characteristics can take place, is avoided.

Under the microscope, the fibres appear as smooth rods having circular cross-sections, though by using spinneret holes with shapes other than round, fibres can be produced having a variety of cross-sections, the most common being the so-called 'trilobal' form.

Nylon-6.6 has a density of 1.17g.cm^{-3} and its moisture regain is low at 4.3%, determined at R.H. (relative humidity) 65%. Its tenacity, both wet and dry, is high at 5g/denier and it has a good elasticity, recovering completely from extensions of up to 8%. Its abrasion resistance is outstanding.

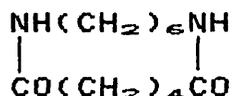
As the temperature is raised, nylon-6.6 filaments exhibit thermoplastic properties, becoming tacky at 230°C and melting at 250°C . The material does not burn easily, but hot molten beads can fall from it when it is held in a flame. Long exposure to light produces some fall off in strength; this can be prevented to some extent by the inclusion of anti-oxidants in the material. This slight oxidation generated by long exposure does not cause discolouration of the fibres.

Nylon-6.6 is attacked by concentrated, and by hot diluted, acids. It is inert to alkalis, cold dilute acids and the common organic solvents, but it is dissolved by some phenolic solutions. Nylon-6.6 is a

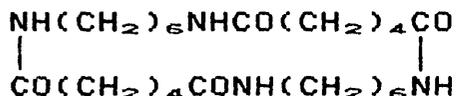
good, all purpose fibre. It is strong, outstandingly tough, has a high melting point and can be heat-set and shaped under the influence of heat. The fibres have a good elasticity and this together with their strength and resistance to abrasion make nylon-6.6 the preferred material from which to produce fine gauge stockings, carpets, overalls, rainwear etc.

1.2. NYLON-6.6 OLIGOMERS.

Nylon-6.6 polymer and yarn is known to contain low levels of oligomeric material^{3,4}. When an equimolar mixture of hexamethylenediamine and adipic acid is heated, the conversion to polymer is not complete. The result is an equilibrium mixture consisting of high molecular weight linear polyamide and much smaller amounts of nylon oligomers. These oligomers are mainly the cyclic monomer (I) together with smaller amounts of the cyclic dimer (II), trimer etc.



I



II

In the molten polymer the equilibrium is dynamic, with three possible reactions occurring, these being;

- i) aminolysis
- ii) acidolysis and, in the presence of water
- iii) hydrolysis

Intramolecular acidolysis or aminolysis can lead directly to the cyclic oligomers. Hydrolysis, intermolecular acidolysis or aminolysis can produce linear oligomers which may then undergo ring formation to produce cyclic oligomers.

The cyclic oligomer content of nylon-6.6 is low relative to some nylons, containing only about 1-2% compared to about 10% in nylon-6. The problems caused are therefore less severe for nylon-6.6 but are still worthy of consideration. The oligomers in nylon-6.6 are responsible for some processing problems, such as the sublimation and subsequent deposition of the cyclic monomer from high throughput spinning processes.

The content of low molecular weight fractions in molten nylon-6.6 in a sealed system is known to be both time and temperature-dependent. This is shown in tabular form below⁵.

Table 1.1. Effect of Temperature^a

<u>Temp/°C</u>	<u>wt. % oligomers</u>
untreated	1.42
290	2.38
310	3.14, 3.04

^a vacuum sealed and heated for 4 hours.

Table 1.2 Effect of Time

<u>Time at 290°C</u>	<u>wt. % oligomers</u>
2 hrs.	1.03
4 hrs.	0.90, 1.08, 0.98
8 hrs.	1.33, 1.70
12 hrs.	2.28, 2.20

Further work at ICI⁴ suggests that oligomer generation is both time and temperature dependent with a linear

relationship between the percentage content of oligomer generated and molecular weight increase. Therefore under the conditions necessary to achieve an RV (relative viscosity, which is related to molecular weight) increase of, for example, 50 units, up to 0.05% of cyclic oligomer could be evolved - equivalent to 250g.hr⁻¹ at a throughput of 500kg.hr⁻¹.

The re-equilibrium of oligomer free (i.e. extracted) nylon-6.6 is comparatively slow³, so that at 290°C under steam only 60% of equilibrium oligomer content is produced after 60 minutes heating, and the rate of the forward reaction decreases as the system approaches equilibrium. Therefore, the spinning of extracted polymer should result in a considerable lowering of the normal oligomer content of the yarn.

Table 1.3. Re-equilibrium

<u>Heating time/mins^a</u>	<u>wt.% oligomers^b</u>
20	0.44
40	0.61
60	0.67
90	0.75
180	0.83
300	0.90
450	1.02

^a at 290°C

^b oligomer content of original yarn 1.22%

Similar results to these were also obtained for samples of nylon-6.6 that were doped with high levels of

oligomers and which were subsequently allowed to re-equilibriate⁵.

As well as causing problems during the processing of nylon, the oligomer content is also known to have marked detrimental effects on the thermal stability and the ' ΔH ' value and to some small extent on the crystallization of nylon-6.6⁵. ' ΔH ' refers to the exothermic transition which occurs at 70°C in nylon-6.6 when it has been melted and quenched in liquid nitrogen.

Oligomers have been shown to form degradation products at twice the rate of nylon-6.6 polymer when heated to 290°C. Also by incorporating high levels of oligomers in the polymer by melt blending the rate of gelation is increased. These two observations would suggest the oligomers could be intermediates in the degradation of the nylon polymer. Also measurements of an exothermic transition occurring at 70°C in nylon-6.6, which is thought to be related to the yarn properties, shows a decrease of ' ΔH ' with the increase in percentage content of oligomers. It has been implied that the oligomers cause a decrease in the quality of the yarn. The presence of oligomers was also shown to produce a slight decrease in crystallization rate.

From this it can clearly be seen that a locally high concentration of nylon-6.6 oligomers in the polymer, which could be caused by effects such as the sublimation of the oligomers on the lid of the autoclave and the subsequent deposition into the melt, could have serious consequences and adversely effect the quality of the yarn.

The mechanistic routes for the thermal decomposition of nylon-6.6 have been studied using mass spectrometry^{6,7}. From this work the presence of cyclic oligomers is indicated along with nylon-6.6 fragments i.e. linear oligomers.

Some work at ICI has attempted to use various short linear oligomers as additives to tackle problems associated with surface finish improvements. For reasons of confidentiality, however, this work cannot be detailed here.

It should also be noted that very little work concerning the linear oligomer content of nylon-6.6 has been performed. Although the content of these linear oligomers is lower than for the cyclic oligomers it may still have as yet unknown effects on the polymer and the finished yarn. This is one of the motivations for the synthesis of high purity linear oligomers.

1.3. POLYMER MORPHOLOGY.

Crystalline polymers show ordering at a number of dimensional levels, from interatomic spacing to macroscopic levels. Polymer morphology is the branch of polymer science that is primarily concerned with understanding this ordering, and it is important if a true understanding of the mechanical behaviour is to be achieved.

The first detailed knowledge of polymer morphology was based on crystalline structures i.e. chain packing, studied by the use of X-ray crystallography. It was shown that in addition to the main sharp and orientated crystalline reflections used for structural analysis, polymer samples also showed diffuse liquid-like diffraction intensity i.e. amorphous regions. An example of this can be seen (for polyethylene) in figure 18 (page 14) which shows the X-ray diffraction patterns for three drawn polyethylenes.

A much stronger diffuse ring can be seen in the very high molecular mass polymer (b) and the branched material (c) than in the typical linear polymer (a). This would suggest the presence of molecular arrangements which are more disordered than the crystal arrangements - these disordered arrangements commonly

being referred to as 'amorphous' areas. Terms such as 'orientated amorphous areas', however, recognise the fact that such areas are probably not totally without order. As a consequence terms such as 'disordered' and 'less ordered' are sometimes preferred to 'amorphous'. It should be noted that there is a clear distinction between crystal (sharp diffraction peaks, DSC melting peak) and amorphous regions (diffuse diffraction peaks, no DSC melting peak). The apparent presence of both crystalline and disordered molecular arrangements led to the early fringed-micelle model seen in figure 2⁶.

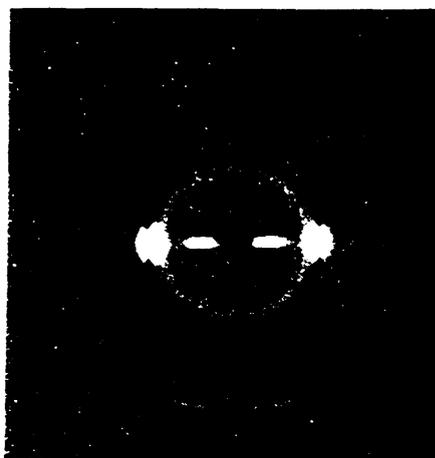
This model was developed to explain the effect shown in the X-ray diffraction patterns, in figure 1: with sufficiently long molecules, there is likely to be partial entanglement and the regions of crystalline order will therefore be restricted in size. An individual chain would be likely to pass through different regions of order and disorder. Therefore the whole structure comprises crystalline regions embedded in a continuous amorphous matrix. This model proved useful in providing an explanation for the variable properties such as density and melting point as shown by crystalline polymers. The fringed-micelle model is applicable, at most, to only a few crystalline polymers, an uncritical application of this concept can give rise

FIGURE 1 : X-RAY DIFFRACTION PATTERNS
FOR THREE DRAWN POLYETHYLENES

a) COMMERCIAL LINEAR
POLYMER



b) VERY HIGH MOLECULAR
MASS POLYMER



c) BRANCHED POLYMER

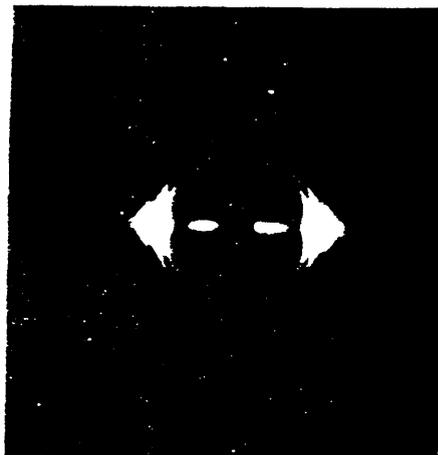
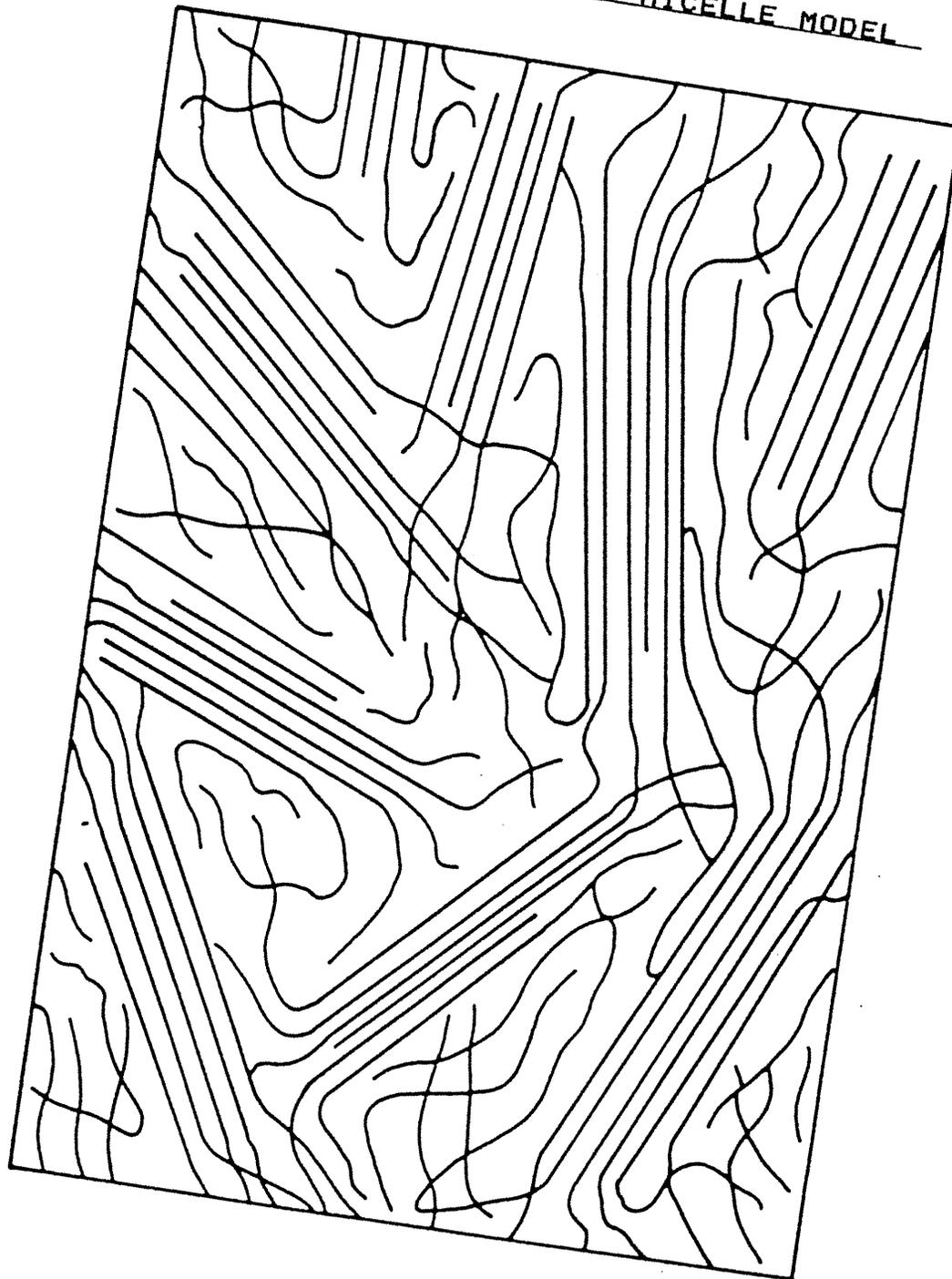


FIGURE 2 : THE FRINGED MICELLE MODEL



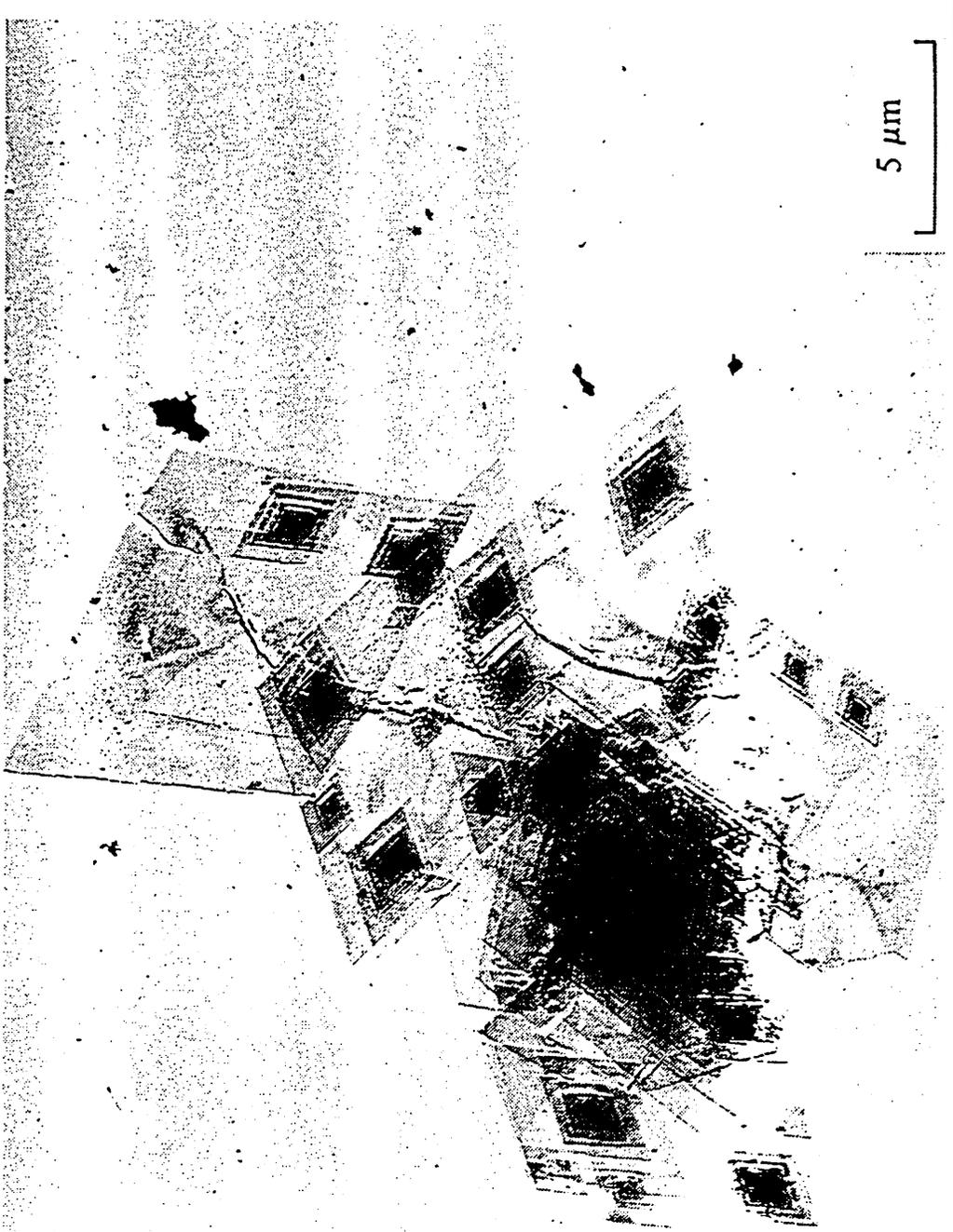
to an oversimplification of the morphology to a misleading extent.

The textural scale of the fringed-micelle model was believed to be of a few tens of nanometers, on the basis of crystalline sizes estimated from the widths of X-ray diffraction rings. In 1945, however, it was found that there was additional ordering on the scale of a few micrometers due to the prevalent melt crystallization of high polymers as spherulites, these being literally little spheres. The fringed-micelle model was found to be incompatible with spherulites, which were two orders of magnitude larger, particularly in view of the fact that the molecular chain is generally tangential to the spherulites instead of being radial as had been expected.

With the introduction of the Electron Microscope came the discovery of individual polymer crystals, or lamellae, which were grown from very dilute solutions. Examples of these, for polyethylene, can be seen in figure 3.

The idea of polymer molecules forming separate crystals was alien to the fringed-micelle model. It has however been shown that, for example, a whole sample of linear polyethylene can be precipitated as crystals of say 12nm

FIGURE 3 : SOLUTION GROWN LAMELLAE OF
POLYETHYLENE



thick by $10\mu\text{m}$ wide, bearing a striking resemblance to those of the aliphatic n-paraffins (polyethylenes of very low molecular weight). This similarity suggested the even more remarkable fact, correctly deduced by A. Keller in the mid 50's, that molecules, typically $5-10\mu\text{m}$ long, are aligned with the molecular long axis parallel (or nearly so) to the crystal thickness of the lamellae. The inescapable conclusion was that the chains must fold back on themselves repetitively at each crystal surface alternately. This phenomenon, now known to be widespread, is termed chain-folding. See figure 4 for a schematic representation of chain-folding.

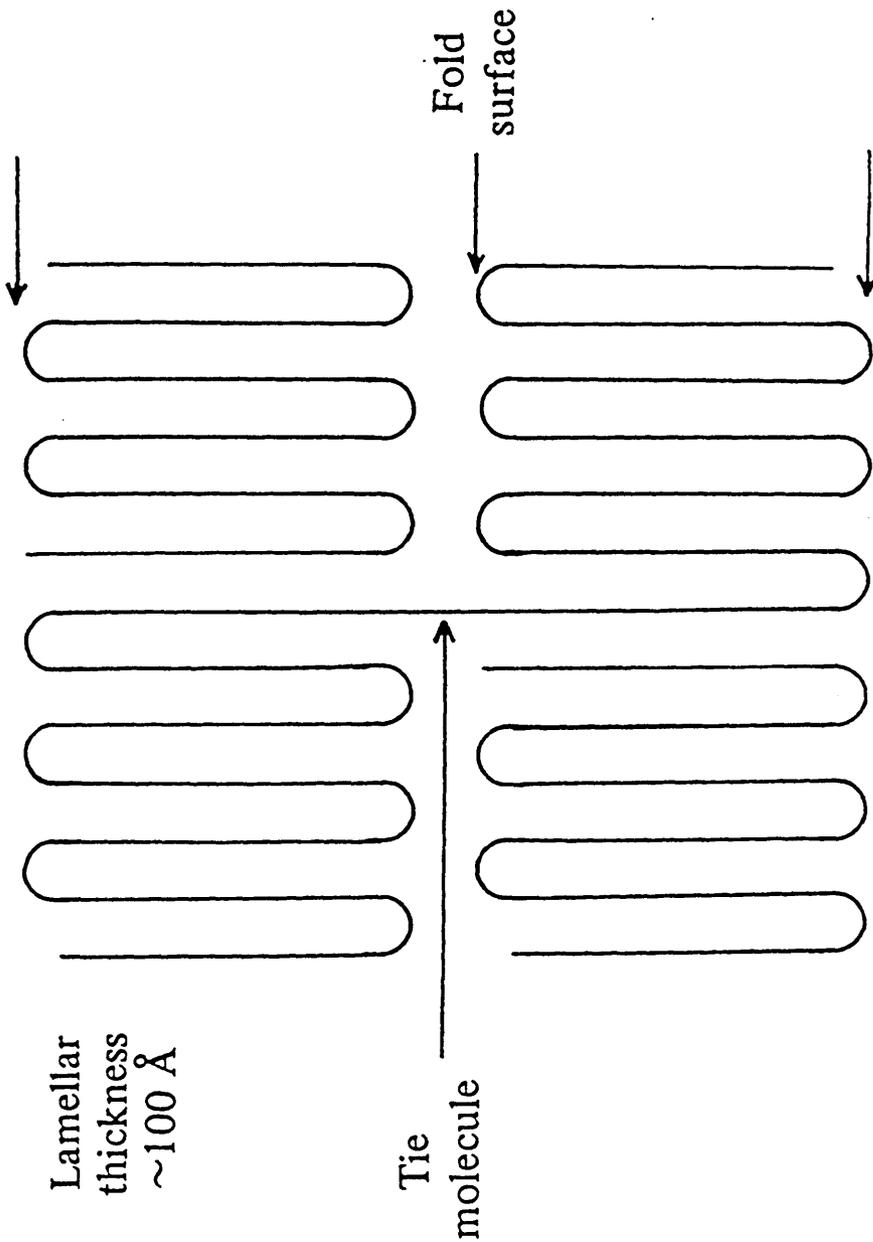
The twin discovery of polymer lamellar crystals and chain-folding now lies at the heart of the modern understanding of polymer morphologies.

With samples consisting almost entirely of individual crystals and a variety of morphological evidence suggesting ordered folding, there was a period when it became difficult to locate the 'amorphous' region associated with crystalline polymers. These were soon identified with regions at or between the fold surfaces (i.e. the large basal surface where molecules turn back on themselves).

Polyethylene has proved to be the most suitable test

FIGURE 4 : SCHEMATIC REPRESENTATION OF
CHAIN FOLDING

Solution-grown lamellae of polyethylene.



substance mainly due to the chemical simplicity of its molecules. Its study can bring out the effects associated with chain-folding without being complicated by the specificity of distinct chemical groups. It can be considered in terms of a continuous chain. It is expected that folding in chains of greater complexity will be influenced by the specific chemical groups situated along them, giving directional inter-stem interactions such as hydrogen-bonding, to enable the most favourable energetic interaction between fold stems.

Single crystals of polyamides have been observed repeatedly using Electron Microscopy^{9,10}. The precise nature of the fold structure is still subject to much debate. Many questions are raised regarding the chain-folded crystallization of polyamides:

1) Does the molecule double back on itself with the fold occupying the minimum possible number of chain bonds?

ii) Does the chain form a loose loop at the basal surface?

iii) Does the chain re-enter the crystal at the nearest (adjacent) site or elsewhere?

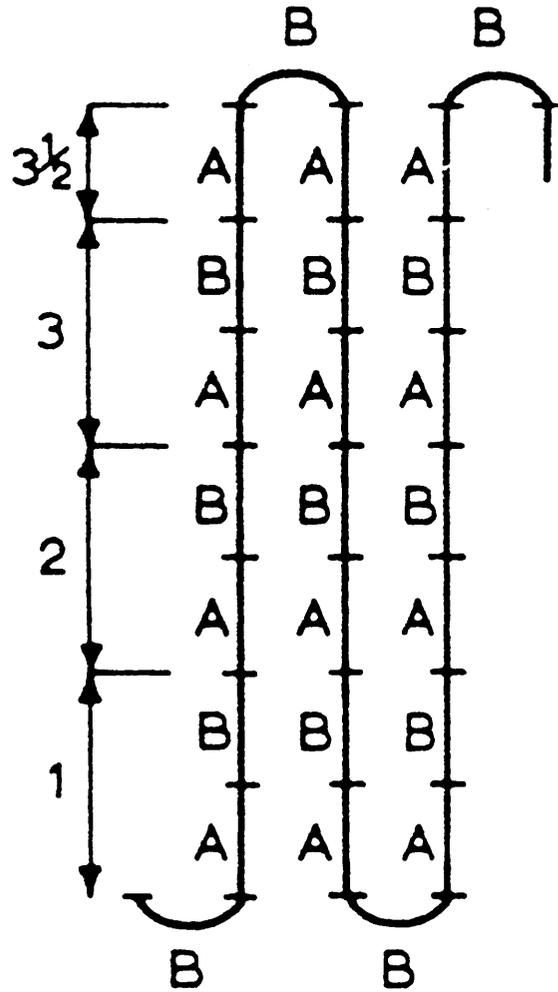
iv) What determines the fold length and at what oligomer length does folding start to occur?

The techniques used in attempting to answer these, and other, questions are essentially infrared spectroscopy¹¹, low- and wide-angle X-ray diffraction^{12,13,13a} and, more recently, neutron scattering¹⁴.

As stated previously, single crystals of polyamides have been observed repeatedly. Although these have not been as well developed as in polyethylene samples, they are lamellar with chains perpendicular to the lamellar interface.

In the early 1970's, Dreyfuss and Keller¹² showed by means of detailed X-ray studies, on nylon-6.6, 6.10 and 6.12, that the crystal layers correspond to four monomer lengths. They suggested that the straight stem could not be four monomer units long, as in figure 5, for two reasons. Firstly this would mean that there is no additional space for the fold and interlamellar gap. The resulting intermeshing of the folds in consecutive layers would be sterically unlikely. Secondly, as can be seen in figure 5, this arrangement (or any other integer monomer number in the straight stem) would lead to alternating acid and amine folds. Thus the two opposing crystal surfaces would have different 'polarities', for which the authors of this paper could find no other indication.

FIGURE 6 : SCHEMATIC REPRESENTATION OF FOLDING
WITH STEMS $3\frac{1}{2}$ MONOMER UNITS LONG



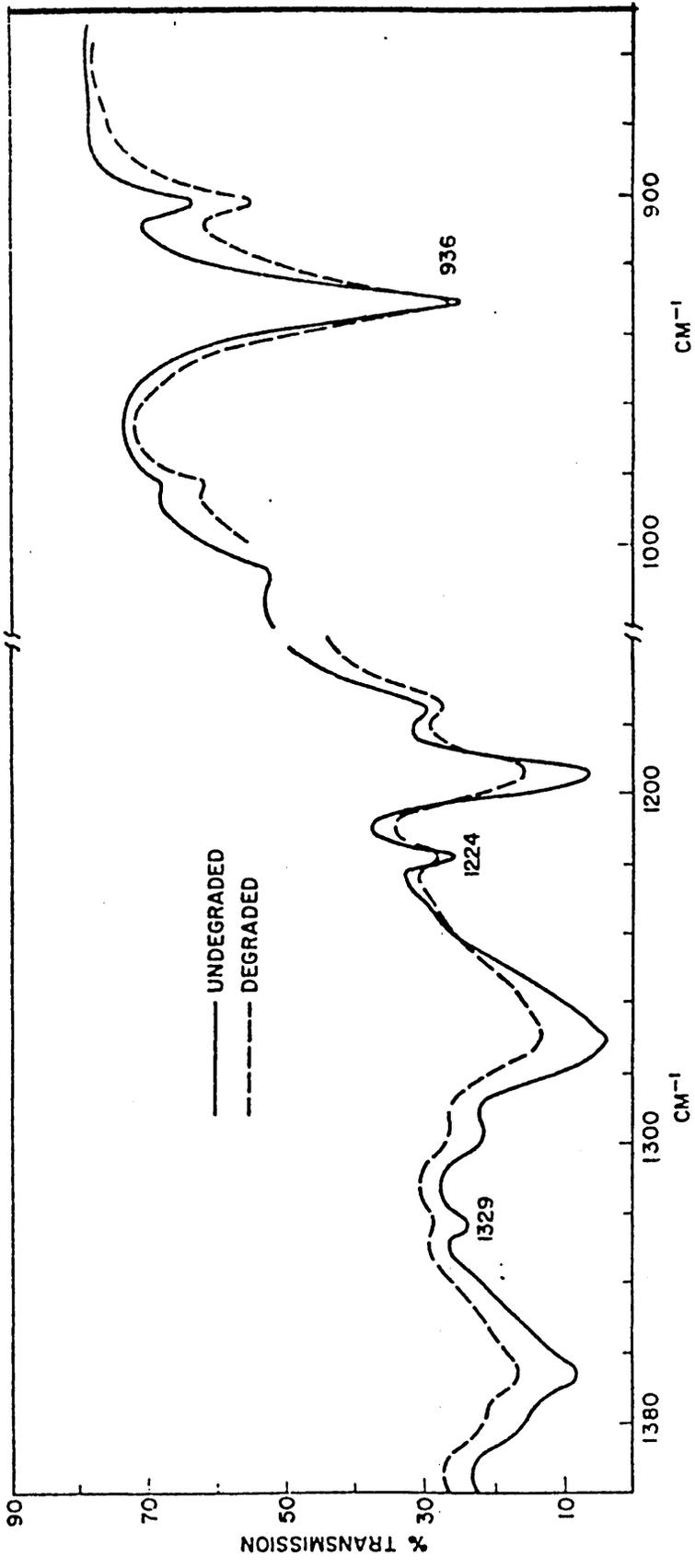
A=THE ACID COMPONENT
 B=THE AMINE COMPONENT

They concluded that straight stems of $3\frac{1}{2}$ monomer units were most likely. By assigning more space to the fold and interlamellar gap the additional 0.5 monomer unit can be taken up by the fold as shown in figure 6. Again assuming the fold to take up either an acid or an amine group there would be sufficient space between layers to avoid intermeshing. This would also mean the folds on both sides of the layer to be of the same type.

Dreyfuss and Keller also showed¹² the ratio of number of monomer units to layer thickness was virtually identical for all three of the nylons studied. They deduced from this that the fold structure must be identical in all three and that this could not be the case unless the fold consisted of either no more than about six carbon atoms or at least one and a half monomer units. The one component common to all three nylon samples, the hexamethylenediamine component, must therefore form the chain fold.

In 1968, Koenig and Aboatwalla¹¹ used infrared studies to come to the same conclusion. Earlier work had shown that IR spectroscopy could be utilized to detect contributions to the spectra from folded, crystalline, crystallizable and non-crystallizable components of the chain. By applying this technique to nylon-6.6 they showed that bands at 1329 and 1224cm^{-1} in the infrared

FIGURE 7 : CHANGES IN 1224 AND 1329 cm^{-1} BANDS
DURING HYDROLYSIS



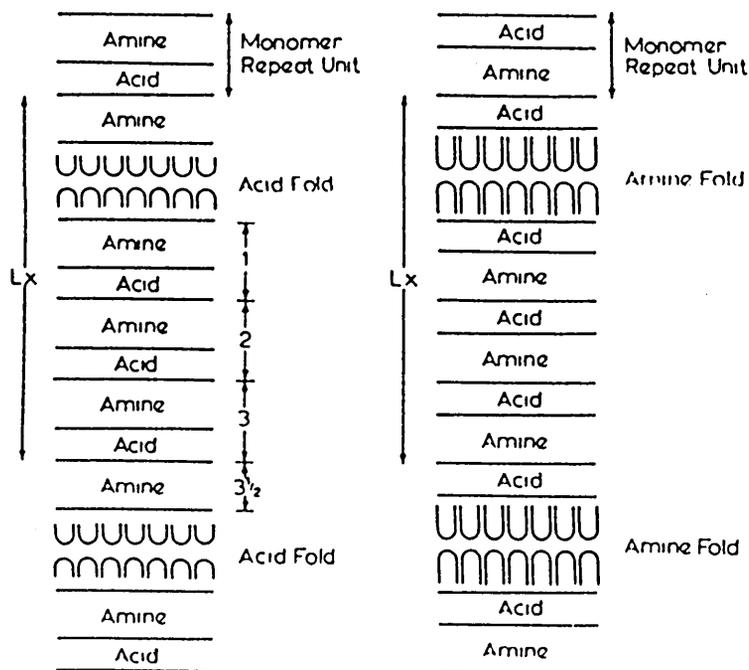
spectra could be assigned to the folded chain regions. These bands were weak due to the low concentration of folds. They also showed that the infrared band at 936cm^{-1} was a contribution of the stems of the fold. Degradation of the fold surface was achieved by heating nylon-6.6 single crystal mats at 98°C with dilute sodium hydroxide solution. The crystalline regions were shown to be unaffected as no significant change in the 936cm^{-1} band was observed. But comparison of the infrared spectra of the same sample before and after hydrolysis showed the intensity of the bands at 1329 and 1224cm^{-1} had decreased relative to that of the 936cm^{-1} band (see figure 7). In conjunction with X-ray diffraction work they showed that the 1329 and 1224cm^{-1} bands could be assigned to the interaction of the amide III band with the wagging and twisting of the N-vicinal CH_2 groups. They concluded from this, as above, that the amine component of the nylon series must make up the chain fold.

Four years after the above paper work by Atkins, Keller and Sadler^{13a} claimed that the majority of the folds in nylon-6.6 are made from the acid component. Their work involved elucidating information on the fold surface by studying the relationship between the diffraction from periodic variations within a single lamella and diffraction from the stacking of lamellae (crystals).

They recorded low- and wide-angle diffractions simultaneously, this provided information on interlamellar (low-angle) and intralamellar (wide-angle) diffraction.

They confirmed previous low-angle work on the crystal lattice by showing the lamella thickness to be approximately four monomer units. This has been shown to consist of $3\frac{1}{2}$ monomer units in the stem and the remaining $\frac{1}{2}$ unit making up the fold. In principle this leads to two models, one with acid folds and one with amine folds as shown below.

FIGURE 8 : SEQUENCES OF PLANES WITHIN LAMELLAE CORRESPONDING TO OXYGEN ATOMS FOR ACID (a) AND AMINE (b) FOLD TYPES



There are eight planes of oxygen atoms, shown above as lines, arising from the four monomer units. The only difference between the two models is the spacing of the oxygen planes. Two subsidiary maxima are observed between the 001 and 002 peaks corresponding to these oxygen planes. These were shown to correspond to the acid fold model. The amine model was calculated to give only one subsidiary maxima.

The discrepancy with infrared data was explained as the X-ray diffraction data was more direct, "in fact based on primary data". They do state, however that their work would allow for a minor fraction of amine folds which may be sufficient to explain the IR evidence.

A more recent paper by Spells, Sadler and Keller¹⁴ also suggests that the fold surface, for solution crystallized samples, consists of a majority of acid type folds, the proportion of which is estimated at 0.58 for nylon-6.6 single crystals. This was shown by using d_8 -adipic acid in the preparation of d_8 -nylon-6.6, and then carrying out a neutron diffraction study. They demonstrated a shift in the 001 peak position on changing the swelling agent from 1,4-butanol to the d_8 analogue which they related to the arrangement of the acid and amine components of nylon-6.6.

It is because of different conclusions such as these that it was deemed important to study the fold surface in greater detail. Previous studies have used nylon-6.6 polymers or fractionated samples and are therefore not monodisperse. It is hoped that the use of monodisperse oligomeric nylon-6.6 will give a clearer view in the effort to answer the questions concerning the nature of the fold and other questions such as the onset of chain folding etc.

1.4. OVERVIEW OF THE PROJECT.

Nylon materials were amongst the earliest output of the polymer industry. Manufacturing and processing protocols have been in place, more or less unchanged, for many years. What fundamental chemical developments have occurred have tended to be peripheral to the actual chemistry of polymer formation and reactivity (e.g. developments in suitable colouring technologies).

The project discussed here grew from an interest in the application of chemical synthesis to the solution of problems of polymer science and technology. In particular the project is a development from work, involving the supervisors of this project, on the synthesis and evaluation of monodisperse polyethylene oligomers (e.g. E. Igner, O.I. Paynter, D.J. Simmonds and M.C. Whiting, J. Chem. Soc., Perkin trans., 1, 2447, (1987); G. Ungar and A. Keller, Polymer, 27, 1835, 1986). The strategy of relevant oligomer synthesis appealed to nylon scientists at ICI Fibres and a series of meetings took place.

At the early discussion stage of this project three main points emerged. Firstly there has been very little fundamental chemistry research into the controlled, targeted synthesis of nylon analogues or oligomers.

Secondly there are genuine problems in nylon technology which might benefit from studies involving monodisperse oligomers (cf Section 1.2.). Thirdly (and ominously) those problems related largely to the lability of nylon structures which would probably cause handling difficulties during any oligomer project also. Since there was already interest in preparing oligomers for chain folding-studies, the programme described here was initiated but the focus changed somewhat from the original objective whereby synthesis was a means to an end of elucidating information on chain-folding.

The new focus put synthesis itself at the centre of attention. A review of the nylon literature showed that chain-folding was the only major ongoing area of fundamental research. Studies of synthetic chemistry had been rather dormant since work, mainly by Zahn et al¹⁹, in the 1960's. Since no other groups have subsequently confirmed or built on Zahn's methods for oligomer synthesis, and as he was unable to test his products by Gel Permeation Chromatography, it seemed timely to re-examine his and other methodologies. It soon became apparent that nylon synthesis was far from simple and that oligomer integrity would be very difficult to confirm, so the new focus of the work reported here became an exercise in problem solving with monodisperse

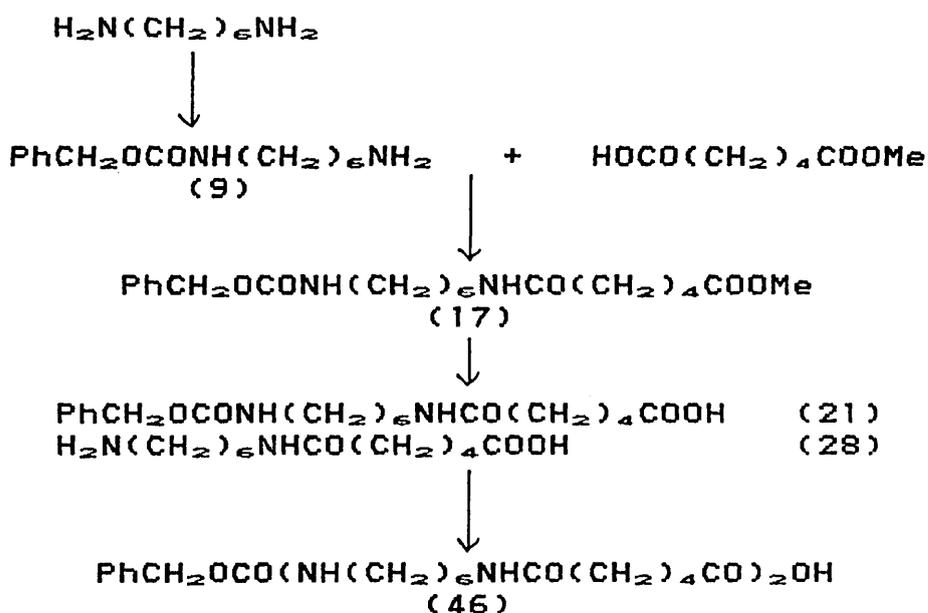
oligomers for physical evaluation a desirable objective, but an elusive one.

The following chapter describes the gradual development of a reasonably successful strategy for nylon oligomer synthesis, while chapter 4 summarizes the methods used. The majority of the work addresses two series of nylon-6.6 oligomers; the oligomers per se (viz. monomer, dimer, tetramer and octomer) referred to as "integer oligomers", and "non-integer oligomers" having degree of polymerization (DOP) of 1.5, 2.5, 3.5 and 8.5. The non-integer oligomers involved two sub-sections, acid terminated and amine terminated. A large number of investigations were required to arrive at these two series of oligomer preparations, as discussed later. Here, we summarize the synthetic sequences arrived at as being the most promising.

Scheme 1 outlines the approach devised for integer oligomers starting from commercially available hexamethylenediamine and methyl hydrogen adipate. Monoprotection of hexamethylenediamine gave a mono-N-carbobenzoxy derivative (9) that led to doubly protected monomer (17), that could be partially deprotected to the carboxylic acid (21) or fully deprotected to aminoacid (28). To prepare the dimer (46), the monomer carboxylic acid (21) was converted to an unsymmetrical anhydride

(using n-butyl chloroformate and triethylamine) that coupled successfully with the amine (28) without apparent interference by the carboxylic acid (27). A similar approach was used to obtain the tetramer from protected dimer (46).

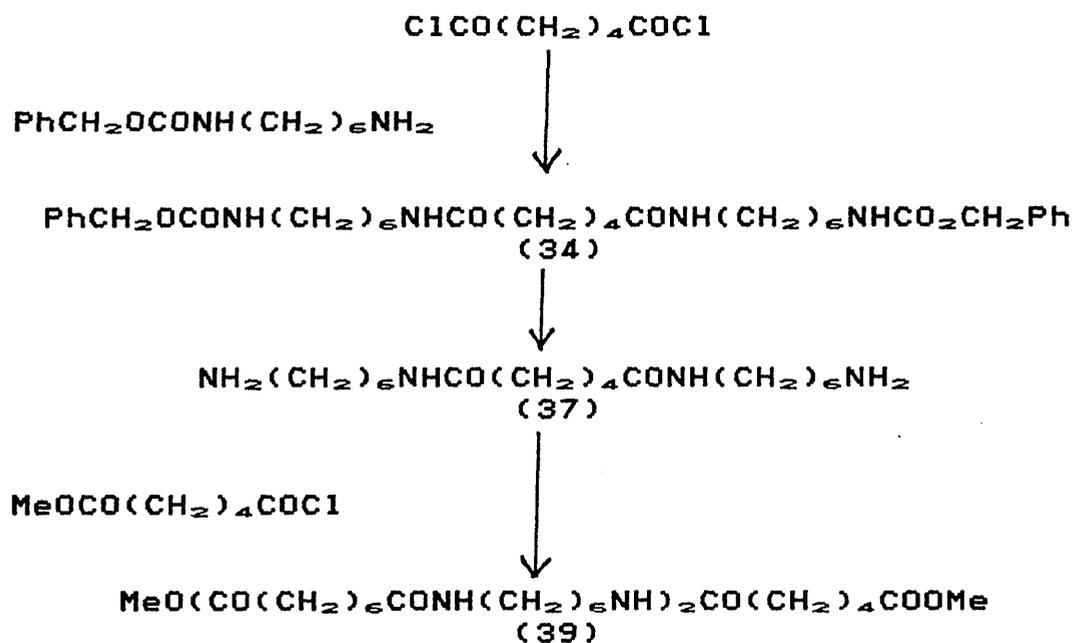
SCHEME 1. INTEGER OLIGOMER SYNTHESIS.



Non-integer oligomers were constructed by building outwards onto both ends of either a reactive "adipyl component" or hexamethylenediamine. For example Scheme 2 illustrates the former approach where the reactive bisacyl chloride of adipic acid condenses at both ends with a monoprotected hexamethylenediamine (9). This gives oligomer (34) that has DOP = 1.5 since one of the hexamethylenediamine units completes the adipamide

monomer while the second is effectively one half of a second nylon-6.6 monomer unit. Deprotection of (34) gave a new central unit for outwards construction, this time having amino functionality at each of the growing ends (37). Thus oligomer growth now required a suitable monoprotected adipyl component (reactive at the second site) and the methyl ester acyl chloride derivative fitted the bill. When condensed with diamine (37) the acyl chloride delivered an adipyl unit at each end increasing the DOP by one to 2.5. This attractive synthetic route was taken further as discussed later, and also an analogous route using hexamethylenediamine as the original central unit was investigated.

SCHEME 2. ONE APPROACH TO NON-INTEGER OLIGOMERS.



Once optimised the routes summarized above appeared to facilitate oligomer synthesis insofar as reactions proceeded smoothly leading to clean products whose IR spectra in particular seemed highly consistent with successful homologation (e.g. relative amplitudes of carbonyl absorption maxima). Full details of these, and other experimental approaches that were attempted form the body of this thesis.

2. DISCUSSION.

2.1. SYNTHETIC STRATEGIES.

The primary aim of the work described in this thesis was the investigation of potential routes for the synthesis of selected oligomers of nylon-6.6, trial syntheses using these routes and assessment of the purity of the products. Monodisperse oligomers are required for reliable studies of oligomer/polymer interactions, and an important secondary aim of the work was an assessment of the dispersity of the oligomer products. While synthetic methods were adopted only if they seemed to lead to monodispersity, the known lability of nylon structures, as described previously, leads us to a cautious approach in this work and demands a careful analysis of reaction products.

Once a general synthetic route to pure oligomers is available it can be applied to the preparation of oligomers of increasing length, while maintaining purity for future characterization studies. This chapter presents a discussion of the development of the most promising general synthetic route. The "nylon intermediates" are not readily amenable to the reaction conditions involved in more conventional syntheses due to solubility, lability etc. The project, therefore,

rapidly developed into a series of problem solving episodes.

In developing the synthetic route several factors had to be kept in mind throughout.

i) High yields are important for each stage of the synthesis as a molecular doubling route is proposed.

ii) Oligomers produced should be monodisperse as polydispersity would be a cumulative problem. Separation of the oligomers would be difficult due to the chemical and physical similarities; this would also defeat the purpose of the synthesis.

iii) Protecting groups used for amines and carboxylic acids must offer total selectivity in the isolated product, and high yields for attachment and removal.

The synthetic route initially proposed was the molecular doubling from the monomer to the dimer, tetramer, octamer etc. This has, however, been studied in conjunction with a second route, that of producing 'non-integer' oligomers. Here the products are oligomers with either acid or amine end groups, unlike the 'integer' oligomers which contain one of each. However, molecular doubling is an attractive approach since it maximises the differences between products and unreacted starting material (which will be only about half the size of the

product) offering greater potential for the purification of the products.

From the literature it can be seen that very little work has been done so far on this topic. The two main approaches have involved solid-phase and solution methods. The solid-phase technique (i.e. the Merrifield method) was used by Peter Kusch¹⁵ for nylon-6.6 oligomers and by M. Rothe and W. Dunkel¹⁶ for nylon-6 oligomers. The solution based technique was used for short oligomers by Helmut Zahn^{17,18}. Both these approaches require nylon-6.6 monomer as the primary starting material. The preparation of this monomer is detailed by Zahn¹⁸, and requires monoprotected adipic acid and monoprotected hexamethylenediamine (i.e. 1,6-diaminohexane). The former is available as a commercial product (methyl hydrogen adipate; Lancaster²⁰). It is, however, necessary to synthesize the monoprotected hexamethylenediamine.

As stated earlier two main approaches were considered for increasing the chain length of the oligomers, the Merrifield method^{15,16} and that used by Zahn^{17,18}. Both require the gradual, stepwise construction of the oligomers. This is important because of the difficulties, if not impossibilities, that are encountered in the attempted separation of polymeric

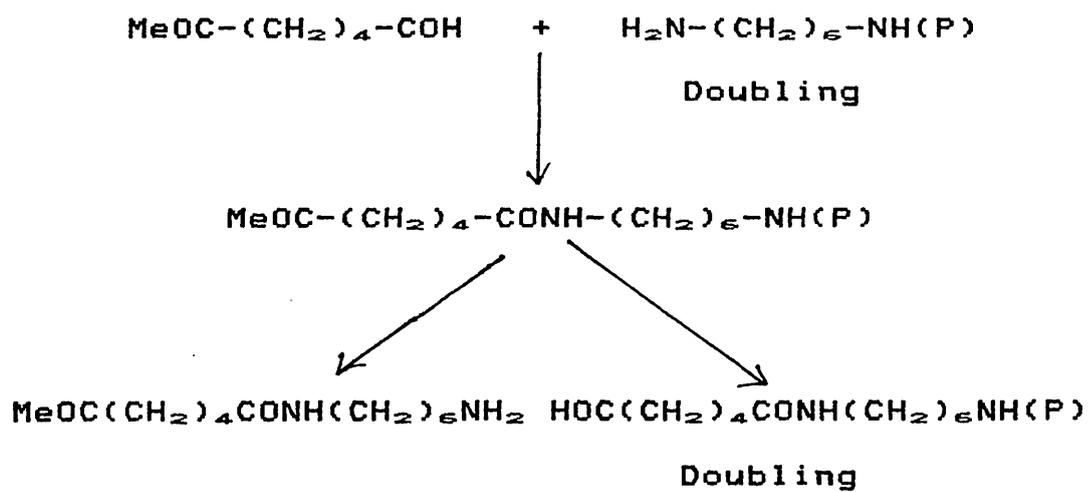
homologous series of macromolecules into fractions containing molecules of identical and exactly defined chain length. It would, therefore, appear necessary to achieve quantitative peptide-type coupling. Neither approach achieves this, the Merrifield method reportedly giving yields of around 75-80%¹⁶, and Zahn's technique around 70%¹⁸. The Merrifield method obtains these slightly higher yields by the use of large excesses of reagents being coupled with the bound oligomer. Some of our own observations lead us to doubt some of the reported results in the light of more sensitive analytical techniques that are available nowadays.

Zahn's method^{17, 18} was chosen as a starting point for this project as it is more economical with reagents. This is of greater importance as the products of one reaction become the reagents for the next. Also, the degree of polymerisation (D.O.P.) achieved by Zahn was only 3^{17, 18}, providing scope for development. Most importantly it was further anticipated that the Zahn method would provide a cleaner method of synthesis without homologous side-products.

It was hoped that the use of this technique would provide levels achieved by Kursch¹⁵ (D.O.P.=16, but for nylon-6 rather than our target, nylon-6.6). Molecular

doubling was also seen as potentially more far reaching than the earlier 'one-off' oligomer preparations¹³.

GENERAL SCHEME FOR MOLECULAR DOUBLING



etc

2.1.1. MONOPROTECTION OF STARTING MATERIALS.

Nylon-6.6 may be considered as a copolymer of hexamethylenediamine (6) and adipic acid (33), as such these two compounds are the monomeric units. However, in order to avoid later confusion the term "monomer" will be used to describe the repeating unit of nylon-6.6 i.e.



Synthesis of the nylon-6.6 monomer (i.e. the above but with terminal groups H and OH respectively) can only be achieved by the quantitative coupling of the monoprotected hexamethylenediamine with monoprotected adipic acid. The protecting groups are employed to introduce selectivity of reaction by limiting the number of reactive sites. This should allow the controlled coupling of the two components.

The protecting groups used were, initially, chosen for the following reasons;

i) The reagents to introduce them are readily available.

ii) Reported ease of selective introduction in high yield (preferably quantitative).

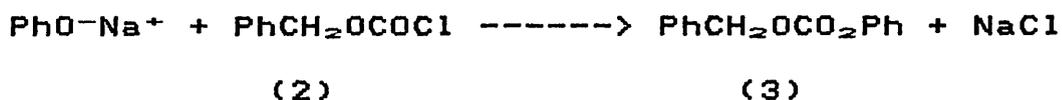
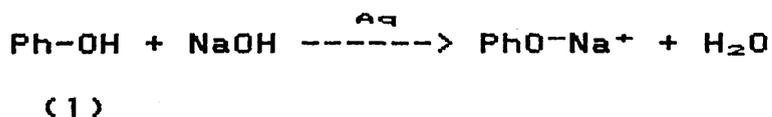
iii) Reported ease of selective removal in high yield (preferably quantitative).

2.1.1.1. ADIPIC ACID

Monoprotected adipic acid is readily available as a commercial product from Lancaster²⁰. In this work the monomethyl ester, methyl hydrogen adipate (15), was used (see page 51).

2.1.1.2. HEXAMETHYLENEDIAMINE (6)

Initially the Zahn approach¹⁸ was attempted. Here the protecting moiety was the carbobenzoxy (Cbz) group, from the reagent phenylbenzyl carbonate (3). This in turn was prepared by the condensation of benzyl chloroformate (2) with phenol (1).



A small scale reaction gave a low yield, 22%, but a highly pure material, as shown by gas chromatography (GC). Attempts to scale up the reaction consistently failed. The phenylbenzyl carbonate (3) was shown by infrared spectroscopy (IR) to be present in the ether layer after the solvent had been removed on a rotary

evaporator. After vacuum distillation, however, the phenylbenzyl carbonate (3) was hardly traceable in any of the fractions. Attempts to prevent this breakdown of the product during distillation included increasing the size of the joints of the glassware to reduce pressure build-up at these points. This was partially successful but not sufficiently so for practical purposes as large quantities of phenylbenzyl carbonate would be required. Even attempts at re-distillation of the low quality product from the modified scaled up reaction failed to yield any significant amount of the required product.

Due to the difficulties encountered in preparing large stocks of phenylbenzyl carbonate (3) it was decided to investigate other protecting groups. These included N-carboethoxyphthalimide^{21,22} (4), acetic acid²³ (5) and the direct use of benzylchloroformate (2). With N-carboethoxyphthalimide (4) three approaches were tried including a two phase system designed to reduce contact between the two reagents. Unfortunately as the mono-N-phthaloylhexamethylenediamine (7) was produced it crystallized out at the interface and was quickly converted to the bis-product. The method using acetic acid (5) was problematic due to the difficulty in maintaining a low enough pressure throughout the distillation and because of solidification of the fractions in the vacuum lines and the condenser. The

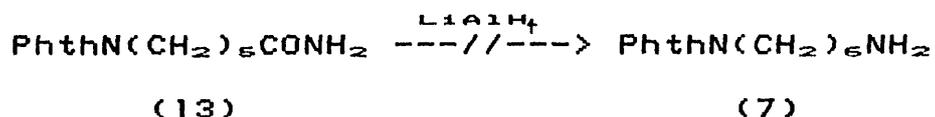
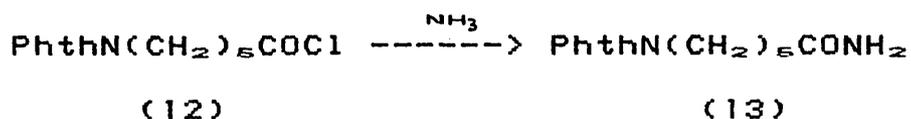
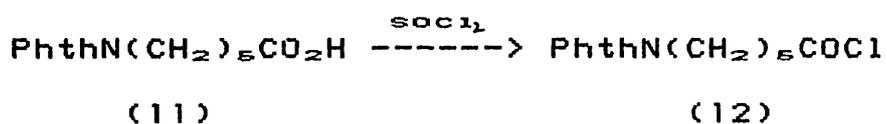
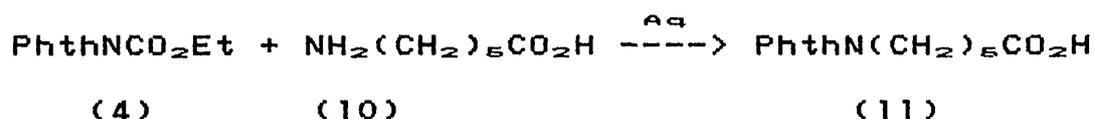
Table 2.1. Yields From Monoprotection Reactions

<u>Reagent</u>	<u>Ratio^a</u>	<u>Yield</u>
N-CEP	1:1	20%
N-CEP	1:1 (two phase)	0%
Acetic Acid	1:1	24%
Benzyl- chloroformate	1:1	20%
Benzyl- chloroformate	2:1	19%
Benzyl- chloroformate	5:1	20%
Benzyl- chloroformate	10:1	22%
Benzyl- chloroformate (Schotten-Baumann)	2:1	25%
Benzyl- chloroformate (Schotten-Baumann)	4:1	27%

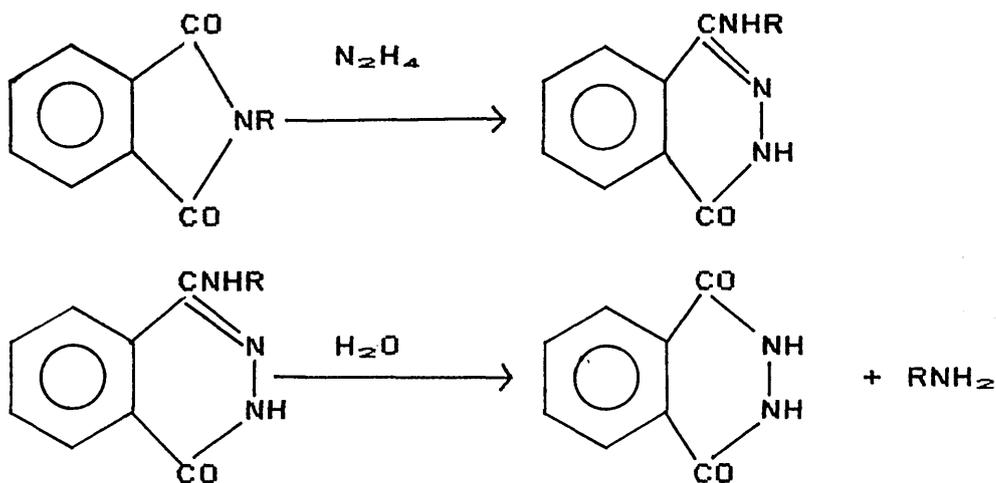
^a ratios given as HMD:reagent

Another attempt to produce mono-N-phthaloyl hexamethylenediamine (7) was via 6-aminocaproic acid (10). This would have allowed protection of the amine to be unhindered by the presence of a second amine. The protecting group was introduced²¹ to give phthaloyl-N-6-aminocaproic acid (11) with a yield of 50%. The carboxy group was converted to the amide (13) via the acid chloride²⁴ (12) in high yield. The reduction of the amide (13) to the amine (7), however, was not possible

due to preferential reduction of the phthaloyl group over the amide giving hexamethylenediamine (6) as the product. Had the preparation of phenylbenzyl carbonate (3) not ultimately been successful this approach to monoprotection would have been further investigated with other protecting groups due to the ease and success of the early stages.



Mono-deprotection of the bis-protected products of the above reactions was also considered. This was attempted on the bis-N-phthaloylhexamethylenediamine (14) using hydrazine^{25, 26}. The reaction attempted involved standing the bis-product in an aqueous solution of hydrazine for decreasing times of between two days and twelve hours and refluxing in a methanolic solution for two hours. A possible mechanism for this deprotection is²⁵;

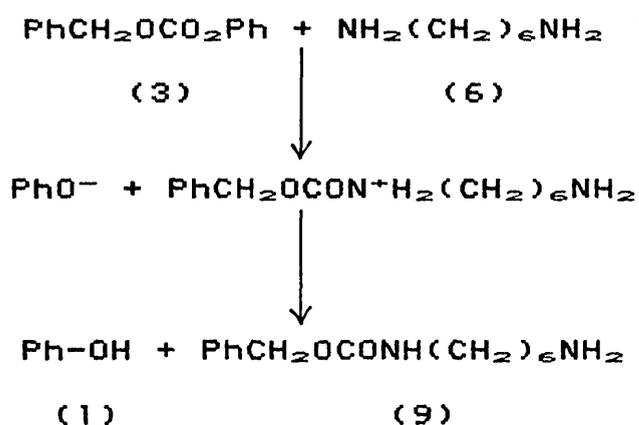


The methods turned out to be far too successful as the phthaloyl group was removed from both amine groups. Decreasing the ratio of hydrazine to bis-N-phthaloyl hexamethylenediamine (14) did not improve the situation to any worthwhile extent as there was still preferential deprotection giving hexamethylene diamine and bis-N-phthaloylhexamethylenediamine as the products.

All these approaches, although showing promise to various degrees, were abandoned in favour of using phenylbenzyl carbonate (3). The difficulties initially encountered in the synthesis were eventually overcome by increasing the reaction time from 4 to 24 hours as well as increasing the number of washes at each stage. There were some problems with water contamination which were solved by drying the ether layer twice. This provided a highly pure product after rotary evaporation to remove

the ether solvent, thus eliminating the need for routine distillation. Yields of about 85% could now be achieved.

The reaction of phenylbenzyl carbonate (3) with hexamethylenediamine (6) proved to be the most successful route to mono-N-carbobenzoxyhexamethylene diamine¹⁸ (9).



Initial problems due to phenol contamination were solved by repeatedly stirring the final product in ether and filtering. Another problem which regularly occurred was the presence of a second substance which appeared to be identical by nuclear magnetic resonance (NMR) but showed an extra peak in the carbonyl region of the IR. The compound was discovered because it crystallized out slightly before the mono-N-carbobenzoxyhexamethylene diamine (9). The melting point of this substance was higher, at around 160°C, than for mono-N-carbobenzoxy hexamethylenediamine (9), 101-102°C. Although the

contaminant could not be positively identified it was thought to be the result of the free amine (9) reacting with carbon dioxide in the air giving rise to carbamides. The problem was easily (and usually successfully) solved by recrystallization. On occasions, however, the product consisted mainly of the "carbamides" and the entire batch would have to be rejected.

Following the successful preparation of monoprotected hexamethylenediamine using the carbobenzoxy group it was now possible to start work on the coupling reactions.

2.1.2. NYLON-6.6 MONOMER.

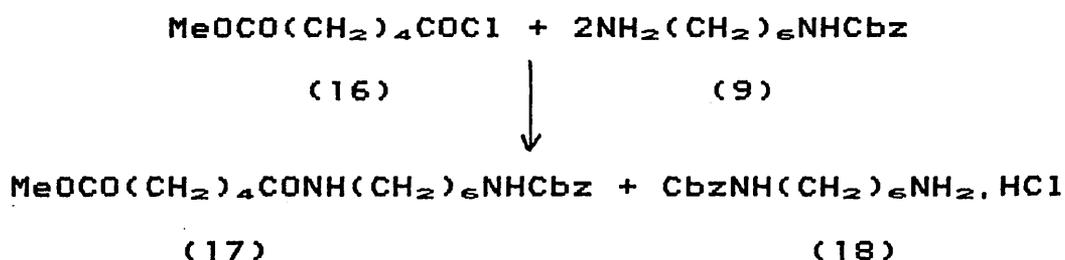
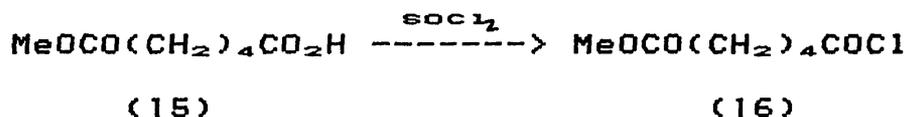
The coupling of mono-N-carbobenzoxyhexamethylenediamine (9) with methyl hydrogen adipate (15) was, as with all stages in the synthesis, required to meet certain standards. These included:

i) A high yield of the isolated product, preferably quantitative (although this was perhaps optimistic), as the product would have to undergo several more reaction stages).

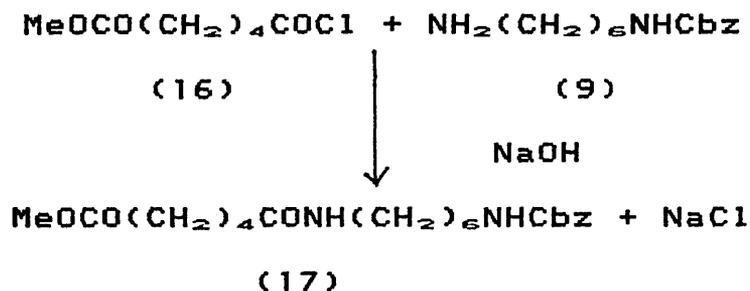
ii) A very high degree of purity i.e. monodispersity. As it is hoped to use the product in determining the onset and nature of chain-folding it is of extreme importance that contamination by other chain lengths is omitted. Any contamination would also be cumulative with each increase of the chain length adding to the polydispersity. A part of the project brief was a feasibility study for future projects that would only be possible if monodispersity could indeed be achieved.

Coupling of the two monoprotected reagents was initially to be performed using a Schotten-Baumann method¹⁶ to prepare an N-carbobenzoxy C-methyl ester monomer (17). Here the methyl hydrogen adipate (15) would be converted to the acyl chloride (16) and reacted with mono-N-carbobenzoxy hexamethylenediamine (9). In the expected reaction between the two reactants, one equivalent of

hydrogen chloride is formed. Because of this two equivalents of the amine must be used in order to account for the formation of the ammonium salt (18).



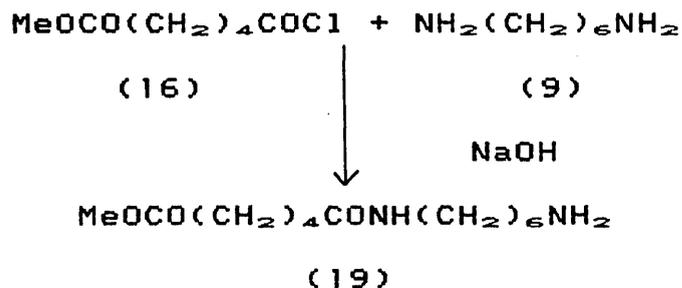
The excess mono-N-carbobenzoxyhexamethylenediamine (9) would have been relatively easy to recover by isolation and neutralization. Alternatively sodium hydroxide could be added simultaneously to neutralize the hydrogen chloride.



The acyl chloride, (16), being less soluble in water, reacts slowly with the sodium hydroxide. The amine (9) dissolves in the acid chloride (16) and reacts rapidly. The amine hydrochloride (18) formed, should then dissolve in the aqueous phase and react rapidly with the hydroxide ion to regenerate the mono-N-carbobenzoxy hexamethylene diamine (9).

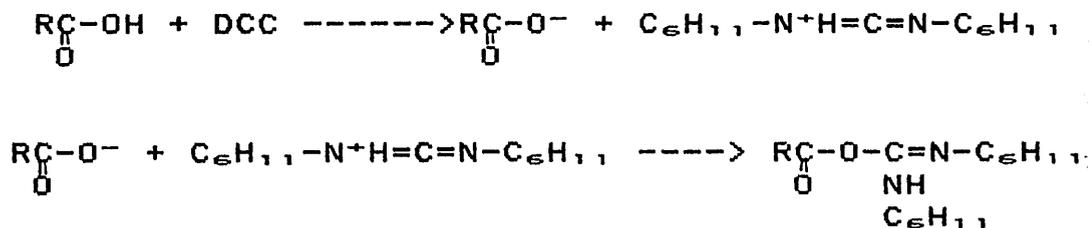
The yield of this reaction was far lower than hoped at around 20%. This could be explained if the solubility of the acid chloride (16) in water was greater than expected and it was reacting directly with the sodium hydroxide. Increasing the ratio of the acyl chloride (16) to the mono-N-carbobenzoxyhexamethylenediamine (9) had little effect as did a reduction of the reaction temperature.

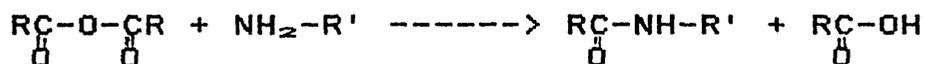
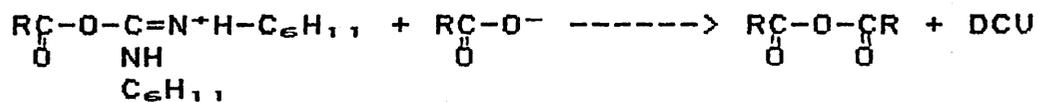
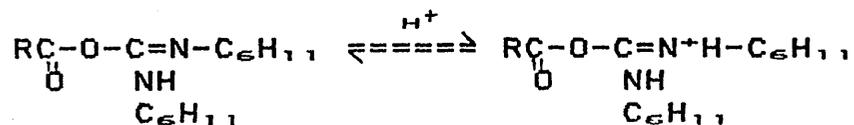
As mentioned previously, prior to the successful formation of mono-N-carbobenzoxyhexamethylenediamine several other monoprotection reactions had been investigated. Within this work was an attempt to "monoprotect" hexamethylenediamine (6) by coupling with methyl adipoyl chloride (16). This experiment was designed to remove the need for mono-N-protection of hexamethylenediamine and lead directly to the C-methyl ester monomer (19).



The aqueous Schotten-Baumann¹⁸ reaction was used but again gave low yields (17%) despite increasing ratios of the hexamethylenediamine (6) to the methyl adipoyl chloride (16).

The direct coupling of methyl hydrogen adipate (15) with hexamethylenediamine (6) was also tried using dicyclohexylcarbodiimide (DCC). This reaction is considered to be one of the most important in peptide synthesis²⁷, due to the simplicity of the procedure. The mechanism is not totally understood but one protocol involves the activation of the carboxyl group by way of a symmetrical anhydride²⁸ which can then be used to acylate the monoprotected amine. DCC is simultaneously converted to dicyclohexylurea (DCU).





The C-methyl ester monomer (19) was again the minor product with yields of around 15%. As with the monoprotection reactions the statistical approach gave far more of the bis product than was anticipated. Once the preparation of mono-N-carbobenzoxy hexamethylenediamine (9) was achieved this and the previous approach were dropped.

An alternative method for the synthesis of N-carbobenzoxy C-methyl ester monomer (20) was a non-aqueous version of the Schotten-Baumann reaction using pyridine to remove the hydrogen chloride and as the solvent. In small scale trials, yields of up to 62% were obtained. On scale-up the exothermic reaction became too extreme essentially 'cooking' the reaction mixture. Separation of the product from the charred mixture was possible but was time consuming and gave vastly reduced yields. Intermediate scales produced gradual decreases in percentage yields suggesting the original trial to be

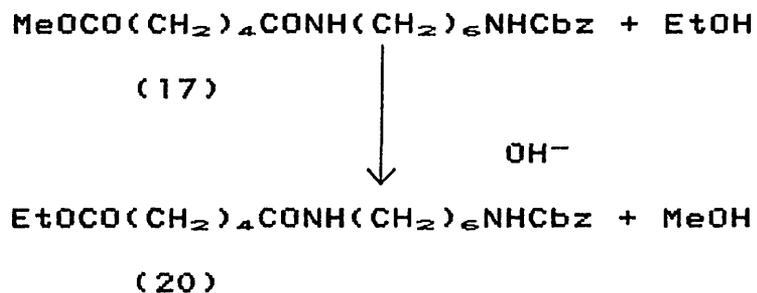
decarbonylation of the bisprotected monomer (17). The main factors concerned with these deprotection reactions are

i) total cleavage of protecting groups in the final isolated product. Failure to achieve this criterion would again lead to increasing polydispersity in successive reactions.

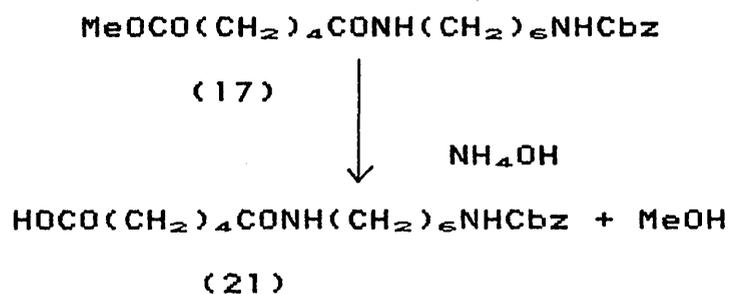
ii) Complete selectivity between the decarbonylation and de-esterification of the carbonyl methyl ester monomer.

iii) High isolated yield of the pure deprotected products.

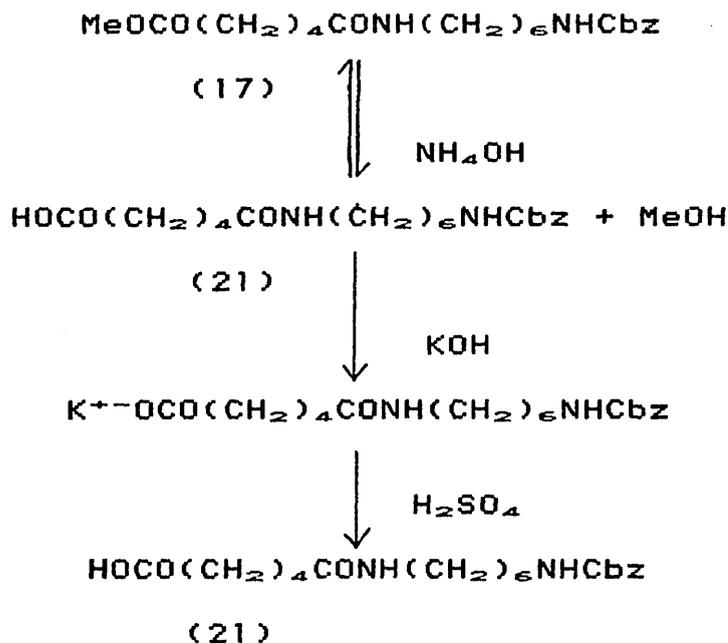
De-esterification using potassium hydroxide in absolute ethanol gave a transesterified material as the major product. IR showed the product still contained the ester group. Mass spectrometry of the product gave the molecular ion at m/z 406 corresponding to N-carbonyl C-ethyl ester monomer (20).



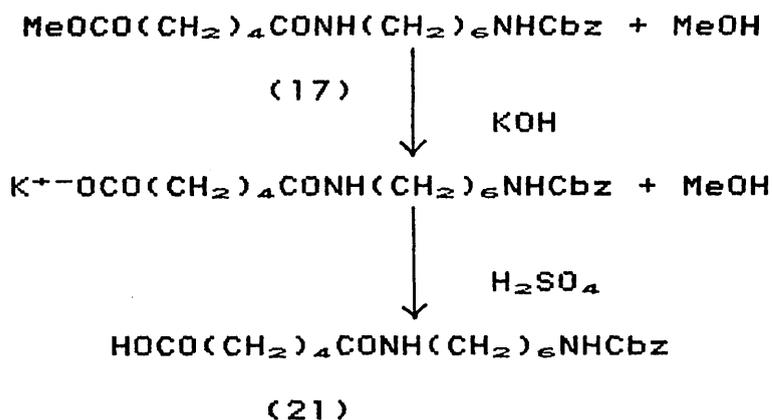
The saponification of carbobenzoxy methyl ester monomer (17) was then tried in aqueous conditions, again using potassium hydroxide. The results were disappointing giving a yield of only 20%. Using ammonium hydroxide as a base in aqueous conditions gave an improved yield, typically 52%. This yield was far too low to be of any real practical use. Although the unreacted starting material could easily be recovered and the saponification reaction repeated, this would be time consuming, and undesirable.



It was decided to investigate a combination of this reaction, which sets up an equilibrium, and the previous potassium hydroxide method, in order to shift the equilibrium to the right by formation of the potassium salt of the N-carbobenzoxy monomer (21). The free N-carbobenzoxy monomer (21) could subsequently be neutralized and the desired product, the N-carbobenzoxy monomer, crystallized out of solution using sulphuric acid.

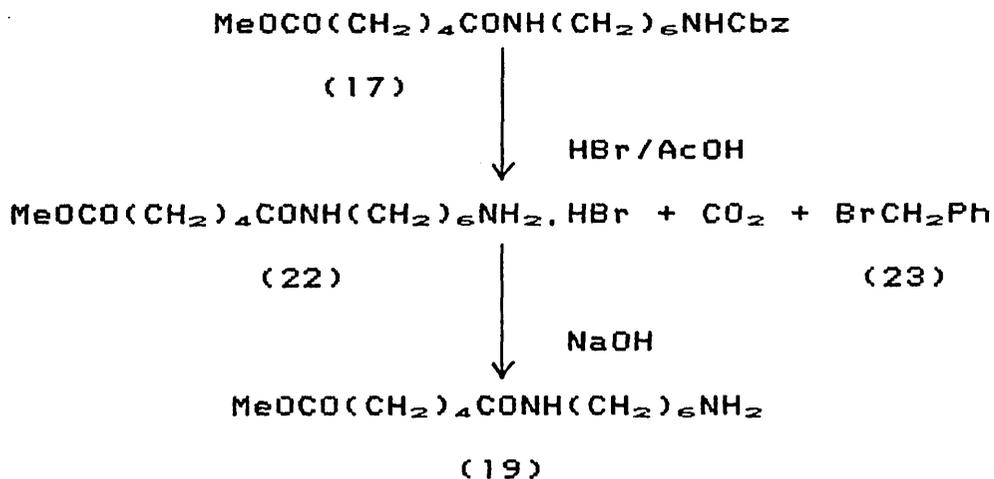


The yield was slightly improved, around 60%, compared to the ammonium hydroxide method but not sufficiently so to make the reaction practical in the long term. The method which finally proved successful was saponification using potassium hydroxide in dry methanol. The transesterification reaction was eliminated and the method gave pure N-carbobenzoxy monomer (21) with yields of up to 98%.



The selective decarbobenzoxylation of the bisprotected monomer (17) proved to be extremely difficult. The various methods under which the carbobenzoxy groups may be cleaved are stated²⁹ to be the use of hydrogen bromide in acetic acid, or heating in concentrated hydrochloric acid, or catalytic hydrogenation with palladium catalysts or sodium in liquid ammonia. Another more recent method involves the use of trimethylsilyl iodide^{30,51}, although this approach was not used at this stage as the relevant papers were not found until the next section of work had been started.

The use of hydrogen bromide in acetic acid was chosen as it is widely used in the literature concerning peptide synthesis³²⁻³⁶.



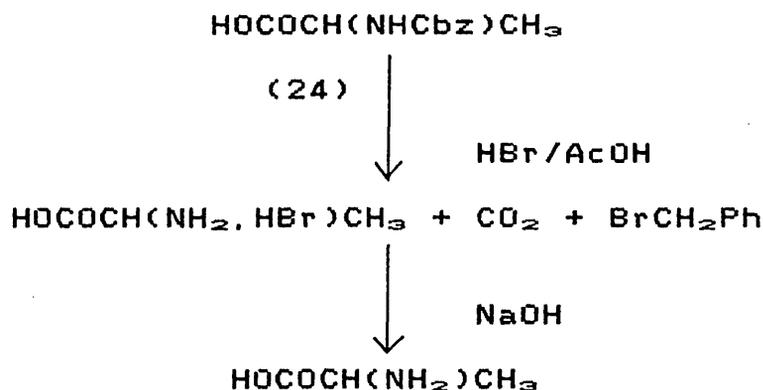
In general and for present purposes the reaction involves dissolving the N-carbobenzoxy methyl ester

monomer (17) in a minimum amount of a fresh, anhydrous solution of hydrogen bromide in glacial acetic acid usually at room temperature, although occasionally heating is required. The progress of the reaction can be followed by the evolution of carbon dioxide.

The hydrobromide product (22) is usually precipitated in crystalline form upon the addition of dry ether, which also dissolves the benzyl bromide side product (23). The reaction conditions need to be strictly maintained and monitored. Under anhydrous conditions amide groups are not cleaved³⁵ but in the presence of a small volume of water slow hydrolysis takes place³⁶. If the reaction time at room temperature exceeds an hour then transesterification between acetic acid and the ester protected group should not occur³⁵. If the reaction time exceeds an hour at 50°C then some transesterification is likely to be observed³⁴. This can usually be counteracted by the addition of a small volume of the corresponding alcohol.

The reaction on the protected monomer (17) was seen to be proceeding as carbon dioxide was evolved. Initially the reaction only yielded a thick, tarry oil which could not be identified as the free amine or its salt. Because of the failure of this standard (at least in peptide chemistry) reaction on the N-carbobenzoxy methyl

ester monomer (17) it was tried on N-carbobenzoxy alanine (24) in a model reaction. This was done in order to ensure that the hydrogen bromide/acetic acid solution was not substandard and that the conditions being used were suitable.

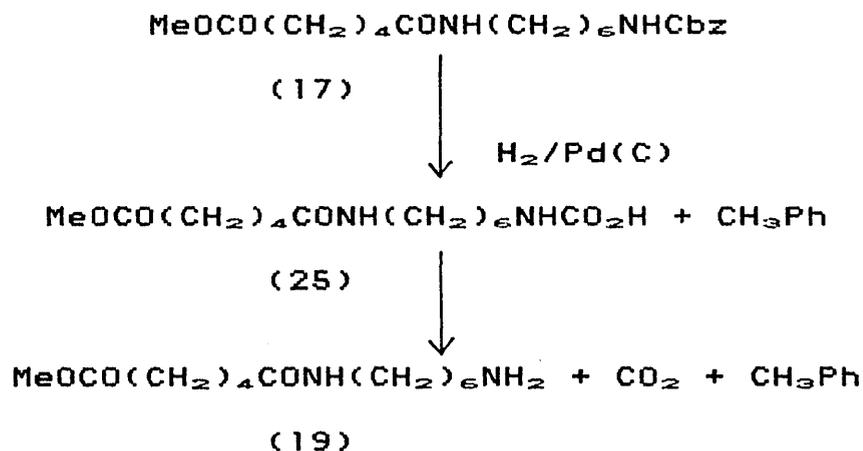


The results were excellent, with yields of around 85-90%, (comparable to literature values³²). When, however, the reaction was retried on the bisprotected monomer (17) the resulting product was still the oil. Attempts were made to isolate the hydrobromide salt of the amine (22) by repetitively dissolving the salt in dry methanol and precipitating from dry ether in several stages. The purity of this material was found to be high although the salt (22) was extremely hygroscopic and the yield was greatly decreased by the number of steps involved in the work-up. It was also difficult to crystallize the free amine (19) after neutralization with sodium hydroxide. For the monomer this was not seen as an approach worth pursuing, due to the problems with

isolation. With more work it was still hoped that this reaction would provide a standard approach to decarbobenzoylation at further stages. It is also envisaged that this step will become more simple with increasing chain length as solubility decreases, and separation occurs more or less automatically from the acetic acid medium.

Other conditions employed for the decarbobenzoylation of the bisprotected monomer (17) were catalytic hydrogenation^{38,39}, concentrated hydrochloric acid¹⁸ and trifluoroacetic acid (TFA)^{40,41}.

Catalytic hydrogenation is the oldest and most widely used method for the decarbobenzoylation of protected amines^{36,37}. It allows the removal of the carbobenzoyloxy group under mild conditions. It is presumed the reaction proceeds via the carbamic acid (25), forming toluene and carbon dioxide³⁷.



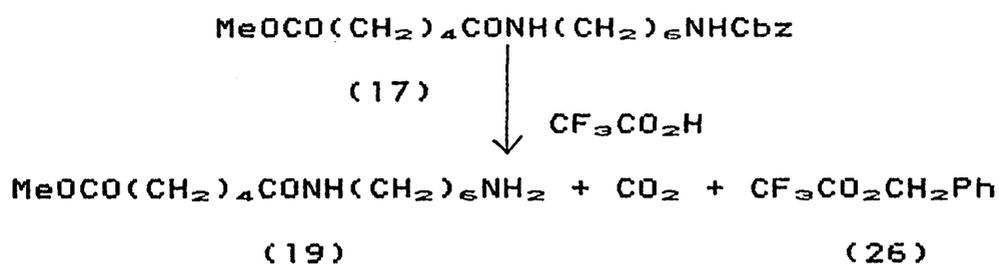
The catalyst used was palladium black (5% and 10% on carbon), and the solvent system was, initially, methanol. The progress of the reaction was to have been monitored by the escape of carbon dioxide gas. This was not observed so reaction times of between twelve hours and two days were tried. The method failed to yield anything other than starting material despite it's efficiency with simpler trial systems, such as the N-carbobenzoxy alanine (24).

The hydrogenolysis approach was modified by acidification of the solvent with glacial acetic acid in an attempt to facilitate the reduction³⁶. The reaction conditions were also modified by using platinum hexachloride as the catalyst. Both these adaptations also failed to achieve decarbobenzoylation of N-carbobenzoxy methyl ester monomer (17) to any detectable degree. It has been stated³⁷ that if hydrogenation is carried out in a closed system, as this was, care must be taken to remove the carbon dioxide formed, as this may lead to problems. Being unaware of this potential problem at the time no precautions were taken and this may explain the failure of the approach, although it was successful with the model reaction.

It was noted by Merrifield and Woolley⁴² that both catalytic hydrogenation and treatment with hydrogen

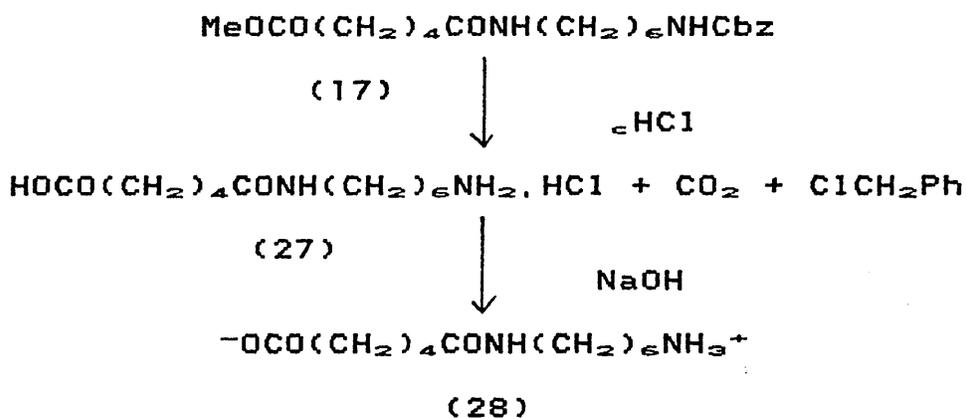
bromide in acetic acid failed in the decarbobenzoylation of a N-carbobenzoxy ethyl ester pentapeptide. Their solution was to use the, then novel, approach of using concentrated hydrochloric acid at 37°C for deprotection. This resulted in cleavage of both the carbobenzoxy group and the ester, achieving their aim since they were attempting bis-deprotection. This method was, therefore, to be a last resort for our work, as the selective removal of the amine protecting group was still hoped for.

The trifluoroacetic acid method^{40,41} of N-decarbobenzoylation again proceeds with the evolution of carbon dioxide, and the formation of the benzyl ester of trifluoroacetic acid³⁷ (26). As with the previous two approaches this method yielded mainly starting material and was abandoned.



Sodium in liquid ammonia was not used as it is known to be non-selective between ester and carbobenzoxy protecting groups and leads to side reactions with the ester²⁹.

Although the use of concentrated hydrochloric acid^{18,37} was expected to give the bis-deprotected product it became the only available option as far as efficient methods with large scale potential were concerned. The reaction conditions are quite severe with temperatures of 40°C being maintained for three hours. This led to fears of the amide bond being broken as the use of this method has a tendency to cleave peptide bonds²⁹. No evidence for such cleavage was observed and in other systems^{42, 43} the use of similar approaches led to no appreciable cleavage of peptide bonds. The residue obtained from the evaporation of the hydrochloric acid solution was dissolved in a minimum amount of acetic acid. The hydrochloride (27) was first obtained as an oil after the initial precipitation by added dry ether. This oil was dissolved in water and the solution extracted with ether and then neutralized with sodium hydroxide.



The yields of unprotected monomer zwitterion (28) using this method was excellent at 96%.

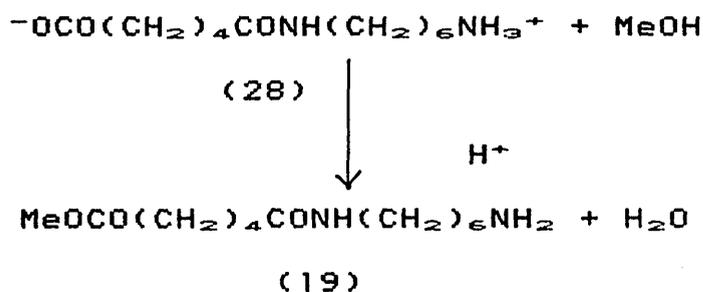
This obviously gave rise to a new problem, that of the subsequent reprotection of the carboxylic acid. This would be a far from ideal situation and a method for selective deprotection was still needed.

There are a number of protecting groups available for the carboxyl group. These include the formation of amides^{44,45} or hydrazides⁴⁴. The use of amides, however, is limited as they can only be cleaved with the preservation of the peptide bond in exceptional cases and the hydrazine group is prone to acylation during peptide synthesis⁴⁴. This can be prevented by blocking the hydrazide function with an amino-protecting group. However as the hydrazide bond cannot be cleaved with the formation of the free acid, this type of protection is suitable only where the azide method of chain extension is proposed. Since in this work the free amino acid is required at each stage, the hydrazide method could not be used.

Certainly the usual protecting group for carboxyl functions is the ester moiety. There are several esters which are regularly used for this purpose, including the simple methyl and ethyl esters, the *tert*-butyl esters,

benzyl esters and some modified benzyl esters⁴⁴. The *tert*-butyl ester group has the advantage that it can be removed under far less vigorous conditions than are used with the corresponding methyl ester. As cleavage of the peptide bond and the carbobenzoxy group does not occur under the conditions for removal of a methyl ester this use of milder conditions is not a prerequisite. The benzyl ester was one of the first protecting groups for carboxylic acids but it offers no real advantage over methyl esters.

It was decided to concentrate on the methyl ester as no real advantage could be gained using other groups. Also the deprotection reaction had already been successful. Several standard methods^{44,46-49} of introducing the methyl ester were investigated. These included the use of acid catalysis, acyl chlorides, dicyclohexylcarbodiimide^{46,47,48} and isocyanides^{46,48}. Carboxylic acids react rapidly with alcohols in the presence of catalytic amounts of mineral acids to yield esters. This reaction has a relatively low equilibrium constant so the reaction needs to be driven to the right by increasing the relative concentration of one of the reactants (Le Châtelier's principle). Here, for practical reasons, the alcohol would have to be in excess.



The C-methyl ester monomer (19) is initially obtained as the ammonium salt. The re-esterification of the unprotected monomer proved less than satisfactory. The reaction times were increased to eighteen hours under reflux but a yield of only 39% after purification was considered too low.

An acid catalysed esterification was also attempted using thionyl chloride in methanol⁴⁴. Here the excess of methanol can be lower as water is not formed during the reaction. The alcohol is mixed with 1.1 moles of thionyl chloride at -10°C , giving a chlorosulphinic acid ester as the esterifying reagent.

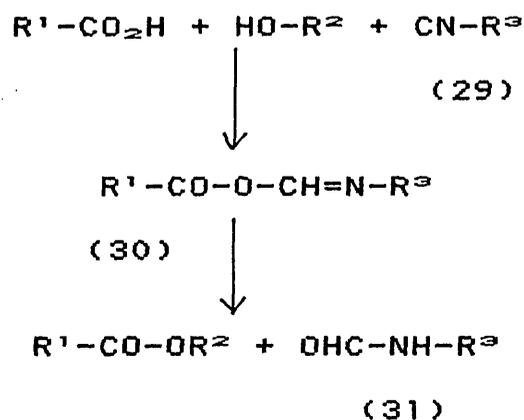


The esterification product is again initially obtained as the ammonium salt. This method, however, proved to be slightly worse than using hydrochloric acid as the catalyst, giving yields of around 36-38%.

Acyl chlorides could not be used in the presence of the free amine as the formation of the amides and the amine hydrochloride would occur. This is, in effect, re-protection of the amine by amide formation.

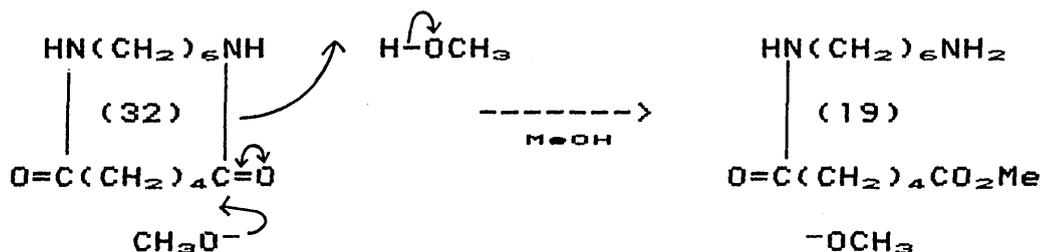
The reaction is also not viable using dicyclohexylcarbodiimide in the presence of a free amine as the coupling side reaction is a probability.

Isocyanides are useful dehydrating reagents for the preparation of esters from carboxylic acids and alcohols under mild conditions. The typical conditions for the reactions are 0-20°C with no catalysis by strong acids⁴⁸. The reaction is thought to proceed via the α -adduct (30) of the acid component. In the conversion of the isocyanide (29) to the formamide (31) the water produced is taken up providing the driving force to the reaction. For this reason additional moisture must be rigorously excluded.



The end of the reaction is detected by the disappearance of the isocyanide (29). The reaction time is given⁴⁸ as between three to nine days with typical yields of 40%. In our case, after fourteen days the reaction of unprotected monomer (28) with methanol and *t*-butyl isocyanide (29) gave no C-methyl ester monomer (19). It is possible that the methanol used was not as dry as it should have been and the water present had reacted with the isocyanide (29) despite precautions. The reaction may have proved to be of some use had a better standard of totally anhydrous methanol been available.

One final method, although eventually unsuccessful, is worthy of note. Samples of impure cyclic monomer were supplied by ICI from their processing plants. This material was purified by recrystallization from methanol and ethyl acetate giving pure, isolated nylon-6.6 cyclic monomer (32). This was verified by mass spectrometry and infrared spectroscopy. Various attempts were made at ring opening this material using sodium methoxide.



The reaction was monitored by infrared spectroscopy as a simple and reliable thin layer chromatography (t.l.c.) system could not be developed. On ring opening there would have been a reduction in the amide carbonyl band at 1650cm^{-1} and a corresponding increase in the ester carbonyl band ($1700\text{-}1750\text{cm}^{-1}$). This was not observed despite many variations in conditions. The result again underlines the stability of the cyclic monomer in the absence of acidic catalyst.

If this could have been made to work it would not only provide a massive short cut to the C-methyl ester monomer (19), but would turn a waste material into a product that could have been repolymerized under control to provide oligomers as required.

It was hoped to try further work on this ring opening method but due to extreme problems in the preparation of the oligomers time could not be spared.

2.1.3. NYLON-6.6 OLIGOMERS.

From the previous work the materials available were the protected N-carbobenzoxy monomer (21), the doubly protected N-carbobenzoxy C-methyl ester monomer (17) and the unprotected monomer (27). Without a suitable method for selective N-decarbobenzoxylation avoiding concomitant de-esterification, the route to the integer oligomers could not be followed satisfactorily. This route could only be achieved at present if the bis-deprotection route followed by re-esterification to give the C-protected products, could be improved. The results of this approach when tried on the monomer were disappointing and no method of improvement could be envisaged. It was hoped, however, that the use of hydrogen bromide in acetic acid may yield mono-C-protected products due to the reduced solubility of the longer chain molecules though this would not help with the initial step from monomer to dimer.

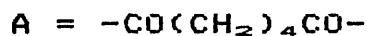
For this reason it was decided to start work on the non-integer oligomers. Here the need for selective deprotection is no longer a factor as chain-growth products would have identical end groups. Methods for de-esterification, i.e. saponification, and N-decarbobenzoxylation, using concentrated hydrochloric acid at 40°C, had already been satisfactorily achieved

at high yields for the monomer. It was expected that these good results could be maintained with the non-integer oligomers.

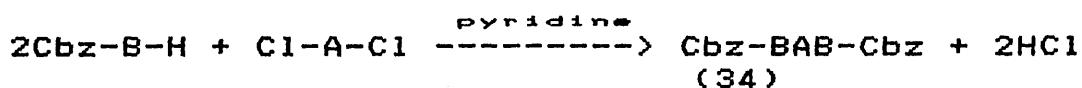
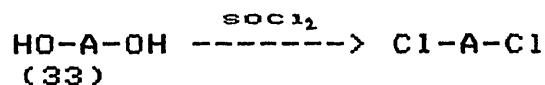
The method previously used for coupling mono-N-carbobenzoxyhexamethylenediamine (9) and methyl hydrogen adipate (15) was the non-aqueous Schotten-Baumann reaction. This gave yields of around 60% which, while not entirely satisfactory, would suffice. The main problem was that the method is limited, in terms of safety, to very small quantities due to the exothermic nature of the reaction. This would require numerous batches of each oligomer to be prepared to provide sufficient material for consecutive reactions.

The non-aqueous Schotten-Baumann method was used on both hexamethylenediamine (6) reacted with methyl hydrogen adipate (15), and also on adipic acid (33) reacted with mono-N-carbobenzoxyhexamethylenediamine (9). This approach produced the two non-integer oligomers with a degree of polymerization (D. O. P.) of 1.5. These reactions produced the bis-N-carbobenzoxy compound (34) and the bis-C-ester (35) respectively. The GPC data showed both of these to be pure products although the yields for the reactions were considerably lower than was expected with only around 39-42% for the bis-N-

carbobenzoxy product (34) and only 32-34% for the bis-C-ester product (35).



Cbz-BAB-Cbz (34)



MeO-ABA-OMe (35)



These products were deprotected by the same methods used for the bis-protected monomer (20), i.e. decarbobenzoylation using concentrated hydrochloric acid at 40°C and saponification using potassium hydroxide in dry methanol under reflux. These reactions gave high yields, of the bis-amine (36) and bis-carboxylic acid (37) respectively, in excess of 95% after neutralization.

It was possible to achieve a D.O.P. of 2.5 for both the bis-N-carbobenzoxy (38) and the bis-C-ester (39) non-integer oligomers before it was found that the heat evolved from the coupling reaction increased as the chain length was increased, effectively ruling this method out as a viable route to oligomers of any worthwhile degree of polymerization. An alternative method was required bearing in mind that such methods as the Schotten-Baumann method originally proposed had failed, as had the use of DCC. The answer to this problem emerged after investigating and adapting a method based on a mixed anhydride coupling method⁵⁰.

The mixed anhydride of a carboxylic acid with an alkyl acid carbonate (HOCOOR) is an efficient reagent for the acylation of amines. In the standard procedure an amino-acid is protected as its N-carbobenzoxy (Cbz) derivative which is treated in an inert solvent (eg. tetrahydrofuran, THF) with enough base (eg. triethylamine, TEA) to form the salt, and subsequently with an alkyl chloroformate. The mixed anhydride produced need not be isolated, and the addition of an amino-acid (usually as an ester) forms the N-substituted peptide ester, usually in excellent yield with the release of carbon dioxide.

It was hoped that this method would offer higher yields and cleaner reaction products with larger scale reactions as the localized heat produced would be far less severe than for the pyridine method and partial charring and danger would be eliminated. Three acid chloroformates were used to investigate this reaction for the synthesis of bis-C-ester non-integer oligomers (D. O. P. = 1.5). Benzyl chloroformate gave extremely poor yields, less than 10%, and the product was found to be very impure. Ethyl chloroformate gave higher yields of around 60% but with the production of the disproportionation product of the mixed anhydride.

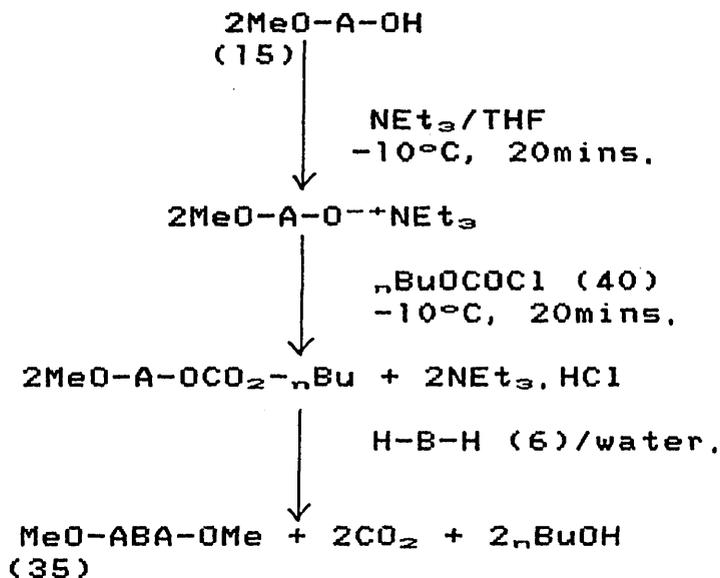


This side reaction was limited by the use of a lower temperature, -10°C rather than -5°C , and reduced reaction times for the formation of the mixed anhydride. It was, however, still not reduced sufficiently to make the method attractive as this contaminant proved very difficult to remove. The final solution was to use n-butyl chloroformate (40). Here the side product was virtually eliminated by carefully controlling reaction conditions. The reaction temperature was again held at -10°C for the first two stages of the reaction. The reaction time was optimized at twenty minutes allowing

near completion of the reaction with only minimal amounts of the disproportionation product.

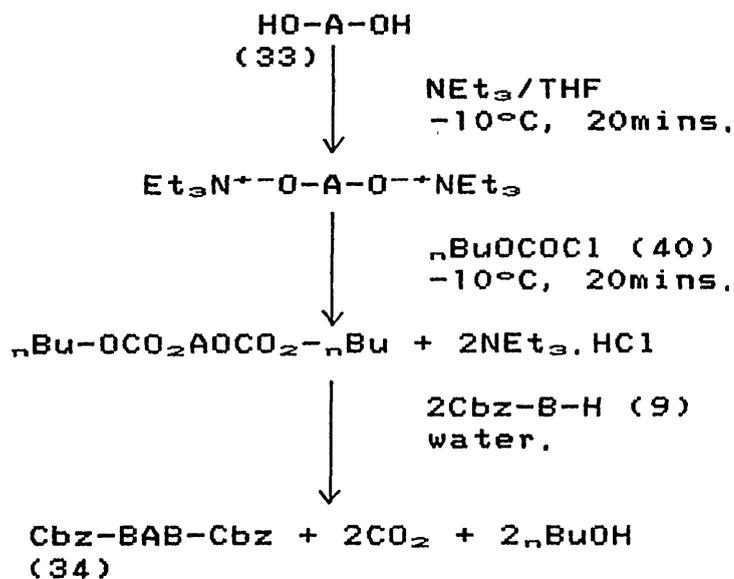
The work up of this reaction was simply to filter off the white solid produced and to recrystallize it from the appropriate solvent (see table below). The yield was ca. 90% and the product (35) appeared extremely pure by analysis with GPC.

MeOABAOMe (35)



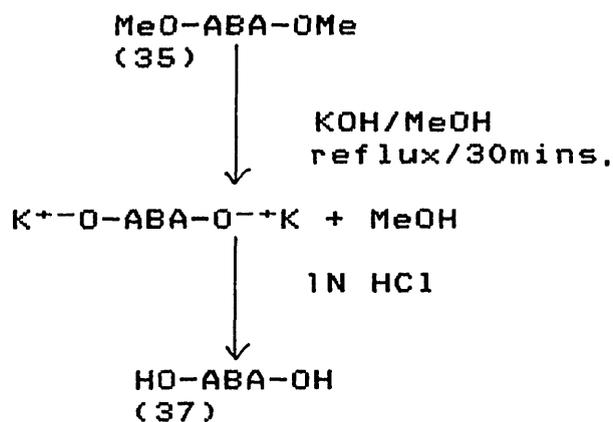
The reaction worked as well when applied to the preparation of the bis-N-carbobenzoxy non-integer oligomer, D.O.P.=1.5 (34). The yield was around 87-90% and again GPC showed that the product was pure.

Cbz-BAB-Cbz (34)



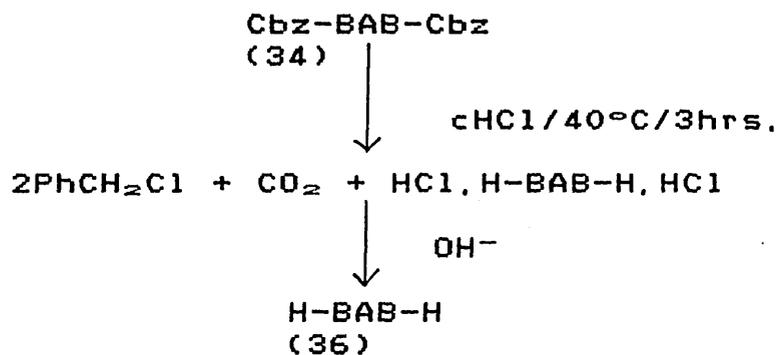
The de-esterification was performed by using potassium hydroxide in dry methanol to give the bis-C-carboxylic acid (37). Once optimised this method gave a high yield (typically in the region of 95%+), a clean product, and was perfected into a very simple technique.

De-esterification



For decarbobenzoylation to the diamine (36) the three methods used were essentially as before. First was catalytic hydrogenation, but again little success was achieved with these materials with low yields and high levels of impurity. Hydrogen bromide in glacial acetic acid again gave low yields and the procedures were extremely 'tricky' involving several recrystallizations. Concentrated hydrochloric acid at 40°C provided far higher yields, an easier work up and a far cleaner product. This reaction also has the considerable advantage that it can be easily monitored by the release of CO₂ during the reaction.

Decarbobenzoylation



The coupling reaction used here, along with the deprotection reactions, have the advantage that they do not require the materials to be in solution but work equally well if a suspension is used. This implies that the scheme should be of equal value as the D.O.P.

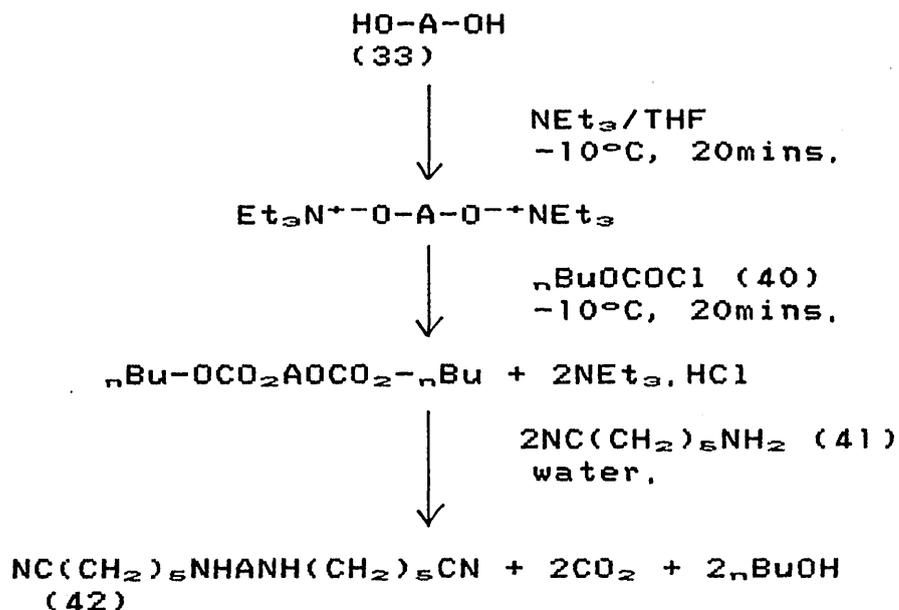
increases beyond 1.5 although careful monitoring is essential. It should also be noted that the deprotected products of both sets of non-integer oligomers could be recrystallized in the same solvents as their protected counterparts. Although this could be expected to present problems in removing unreacted material in the purification of the deprotected derivatives of non-integer oligomers, earlier stages in these reactions are essentially self-purifying.

Another approach, attempted in order to attain the amine end groups, was the use of nitrile groups in place of protected amines (the nitrile group being in effect a latent amine by reduction). This was investigated using 6-aminocapronitrile (41) in a mixed anhydride reaction, in place of mono-protected hexamethylene diamine (9). This reaction was used to produce molecules to a D.O.P. of 2.5 giving the bis-nitrile product as shown below.

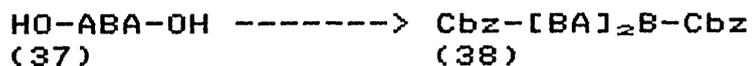
Attempts to reduce the nitrile (42) back to the amine (36) included catalytic hydrogenation¹⁹, reduction using lithium aluminium hydride⁵¹ and sodium and ethanol⁵². The results of all these attempts were unsuccessful and the nitrile approach was abandoned. Clearly reactions that work with small molecules, or with peptides (more akin to nylon-2 and nylon-6 than to nylon-6.6) are not necessarily amenable to nylon-6.6 segments. This has

been a major, and unforeseen difficulty, throughout the project.

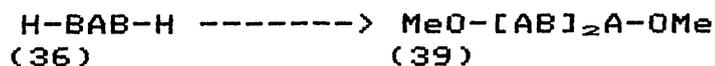
BIS NITRILE / D.O.P. 1.5



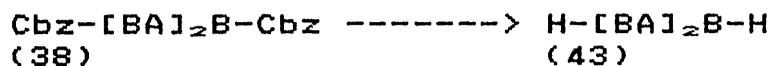
Continuing with the preparation of non-integer oligomers using mixed anhydrides, to a D.O.P. of 2.5, gave reasonably high yields, ca. 77% for the conversion of the bis-carboxylic acid D.O.P. = 1.5 (37) to the bis-N-carbobenzoxy oligomer D.O.P. = 2.5 (38);



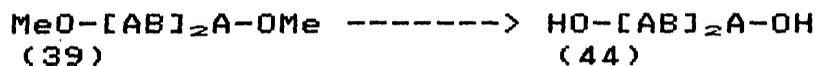
and ca. 70% for the conversion of the corresponding diamine (36) to the bis-C-ester D.O.P. = 2.5 (39);



The yield for the decarbobenzoylation reaction, on Cbz-[BA]₂B-Cbz (38) to the corresponding diamine (43), also dropped though only to around 80%.



The de-esterification of MeO-[AB]₂A-OMe to HO-[AB]₂A-OH (44) by saponification gave a very pure product in a high yield of 97%



The scheme was taken to a D.O.P. of 3.5 for both the amine end group, and acid end group oligomers. Again there was a decrease in the yield of the protected oligomers. The bis-N-carbobenzoxy oligomer was produced in a yield of around 60% while the yield for the bis-C-ester oligomer was slightly better at around 64%. This decrease in yield was disappointing as although the material was of higher quality it was now approaching the levels obtainable by the non-aqueous Schotten-Baumann method. There was a further decrease in the yield of the decarbobenzoylation reaction, but the saponification reaction still gave yields in the region of 95%+.

As previously mentioned the protected non-integer oligomers and their unprotected counterparts could be successfully recrystallized in the same solvents. A table is given below.

Table 2.2. Recrystallization Solvents for Non-Integer Oligomers

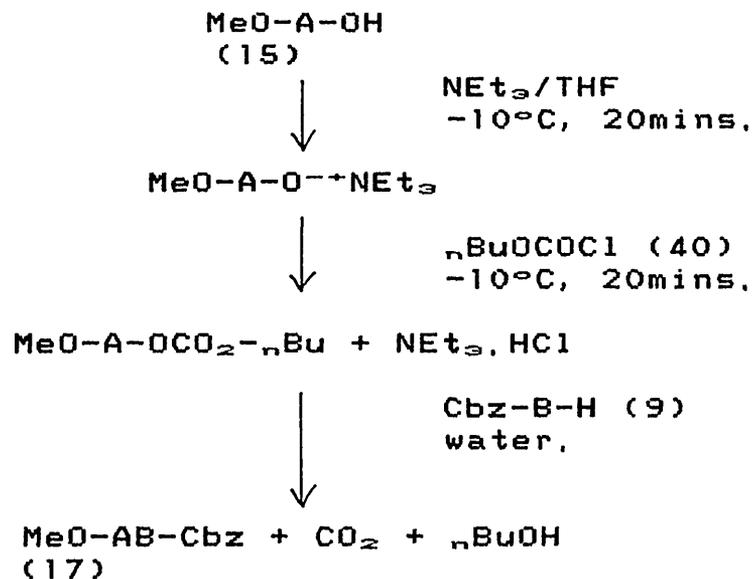
<u>Product</u>	<u>Solvent</u>
MeO-ABA-OMe	Ethanol
Cbz-BAB-Cbz	Ethanol
MeO-[AB] ₂ A-OMe	Water
Cbz-[BA] ₂ B-Cbz	Water
MeO-[AB] ₃ A-OMe	DMF
Cbz-[BA] ₃ B-Cbz	DMF

The reason why progression was halted at this point was the need to work on integer oligomers. There was hope of success in the use of hydrogen bromide in acetic acid to produce the C-protected oligomers and by using the mixed anhydride coupling it was expected that high D.O.P. values should be attainable in the integer oligomer series.

Work on the integer oligomers using the mixed anhydride method started with the N-carbobenzoxy methyl ester monomer (17) as the non-aqueous Schotten-Baumann method was limited in the quantity that could be made at any

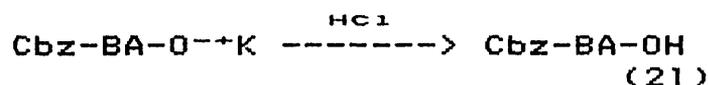
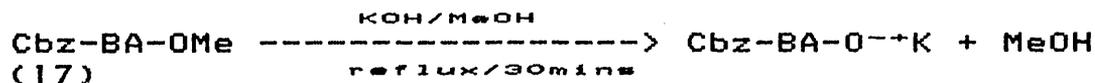
one time. The product (17) appeared by tlc to be of higher purity than that produced using the non-aqueous Schotten-Baumann method.

MeO-AB-Cbz (17)

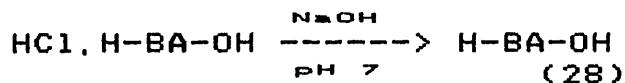
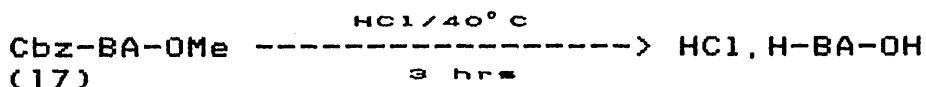


The yield of this reaction was around 85%, again an improvement on the previous method. The monomeric products obtained by the use of the two standard deprotection reactions were Cbz-BA-OH (21) and H-BA-OH (28).

DE-ESTERIFICATION



BIS-DEPROTECTION

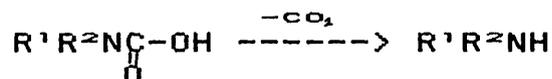
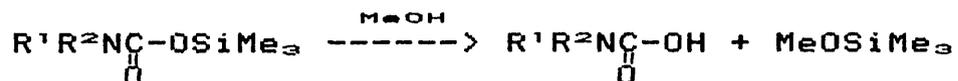
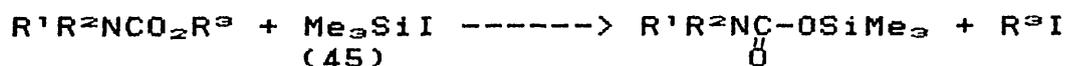


These reactions again gave high yields and clean products. The decarbobenzoylation reaction gave 96% of the theoretical yield and the saponification reaction gave yields of up to 94%.

Attempts at preparation of the C-methyl ester monomer, HBAOMe, (19) using hydrogen bromide in acetic acid again failed despite the higher purity of the carbobenzoxy methyl ester monomer (17). It had been hoped that this better quality material may lead to selective decarbobenzoylation so that coupling to produce molecular doubling products could be undertaken on a large scale to bring the synthetic programme to a useful, benchmark position by making the tetramer and, eventually the octamer.

Along with the failure of this method the catalytic hydrogenation method also failed. As previously mentioned a new approach was attempted, that of using trimethylsilyl iodide^{9,50} (45). Developed as a method for N-decarbobenzoylation in 1978 it is claimed that it

"affords high yields of the corresponding amines". The reaction involves the hydrolysis of the trimethylsilyl carbamate.



As with many of the other standard reactions (i.e. reactions developed for smaller, simpler substrates) the material obtained in our particular case was starting material. With this method failing there appeared to be no option but to attempt the doubling reactions with the materials available. These being;

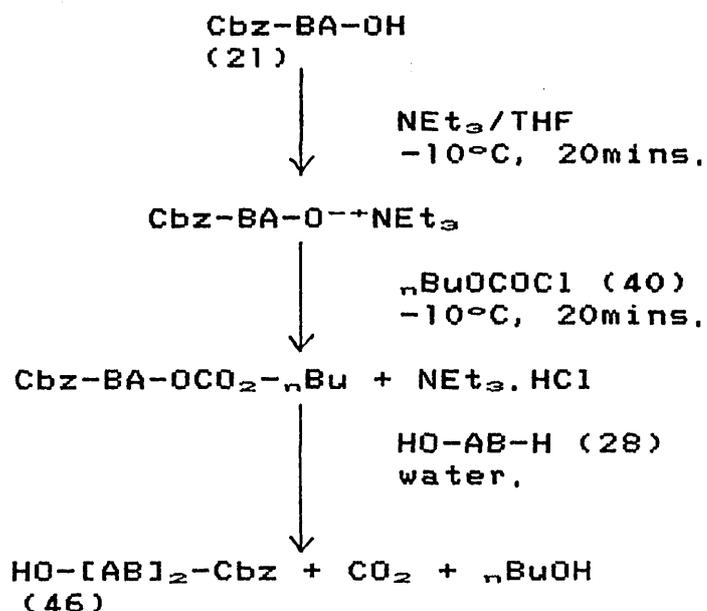
- i) Cbz-BA-OMe, (17);
- ii) Cbz-BA-OH, (21);
- iii) H-BA-OH, (28).

Using these products without the C-methyl ester monomer (19) obviously leaves the coupling reaction open to over reaction leading to, at best, non-integer oligomers and, at worst, polymeric material due to the presence of two unprotected carboxylic acid groups. It was, however, hoped that with the use of the mixed anhydride method it would be possible to avoid this since the acid component of the N-carbobenzoxy monomer (21) is activated prior to

the addition of unprotected monomer (28). This should lead to preferential reaction on the carboxyl group of the carbobenzoxy protected monomer (21).

The reaction was initially attempted on the unprotected monomer, HO[AB]H, (28) with the N-carbobenzoxy monomer, Cbz[BA]OH, (21). The reaction conditions were kept the same as with the non-integer oligomers, with the reaction being maintained at -10°C in order to prevent the disproportionation reaction occurring on the mixed anhydride. The white solid product was purified by recrystallization from methanol with a small amount of water. The yields initially obtainable using this method were not as high as expected (around 60-65%).

N-CARBOBENZOXY DIMER (46)

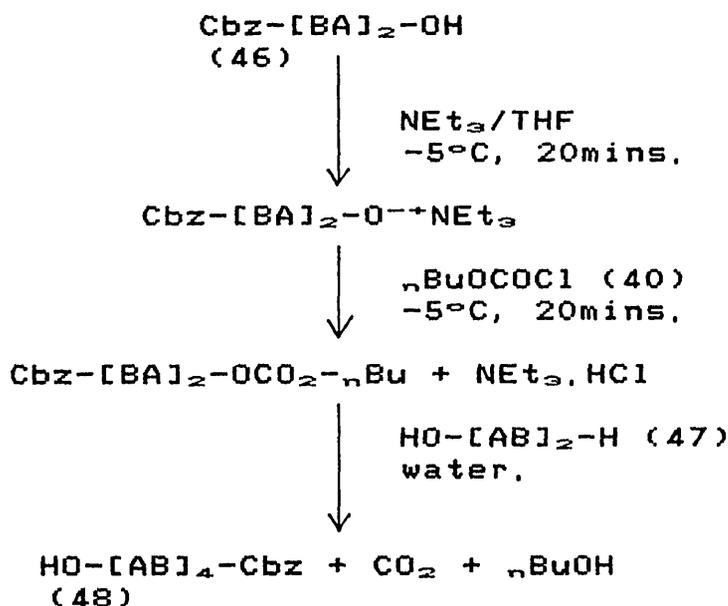


By increasing the reaction temperature to -5°C the yields were slightly improved, reaching about 70-73%. The yields was not significantly improved by any further increase in temperature, so it was thought best to continue at -5°C in order to avoid the possibility of disproportionation by the mixed anhydride. The purity of this material, N-carbobenzoxy dimer (46) was confirmed by G.P.C. and by $^1\text{H NMR}$. Although in the early trials of the reaction very small quantities of higher molecular weight material were detected, these were later removed, quite simply, by repeated recrystallization of the product. This simple separation would undoubtedly not have been possible had both the D.O.P. and quantity of the contaminant oligomer not been so low.

The N-carbobenzoxy dimer (46) was successfully deprotected by the use of concentrated hydrochloric acid in yields of around 90%.

This provided the unprotected dimer (47) to be reacted with the N-carbobenzoxy dimer (46) to give N-carbobenzoxy tetramer (48). The use of a selective method of decarbobenzoylation was not required as, obviously, no ester group was present.

N-CARBOBENZOXY TETRAMER (48)



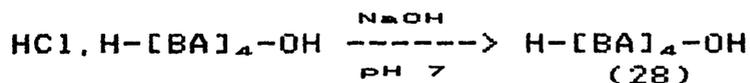
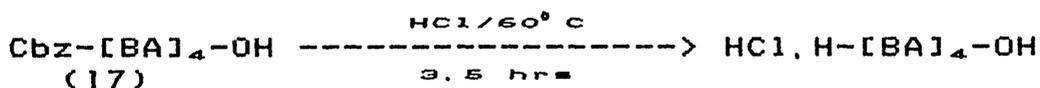
Again a white solid precipitate was recovered from the reaction mixture. Analysis by G.P.C. and IR showed that at the first attempt this reaction had hardly occurred and that the majority of the white solid was of dimeric size. The melting point was found to be higher, at 219-220°C, than that of N-carbobenzoxy dimer (46) with a value of 177°C. The NMR data for this material matched that for the N-carbobenzoxy dimer (46). The IR showed an additional carbonyl group. Identical spectral data and the higher melting point were seen previously in the preparation of mono-N-carbobenzoxyhexamethylenediamine (9). Here the conclusion was that the free amine had reacted with atmospheric carbon dioxide to give the carbamide. As before, this could not be confirmed but appeared to be the most likely explanation. The point at

which these "carbamides" were formed is also unknown but as in future stages this reaction became a minor side reaction it was deemed relatively unimportant and could be dealt with by recrystallization.

With no change to the conditions the reaction was repeated successfully but with very low yields (in the order of 40-45%). This was later improved to around 60%, by a slight increase in the reaction time to 30 minutes for each of the first two stages. But further increases in reaction time or temperature had little to no effect on the yield.

The N-carbobenzoxy tetramer was deprotected using concentrated hydrochloric acid.

DEPROTECTION OF N-CARBOBENZOXY TETRAMER

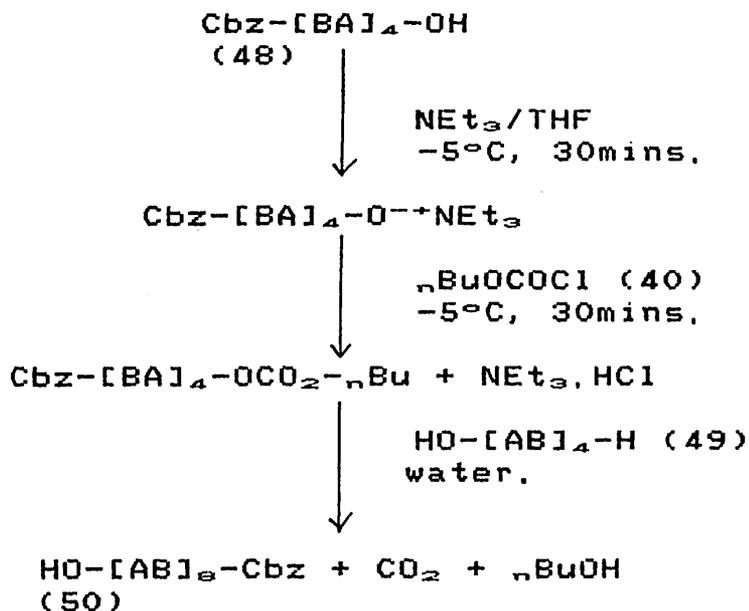


The yield was disappointing (around 57%) and also the product was found to contain a fairly high proportion of the carbobenzoxy protected tetramer. This could be seen by IR and NMR. It was also later clarified by GPC which did however show that the vast majority of the material was tetrameric with small amounts of dimeric and

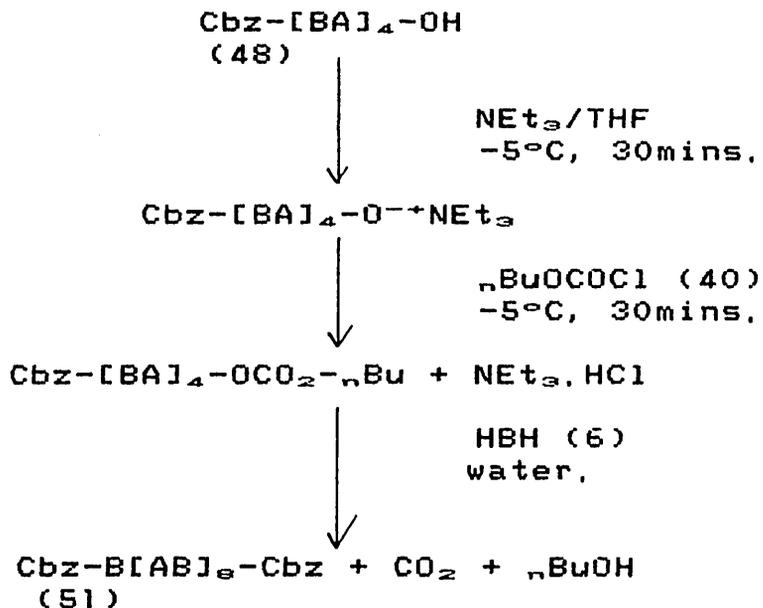
octameric material. This situation was improved by increasing the temperature to 60°C and the reaction time to three and a half hours. The N-carbobenzoxy tetramer and the unprotected tetramer were then combined using the mixed anhydride method to yield the N-carbobenzoxy octamer.

The N-carbobenzoxy tetramer was also used to prepare the non-integer oligomer with a D.O.P. of eight and a half. The conditions used were as with the corresponding integer oligomer, HO[AB]₈Cbz, i.e. using a temperature of -5°C and a reaction time of thirty minutes.

N-CARBOBENZOXY OCTAMER (50)



BIS-CARBOBENZOXY OLIGOMER D.O.P. 8.5 (51)



The yield of this reaction was 36% and for the N-carbobenzoxy octamer a yield of 43% was obtained. GPC data for the integer mono-carbobenzoxy octamer showed the product to still be mainly tetrameric with only small amounts of octamer. The GPC data for the non-integer bis-carbobenzoxy oligomer with D.O.P. = 8.5 shows a slightly more encouraging picture, around half of the tetrameric material being converted to octameric product. This indicates that the reaction scheme is still viable at these higher degrees of polymerization and could probably be taken on to even higher degrees.

2.2. ANALYSIS & CHARACTERIZATION.

This project centred on the synthesis of mono-disperse oligomers of nylon-6.6 (with an eye on nylon-6 also) especially from the viewpoint of feasibility. Could the rather labile oligomers be isolated pure and were earlier claims justified in the light of modern analytical investigations? As such, determining the chain length and purity of each material prepared was of considerable importance. The techniques which were of most importance in achieving this were infrared spectroscopy (IR), proton nuclear magnetic resonance (¹H NMR), gel permeation chromatography (GPC) and mass spectrometry. Mass spectrometry was however only applied to the shorter oligomers due to instrumental restrictions. This section is primarily concerned with the application of these techniques. The oligomers, and the intermediates en route to them, were difficult to handle, of poor solubility and hydrolytically unstable. Rapid spectroscopic analysis was of critical importance during this project.

In addition to determining purity and chain-length, accurate characterization of a range of nylon-6.6 oligomers will permit a better understanding of the morphology of the polymer. As previously stated several techniques have been used in this type of

characterization. These include, in addition to those mentioned above, F.T.I.R. spectroscopy, differential scanning calorimetry (DSC), X-ray diffraction, and neutron diffraction. Although these approaches played little or no part in this study they are worthy of note as they would all probably form the basis of any future studies of chain-folding in the nylon-6.6 oligomers.

2.2.1. INFRARED SPECTROSCOPY.

In attempting to characterize polymeric materials recourse will inevitably be made to some form of vibrational spectroscopy. Indeed the crucial role of infrared spectroscopy in probing for chain-folding has already been mentioned (section 1.3.) and measurements on our oligomers have been made.

The infrared region of the spectrum encompasses radiation within wavenumbers ranging from about 12,000 to 10cm^{-1} . This range is, for reasons of instrumentation, subdivided into near, middle and far infrared. The majority of analytical applications are confined to a portion of the middle region extending from 4,000 to 670cm^{-1} .

Infrared spectroscopy measures the absorption of electromagnetic radiation in the middle infrared region

resulting in changes in the vibrational energy of the molecule. A molecule can only absorb energy if there is a net change in the dipole moment during a particular vibration, a condition fulfilled by virtually all polyatomic molecules.

The most important use of infrared spectroscopy is in the identification of organic compounds as their spectra are often complex providing numerous maxima and minima for comparison purposes. The infrared spectrum of an organic compound represents one of its unique properties essentially giving it a "fingerprint".

The macromolecules produced from the oligamides show four strong bands in the range of $3350-2850\text{cm}^{-1}$. The strongest band, at 3300cm^{-1} , is the NH- stretching vibration and is attributed to the trans arrangement of the amide group¹⁷.

The absorption bands at 2950 and 2850cm^{-1} are the result of asymmetric $\text{C}_{\text{sp}^3}\text{-H}$ stretching vibration. The main differences in spectra of the lower oligomers compared to that of the polyamide are the displacement of the amide carbonyl stretching band from 1720 to 1640cm^{-1} and the appearance of a further strong band at 1540cm^{-1} . The interpretation of this latter band, recently marked as the amide II band, is, however, still not clear. The

displacement of the amide carbonyl band is usually explained by the occurrence of hydrogen bonding. According to C.G. Cannon⁵³, however, the NH group is acting as neither a proton donor or acceptor for hydrogen "bridging" bonds, and the peptide group associates due to dipole forces.

The oligomers also displayed the following additional bands;

<u>Wavenumber/cm⁻¹</u>	<u>Assignment</u>
1470	CH ₂ deformation
1420	CH ₂ deformation
1280	
1205	
740-720	-(CH ₂) ₄ - rocking

The main uses of IR spectroscopy have been in the rapid identification of end groups, and to give an indication of D.O.P. during the synthetic programme. Both of these applications require a close study of the bands in the carbonyl stretching region (1870-1630cm⁻¹). Since IR became a very valuable technique in these studies, relevant spectral diagnostics are discussed in some detail and illustrative spectra are shown.

Four carbonyl bands are studied; those due to the amide link, the ester protecting group, the free carboxylic acid and the carbobenzoxy protecting group, as shown in the table;

Table. Stretching Bands of C=O Groups

<u>C=O band</u>	<u>Wave-number/cm⁻¹</u>
Amide	1640
Carboxylic Acid	1695
Ester	1735
Carbобензоxy	1690

In protection and deprotection reactions the results are instantly detectable by displacement of the carbonyl band for esterification and de-esterification, and the appearance or removal of the carbonyl band for the amine protection and deprotection.

The non-integer oligomers can be simply categorized as the bis-C-ester, dicarboxylic acid, diamine or the bis-N-carbобензоxy compounds. Similarly the integer oligomers can be categorized as the carbобензоxy-ester, carbобензоxy-carboxylic acid, ester-amine or the amino-acid variation. Each can be easily distinguished due to the appearance of absorption bands corresponding to the functional groups present. Throughout, allowances were made for IR absorption within one homologous series for

the observed decrease in concentration of the end groups.

The diesters produce the band at 1735cm^{-1} due to the carbonyl stretching vibration in accordance with saturated esters. The further stretching band of the ester C-O-C single bonding is at 1185cm^{-1} . The dicarboxylic acids exhibit the expected carbonyl band measured at 1695cm^{-1} . In addition there is the broad band associated with the O-H stretch of a carboxylic acid ranging across $3300\text{-}2500\text{cm}^{-1}$.

The NH and NH_2 groups of the diamines can be detected via one or two bands in the region of 3300cm^{-1} . However these bands, which are in the same region of absorption as OH groups, can become complicated due to any residual moisture in the sample or KBr windows, or by displacement due to the "bridging bonds". The absence of further bands to indicate other functionality demonstrates the presence of the diamine. The dicarbobenzoxy oligomer is detectable by the presence of the carbonyl stretching band at 1690cm^{-1} and the weak $\text{C}_{\text{sp}^2}\text{-H}$ vibration at 3050cm^{-1} .

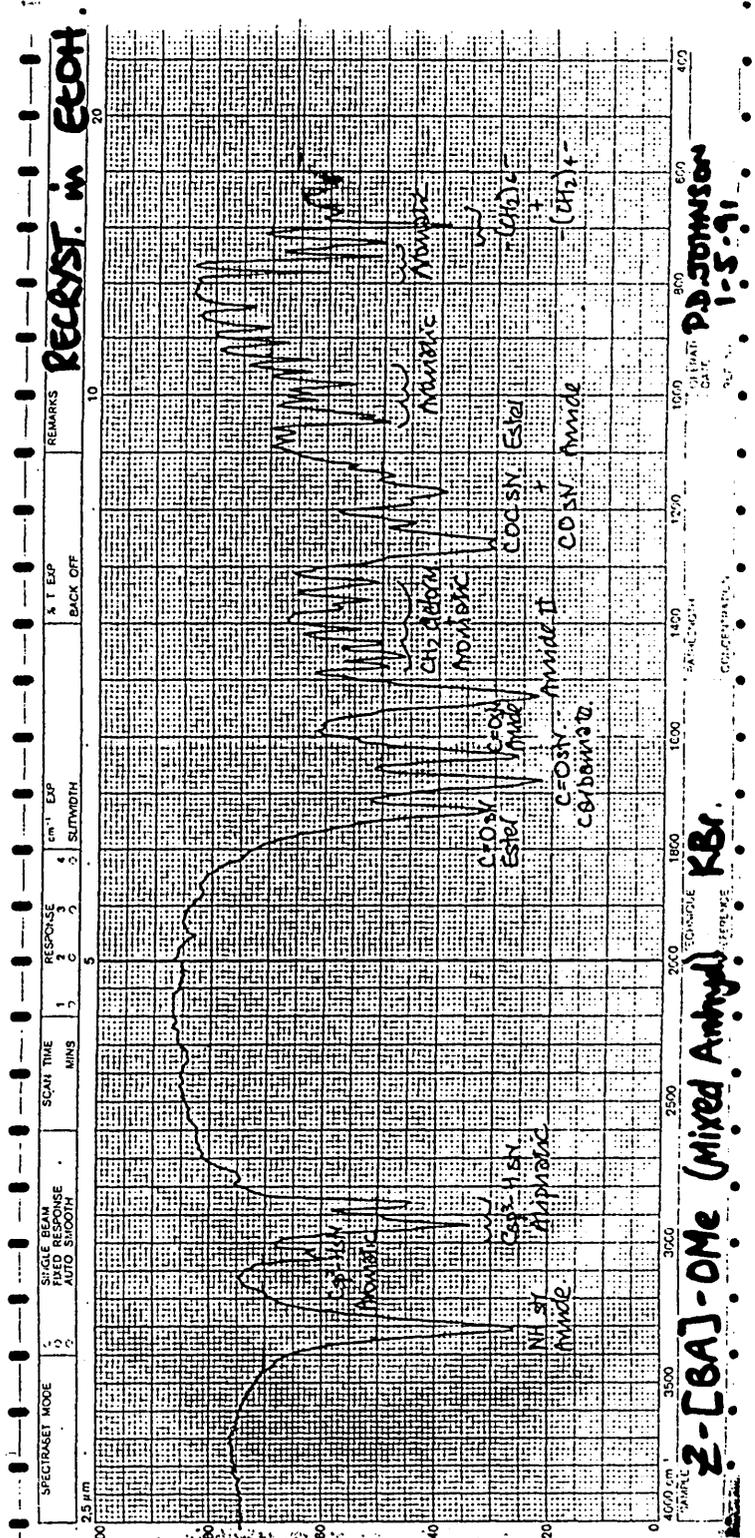
With the amino acids the COO^- ion is responsible for the strong absorption band at 1405cm^{-1} . This indicates the presence of the zwitterion of the amino acids. With the

dicarboxylic acids this band is not present. The ester-
amines have similar, but of course weaker, bands to
those described for the diester. The carbobenzoxy-ester
compound is again instantly recognizable by the presence
of bands corresponding to the carbonyl C=O stretches for
both end groups.

With the carbobenzoxy-carboxylic acid oligomer there is
a strong resemblance to the spectra of the dicarboxylic
acid and dicarbobenzoxy compounds, due to the close
proximity of the carbonyl stretching band for both
functional groups. They are separated as only the
carbobenzoxy-carboxylic acid compound shows both the
broad O-H stretch and the $C_{sp^2}-H$ stretch. Several
spectra have been included (pages 100-102) to show the
major absorption bands.

For estimating D.O.P. the bands due to carbonyl
stretching are again utilized. The number of amide
groups in the central chain is proportional to the size
of the amide carbonyl stretching band at 1640cm^{-1} . The
number of protecting groups or free carboxylic acid
groups is reflected in the size of the corresponding
carbonyl band e.g. 1735cm^{-1} for the ester. The ratio of
the number of amide groups to the number of end groups

FIGURE 11: INFRARED SPECTRUM OF NYLON-6.6 MONOMER (CARBOBENZOXY-ESTER)



should therefore be proportional to the ratio of the sizes of the amide band compared to that of the respective end group carbonyl band.

Since IR signal amplitudes are not directly proportional to the number of absorbing bonds per molecule (nor are amplitudes from different bond types easily comparable), this approach must be applied cautiously. But careful comparisons between samples that vary only in D.O.P. provide useful diagnostic guidelines, especially for these poorly soluble and often labile synthetic intermediates, which are not readily amenable to routine NMR.

Spectra are included (pages 104-106) to show this effect in the non-integer oligomers which are acid terminated. The comparative trends in the relative peak sizes are readily discernible. The carbonyl band at 1700cm^{-1} is due to the free carboxylic acid. Its size relative to the amide band at 1635cm^{-1} can be seen to decrease with increasing chain length.

It should also be possible, if X-ray diffraction was to indicate chain folding, to study (probably by F.T.I.R.) the bands at 936, 1329 and 1224cm^{-1} in the infrared spectra as reported by Koenig and Aboatwalla¹¹ (see 1.3. Polymer Morphology). By a comparison of the infrared

FIGURE 12: INFRARED SPECTRUM OF DICARBOXYLIC ACID D.O.P. 1.5

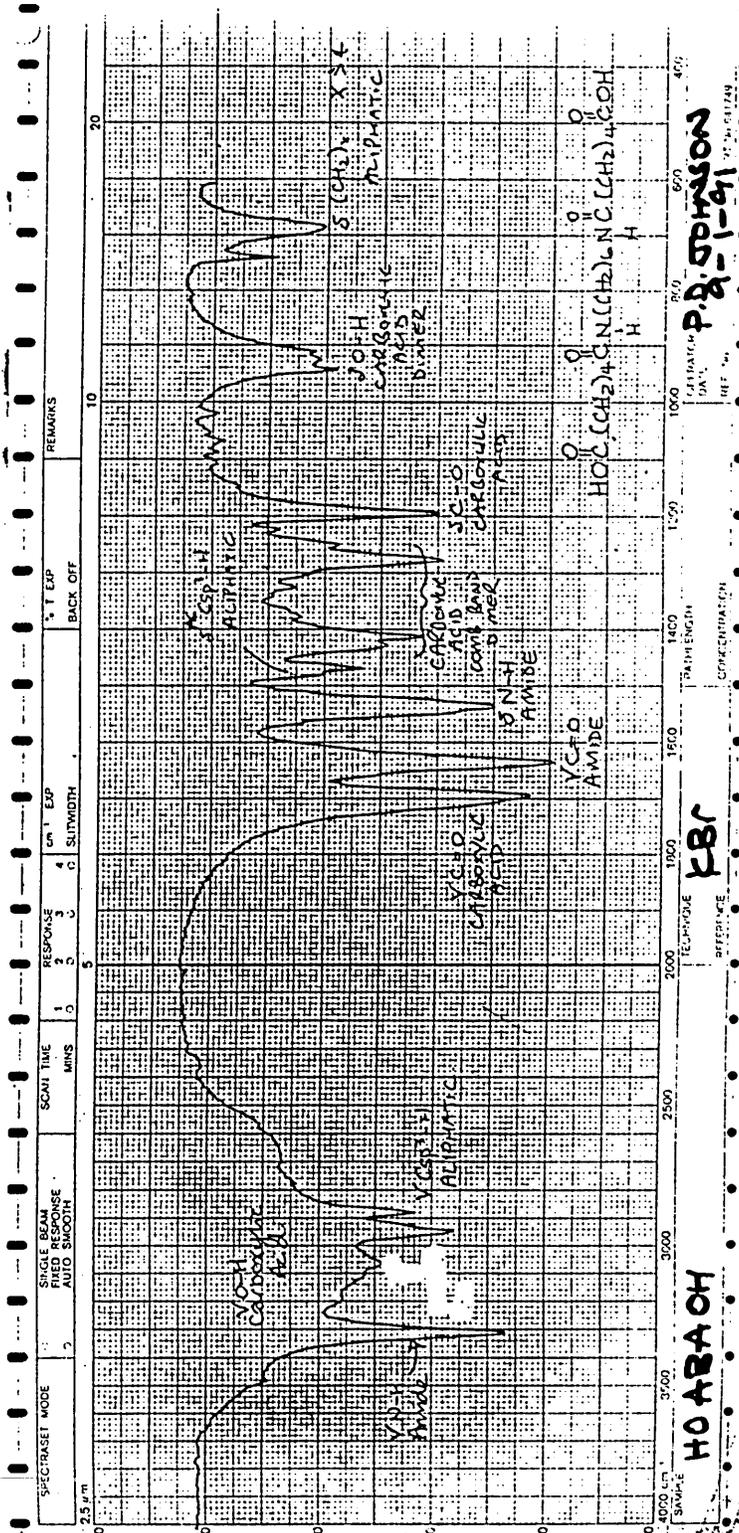


FIGURE 13: INFRARED SPECTRUM OF DICARBOXYLIC ACID D.O.P. 2.5

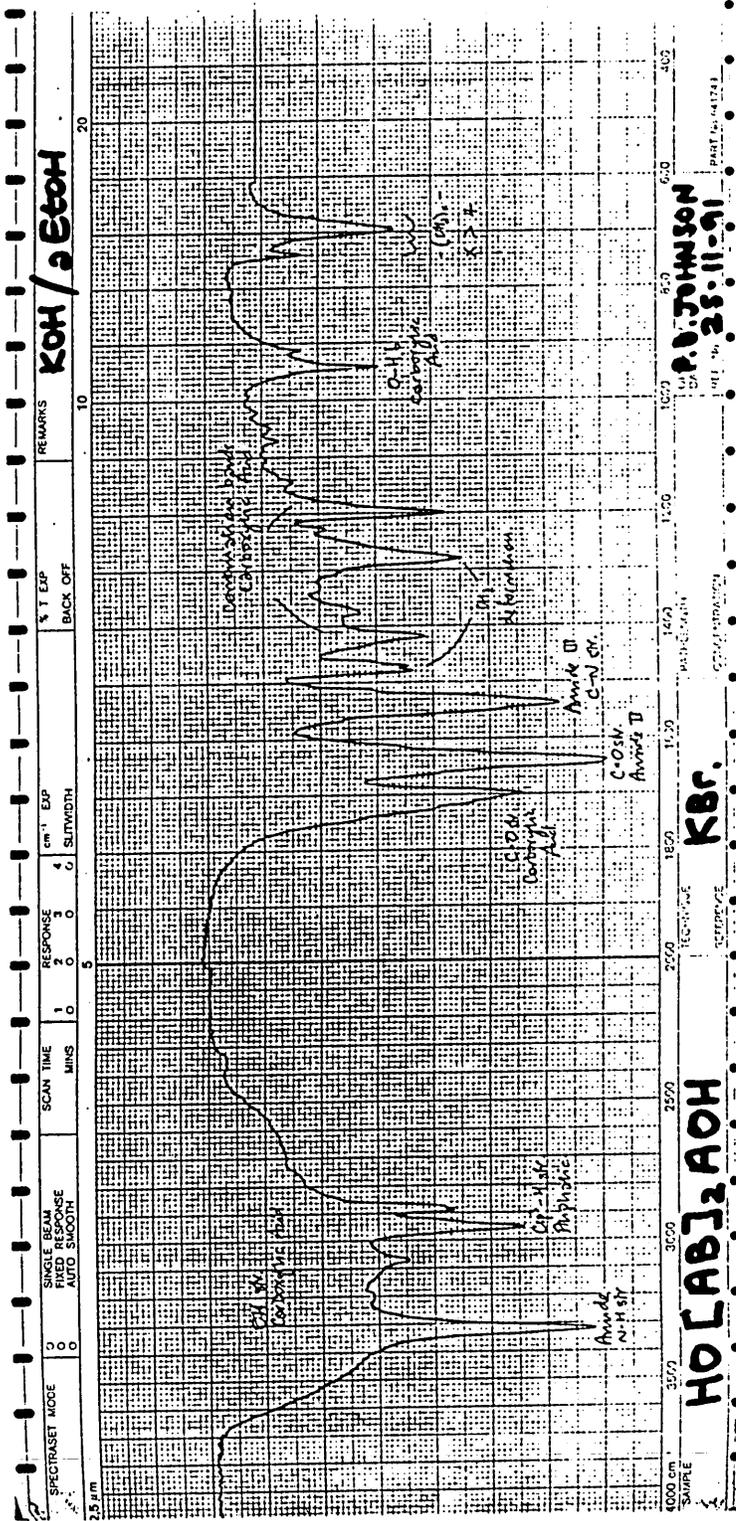
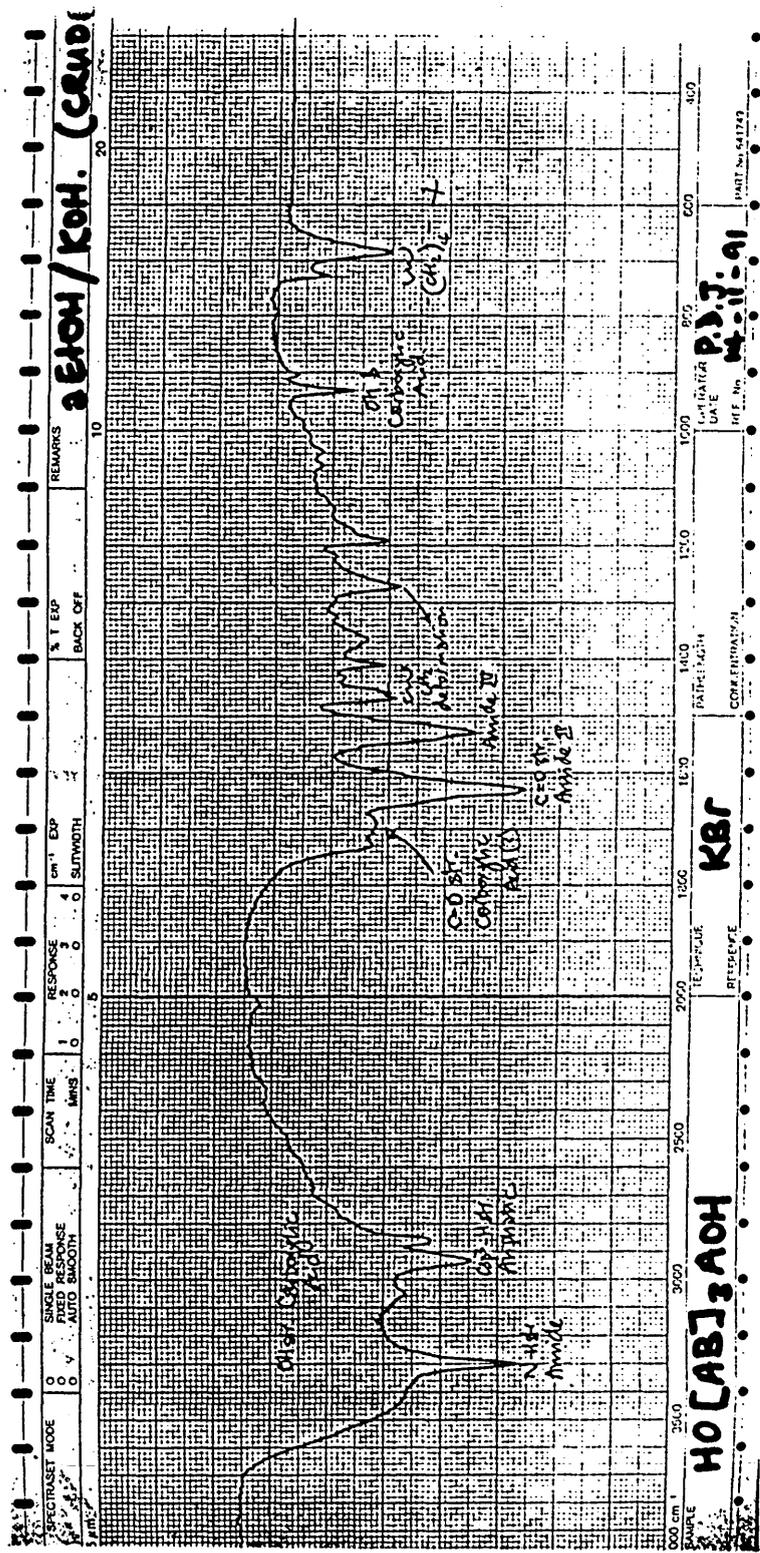


FIGURE 14: INFRARED SPECTRUM OF DICARBOXYLIC ACID D.O.P. 3.5



spectra of single crystal mats of various oligomeric types before and after hydrolysis it may be possible to add more information to these studies. This would include the identification of fold type, preferably both acid and amine.

The studies by Koenig and Aboatwalla¹¹ used infrared spectroscopy to determine the nature of the chain-fold. They assigned the spectral bands for nylon-6.6 at 1329 and 1224cm⁻¹ to folded chain regions. They also showed that the infrared band at 936cm⁻¹ contained a contribution of the stems of the fold. Following degradation of the fold surface with dilute sodium hydroxide solution the crystalline regions were shown to be unaffected as no significant change in the 936cm⁻¹ band was observed. But after hydrolysis they showed the intensity of the bands at 1329 and 1224cm⁻¹ had decreased relative to that of the 936cm⁻¹ band. In conjunction with X-ray diffraction work they showed the 1329 and 1224cm⁻¹ bands could be assigned to the interaction of the amide III band with the wagging and twisting of the N-vicinal CH₂ groups. They concluded from this that the amine component of the nylon series must make up the chain fold.

The use of Fourier transform (F.T.I.R.) would enhance their findings and the addition of the oligomers would

expand on them. F.T.I.R. is a far more powerful technique than simple infrared spectroscopy. By using F.T. mathematical analysis on interferograms high resolution spectra can be obtained rapidly. The spectra would enable superior data on the variations in the chain induced to study its structure, e.g. degradation of the fold surface as described above. In addition the data handling ability would be vastly improved with the accurate determination of the position and size of the spectral bands. In studying the relatively small bands at 1329, 1224 and 936 cm^{-1} this would provide a major advantage over conventional I.R. spectroscopy.

2.2.2. NUCLEAR MAGNETIC RESONANCE.

With this technique a strong magnetic field causes the energies of certain nuclei (those with a non-zero spin quantum number) to be split into two or more quantized levels due to their magnetic properties. Transitions among the resulting energy levels can then be brought about by the absorption of electromagnetic radiation of suitable frequencies. The energy differences between magnetic quantum levels for atomic nuclei correspond to radiation energies in the frequency range of 0.1 to 100MHz.

Measurement of absorption of this radio-frequency (rf) radiation by nuclei (nuclear magnetic resonance, NMR) forms the basis for qualitative analysis of compounds.

Three main factors give rise to the structural information given by a NMR spectrum. Firstly, the position of the resonance (chemical shift) is determined by the chemical environment of a nuclei. The field experienced by a particular nucleus differs in magnitude from that of the applied field due to the shielding effects by neighbouring electrons. It is due to variations in shielding that protons in different chemical environments absorb at different values of the applied field.

Secondly, a given band may be split into several peaks (multiplets) as a result of interactions of neighbouring nuclei, this is termed spin-spin coupling. For protons the number of peaks in a multiplet is determined by the number of protons in the adjacent group(s) n and is simply $n+1$. Thirdly, the integrated area of an absorption peak is directly proportional to the number of nuclei responsible for the signal. All these factors combine to make NMR a very powerful analytical tool.

Proton nuclear magnetic resonance (^1H NMR) was extensively used for both the identification of any given oligomer and the determination of the purity of that compound. The application of ^1H NMR in the identification of end groups was essentially to confirm the findings from the infrared spectra. Conversely the IR studies aided the interpretation of the NMR spectra by showing which functional groups were present. Any contaminant present in the products would, obviously, result in additional signals in the spectra that could not be assigned to the oligomer under study. This would give an indication of the purity, especially for non-oligomer materials. The presence of polydispersity could also be detected using NMR by comparison of the integration values.

The nylon-6.6 oligomers produced in this project can be categorized in one of eight forms, the bis-N-carbobenzoxy, bis-C-ester, diamine or the dicarboxylic acid non-integer oligomers, as well as the carbobenzoxy-ester, N-carbobenzoxy, C-methyl ester or the amino-acid integer oligomers. Each form, as with IR was instantly recognizable by its ^1H NMR spectrum confirming the success or failure of any given reaction.

The majority of the protons in all of the oligomer variations are to be found in the four $-(\text{CH}_2)-$ groups in the centre of hexamethylene diamine components or the two $-(\text{CH}_2)-$ groups in the adipic acid components. The central protons in these segments give rise to the large signals between δ_{H} 1.3-1.8ppm relative to trimethylsilane (TMS).

The methylene groups adjacent to amine, amide, carboxylic acid or ester groups give the first indication of the molecule's identity. Assuming the resolution of the instrument is high enough the following shifts relative to TMS can be observed.

The methylene groups adjacent to the carboxylic acid (or carboxylate or ester) all give rise to signals with the same chemical shift of around 2.4ppm. The molecules are however easily distinguished. The ester derivative is

obviously accompanied by a signal at 3.6ppm for the methyl group of the ester. The zwitterion is shown by the presence of the protonated amine peak at 3.4ppm. The carboxylic acid function is also present with a second acid group, with non-integer oligomers, or with the carbobenzoxy group in integer oligomers. The existence of the carbobenzoxy group is unmistakably shown by signals at 7.1ppm (ArH) and 5.0ppm (PhCH₂) in a ratio of 5:2, the adjacent methylene group giving a signal at 3.3ppm as with the -CH₂NHCO- methylene group.

<u>Hydrogen environment</u>	<u>δ/ppm</u>
-CH ₂ NH ₂	2.6
-CH ₂ NH ₃ ⁺	3.4
-CH ₂ NHCO-	3.3
-CH ₂ CONH-	2.2
-CH ₂ COOH	2.4
-CH ₂ COO ⁻	2.4
-CH ₂ COOCH ₃	2.4

¹H NMR was also found to be the quickest method for determining the conversion of a carboxylic acid to an acid chloride in preparation for the Schotten-Baumann reactions. The shift of the signal for the methylene group adjacent to the carboxylic acid from 2.4ppm to 3.0ppm was instantly recognizable.

The protons associated with the amide, amine and carboxylic acid groups were not always observable, especially in the oligomers of higher D.O.P. Here the concentration of the end groups is vastly reduced. Because of this they are not always listed in the analysis of the oligomers.

Once the identity of an oligomer had been established and confirmed by infrared spectroscopy the purity of the sample could be examined. The presence of any signals due to oligomers with the incorrect end group or non-oligomer materials was the most obvious sign of any contamination. In addition the chain length could be assessed to determine the presence of contaminant oligomers. This involved measurement of the ratios of the integration values due to certain hydrogen environments. For oligomers containing the carbobenzoxy group the ratio of PhCH_2 protons to the NHCH_2 protons could be compared to the theoretical value. With ester oligomers the ratio of methyl protons to NHCH_2 protons could similarly be used. Any major discrepancy between the theoretical and experimental values would indicate the presence of polydispersity. For oligomers containing both those groups the ratio of PhCH_2 : CH_3O protons would suffice. The unprotected oligomers would involve NHCH_2 protons relative to NH_2CH_2 protons.

Four solvents were used in the NMR studies depending on the D.O.P. and identity of the sample (solubilities varied widely). Deuterated chloroform, CDCl_3 , was sufficient for monomeric and the lower oligomers. It was also used for the analysis of general reagents and starting materials. As the D.O.P. increased deuterated methanol (CD_3OD), and deuterated trifluoroacetic acid (CF_3COOD), were employed. The trifluoroacetic acid could clearly not be used in the presence of free base amine groups. For oligomers with D.O.P. of four and above d_2 -1, 1, 1, 3, 3, 3-hexafluoropropanol, $\text{CF}_3\text{CD}(\text{OD})\text{CF}_3$, was required to overcome the decreasing solubility of the products. The residual absorptions (due to protio-contaminants in deuterated solvents) relative to TMS for each solvent are shown in the table below.

<u>Solvent</u>	<u>Residual Absorption/ppm</u>
CDCl_3	7.25
CD_3OD	3.34, 4.1
CF_3COOD	11.34
$\text{CF}_3\text{CD}(\text{OD})\text{CF}_3$	5.5

Values for the shifts given here for the protons of the oligomers are dependent on temperature and solvent, and the residual absorptions for the solvent depend on temperature and solute. [The residual absorption given

for d_2 -1, 1, 1, 3, 3, 3-hexafluoropropanol is the only one actually observed: although it would be expected that there would be two.

^{13}C NMR was also used but due to difficulties in accurate assignment of shifts it was not pursued.

2.2.3. GEL PERMEATION CHROMATOGRAPHY.

Gel permeation chromatography (GPC) is used to separate materials according to molecular size and shape. This technique is also known as exclusion or molecular-sieve chromatography. GPC is performed on a column by elution of the sample in solution. The degree of retardation is dependent upon the extent to which the solute molecules can penetrate that part of the solution phase that is held within the pores of the highly porous gel-like packing material.

If molecules are larger than the pores of the packing material then they will be excluded completely and will pass quickly through the column. For smaller molecules that can penetrate the pores the retention in the stationary phase will increase slowing the molecules passage through the column. The degree of retardation, and therefore the retention time, for the smaller molecules will be dependent upon the size, shape and sometimes their tendency to be absorbed by the gel.

The detection of eluted solutes will give a measurement of the retention times for the components in a given sample. These in turn give the molecular mass of the components when related to a calibration material. For

this work the cyclic monomer was used for the calibration.

The main application of GPC is for the assessment of molecular weights of high molecular weight materials. This makes GPC the ideal analytical technique for use with the nylon-6.6 oligomers, assuming that they are stable to the experimental conditions.

GPC was used to show the approximate composition of a sample i.e. to determine whether or not it was monodisperse. With the addition of the molecular weight to supplement the array of data even more confidence could be gained in the identity of a given oligomer. It should however be noted that an element of caution had to be applied as the standard used was the cyclic monomer of nylon-6.6 and not a linear analogue of the oligomers. This shape difference meant that the technique could not be totally relied upon to give absolute values for molecular weights although good separation of oligomer peaks was achieved.

Some general observations should be made at this point concerning the appearance of the peaks on the GPC. It was noted that the presence of an unprotected amine end group in the oligomer would cause a tailing effect towards a lower molecular weight. This would

consequently give rise to lower values than expected for the average molecular weight for samples of this type. Also the presence of a N-carbobenzoxy protected amine, a C-ester protected carboxylic acid or the free carboxylic acid would result in a slight but noticeable increase in the molecular weight value obtained.

Although absolute values of the molecular weight could not be obtained, gel permeation chromatography proved to be invaluable for the assessment of purity. This became particularly important as a completely reliable thin layer chromatography (tlc) system could not be established. However GPC data are superior to tlc data in providing quantitative information (the latter was however routinely available while GPC was not). Also, mass spectrometry was not readily available for most of the oligomers as the available instrumentation was intended for lower molecular weight molecules than those involved here. This meant that gel permeation chromatography became the only usable technique for establishing molecular weight.

GPC analyses were performed at ICI Wilton. Illustrative chromatograms appear on the following pages, and show either that monodisperse synthesis of the oligomers is not readily attainable or that sample storage, sample preparation or the GPC experiment itself is detrimental

to the monodispersity of synthetic nylon oligomers. There is no precedent available since nylon GPC has previously been used with much higher molecular weight materials where near homologues are undetected within broad, envelope eluate peaks.

It can be seen from the GPC chromatograms included (pages 120-122) that the quality of the samples deteriorates as the D.O.P. increases. The GPC analysis was carried out at high temperature and may have caused some deterioration of the samples. Sample preparation and storage may also have had a detrimental effect on the oligomers. These possibilities are given credence as GPC shows species that are not evident using ¹H NMR or IR spectroscopy. It should also be noted that the diamine (D.O.P. 8.5) sample was from an early experiment and was not expected to be of high purity.

FIGURE 15: GPC CHROMATOGRAM OF Z-BA-OH AND Z-[BA]₂-OH WITH CYCLIC MONOMER AS REFERENCE

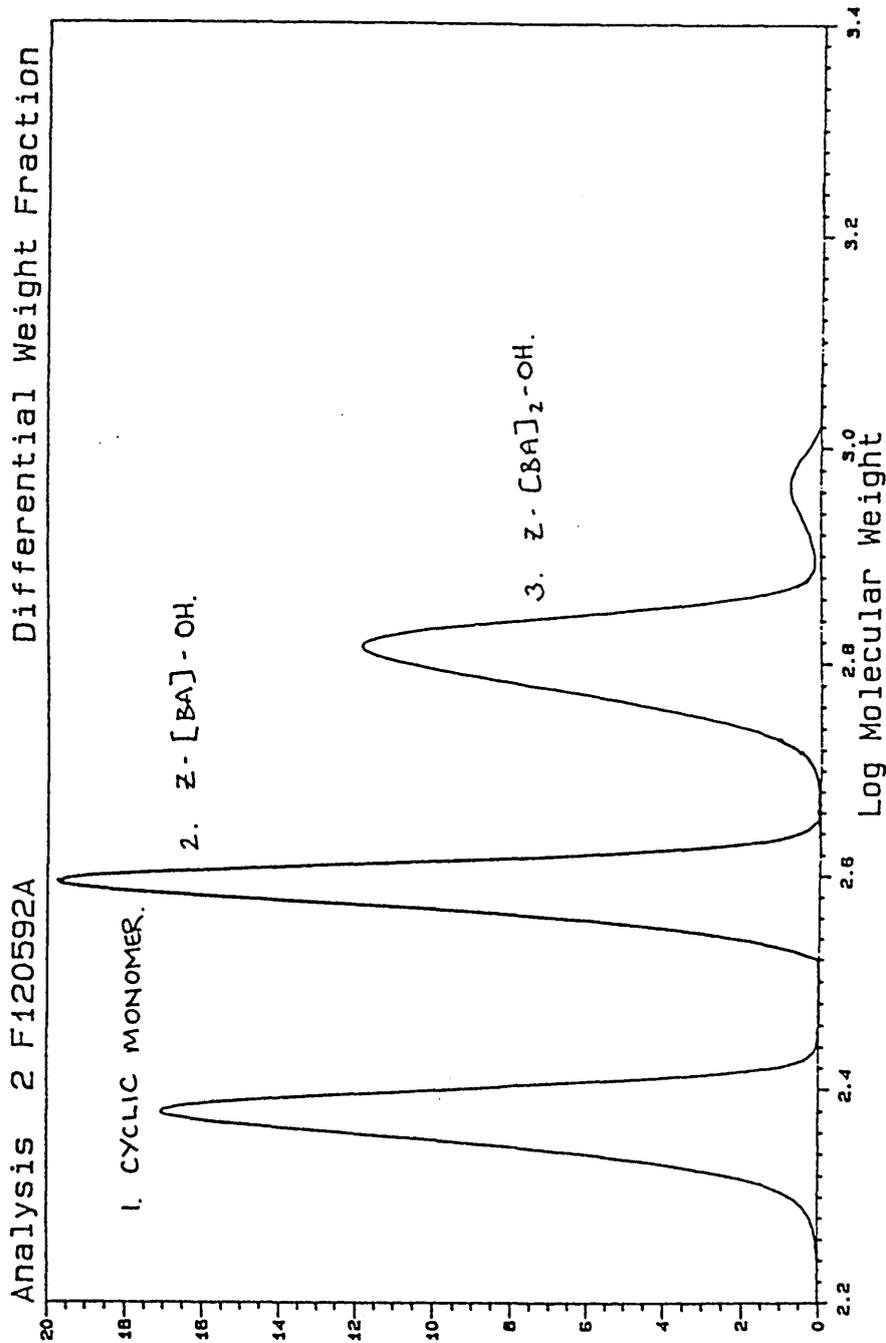


FIGURE 16: GPC CHROMATOGRAM OF Z-[BA]₄-OH

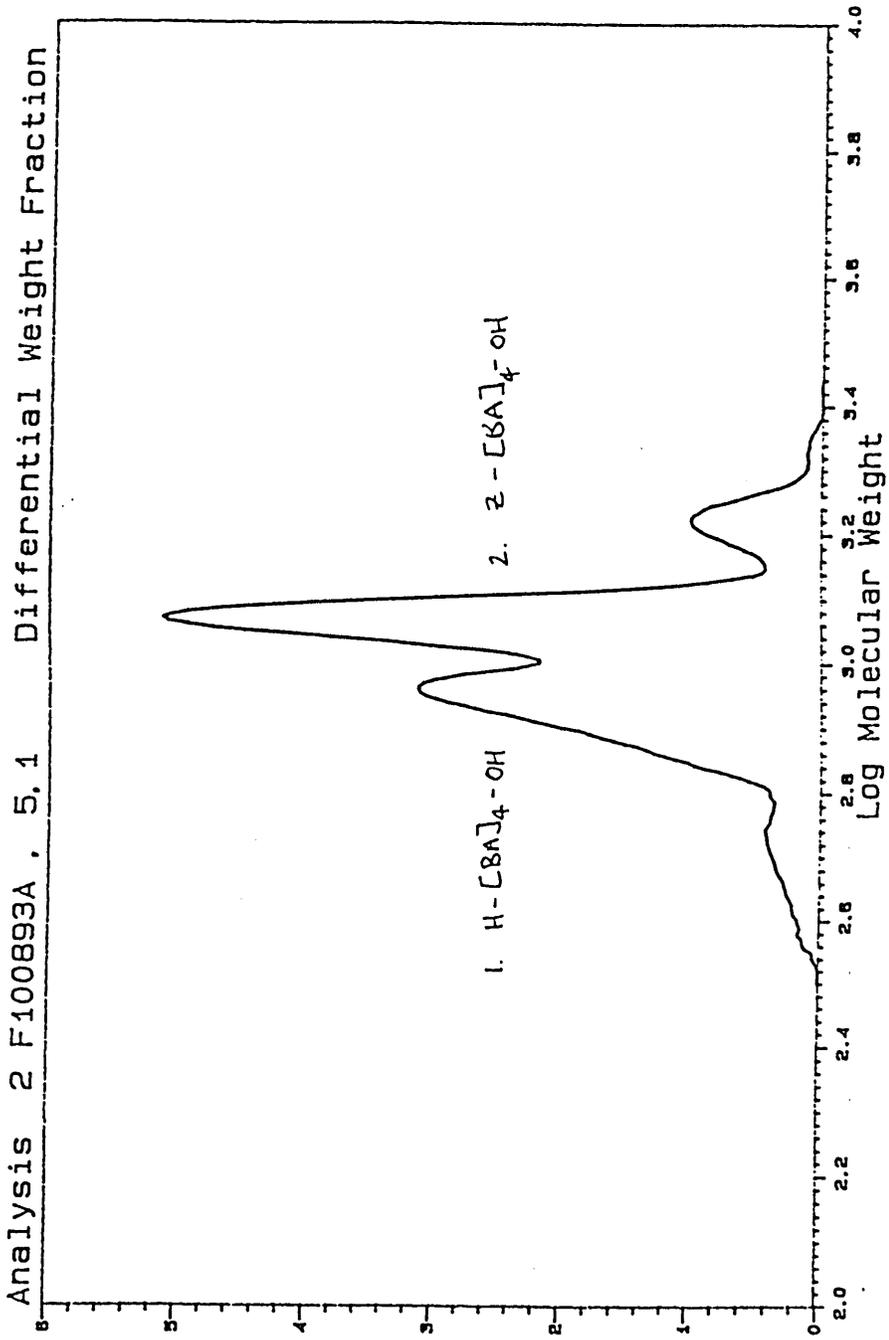
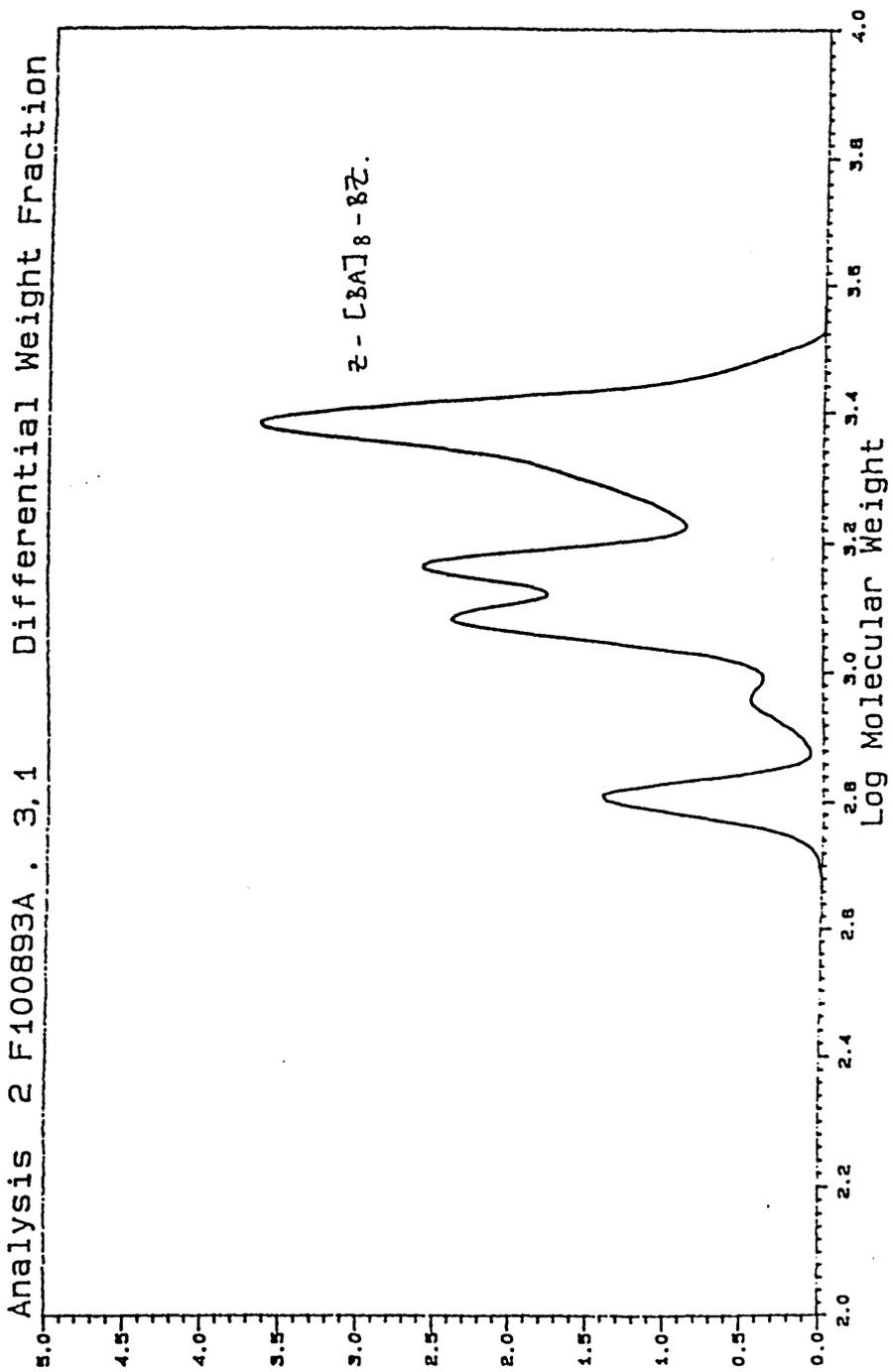


FIGURE 17: GPC CHROMATOGRAM OF Z-[BA]₈-BZ



2.2.4. MASS SPECTROMETRY.

Mass spectroscopy involves the ionization and fragmentation of materials by either using a high energy electron beam or by chemical ionization. The fragments are then resolved on the basis of their mass-to-charge ratio. This is achieved by accelerating the positively charged fragment ions through a potential gradient under vacuum and separating them in a magnetic field. The flight path through the magnetic field is curved so the smaller, or lighter ions take a shorter path than heavier ions as they experience greater deflection. The fragment ions are then usually detected by using an earthed electrode (collector plate).

The recorded mass spectrum is, usually, in the form of a line diagram expressing fragment abundance as a percentage of the most abundant one against the mass-to-charge ratio. The fragmentation, or cracking, pattern is unique for a given substance enabling identification. The structure of the substance can sometimes be determined as its fragmentation will follow general rules. The molecular weight of a molecule can be determined if the parent or molecular ion peak can be observed. This occurs when the molecule ejects only a single electron on ionization.

Organic mass spectrometry finds its main application in the identification and structural analysis of small organic compounds. Used in conjunction with IR, NMR and GPC mass spectrometry becomes an extremely valuable technique. As well as giving the molecular mass of a material it can confirm that the anticipated structure of that material is correct, via fragmentation.

The use of mass spectrometry in this study was, however confined to the low molecular weight compounds due to the extreme limitations of the instrument available at the time. It was therefore mainly used for the analysis of the starting materials and oligomers to a D.O.P. of 1.5. Despite this the use of mass spectrometry proved valuable as many of the protection, deprotection and coupling reactions were performed on the integer and non-integer "monomers". These could be studied using this technique together with IR and NMR. For example in attempting the de-esterification of the monomer with ethanol as the solvent, transesterification resulted. This was shown most graphically by mass spectrometry.

For molecules with a higher D.O.P. GPC was the preferred technique, being more appropriate and giving far clearer results in terms of purity.

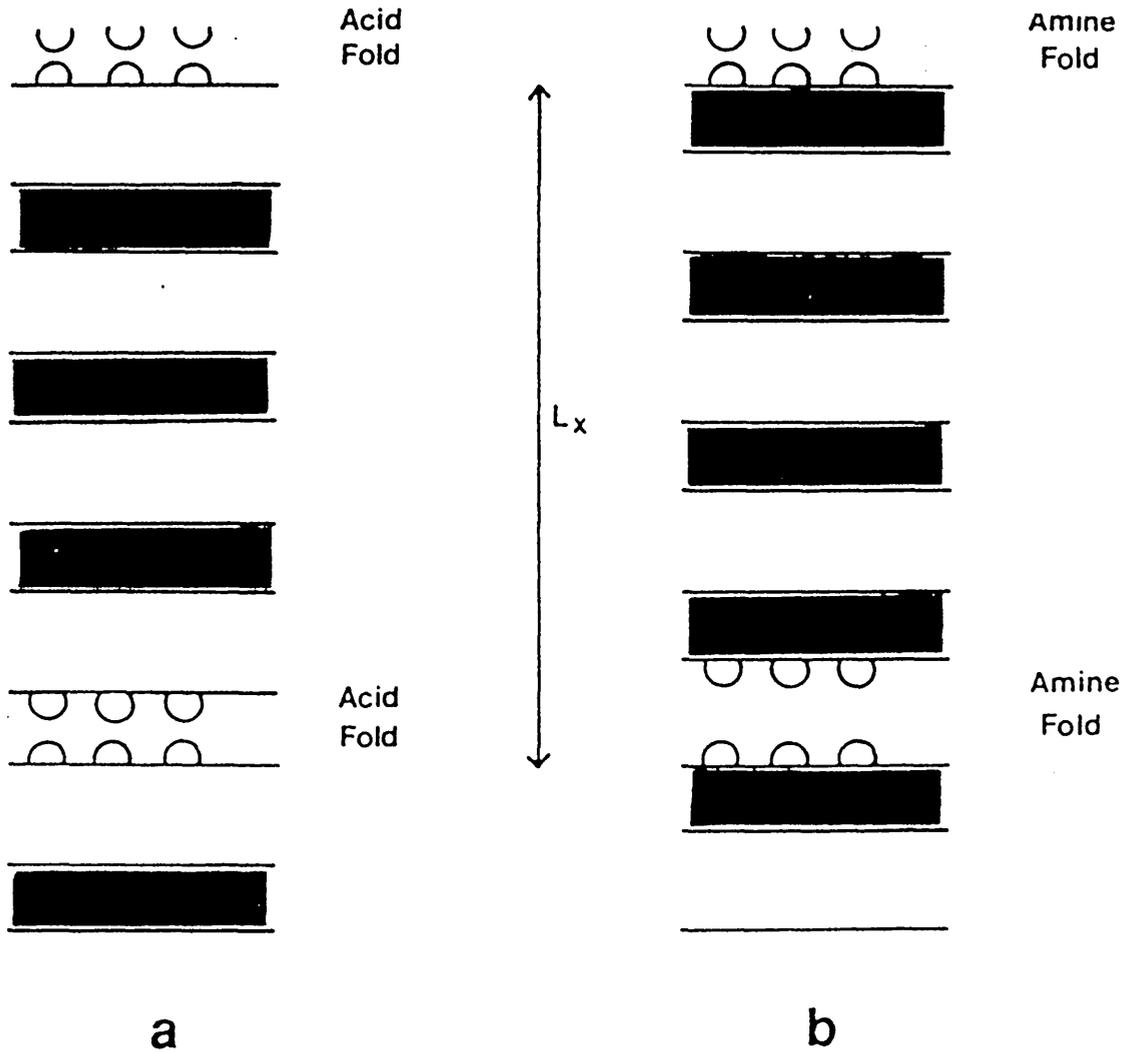
2.2.5. LOW ANGLE X-RAY DIFFRACTION.

Low, or small, angle X-ray diffraction is an important tool for the investigation of the microstructure of matter at the molecular level. The technique relies on the interaction of X-radiation with the electrons of the matter through which it passes resulting in scattering. The scattering of X-rays by the orientated environment in a crystal constructive and destructive interference occurs as the distance between the scattering centres are of the same magnitude as the wavelength of the radiation. Diffraction is the result.

The technique would be used to investigate the onset of folding and, through this, the nature of chain-folding in each of the three various oligomeric types i.e. diamine non-integer oligomers, dicarboxylic acid non-integer oligomers and the integer oligomers.

This would be achieved by observation of the periodicity of crystals stacks (long spacing, d) using low angle X-ray scattering. The periodicity of the lamellar crystals is the distance between the upper basal surface of one lamella and the next. This includes the amorphous as well as the crystal regions. For a sample with a high degree of crystallinity d would approximate to the crystal thickness.

FIGURE 18: PERIODICITY OF THE CRYSTAL STACKS



Schematic cross section of 6,6-nylon lamellae showing (a) the acid section of the repeat unit forming the fold and (b) the amine section forming the fold. The acid segments within the lamellae are shown shaded. L_x is the X-ray long spacing

This technique gives maxima at diffraction angles 2θ that can be related to d by the Bragg equation, $n\lambda = 2d\sin\theta$, for wavelength λ . On striking a crystal surface a portion of an X-ray will be scattered the remainder will penetrate to be scattered by the second or third layer. The cumulative effect leads to diffraction from the regularly spaced crystal surfaces. W.L. Bragg treated this diffraction as shown in the diagram below, showing that scattering occurs from atoms located at O, P and R. Assuming

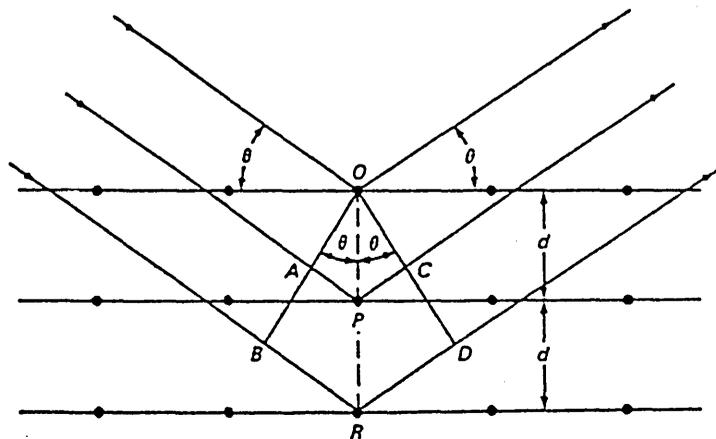
$$AP + PC = n\lambda$$

where n is an integer, the radiation will be in phase at OCD. It can be seen that

$$AP = PC = d\sin\theta$$

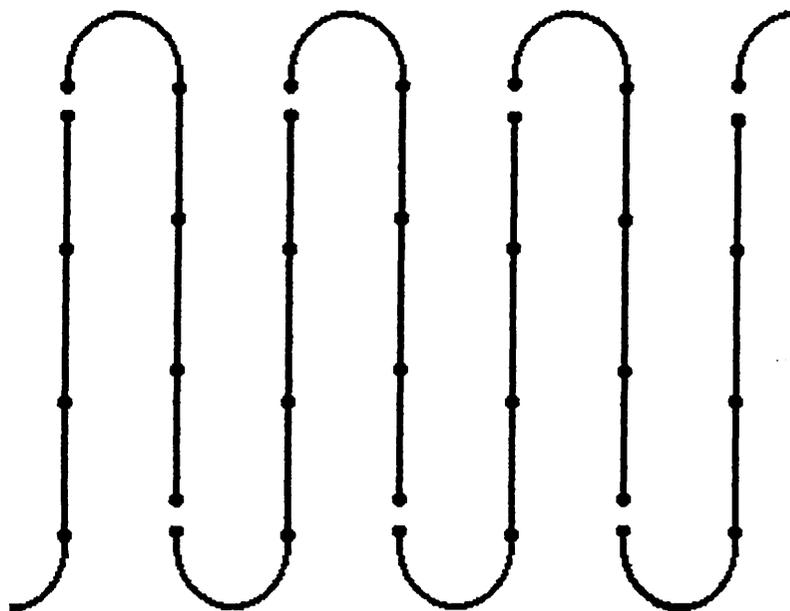
This gives the Bragg equation as above.

FIGURE 19: DIFFRACTION OF X-RAYS BY A CRYSTAL



The long spacing would be expected to increase proportionally with the chain length of the oligomer until chain-folding occurred. At this point, for a singly folded oligomer, the long spacing should appear at approximately half the value expected for the unfolded chain. Differences in the onset of chain folding between the different oligomer types would give an insight to the identity of the fold, showing it to be the acid component, the amine component or possibly a combination of the two. It would also be possible to determine whether only complete folds are present or a "walking stick" fold could occur.

FIGURE 20: "WALKING STICK" CHAIN-FOLDING



This technique was not utilised to any great extent, as samples of all the oligomers types at a sufficiently high chain length suitable for folding were not attained. With the lower chain length oligomers, where chain-folding does not occur, the use of low angle X-ray diffraction would not be very informative. It is expected, however, that small angle X-ray diffraction will provide the basis of characterization data for these samples in any future studies. From the basis of polymer crystal results, section 1.3., it is expected that folding would start at about the tetramer stage.

Dreyfuss and Keller¹² showed by means of detailed X-ray studies, on nylon-6.6, 6.10 and 6.12 polymers, that the crystal layers correspond to four monomer lengths. They went on to conclude that in order to incorporate the fold, straight stems of 3.5 monomer units were most likely, the additional 0.5 monomer unit being taken up by the fold itself. Assuming the fold to take up either an acid or an amine component would also mean that folds on both sides of the layer were of the same type. They showed the ratio of the number of monomer units to the layer thickness to be virtually identical for all three nylon types. The one component common to all three nylon samples, the hexamethylenediamine component, must therefore form the chain fold.

In addition to this work there is also the work by Atkins, Keller and Sadler^{193m} which shows that the fold surface consists of only or mainly acid components.

The use of X-ray diffraction with nylon-6.6 oligomers, of both integer and non-integer, types could only add to this work. More information on the position of the amine and acid segments in the fold could be gained if the exact nature and length of the components of the samples were already known.

2.2.6. DIFFERENTIAL SCANNING CALORIMETRY.

Differential scanning calorimetry (DSC) provides information on crystal annealing, crystallization and crystal melting. With polymeric, or high D.O.P. oligomeric materials this information would include the glass transition, and the temperature at which crystallization, melting and decomposition occurs. The technique works by monitoring additional heat that must be supplied to the sample or to an inert reference in order to keep both at the same temperature when the former passes through some thermal transition.

DSC thermograms (both heating traces and cooling traces) were obtained for several of the nylon-6.6 oligomers. The information that could be gained from them was essentially limited to the melting point as they are still of a relatively low D.O.P. Any impurities present e.g. solvent or starting material would be discernible due to low temperature peaks that were not repeated on the cooling thermogram. This information, although useful in its own right, did not really add to the study at this stage.

In studying the nature of chain-folding the work of H. Mitomo⁵⁴ would be of interest. This work studied the relationship between layer thickness of solution grown

and dry, annealed single crystals of nylon-6.6 with the melting point observed with DSC. On increasing the annealing temperature the layer thickness increases accordingly. Using melting point data Mitomo concluded from his study that the process occurred in a stepwise fashion disputing existing theories that the thickening occurred in a continuous fashion.

The results of this work are not of any immediate value to proposed fold studies with the oligomers. The ability to measure the layer thickness from the melting point, however, would be useful, and the above work provides an equation for this purpose. An example of a DSC trace is included below.

FIGURE 21: DSC HEATING TRACE OF Z-LBAJ-OH

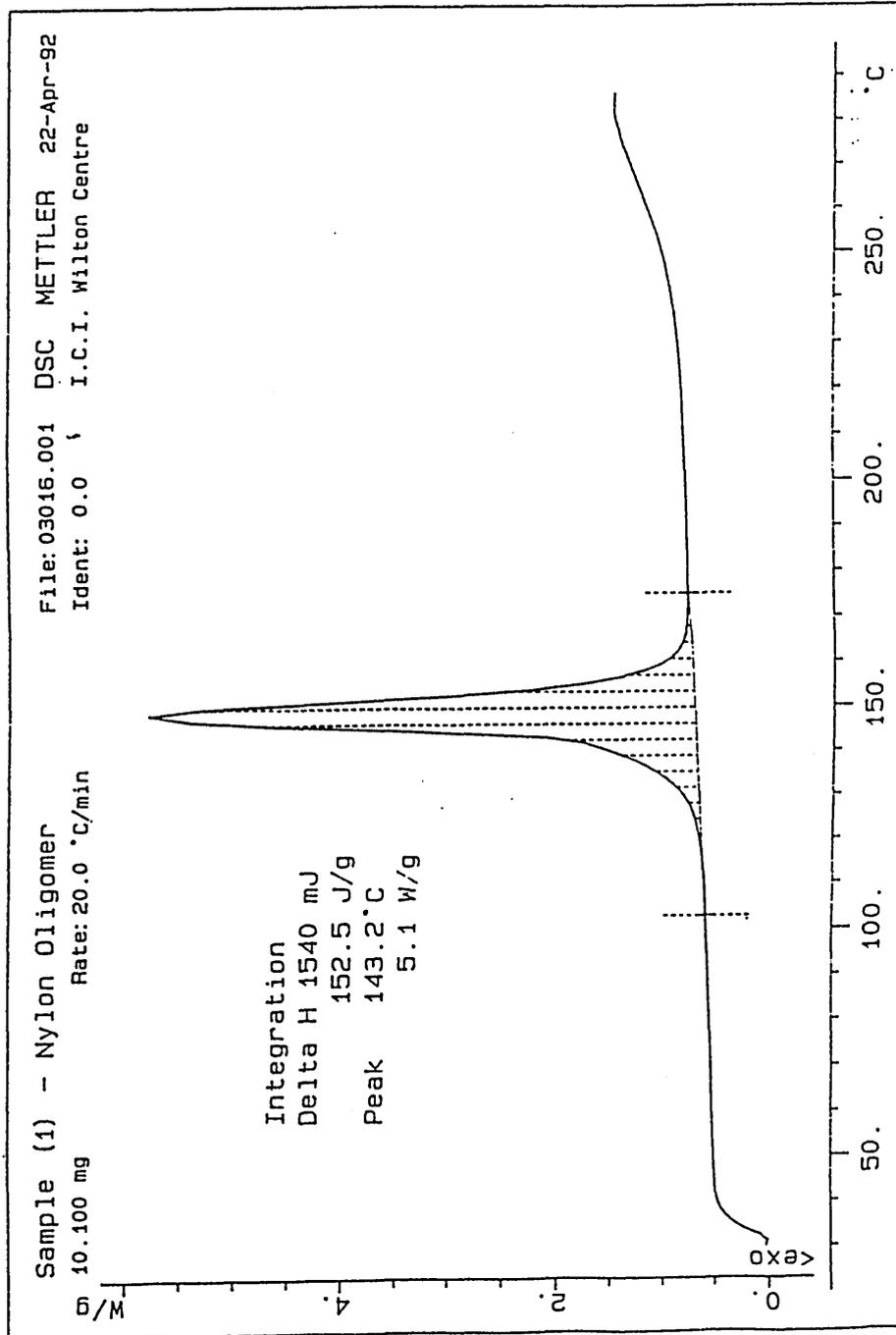
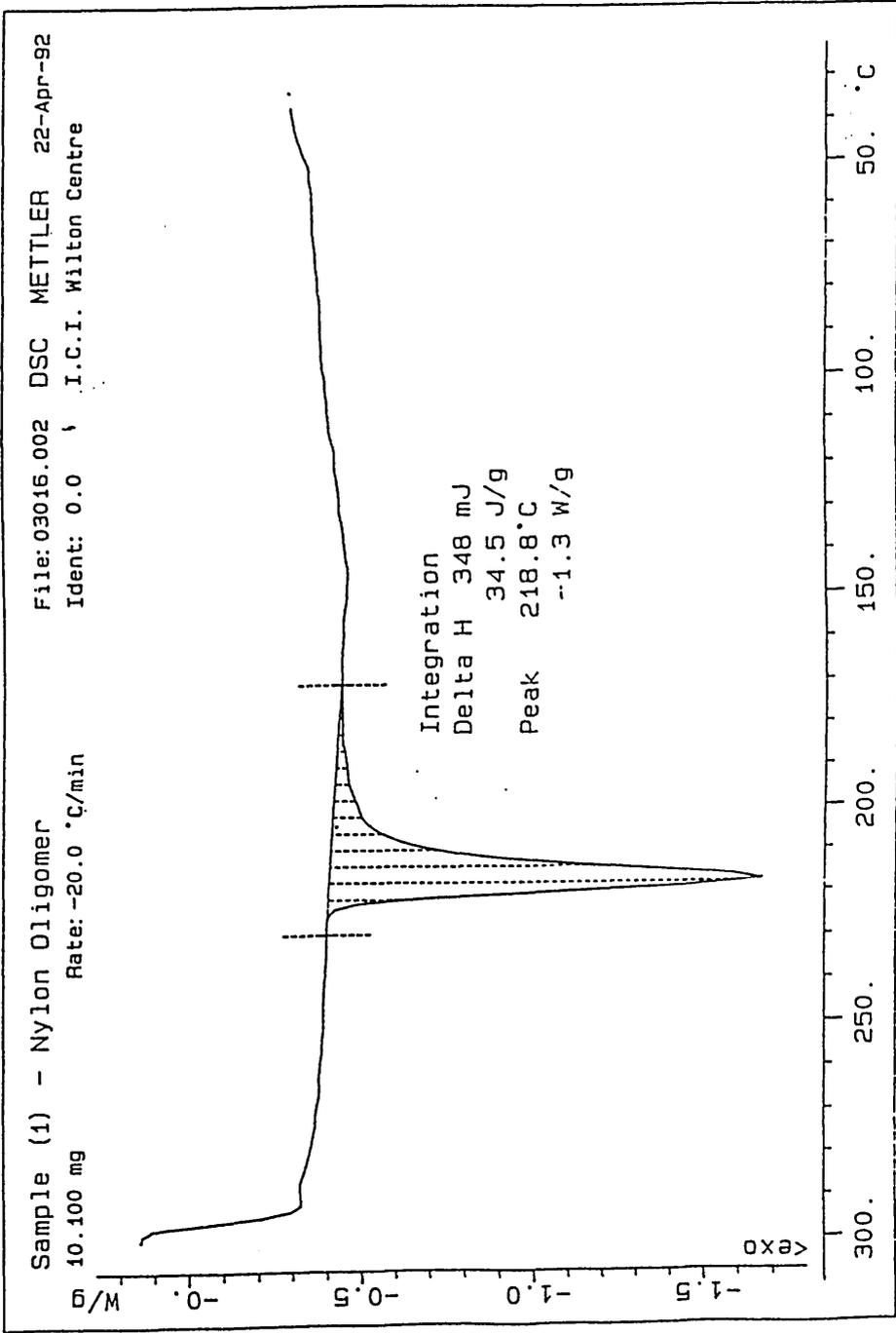


FIGURE 22: DSC COOLING TRACE OF Z-[BA]-OH



2. 2. 7. NEUTRON DIFFRACTION.

Neutron diffraction was not used in this study for essentially the same reasons as X-ray diffraction. This technique would similarly be expected to become more important with the onset of chain-folding.

As previously mentioned, recent work by Spells, Sadler and Keller¹⁴ used neutron diffraction in a study of the fold surface. They used d_3 -adipic acid in the preparation of d_3 -nylon-6.6. These fully deuterated acid blocks provided a contrast in neutron scattering to the hydrogenous amine blocks. From here they went on to conclude that the most probable model for chain-folding in nylon-6.6 was that involving only the acid component at the fold surface. This is in total contrast to the findings of Koenig and Aboatwalla¹¹.

If this work were to be repeated using partially deuterated analogues of nylon-6.6 oligomers, further insight into chain-folding may be gained. With the oligomers of defined length, there is no ambiguity in the chemical nature of the fold and the neutron diffraction technique has the potential to end the controversy surrounding this subject.

3. CONCLUSIONS AND FURTHER WORK.

The primary aim of this project has been the investigation of potential routes for the synthesis of selected monodisperse oligomers of nylon-6.6 and trial syntheses using these routes. It was hoped to devise a general synthetic route to pure oligomers that could be applied to the preparation of oligomers of increasing length, while maintaining purity for future characterization studies.

The work was initially only intended to involve the integer oligomers but was, however, expanded to include the non-integer equivalents. This provides greater potential in the proposed future chain-folding studies as the end groups of the oligomers would be expected to have a considerable effect on the nature of folding. The addition of these non-integer oligomers also gives a greater and more comprehensive range of chain lengths effectively "filling the gaps" between the integer oligomers.

The "nylon intermediates" were soon found to be scarcely amenable to the reaction conditions involved in more conventional amide syntheses (e.g. as used in peptide synthesis) due to their solubility, hydrolytic lability etc. The project, therefore, rapidly developed into a

series of problem solving exercises. These started with the mono-protection of the starting material, hexamethylenediamine. Here the tendency of the reaction was towards disproportionate amounts of the bis-protected product. This was regardless of the protecting moiety involved. Once the synthesis of the phenylbenzyl carbonate derivatives had been perfected, the mono-protection of hexamethylenediamine became a standard preparation.

The coupling of mono-N-carbobenzoxyhexamethylenediamine and methyl hydrogen adipate was initially to be achieved with an aqueous Schotten-Baumann reaction. This was unsuccessful and a non-aqueous version was developed. This enabled the monomeric derivatives, carbobenzoxy methyl ester monomer, N-carbobenzoxy monomer and unprotected monomer, to be prepared.

With the lack of an adequate method for the C-methyl ester monomer, the route to the integer oligomers was temporarily suspended. Because selective deprotection is not required for the non-integer oligomers, work was focussed in this direction. The coupling reaction started to become unworkable, due to the extreme exothermic nature of the reaction, at a D.O.P. of 2.5. It seems possible that these longer molecules might assemble in some way to concentrate the functional

groups into a microstructure (e.g. H-bonded) that created severe hot spots when reaction was attempted. Even with a reduction of the temperature and the quantities of the reactants this could not be overcome. This prompted a comprehensive study of coupling methods. From this the method showing the greatest potential was found to be the mixed anhydride approach detailed earlier. This yielded cleaner and purer products than any of the other methods attempted, most of which failed. The non-integer oligomers were taken to a D.O.P. of 3.5 using mixed anhydride coupling.

Work was then continued on the integer oligomers although there was still no selective decarbobenzoylation reaction available. The reactions were attempted using the unprotected oligomers with the N-carbobenzoxy protected oligomers. As was expected side reactions dominated the scheme. Despite this the D.O.P. was successfully increased to four. On extending the method to D.O.P. values of 8 and 8.5 the products were found to contain large elements of contaminant oligomers, mainly tetrameric in length. This was thought likely to be due to the reaction not going to completion rather than any fundamental failure in the process.

It was felt that, as with all the previous stages of the synthetic scheme, the preparation of these longer chain

oligomers could be refined into a working method. This would undoubtedly be aided by the development of selective decarbobenzoylation. This should result in eliminating the possibility of side reactions by presenting only one reactive site. A successful method of bis-deprotection with subsequent reprotection of the carboxylic acid end group would also achieve this step and may be a more realistic option in future. However, this would obviously be less desirable as a single step would be less likely to introduce contaminants. It should also be noted that the tetramer was prepared even without this type of deprotection. There is no reason to suggest this would not be the case with the octamer or even with the higher oligomers. It may also be desirable, mainly as a precaution, to end the use of concentrated hydrochloric acid for deprotection. This reaction is noted in literature to run the risk of chain cleavage²⁵, although the effect has not been observed in the products up to and including the tetramer, although close control of the reactions was essential.

The octamer has been considered a suitable point for the study of chain-folding in nylon-6.6. This would, according to previous studies on the polymer¹², give a complete single fold with the chain being doubled over. This work has resulted in a scheme that is only a few steps from the synthesis of pure, monodisperse octamer,

suggesting that the method could be developed, even against the odds.

The majority of further work would be centred on using these oligomers, both integer and non-integer, in a study of chain-folding in nylon-6.6. Earlier in this report several questions were put forward regarding the nature of the fold, as follows

1) Does the molecule double back on itself with the fold occupying the minimum possible number of chain bonds?

ii) Does the chain form a loose loop at the basal surface?

iii) Does the chain re-enter the crystal at the nearest (adjacent) site or elsewhere?

iv) What determines the fold length and at what oligomer length does folding start to occur?

Many such questions remain without a conclusive answer. Not least of these is the controversy surrounding the actual identity of the chain-fold, i.e. does it consist of the acid or the amine component. It is anticipated that the answers to these questions can, conclusively or at least in part, be obtained by the use of pure oligomers. The discussion of the analytical techniques demonstrates how this may be achieved. The defined chain length and monodispersity of these compounds should

allow the folds to be studied as they form. With the end groups and chain length already determined a lot of the variables and doubt would be removed.

This project has laid the foundations for an in depth and novel study of this phenomenon by the synthesis of the materials required. Because of this, the opportunity for a greater insight into the detailed morphology of adipate polyamides now exists.

Progress in this project was severely hampered, from an early stage, by the awkwardness of the compounds involved. While difficulties in obtaining monoprotected starting diamines were expected (and eventually overcome), other problems arose which are probably inherent in the structures involved. The poor solubility of even small oligomers was rather surprising, and a serious drawback. It precluded routine analysis (e.g. by tlc or paper chromatography) that was essential for effective monitoring of reactions, and it rendered difficult routine structural confirmation using standard spectroscopic methods in many instances. Furthermore aspects of the reactivity (or unreactivity) of the compounds raised the prospect that even when dissolution was achieved the molecules remained associated, in many cases, into microstructures where "simple functional group" transformations were inefficient. On the other

hand it seems possible that prolonged exposure of the compounds to solvents in an attempt to effect complete dissolution jeopardies the integrity of oligomers and risked (solvolytic) degradation. In some cases it seemed inevitable that either unreactivity was leading to incomplete conversions or vigorous exposure to solvents was leading to degradation.

With the benefit of hindsight (such as with the previous paragraph) and other insights gained during this project, it is possible to propose a program of further work that might realistically afford further progress towards the provision and use of nylon-6.6 oligomers. Since the present work was hampered by the lack of reliable and routine information about purity and/or monodispersity, it seems access, in-house, to GPC analysis is a sine qua non for further work (there was a delay of several months in some instances here). With that proviso the author proposes that the synthetic route to mono-N-protected monomer, dimer and tetramer should be followed as described here. Thereafter the methodology for non-integral oligomers should be used as it removes the necessity for selective deprotection which was a particularly difficult aspect of the work. For example, reaction of the diamine oligomer (D.O.P. = 3.5) with two equivalents of N-monoprotected tetramer using the mixed anhydride procedure developed during

this project would provide access to an oligomer having D.O.P. = 11.5. The route to non-integer diamine oligomers could be extended to larger D.O.P.s to give higher oligomers by reaction with the tetramer, or the D.O.P. = 11.5 product after N-deprotection could be used to condense with non-integral acid terminated oligomers (2 equivalents) for chain extension. It seems that, despite the severe handicaps that affected this project so radically, methods have now been developed that offer a realistic route to oligomers of genuine interest.

4. EXPERIMENTAL.

General Information

For this work standard chemicals were supplied by either Aldrich Chemical Co Ltd or Lancaster Synthesis. Analar standard was used where available and appropriate. The hexamethylenediamine, adipic acid and cyclic monomer was supplied by ICI Fibres, Wilton.

Analysis was performed using the following instrumentation:

Infrared spectra were obtained using a Pye-Unicam SP3-100 spectrophotometer. Samples were prepared as potassium bromide (KBr) discs or liquid films.

¹H NMR were obtained using a Joel JNM PMX-60MHz spectrometer or a Bruker 250MHz spectrometer. The internal standard used was tetramethylsilane (TMS). Abbreviations used are s (singlet), d (double), t (triplet), q (quartet), m (multiplet) and b (broad).

Mass Spectra were obtained using a VG Micromass 7070F.

Melting points were obtained using an Electrothermal melting point apparatus.

Dry ether refers to diethyl ether obtained through standing over sodium metal. Dry tetrahydrofuran was

obtained by reflux over sodium metal. Dry methanol was obtained by distillation and storage over a molecular sieve.

Pure hexamethylenediamine was obtained by vacuum distillation prior to use.

Petrol refers to that fraction of petroleum boiling between 40 and 60°C.

Potassium bromide was stored in an oven at 60°C.

Unless otherwise stated, alkaline and acid solutions refer to 2M sodium hydroxide and 2M hydrochloric acid solutions respectively.

Unless otherwise stated, solvents, especially those used in recrystallization, were not treated.

4.1. MONO-PROTECTED HEXAMETHYLENEDIAMINE.

PHENYLBENZYL CARBONATE (3).

A solution of phenol (11.7g; 0.125mol) in aqueous sodium hydroxide (10%, 50ml) was prepared under stirring at 0°C in a 250ml round bottomed flask. At between 0-5°C benzylchloroformate (21.5g; 0.126mol) was added. The solution was then allowed to stand for four hours in a fume-cupboard. The resulting layers were separated, the aqueous layer was extracted several times with ether, and the combined ether layers were added to the organic layer. Any unreacted benzylchloroformate was removed by the dropwise addition of pyridine. Dilute hydrochloric acid (2M) was added and the solution washed several times with water. The ether solution was twice dried over sodium sulphate and evaporated. The phenylbenzyl carbonate was isolated by vacuum distillation at a pressure of 0.1mmHg. Yield 6.3g, 22%. Bpt. 127-131°C/0.1 mmHg.

¹H NMR (CDCl₃) δ_H 5.0 (2H, s, PhCH₂), 6.9-7.1 (10H, m, 10xArH). IR (Liquid Film) 1762 (C=O)cm⁻¹.

PHENYLBENZYL CARBONATE (3).

Scaled up reaction.

A solution of phenol (47g; 0.5mol) in sodium hydroxide (10%, 200ml) was prepared under stirring at 0°C. At between 0-5°C benzylchloroformate (86g; 0.504mol) was added. The solution was allowed to stand for 4 hrs in a fume-cupboard. The resulting layers were separated, and the aqueous layer was extracted several times with ether. The ether layers were combined with the organic layer. Any unreacted benzylchloroformate was removed by pyridine. Dilute hydrochloric acid (2M) was added and the solution washed several times with water. The ether layer was dried over sodium sulphate. The phenylbenzyl carbonate was removed by vacuum distillation. Yield 19.4g, 17%. Bpt. 127-131°C/0.1 mmHg.

¹H NMR (CDCl₃) δ_H 5.0 (2H, s, PhCH₂), 6.9-7.1 (10H, m, 10xArH). IR (Liquid Film) 1762 (C=O)cm⁻¹.

PHENYLBENZYL CARBONATE (3).

redistillation.

The various fractions (30g) collected from several attempts to prepare phenylbenzyl carbonate were placed in a 250ml pear shaped flask. The phenylbenzyl carbonate

was obtained by vacuum distillation. Yield 3.0g. Bpt.
127-131°C/0.1 mmHg.

^1H NMR (CDCl_3) δ_{H} 5.0 (2H, s, PhCH_2), 6.9-7.1
(10H, m, 10xArH). IR (Liquid Film) 1762 ($\text{C}=\text{O}$) cm^{-1} .

MONO-N-PHTHALOYL HEXAMETHYLENEDIAMINE (7).

a) A solution of N-carboethoxyphthalimide (3.8g; 0.017mol) in water (30ml) was added dropwise to a solution of freshly distilled hexamethylenediamine (2g; 0.017mol) in water (20ml). The mixture was stirred for 15 minutes. The solution was acidified and filtered. The filtrate was made alkaline and the precipitate collected and dried. Yield 0.8g, 20%.

^1H NMR (CDCl_3) δ_{H} 1.4 (8H, m, 4x CH_2), 3.7 (4H, t, 2x CH_2N),
7.7 (4H, m, 4xArH). IR (KBr disc) 3350 (NHstr) cm^{-1} ,
1720 ($\text{NC}=\text{O}$) cm^{-1} .

b) A suspension of N-carboethoxyphthalimide (3.8g; 0.017mol) in dry tetrahydrofuran (30ml) was added dropwise to a solution of freshly distilled hexamethylenediamine (2g; 0.017mol) in dry tetrahydrofuran (20ml). The mixture was stirred for 15 minutes then filtered. The solid was suspended in warm hydrochloric acid. This was filtered, the filtrate made

alkaline and the precipitate collected and dried. Yield 0.6g, 14%.

^1H NMR (CDCl_3) δ_{H} 1.4 (8H, m, $4 \times \text{CH}_2$), 3.7 (4H, t, $2 \times \text{CH}_2\text{N}$), 7.7 (4H, m, $4 \times \text{ArH}$). IR (KBr disc) $3350 (\text{NHstr}) \text{cm}^{-1}$, $1720 (\text{NC=O}) \text{cm}^{-1}$.

c) A suspension of N-carboethoxyphthalimide (3.8g; 0.017mol) in toluene (200ml) was carefully added to a solution of freshly distilled hexamethylenediamine (2g; 0.017mol) in water (200ml) without mixing. The system was gently agitated, without breaking the surface, overnight. The resulting precipitate was filtered off. The solid was suspended in warm hydrochloric acid. This was filtered and the filtrate made alkaline.

Only bis-protected hexamethylenediamine was produced due to crystallization at the interface.

MONO-N-ACETYL HEXAMETHYLENEDIAMINE (8).

A solution of acetic acid (60g; 1mol) in methanol (100ml) was added over a period of 1 hour to a solution of freshly distilled hexamethylenediamine (116g; 1mol) in methanol (400ml) while keeping the temperature below 35°C with an ice bath. The mixture was stood overnight.

The methanol was removed on a rotary evaporator and the residue heated at 150-160°C for 5 hours. The reaction mixture was distilled under high vacuum. The fraction collected at 120-175°C/0.06 mmHg was redistilled and the fraction at 136-138°C/0.12 mmHg. Yield 37.9g, 24%.

¹H NMR (CDCl₃) δ_H, 1.3 (8H, m, 4xCH₂), 1.8 (3H, s, CH₃), 2.5 (2H, t, CH₂NH₂), 3.3 (2H, t, CH₂NH), 5.8 (1H, bs, NH). IR (KBr disc) 3350 (NHstr)cm⁻¹, 1705 (NC=O)cm⁻¹.

MONO-N-CARBOBENZOXYHEXAMETHYLENEDIAMINE (9).

Using Benzylchloroformate (2).

a) A mixture of benzylchloroformate (17.6g; 0.1mol) in dry tetrahydrofuran (70ml), and freshly distilled hexamethylenediamine (23g; 0.2mol) in dry tetrahydrofuran (80ml), was refluxed for 2 hours (or left stirring for 12 hours at room temperature). The bis-N-carbobenzoxy hexamethylenediamine and tetrahydrofuran were removed under vacuum and the syrupy residue dissolved in warm hydrochloric acid (2M; 500ml). The filtrate was neutralized with dilute sodium hydroxide (2M) and allowed to stand for 24 hours in a fridge. The product that crystallized out of the water was oven dried at 60°C. The white solid was recrystallized from ethyl acetate and methanol. Yield 5g, 19%. Mpt 99-102°C.

^1H NMR (CDCl_3) δ_{H} 1.4-1.7 (8H, m, $4\times\text{CH}_2$), 2.7 (2H, t, CH_2NH_2), 3.2 (2H, t, CH_2HN), 5.1 (2H, s, ArCH_2), 6.8 (1H, bs, NH), 7.2 (5H, s, $5\times\text{ArH}$). IR (KBr disc) 1680 (NC=O), 3340 (NH) cm^{-1} .

b) To a solution of freshly distilled hexamethylene diamine (14g; 0.124mol) in water (30ml) was added benzylchloroformate (10.6g; 0.062mol) and a solution of sodium hydroxide (2M, 40ml) simultaneously. The solution was stirred for 15 minutes. The product crystallized out of solution and was oven dried at 60°C . The white solid was recrystallized from ethyl acetate and methanol. Yield 3.88g, 25%. Mpt $101-103^\circ\text{C}$.

^1H NMR (CDCl_3) δ_{H} 1.4-1.7 (8H, m, $4\times\text{CH}_2$), 2.7 (2H, t, CH_2NH_2), 3.2 (2H, t, CH_2HN), 5.1 (2H, s, ArCH_2), 6.8 (1H, bs, NH), 7.2 (5H, s, $5\times\text{ArH}$). IR (KBr disc) 1680 (NC=O), 3340 (NH) cm^{-1} .

MONO-N-PHTHALOYLHEXAMETHYLENEDIAMINE (7).
From 6-aminocaproic acid (10).

Monoprotection of 6-aminocaproic acid.

A solution of N-carboethoxyphthalimide (9g; 0.041mol) in water (100ml) was added dropwise to a solution of 6-aminocaproic acid (5g; 0.04mol) and sodium carbonate (4g; 0.04mol) in water (70ml). The mixture was stirred

for 15 minutes. The solution was filtered and acidified. The precipitate was collected and dried. Yield 5.4g, 50%.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (6H, m, $3\times\text{CH}_2$), 2.3 (2H, t, CH_2COOH), 3.6 (2H, t, CH_2N), 7.4 (4H, s, $4\times\text{ArH}$). IR (KBr disc) $3350(\text{NHstr})\text{cm}^{-1}$, $3300-2500(\text{OHstr})\text{cm}^{-1}$, $1720(\text{NC=O})\text{cm}^{-1}$.

Chlorination of carboxylic acid.

The N-phthaloyl amino acid was stirred with thionyl chloride (7ml; 0.06mol 1:1.5 molar ratio) and 2 drops of dimethylformamide for 30 minutes. The excess thionyl chloride was removed by distillation (Bpt. 78°C) leaving the crude acid chloride, used without further purification. Yield 6.2g, 100%.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (6H, m, $3\times\text{CH}_2$), 2.9 (2H, t, CH_2COCl), 3.6 (2H, t, CH_2N), 7.4 (4H, s, $4\times\text{ArH}$). IR (KBr disc) $1800(\text{NC=O})\text{cm}^{-1}$.

Preparation of amide from acid chloride.

To the acid chloride 2 molar equivalents of ammonia solution (sp. gr 0.88) was added dropwise. The solution was warmed for 5 minutes then evaporated to dryness and the solid recrystallized from dilute methanol. Yield 4.6g, 80%.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (6H, m, $3 \times \text{CH}_2$), 2.3 (2H, t, CH_2CONH_2), 3.6 (2H, t, CH_2N), 6.8 (2H, s, CONH_2), 7.4 (4H, s, $4 \times \text{ArH}$). IR (KBr disc) $3350 (\text{NHstr}) \text{cm}^{-1}$, $1725 (\text{NC=O}) \text{cm}^{-1}$.

Reduction of amide to amine.

a) A solution of lithium aluminium hydride (0.6g; 0.016mol) in dry tetrahydrofuran (50ml) was placed in a 150ml two-necked flask equipped with a condenser and a magnetic stirrer. The solution was gently refluxed while the amide (4g; 0.015mol) was slowly added over a period of 30 minutes. The mixture was refluxed for an additional 2 hours. The reaction mixture was worked up by the addition of water (10ml). After filtration to remove the solid aluminium and lithium salts, the tetrahydrofuran was evaporated. The product was recrystallized from methanol.

Due to preferential reduction of the phthaloyl group only hexamethylenediamine was produced.

b) A solution of lithium aluminium hydride (0.6g; 0.016mol) in dry tetrahydrofuran (50ml) was placed in a 150ml two-necked flask equipped with a condenser and a magnetic stirrer. The solution was stirred at room temperature while the amide (4g; 0.015mol) was slowly added over a period of 30 minutes. The mixture was

stirred for an additional 2 hours. The reaction mixture was worked up by the addition of water (10ml). After filtration to remove the solid aluminium and lithium salts, the tetrahydrofuran was evaporated. The product was recrystallized from methanol.

Due to preferential reduction of the phthaloyl group only hexamethylene diamine was produced.

MONO-N-PHTHALOYLHEXAMETHYLENEDIAMINE (7).
Mono-deprotection using hydrazine.

a) A solution of hydrazine hydrate (1g; 0.02mol) in water (100ml) was prepared in a 250ml round bottomed flask. Bis-N-phthaloylhexamethylenediamine (15g; 0.04mol) was added and the solution stirred for twelve hours. The solution was filtered and the water was then removed under vacuum. Hydrochloric acid (2M) added to the residue. The filtrate was then neutralized but no mono-protected product could be obtained.

b) A solution of methanol (100ml) and hydrazine hydrate (1g; 0.02mol) was prepared in a 250ml round bottomed flask fitted with a reflux condenser. Bis-N-phthaloyl hexamethylenediamine (15g; 0.04mol) was added and the solution refluxed for two hours. The methanol was then removed under vacuum and hydrochloric acid (2M) added to

the residue. The filtrate was then neutralized but no mono-protected product was obtained.

PHENYLBENZYL CARBONATE (3).

Modified method.

A solution of phenol (47g; 0.5mol) in sodium hydroxide (10%, 200ml) was prepared under stirring at 0°C. At between 0-5°C benzylchloroformate (86g; 0.504mol) was added. The solution was allowed to stand for 12 hrs in a fume-cupboard. The resulting layers were separated and the aqueous layer was extracted several times with ether. The ether layers were added to the organic layer. Any unreacted benzylchloroformate was removed by pyridine. Dilute hydrochloric acid (2M) was added and the solution washed many times with water. The ether layer was dried twice over sodium sulphate. The ether was removed on a rotary evaporator. Yield 97g, 85%.

¹H NMR (CDCl₃) δ_H 5.0 (2H, s, PhCH₂) 6.9-7.1 (10H, m, 10xArH). IR (Liquid Film) 1762 (C=O)cm⁻¹.

MONO-N-CARBOBENZOXYHEXAMETHYLENEDIAMINE (9).

A mixture of phenylbenzyl carbonate (22.8g; 0.1mol) in dry tetrahydrofuran (70ml) and freshly distilled hexamethylenediamine (23g; 0.2mol) in dry tetrahydrofuran (80ml) was refluxed for 2 hours (or left stirring for 12 hours at room temperature). The bis-N-carbobenzoxy hexamethylenediamine and tetrahydrofuran were removed under vacuum and the syrupy residue dissolved in warm hydrochloric acid (2M; 500ml). The filtrate was extracted several times with ether (removal of phenol from esteraminolysis) and neutralized with dilute sodium hydroxide (2M) before being allowed to stand for 24 hours in a fridge. The crystallized product was filtered and oven dried at 60°C. The reaction product was stirred in dry ether to remove any remaining phenol. The white solid was recrystallized from ethyl acetate and methanol, removing what were thought to be carbamate contaminants. Yield 12.5g, 50%. Mpt 101-102°C.

¹H NMR (CDCl₃) δ_H 1.4-1.7 (8H, m, 4xCH₂), 2.7 (2H, t, CH₂NH₂), 3.2 (2H, t, CH₂NH), 5.1 (2H, s, ArCH₂), 6.8 (1H, bs, NH), 7.2 (5H, s, 5xArH). IR (KBr disc) 1680 (NC=O), 3340 (NH) cm⁻¹.

A second product was crystallized out of water prior to the mono-N-carbobenzoxyhexamethylenediamine. Mpt. 160°C,

IR (KBr disc) 1680 (NC=O), 1630 (C=O?), 3340 (NH) cm^{-1} . The ^1H NMR was identical to mono-N-carbobenzoxy hexamethylenediamine and the only conclusion was that the product was the carbonate produced by reaction with atmospheric carbon dioxide. Further analysis was not attempted.

4.2. MONOMERIC DERIVATIVES.

CARBOBENZOXY METHYL ESTER MONOMER (17).

Via the Schotten-Baumann reaction.

In a 50ml round-bottomed flask methyl hydrogen adipate (5g; 0.031mol) was stirred with thionyl chloride (7g; 0.06mol) and two drops of N,N'-dimethylformamide. After 30 minutes the excess thionyl chloride was removed under vacuum, leaving the crude acid chloride.

^1H NMR (CDCl_3) δ_{H} 1.7 (4H, m, $2\times\text{CH}_2$), 2.4 (2H, t, $\text{CH}_2\text{C}=\text{O}$), 3.0 (2H, t, CH_2COCl), 3.6 (3H, s, CH_3).

Using a magnetic stirrer a suspension of mono-N-carbobenzoxyhexamethylenediamine (5g; 0.02mol) in water (75ml) was prepared at 0°C . The crude methyl adipyl chloride (3.3g; 0.019mol) and sodium hydroxide (2M; 20ml) were added simultaneously. After four hours on a rotary evaporator at 40°C the residue was recrystallized from ethyl acetate. Yield 1.64, 22%. Mpt $101-103^\circ\text{C}$.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (12H, m, $6\times\text{CH}_2$), 2.2 (4H, t, $2\times\text{CH}_2\text{C}=\text{O}$), 3.3 (4H, t, $2\times\text{CH}_2\text{NH}$), 3.6 (3H, s, CH_3), 5.0 (2H, s, PhCH_2), 7.1 (5H, s, $5\times\text{ArH}$). IR (KBr disc) 1730 (C=O ester), 1680 (C=O carbamate), 1640 (C=O amide) $3300(\text{NH})\text{cm}^{-1}$. EIMS 392 (M^+)

CARBOBENZOXY METHYL ESTER MONOMER (17).

Using dicyclohexylcarbodiimide.

Methyl hydrogen adipate (16g; 0.1mol) was dissolved in dry tetrahydrofuran (500ml). The solution was cooled to 0°C and mono-N-carbobenzoxyhexamethylenediamine (25g; 0.1mol) was added followed by dicyclohexylcarbodiimide (20.6g; 0.1mol). The solution was refluxed for one hour and then left stirring overnight. The resulting precipitate, dicyclohexylurea, was filtered off and washed with dry tetrahydrofuran. The tetrahydrofuran solutions were taken down on a rotary evaporator and the resulting solid recrystallized from methanol. Yield 5.9g, 15%. Mpt 103°C.

¹H NMR (CDCl₃) δ_H 1.3-1.8 (12H, m, 6xCH₂), 2.2 (4H, t, 2xCH₂C=O), 3.3 (4H, t, 2xCH₂NH), 3.6 (3H, s, CH₃), 5.0 (2H, s, PhCH₂), 7.1 (5H, s, 5xArH). IR (KBr disc) 1730 (C=O ester), 1680 (C=O carbamate), 1640 (C=O amide) 3300 (NH) cm⁻¹.

CARBOBENZOXY METHYL ESTER MONOMER (17).

Via the non-aqueous Schotten-Baumann reaction.

In a 50ml round-bottomed flask methyl hydrogen adipate (5g; 0.031mol) was stirred with thionyl chloride (7g; 0.06mol) and two drops of N,N-dimethylformamide.

After 30 minutes the excess thionyl chloride was removed under vacuum leaving the crude acid chloride.

^1H NMR (CDCl_3) δ_{H} 1.7 (4H, m, $2 \times \text{CH}_2$), 2.4 (2H, t, $\text{CH}_2\text{C}=\text{O}$), 3.0 (2H, t, CH_2COCl), 3.6 (3H, s, CH_3).

In a 100ml conical flask fitted with a calcium chloride drying tube were placed mono-N-carbobenzoxy hexamethylenediamine (2.5g; 0.01mol), methyl adipyl chloride (2.68g; 0.015mol) and pyridine (30ml). The temperature of the reaction mixture rose spontaneously, and when no further heat was evolved (around 15 minutes) the mixture was poured with good stirring into hydrochloric acid (3%; 600ml) containing crushed ice (200g). The product was collected on a Büchner funnel and washed with methanol (20ml), then with water (20ml). The product was sucked as dry as possible and air-dried at room temperature. The crude product was recrystallized from methanol and the carbobenzoxy methyl ester monomer obtained as a white solid. Yield 2.4g, 62%. Mpt 102-104°C.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (12H, m, $6 \times \text{CH}_2$), 2.2 (4H, t, $2 \times \text{CH}_2\text{C}=\text{O}$), 3.3 (4H, t, $2 \times \text{CH}_2\text{NH}$), 3.6 (3H, s, CH_3), 5.0 (2H, s, PhCH_2), 7.2 (5H, s, $5 \times \text{ArH}$). IR (KBr disc) 1730 (C=O ester), 1680 (C=O carbamate), 1640 (C=O amide) $3300 (\text{NH}) \text{cm}^{-1}$. EIMS 392 (M^+)

CARBOBENZOXY METHYL ESTER MONOMER (17).
Scaled up.

In a 50ml round-bottomed flask methyl hydrogen adipate (20g; 0.12mol) was stirred with thionyl chloride (28g; 0.24mol) and two drops of N,N-dimethylformamide. After 30 minutes the excess thionyl chloride was removed under vacuum leaving the crude acid chloride.

$^1\text{H NMR}$ (CDCl_3) δ , 1.7 (4H, m, $2 \times \text{CH}_2$), 2.4 (2H, t, $\text{CH}_2\text{C}=\text{O}$), 3.0 (2H, t, CH_2COCl), 3.6 (3H, s, CH_3).

In a 500ml conical flask fitted with a calcium chloride drying tube were placed mono-N-carbobenzoxy hexamethylenediamine (10.0g; 0.04mol), methyl adipyl chloride (10.72g; 0.06mol) and pyridine (120ml). The temperature of the reaction mixture rose spontaneously, and when no further heat was evolved (around 15 minutes) the mixture was poured with good stirring into hydrochloric acid (6%; 1.2l) containing crushed ice (800g). The product was collected on a Büchner funnel and washed with methanol (80ml), then with water (80ml). The product was sucked as dry as possible and air-dried at room temperature. The crude product was recrystallized from methanol and the carbobenzoxy methyl ester monomer obtained as a white solid. Yield 1.7g, 10-12%. Mpt 101-103°C.

¹H NMR (CDCl₃) δ_H 1.3-1.8 (12H, m, 6xCH₂), 2.2 (4H, t, 2xCH₂C=O), 3.3 (4H, t, 2xCH₂NH), 3.6 (3H, s, CH₃), 5.0 (2H, s, PhCH₂), 7.1 (5H, s, 5xArH). IR (KBr disc) 1730 (C=O ester), 1680 (C=O carbamate), 1640 (C=O amide) 3300 (NH) cm⁻¹. EIMS 392 (M⁺)

CARBOBENZOXY METHYL ESTER MONOMER (17).

Modified method.

In a 50ml round-bottomed flask methyl hydrogen adipate (8g; 0.05mol) was stirred with thionyl chloride (10g; 0.09mol) and two drops of N,N-dimethylformamide. After 30 minutes the excess thionyl chloride was removed under vacuum leaving the crude acid chloride.

¹H NMR (CDCl₃) δ_H 1.7 (4H, m, 2xCH₂), 2.4 (2H, t, CH₂C=O), 3.0 (2H, t, CH₂COC1), 3.6 (3H, s, CH₃).

In a 100ml conical flask fitted with a calcium chloride drying tube were placed mono-N-carbobenzoxy hexamethylenediamine (3.75g; 0.015mol) and pyridine (45ml), this mixture was cooled to -10°C. The temperature of the reaction mixture was maintained at around -10°C and methyl adipyl chloride (4.0g; 0.023mol) was added dropwise over 30 minutes. The mixture was poured with good stirring into hydrochloric acid (3%; 900ml) containing crushed ice (300g). The product

was collected on a Büchner funnel and washed with methanol (30ml), then with water (30ml). The product was sucked as dry as possible and air-dried at room temperature. The crude product was recrystallized from methanol and the carbobenzoxy methyl ester monomer obtained as a white solid. Yield 3.5g, 60%. Mpt 101-102°C.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (12H, m, $6 \times \text{CH}_2$), 2.2 (4H, t, $2 \times \text{CH}_2\text{C}=\text{O}$), 3.3 (4H, t, $2 \times \text{CH}_2\text{NH}$), 3.6 (3H, s, CH_3), 5.0 (2H, s, PhCH_2), 7.1 (5H, s, $5 \times \text{ArH}$). IR (KBr disc) 1730 (C=O ester), 1680 (C=O carbamate), 1640 (C=O amide) $3300 (\text{NH}) \text{cm}^{-1}$. EIMS 392 (M^+)

N-CARBOBENZOXY MONOMER (21).

Using potassium hydroxide in ethanol.

Potassium hydroxide (3.0g; 0.05mol) was dissolved in water (5ml) in a 50ml round bottomed flask and ethanol (10ml) added. Carbobenzoxy methyl ester monomer (1.0g; 3×10^{-3} mol) was introduced with stirring. A reflux condenser was then attached and the solution refluxed for one hour. The ethanol was removed on a rotary evaporator and the residue dissolved in a small amount of warm water and filtered. The solution was cooled in an ice bath and sulphuric acid (2M) was added dropwise under stirring until no more product was precipitated.

The product was filtered and washed with water (20ml) and dried in an oven at 60°C.

The product obtained was the trans-esterification product. ^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (15H, m, $6 \times \text{CH}_2$, CH_3), 2.2 (4H, t, $2 \times \text{CH}_2\text{C}=\text{O}$), 3.3 (4H, t, $2 \times \text{CH}_2\text{NH}$), 3.5 (2H, s, CH_2), 5.0 (2H, s, PhCH_2), 7.1 (5H, s, $5 \times \text{ArH}$). IR (KBr disc) 1735 ($\text{C}=\text{O}$ ester), 1680 ($\text{C}=\text{O}$ carbamate), 1640 ($\text{C}=\text{O}$ amide) $3300 (\text{NH}) \text{cm}^{-1}$. EIMS 406 (M^+)

N-CARBOBENZOXY MONOMER (21).
Using aqueous potassium hydroxide.

Carbobenzoxy methyl ester monomer (1.0g; 3×10^{-3} mol) was dissolved in water (10ml) in a 50ml round bottomed flask and potassium hydroxide (2.5g; 0.045mol) was introduced with stirring. A condenser was attached and the solution refluxed for one hour, then filtered and cooled in an ice bath. Sulphuric acid (2M) was added dropwise under stirring until no more product precipitated. The product was filtered and washed with water (20ml) and dried in an oven at 60°C. Yield 0.19g, 20%. Mpt 137-139°C.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (12H, m, $6 \times \text{CH}_2$), 2.1 (2H, t, $\text{CH}_2\text{C}=\text{O}$), 2.4 (2H, t, CH_2COOH), 3.3 (4H, t, $2 \times \text{CH}_2\text{NH}$), 5.0 (2H, s, PhCH_2), 7.1 (5H, s, $5 \times \text{ArH}$). IR (KBr disc)

3300(NH), 3300-2500(OHstr) 1680(C=O carbamate, carboxylic acid), 1635(C=O amide)cm⁻¹. EIMS 378(M⁺).

N-CARBOBENZOXY MONOMER (21).

Using aqueous ammonium hydroxide.

A solution of carbobenzoxymethyl ester monomer (1g; 3x10⁻³mol) was prepared in concentrated ammonium hydroxide (0.88, 50ml) in a 100ml round bottomed flask. A condenser was attached and the solution was refluxed for one hour, then cooled in an ice bath before dilute sulphuric acid (2M) was added dropwise under stirring. The product was filtered off and washed with water (2x20ml) and dried in an oven at 60°C. Yield 0.5g, 52%. Mpt 137-139°C.

¹H NMR (CDCl₃) δ_H 1.3-1.8 (12H, m, 6xCH₂), 2.1 (2H, t, CH₂C=O), 2.4 (2H, t, CH₂COOH), 3.3 (4H, t, 2xCH₂NH), 5.0 (2H, s, PhCH₂), 7.1 (5H, s, 5xArH). IR (KBr disc) 3300(NH), 3300-2500(OHstr) 1680(C=O carbamate, carboxylic acid), 1635(C=O amide)cm⁻¹. EIMS 378(M⁺).

N-CARBOBENZOXY MONOMER (21).

Using potassium hydroxide and ammonium hydroxide.

Carbobenzoxymethyl ester monomer (1.0g; 3x10⁻³mol) was dissolved in concentrated ammonium hydroxide (0.88, 40ml) in a 100ml round bottomed flask a reflux condenser

was attached and the solution refluxed for 30 minutes. Potassium hydroxide pellets (2.0g; 0.04mol) were introduced with stirring until all the solids were dissolved. The solution was cooled in an ice bath and filtered. Sulphuric acid (2M) was added dropwise under stirring until no more product precipitated. The product was filtered, washed with water (20ml) and dried in an oven at 60°C. Yield 0.58g, 60%. Mpt 138-139°C.

¹H NMR (CDCl₃) δ_H 1.3-1.8 (12H, m, 6xCH₂), 2.1 (2H, t, CH₂C=O), 2.4 (2H, t, CH₂COOH), 3.3 (4H, t, 2xCH₂NH), 5.0 (2H, s, PhCH₂), 7.1 (5H, s, 5xArH). IR (KBr disc) 3300 (NH), 3300-2500 (OHstr) 1680 (C=O carbamate, carboxylic acid), 1635 (C=O amide)cm⁻¹. EIMS 378 (M⁺).

N-CARBOBENZOXY MONOMER (21).

Using potassium hydroxide in methanol.

Potassium hydroxide (3.0g;) was dissolved in warm, dry methanol (20ml). Carbobenzoxy methyl ester monomer (1.0g; 3x10⁻³mol) was introduced with stirring. A condenser was attached and the solution refluxed for one hour. The methanol was removed on a rotary evaporator and the residue dissolved in warm water and filtered. The solution was cooled in an ice bath and sulphuric acid (2M) was added dropwise under stirring until no

more product precipitated. The product was filtered and washed with water (20ml). Yield 0.92g, 95%. Mpt 139°C.

¹H NMR (CDCl₃) δ_H 1.3-1.8 (12H, m, 6xCH₂), 2.1 (2H, t, CH₂C=O), 2.4 (2H, t, CH₂COOH), 3.3 (4H, t, 2xCH₂NH), 5.0 (2H, s, PhCH₂), 7.1 (5H, s, 5xArH). IR (KBr disc) 3300(NH), 3300-2500(OHstr) 1680(C=O carbamate, carboxylic acid), 1635(C=O amide)cm⁻¹. EIMS 378(M⁺).

N-CARBOBENZOXY MONOMER (21).

Using potassium hydroxide in methanol (scaled up).

Potassium hydroxide (29.0g; 0.52mol) was dissolved in warm, dry methanol (170ml) added. Carbobenzoxy methyl ester monomer (10.0g; 0.026mol) was introduced with stirring. A reflux condenser was attached and the solution refluxed for one hour. The methanol was removed on a rotary evaporator and the residue dissolved in warm water and filtered. The solution was cooled in an ice bath and sulphuric acid (2M) was added dropwise under stirring until no more product precipitated. The product was filtered and washed with water (3x50ml). Yield 9.35g, 97%. Mpt 139°C.

¹H NMR (CDCl₃) δ_H 1.3-1.8 (12H, m, 6xCH₂), 2.1 (2H, t, CH₂C=O), 2.4 (2H, t, CH₂COOH), 3.3 (4H, t, 2xCH₂NH), 5.0 (2H, s, PhCH₂), 7.1 (5H, s, 5xArH). IR (KBr disc)

3300(NH), 3300-2500(OHstr) 1680(C=O carbamate, carboxylic acid), 1635(C=O amide)cm⁻¹. EIMS 378(M⁺).

C-METHYL ESTER MONOMER (19).

Using hydrogen bromide in acetic acid.

Carbobenzoxy methyl ester monomer (1g; 3x10⁻³mol) was dissolved in a solution of hydrogen bromide in acetic acid (37%; 10ml) in a 50ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was left stirring gently at room temperature for two hours. The mixture was evaporated to an oil which was dissolved in water (25ml). The solution was washed with ether (4x20ml), and then evaporated to dryness. The residue was dried completely in a desiccator under vacuum overnight.

No product could be isolated from the residue. As no hydrogen bromide salt could be obtained the method could not proceed.

DECARBOBENZOXYLATION OF N-CARBOBENZOXY ALANINE (24).

Using hydrogen bromide in acetic acid.

N-carbobenzoxy alanine (1g; 4x10⁻³mol) was dissolved in a solution of hydrogen bromide in acetic acid (37%; 10ml) in a 50ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The

solution was left stirring gently at room temperature for two hours. The mixture was evaporated to an oil which was dissolved in water (25ml). The solution was washed with ether (4x20ml), and then evaporated to dryness. The residue was dried completely in a desiccator under vacuum overnight. The product was crystallized from methanol and ether. Yield 0.65g, 85%.

The hydrogen bromide salt of alanine was dissolved in an absolute minimum amount of water. The free amino acid was obtained by neutralization with sodium hydroxide (2M). The precipitate was filtered out, washed with water and oven dried at 40°C. Yield 0.55g, 97%.

¹H NMR (CDCl₃) δ_H 1.6 (3H, d, CH₃), 3.2 (H, m, CH) 2.9 (b, NH₂).

C-METHYL ESTER MONOMER (19).

Using hydrogen bromide in acetic acid (modified).

Carbobenzoxy methyl ester monomer (1g; 3x10⁻³mol) was dissolved in a solution of hydrogen bromide in acetic acid (37%; 10ml) in a 50ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was left stirring gently at 40°C for two hours. The mixture was evaporated to an oil which was dissolved in water (25ml). The solution was washed

with ether (4x20ml), and then evaporated to dryness. The residue was dried completely in a desiccator under vacuum overnight. The product was crystallized repeatedly from methanol and ether. Yield 0.09g, 10%.

The hydrogen bromide salt of carbobenzoxy methyl ester monomer (0.5g, 2×10^{-3} mol) was dissolved in an absolute minimum amount of water. The free amino acid was to be obtained by neutralization with sodium hydroxide (2M).

No product could be isolated.

C-METHYL ESTER MONOMER (19).
Using catalytic hydrogenation (Pd/C).

A 50ml flame dried round bottomed flask was charged with dry methanol (20ml), carbobenzoxy methyl ester monomer (3g; 8×10^{-3} mol) and palladium black (0.3g). The solution was attached to hydrogenation equipment for twelve hours (carbon dioxide evolution could not be observed). The solution was filtered and the material oven dried at 40°C before recrystallization in methanol.

The product obtained was unchanged bis-protected monomer. IR (KBr disc) 1730 (C=O ester), 1680 (C=O carbamate), 1640 (C=O amide) 3300 (NH) cm^{-1} .

DECARBOBENZOXYLATION OF N-CARBOBENZOXY ALANINE (24).
using catalytic hydrogenation (Pd/C).

A 50ml flame dried round bottomed flask was charged with dry methanol (20ml), N-carbobenzoxy alanine (3g; 0.012mol) and palladium black (0.3g). The solution was attached to hydrogenation equipment for twelve hours. The solution was filtered and the product oven dried at 40°C before recrystallization in methanol. Yield 47%.

¹H NMR (CDCl₃) δ_H 1.6 (3H, d, CH₃), 3.2 (H, m, CH).

C-METHYL ESTER MONOMER (19).
Using catalytic hydrogenation (modified).

A 50ml flame dried round bottomed flask was charged with dry methanol (20ml), acetic acid (5ml), carbobenzoxy methyl ester monomer (3g; 8x10⁻³mol) and palladium black (0.3g). The solution was attached to hydrogenation equipment for twelve hours (carbon dioxide evolution could not be observed). The solution was filtered and the material oven dried at 40°C before recrystallization in methanol.

The product obtained was unchanged bis-protected monomer. IR (KBr disc) 1730(C=O ester), 1680(C=O carbamate), 1640(C=O amide) 3300(NH)cm⁻¹.

C-METHYL ESTER MONOMER (19).

Using catalytic hydrogenation (modified).

A 50ml flame dried round bottomed flask was charged with dry methanol (20ml), acetic acid (5ml), carbobenzoxy methyl ester monomer (3g; 8×10^{-3} mol) and platinum hexachloride (0.3g). The solution was attached to hydrogenation equipment for twelve hours (carbon dioxide evolution could not be observed). The solution was filtered and the product oven dried at 40°C before recrystallization in methanol.

The product obtained was unchanged bis-protected monomer. IR (KBr disc) 1730 (C=O ester), 1680 (C=O carbamate), 1640 (C=O amide) 3300 (NH) cm^{-1} .

UNPROTECTED MONOMER (28).

Using concentrated hydrochloric acid.

A solution of carbobenzoxy methyl ester monomer (2g; 5×10^{-3} mol) in concentrated hydrochloric acid (20ml) was prepared in a 50ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was heated to 40°C for three hours (carbon dioxide evolution), then cooled, mixed with water (40ml) and extracted with ether (40ml) to remove the benzyl chloride. The filtrate of the hydrochloride solution was taken down on a rotary evaporator and the residue

dissolved in a minimum amount of glacial acetic acid. This solution was purified by warming with activated charcoal and was then filtered. The hydrochloride was precipitated with dry ether. The resulting oil was again taken down on a rotary evaporator and the residue was mixed with water and ether. The aqueous layer was separated and after neutralization with sodium hydroxide (2M) evaporated to near dryness, on cooling the solid precipitate was recrystallized from methanol and ether. Yield 1.2g, 96%. Mpt 192°C.

¹H NMR (CDCl₃) δ_H 1.4-1.7 (12H, m, 6xCH₂), 2.0 (2H, t, CH₂C=O), 2.3 (2H, t, CH₂COO⁻), 3.3-3.4 (4H, t, CH₂NH, CH₂NH₃⁺). IR (KBr disc) 1640 (C=O amide), 1400 (COO⁻), 3300 (NH) cm⁻¹.

C-METHYL ESTER MONOMER (19).
Using trifluoroacetic acid.

Trifluoroacetic acid (20ml) was added to a 50ml round bottomed flask fitted with a condenser. Carbobenzoxy methyl ester monomer (2g; 5x10⁻³mol) was added and the solution refluxed for two hours. The trifluoroacetic acid was removed under vacuum and the residue recrystallized from methanol. Yield 0.13g, 10%.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (12H, m, $6 \times \text{CH}_2$), 2.2-2.4 (6H, m, $2 \times \text{CH}_2\text{C}=\text{O}$, CH_2NH_2), 3.3 (2H, t, CH_2NH), 3.6 (3H, s, CH_3), 5.9 (2H, s, NH_2). IR (KBr disc) 1740 (C=O ester), 1635 (C=O amide), 3300 (NH) cm^{-1} .

C-METHYL ESTER MONOMER (19).

Via esterification with methanol and hydrochloric acid.

In a flame dried 100ml round bottomed flask fitted with a reflux condenser were placed dry methanol (40ml) and concentrated hydrochloric acid (3ml). Unprotected monomer (5g; 0.02mol) was added and the solution was refluxed for eighteen hours. The excess solvent was removed under vacuum. The residue was dissolved in a minimal amount of water and neutralized with sodium hydroxide (2M). The precipitate was recrystallized from methanol. Yield 39%.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (12H, m, $6 \times \text{CH}_2$), 2.2-2.4 (6H, m, $2 \times \text{CH}_2\text{C}=\text{O}$, CH_2NH_2), 3.3 (2H, t, CH_2NH), 3.6 (3H, s, CH_3), 5.9 (2H, s, NH_2). IR (KBr disc) 1740 (C=O ester), 1635 (C=O amide), 3300 (NH) cm^{-1} .

C-METHYL ESTER MONOMER (19).

Via esterification with methanol and thionyl chloride.

In a flame dried 100ml round bottomed flask fitted with a reflux condenser were placed dry methanol (40ml) at -10°C and thionyl chloride (2.5g; 0.022mol). Unprotected monomer (5g; 0.02mol) was added and the solution was stirred at room temperature for two hours. The excess solvent was removed under vacuum. The residue was dissolved in a minimal amount of water and neutralized with sodium hydroxide (2M). The precipitate was recrystallized from methanol. Yield 37%.

¹H NMR (CDCl₃) δ_H 1.3-1.8 (12H, m, 6xCH₂), 2.2-2.4 (6H, m, 2xCH₂C=O, CH₂NH₂), 3.3 (2H, t, CH₂NH), 3.6 (3H, s, CH₃), 5.9 (2H, s, NH₂). IR (KBr disc) 1740 (C=O ester), 1635 (C=O amide), 3300 (NH) cm⁻¹.

C-METHYL ESTER MONOMER (19).

Via esterification with methanol and thionyl chloride (modified).

In a flame dried 100ml round bottomed flask fitted with a reflux condenser were placed dry methanol (40ml) at -10°C and thionyl chloride (2.5g; 0.022mol). Unprotected monomer (5g; 0.02mol) was added and the solution was refluxed one hour. The solution was cooled and the excess solvent was removed under vacuum. The residue was

dissolved in a minimal amount of water and neutralized with sodium hydroxide (2M). The precipitate was recrystallized from methanol. Yield 39%.

^1H NMR (CDCl_3) δ , 1.3-1.8 (12H, m, $6 \times \text{CH}_2$), 2.2-2.4 (6H, m, $2 \times \text{CH}_2\text{C}=\text{O}$, CH_2NH_2), 3.3 (2H, t, CH_2NH), 3.6 (3H, s, CH_3), 5.9 (2H, s, NH_2). IR (KBr disc) 1740 (C=O ester), 1635 (C=O amide), 3300 (NH) cm^{-1} .

C-METHYL ESTER MONOMER (19).
Using t-butyl isocyanide.

A solution of unprotected monomer (4g; 0.01mol) in anhydrous methanol (50ml) was kept under stirring at room temperature. t-butyl isocyanide (0.83g; 0.01mol) was added giving a cloudy solution. The reaction mixture was left stirring for the disappearance of the isocyanide to indicate completion of the reaction. After two weeks there was still no sign of the solution clearing.

The product recovered was unchanged unprotected monomer. IR (KBr disc) 1640 (C=O amide), 1400 (COO^-), 3300 (NH) cm^{-1} .

C-METHYL ESTER MONOMER (19).
From ring opening of cyclic monomer.

In a flame dried 250ml round bottomed flask fitted with a calcium chloride drying tube was added anhydrous

methanol (30ml) and sodium (1g). Once the sodium had reacted a solution of cyclic monomer (10g; 0.04mol) in anhydrous methanol (100ml) was added. The solution was stirred for two days at room temperature. The excess methanol was removed under vacuum and the residue recrystallized from methanol.

Only starting material was recovered.

C-METHYL ESTER MONOMER (19).
From ring opening of cyclic monomer (modified).

In a flame dried 250ml round bottomed flask fitted with a reflux condenser and a calcium chloride drying tube was added anhydrous methanol (30ml) and sodium (1g). Once the sodium had reacted a solution of cyclic monomer (10g;) in anhydrous methanol (100ml) was added. The solution was refluxed for four days. The excess methanol was removed under vacuum and the product recrystallized from methanol. Yield 5%.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (12H, m, $6 \times \text{CH}_2$), 2.2-2.4 (6H, m, $2 \times \text{CH}_2\text{C}=\text{O}$, CH_2NH_2), 3.3 (2H, t, CH_2NH), 3.6 (3H, s, CH_3), 5.9 (2H, s, NH_2). IR (KBr disc) 1740 (C=O ester), 1635 (C=O amide), 3300 (NH) cm^{-1} .

4.3. OLIGOMERIC DERIVATIVES.

4.3.1. NON-INTEGER OLIGOMERS.

BIS-N-CARBOBENZOXY OLIGOMER / D. O. P. = 1.5 (34) Via non-aqueous Schotten-Baumann reaction

In a 250ml round bottomed flask fitted with a calcium chloride drying tube were placed mono-N-carbobenzoxy hexamethylenediamine (5g; 0.02mol) and pyridine (75ml), and the mixture was cooled to -10°C . The temperature of the reaction mixture was maintained at around -10°C while adipoyl chloride (1.43g; 8×10^{-3} mol) was added dropwise over 30 minutes. The mixture was poured with good stirring into hydrochloric acid (3%; 900ml) containing crushed ice (300g), and the product was collected on a Büchner funnel and washed with methanol (30ml), then with water (30ml), then sucked as dry as possible and air-dried at room temperature. The crude product was recrystallized from methanol and the bis-N-carbobenzoxy non-integer oligomer obtained as a white solid. Yield 2.0g, 42% Mpt. 160°C .

^1H NMR (CD_3OD) δ_{H} 1.3-1.8 (20H, m, $10 \times \text{CH}_2$), 2.2 (4H, t, $2 \times \text{CH}_2\text{C}=\text{O}$), 3.3 (8H, t, $4 \times \text{CH}_2\text{NH}$), 5.0 (4H, s, $2 \times \text{PhCH}_2$), 7.1 (10H, s, $10 \times \text{ArH}$). IR (KBr disc) 1685 (C=O carbamate), 1640 (C=O amide), 3310 (NH) cm^{-1} .

DIAMINE OLIGOMER / D. O. P. =1.5 (36)

A solution of the bis-N-carbobenzoxy product D. O. P. 1.5 (2g; 3.3×10^{-3} mol) in concentrated hydrochloric acid (50ml) was prepared in a 100ml round bottomed flask fitted with a reflux condenser and a calcium carbonate guard tube. The solution was heated to 40°C for three hours (carbon dioxide evolution), then cooled, mixed with water (150ml) and extracted with ether (3x40ml) to remove the benzyl chloride. The filtrate of the hydrochloride solution was taken down on a rotary evaporator and the residue dissolved in a minimum amount of glacial acetic acid. This solution was purified by warming with activated charcoal and then filtered. The hydrochloride was precipitated with dry ether. The resulting oil was again taken down on a rotary evaporator and the residue was mixed with water and ether. The aqueous layer was separated and after neutralization with sodium hydroxide (2M) evaporated to near dryness. After cooling the solid precipitate was recrystallized from ethanol. Yield 0.97g, 95%. Mpt. 138-140°C.

¹H NMR (CD₃OD) δ_H 1.3-1.8 (20H, m, 10xCH₂), 2.2 (4H, t, 2xCH₂C=O), 2.7 (4H, t, 2xCH₂NH₂), 3.3 (4H, t, 2xCH₂NH). IR (KBr disc) 1645 (C=O amide), 3315 (NH) cm⁻¹.

BIS-C-ESTER OLIGOMER / D.O.P. = 1.5 (35)
Via non-aqueous Schotten-Baumann reaction

In a 250ml round bottomed flask fitted with a calcium chloride guard tube were placed freshly distilled hexamethylenediamine (0.93g; 8×10^{-3} mol) and pyridine (75ml), and the mixture was cooled to -10°C . The temperature of the reaction mixture was maintained at around -10°C while methyl adipyl chloride (3.57g; 0.02mol) was added dropwise over thirty minutes. The mixture was poured with vigorous stirring into aqueous hydrochloric acid (3%; 900ml) containing crushed ice (300g). The product was collected on a Büchner funnel and washed with methanol (3x30ml) and then with water (3x30ml). The product was sucked as dry as possible and then air-dried at room temperature. The crude product was recrystallized from methanol and the bis-C-ester non-integer oligomer obtained as a white solid. Yield 1.1g, 34%.

^1H NMR (CF_3COOD) δ_{H} 1.3-1.8 (16H, m, $8 \times \text{CH}_2$), 2.3 (8H, t, $4 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (4H, t, $2 \times \text{CH}_2\text{NH}$), 3.6 (6H, s, $2 \times \text{CH}_3$).
IR (KBr disc) 1740 (C=O ester), 1640 (C=O amide), 3310 (NH) cm^{-1} .

DICARBOXYLIC ACID OLIGOMER / D. O. P. =1.5 (37)

Potassium hydroxide (1.4g; 0.025mol) was dissolved in warm, dry methanol (50ml). The bis-C-ester oligomer D. O. P. 1.5 (2g; 5×10^{-3} mol) was introduced with stirring. A reflux condenser was attached and the solution refluxed for one hour. The methanol was removed on a rotary evaporator and the residue dissolved in a minimum amount of warm water and filtered. The solution was cooled in an ice bath and sulphuric acid (2M) was added dropwise under stirring until no more product precipitated. The product was filtered and washed with water (5ml), then recrystallized from ethanol. Yield 1.8g, 96%. Mpt. 192-195°C.

^1H NMR (CD_3OD) δ_{H} 1.3-1.8 (16H, m, $8 \times \text{CH}_2$), 2.2-2.4 (8H, t, $4 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (4H, t, $2 \times \text{CH}_2\text{NH}$). IR (KBr disc) 3310 (NHstr), 3300-2500 (OHstr), 1700 (C=O acid), 1640 (C=O amide) cm^{-1} .

BIS-N-CARBOBENZOXY OLIGOMER / D. O. P. =2.5 (38)

Via non-aqueous Schotten-Baumann reaction

In a 50ml round-bottomed flask the dicarboxylic acid oligomer D. O. P. 1.5 (7.5g; 0.02mol) was stirred with thionyl chloride (9.5g; 0.08mol) and two drops of N,N-dimethylformamide. After 30 minutes the excess thionyl

chloride was removed under vacuum leaving the crude bis acid chloride.

¹H NMR (CDCl₃) δ_H 1.5-1.8 (16H, m, 8xCH₂), 2.4 (4H, t, 2xCH₂C=O), 2.9 (4H, t, 2xCH₂COCl), 3.2 (4H, t, 2xCH₂NH). IR (Liquid film) 1800 (NC=O) cm⁻¹.

In a 250ml round bottomed flask fitted with a calcium chloride drying tube were placed mono-N-carbobenzoxy hexamethylenediamine (5g; 0.02mol) and pyridine (75ml), and the mixture was cooled to -10°C. The temperature was maintained at around -10°C while the dicarboxylic acid chloride D.O.P. 1.5 (3.24g; 8x10⁻³mol) was added dropwise over 30 minutes. The mixture was poured with good stirring into hydrochloric acid (3%; 900ml) containing crushed ice (300g). The product was collected on a Büchner funnel and washed with methanol (30ml), then with water (30ml). The product was sucked as dry as possible and air-dried at room temperature. The crude product was recrystallized from methanol and the bis-N-carbobenzoxy non-integer oligomer obtained as a white solid. Yield 1.8g, 27%

¹H NMR (CD₃OD) δ_H 1.3-1.9 (32H, m, 16xCH₂), 2.3 (8H, t, 4xCH₂C=O), 3.3 (12H, t, 6xCH₂NH), 5.0 (4H, s, 2xPhCH₂), 7.1 (10H, s, 10xArH). IR (KBr disc) 1685 (C=O carbamate), 1640 (C=O amide), 3310 (NH) cm⁻¹.

DIAMINE OLIGOMER / D. O. P. =2.5 (43)

A solution of the bis-N-carbobenzoxy product D. O. P. 2.5 (1g; 1.2×10^{-3} mol) in concentrated hydrochloric acid (20ml) was prepared in a 100ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was heated to 40°C for three hours (carbon dioxide evolution). The solution was then cooled, mixed with water (50ml) and extracted with ether (3x20ml) to remove the benzyl chloride. The filtrate of the hydrochloride solution was taken down on a rotary evaporator and the residue dissolved in a minimal amount of glacial acetic acid. This solution was purified by warming with activated charcoal and was then filtered. The hydrochloride was precipitated with dry ether. The resulting oil was again taken down on a rotary evaporator and the residue was mixed with water and ether. The aqueous layer was separated and after neutralization with sodium hydroxide (2M) evaporated to near dryness, on cooling the solid precipitate was recrystallized from water. Yield 0.47g, 69%. Mpt. 222-227°C.

¹H NMR (CD₃OD) δ_H 1.3-1.8 (32H, m, 16xCH₂), 2.2 (8H, t, 4xCH₂C=O), 2.7 (4H, t, 2xCH₂NH₂), 3.3 (8H, t, 4xCH₂NH). IR (KBr disc) 1645 (C=O amide), 3315 (NH) cm⁻¹.

BIS-C-ESTER OLIGOMER / D. O. P. =2.5 (39)
Via non-aqueous Schotten-Baumann reaction

In a 50ml round-bottomed flask methyl hydrogen adipate (6.4g; 0.04mol) was stirred with thionyl chloride (9.5g; 0.08mol) and two drops of N,N-dimethylformamide. After 30 minutes the excess thionyl chloride was removed under vacuum leaving the crude acid chloride.

$^1\text{H NMR}$ (CDCl_3) δ_{H} 1.7 (4H, m, $2 \times \text{CH}_2$), 2.4 (2H, t, $\text{CH}_2\text{C}=\text{O}$), 3.0 (2H, t, CH_2COCl), 3.6 (3H, s, CH_3). IR (Liquid film) $1800(\text{NC}=\text{O})\text{cm}^{-1}$.

In a 250ml round bottomed flask fitted with a calcium chloride drying tube were placed the diamine D.O.P. 1.5 (2.74g; 8×10^{-3} mol) and pyridine (75ml), this mixture was cooled to -10°C . The temperature was maintained at around -10°C while methyl adipyl chloride (3.57g; 0.02mol) was added dropwise over 30 minutes. The mixture was poured with good stirring into hydrochloric acid (3%; 900ml) containing crushed ice (300g). The product was collected on a Büchner funnel and washed with methanol (30ml), then with water (30ml). The product was sucked as dry as possible and air-dried at room temperature. The crude product was recrystallized from methanol and the bis-C-ester non-integer oligomer obtained as a white solid. Yield 1.3g, 25%.

^1H NMR (CF_3COOD) δ_{H} 1.3-1.8 (28H, m, $14\times\text{CH}_2$), 2.3 (12H, t, $6\times\text{CH}_2\text{C=O}$), 3.2 (8H, t, $4\times\text{CH}_2\text{NH}$), 3.6 (6H, s, $2\times\text{CH}_3$).
IR (KBr disc) 1740 (C=O ester), 1640 (C=O amide), 3310 (NH) cm^{-1} .

DICARBOXYLIC ACID OLIGOMER / D. O. P. = 2.5 (44)

Potassium hydroxide (1.2g; 0.02mol) was dissolved in dry methanol (50ml). The bis-C-ester oligomer D. O. P. 2.5 (2.5g; 4×10^{-3} mol) was introduced and the solution refluxed for one hour. The methanol was removed on a rotary evaporator and the residue dissolved in warm water and filtered. The solution was cooled in an ice bath and sulphuric acid (2M) was added dropwise under stirring until all product was precipitated. The product was filtered, washed with water ($2\times 10\text{ml}$) and recrystallized from water. Yield 2.2g, 93%. Mpt. 203-206°C.

^1H NMR (CD_3OD) δ_{H} 1.3-1.8 (28H, m, $14\times\text{CH}_2$), 2.2-2.4 (12H, t, $6\times\text{CH}_2\text{C=O}$), 3.2 (8H, t, $4\times\text{CH}_2\text{NH}$). IR (KBr disc) 3310 (NHstr), 3300-2500 (OHstr), 1700 (C=O carboxylic acid), 1640 (C=O amide).

BIS-N-CARBOBENZOXY OLIGOMER / D. O. P. =3.5
Via non-aqueous Schotten-Baumann reaction

In a 50ml round-bottomed flask the dicarboxylic acid oligomer D. O. P. 2.5 (12g; 0.02mol) was stirred with thionyl chloride (9.5g; 0.08mol) and two drops of N,N-dimethylformamide. After 30 minutes the excess thionyl chloride was removed under vacuum leaving the crude bis acid chloride.

¹H NMR (CDCl₃) δ_H 1.7 (28H, m, 14xCH₂), 2.4 (8H, t, 4xCH₂C=O), 2.9 (4H, t, 2xCH₂COCl), 3.2 (8H, t, 4xCH₂NH). IR (Liquid film) 1800 (NC=O)cm⁻¹.

In a 250ml round bottomed flask fitted with a calcium chloride drying tube were placed mono-N-carbobenzoxy hexamethylenediamine (5g; 0.02mol) and pyridine (75ml), and the mixture was cooled to -20°C. The temperature was maintained at around -20°C while the dicarboxylic acid chloride D. O. P. 2.5 (5.0g; 8x10⁻³mol) was added dropwise over 30 minutes. The mixture was poured with good stirring into hydrochloric acid (3%; 900ml) containing crushed ice (300g). The product was collected on a Büchner funnel and washed with methanol (30ml), then with water (30ml). The product was sucked as dry as possible and air-dried at room temperature. The crude product was recrystallized from methanol and the bis-N-

carbobenzoxy non-integer oligomer obtained as a white solid. Yield 0.51g, 6%

^1H NMR (CD_3OD) δ_{H} 1.3-1.9 (44H, m, $22 \times \text{CH}_2$), 2.2 (12H, t, $6 \times \text{CH}_2\text{C}=\text{O}$), 3.3 (16H, t, $8 \times \text{CH}_2\text{NH}$), 5.0 (4H, s, $2 \times \text{PhCH}_2$), 7.1 (10H, s, $10 \times \text{ArH}$). IR (KBr disc) 3310 (NH), 1685 (C=O carbamate), 1640 (C=O amide), 1530 (NHb) cm^{-1} .

DIAMINE OLIGOMER / D. O. P. = 3.5

A solution of the bis-N-carbobenzoxy product D. O. P. 3.5 (0.4g; 4×10^{-4} mol) in concentrated hydrochloric acid (10ml) was prepared in a 50ml round bottomed flask fitted with a reflux condenser and a calcium carbonate guard tube. The solution was heated to 40°C for three hours (carbon dioxide evolution), then cooled, mixed with water (30ml) and extracted with ether (3×10 ml) to remove the benzyl chloride. The filtrate of the hydrochloride solution was taken down on a rotary evaporator and the residue dissolved in a minimum amount of glacial acetic acid. This solution was purified by warming with activated charcoal and was then filtered. The hydrochloride was precipitated with dry ether. The resulting solid was dissolved in a minimum amount of water. After neutralization with sodium hydroxide (2M)

the solid precipitate was recrystallized from dimethylformamide. Yield 0.15g, 47%. Mpt. 235-239°C.

¹H NMR (CD₃OD) δ_H 1.3-1.8 (44H, m, 16xCH₂), 2.2 (8H, t, 4xCH₂C=O), 2.8 (4H, t, 2xCH₂NH₂), 3.3 (12H, t, 6xCH₂NH). IR (KBr disc) 1645 (C=O amide), 3315 (NH)cm⁻¹.

BIS-C-ESTER OLIGOMER / D. O. P. =3.5
Via non-aqueous Schotten-Baumann reaction

In a 50ml round-bottomed flask methyl hydrogen adipate (6.4g; 0.04mol) was stirred with thionyl chloride (9.5g; 0.08mol) and two drops of N,N-dimethylformamide. After 30 minutes the excess thionyl chloride was removed under vacuum leaving the crude acid chloride.

¹H NMR (CDCl₃) δ_H 1.7 (4H, m, 2xCH₂), 2.4 (2H, t, CH₂C=O), 3.0 (2H, t, CH₂COCl), 3.6 (3H, s, CH₃). IR (Liquid film) 1800 (NC=O)cm⁻¹.

In a 250ml round bottomed flask fitted with a calcium chloride drying tube were placed the diamine D. O. P. 2.5 (4.5g; 8x10⁻³mol) and pyridine (75ml), and the mixture was cooled to -10°C. The temperature was maintained at around -10°C while methyl adipyl chloride (3.57g; 0.02mol) was added dropwise over 30 minutes. The

mixture was poured with good stirring into hydrochloric acid (3%; 900ml) containing crushed ice (300g). The product was collected on a Büchner funnel and washed with methanol (30ml), then with water (30ml). The product was sucked as dry as possible and air-dried at room temperature. The crude product was recrystallized from methanol and the bis-C-ester non-integer oligomer obtained as a white solid. Yield 0.61g, 9%.

^1H NMR (CF_3COOD) δ_{H} 1.3-1.8 (40H, m, $20 \times \text{CH}_2$), 2.3 (16H, t, $8 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (12H, t, $6 \times \text{CH}_2\text{NH}$), 3.6 (6H, s, $2 \times \text{CH}_3$).
IR (KBr disc) 1740 (C=O ester), 1640 (C=O amide), 3310 (NH) cm^{-1} .

DICARBOXYLIC ACID OLIGOMER / D. O. P. = 3.5

Potassium hydroxide (0.5g; 9×10^{-3} mol) was dissolved in dry methanol (20ml). The bis-C-ester oligomer D. O. P. 3.5 (1.4g; 1.6×10^{-3} mol) was introduced with stirring. A reflux condenser was attached and the solution refluxed for one hour. The methanol was removed on a rotary evaporator and the residue dissolved in warm water and filtered. The solution was cooled in an ice bath and sulphuric acid (2M) was added dropwise under stirring until no more product was precipitated out. The product was filtered, washed with water (2x10ml) and

recrystallized from dimethylformamide. Yield 1.2g, 88%.

Mpt. 220-224°C.

¹H NMR (CD₃OD) δ_H 1.3-1.8 (40H, m, 20xCH₂), 2.2-2.4 (16H, t, 8xCH₂C=O), 3.2 (12H, t, 6xCH₂NH). IR (KBr disc) 3310 (NHstr), 3300-2500 (OHstr), 1700 (C=O carboxylic acid), 1640 (C=O amide)cm⁻¹.

BIS-C-ESTER OLIGOMER / D. O. P. = 1.5 (35)

Via mixed anhydride reaction with benzyl chloroformate

A solution of methyl hydrogen adipate (3.2g; 0.02mol) in dry tetrahydrofuran (100ml) was prepared at -5°C in a 250ml two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (5ml) was added and the solution stirred at -5°C for forty minutes prior to treatment with benzyl chloroformate (3.4g; 0.02mol). The solution was again allowed to react under stirring for forty minutes at -5°C. Freshly distilled hexamethylene diamine (1.16g; 0.01mol) in water (20ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (100ml). The precipitate formed was filtered off and recrystallized from ethanol. The product was then oven dried at 60°C. Yield 0.36g, 9%.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (16H, m, $8 \times \text{CH}_2$), 2.3 (8H, t, $4 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (4H, t, $2 \times \text{CH}_2\text{NH}$), 3.6 (6H, s, $2 \times \text{CH}_3$).
IR (KBr disc) 1740 (C=O ester), 1640 (C=O amide), 3310 (NH) cm^{-1} .

BIS-C-ESTER OLIGOMER / D. O. P. = 1.5 (35)

Via mixed anhydride reaction with ethyl chloroformate

a) A solution of methyl hydrogen adipate (3.2g; 0.02mol) in dry tetrahydrofuran (100ml) was prepared at -5°C in a 250ml two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (5ml) was added and the solution stirred at -5°C for forty minutes prior to treatment with ethyl chloroformate (2.2g; 0.02mol). The solution was again allowed to react under stirring for forty minutes at -5°C . Freshly distilled hexamethylene diamine (1.16g; 0.01mol) in water (20ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (100ml). The precipitate formed was filtered off and recrystallized from ethanol. The product was then oven dried at 60°C . Yield 2.4g, 60%.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (16H, m, $8 \times \text{CH}_2$), 2.3 (8H, t, $4 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (4H, t, $2 \times \text{CH}_2\text{NH}$), 3.6 (6H, s, $2 \times \text{CH}_3$).

IR (KBr disc) 1740 (C=O ester), 1690 (C=O weak), 1640 (C=O amide), 3310 (NH) cm^{-1} . The IR band at 1690 cm^{-1} is thought to be the disproportionation product.

b) A solution of methyl hydrogen adipate (3.2g; 0.02mol) in dry tetrahydrofuran (100ml) was prepared at -10°C in a 250ml two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (5ml) was added and the solution stirred at -10°C for forty minutes prior to treatment with ethyl chloroformate (2.2g; 0.02mol). The solution was again allowed to react under stirring for forty minutes at -10°C . Freshly distilled hexamethylene diamine (1.16g; 0.01mol) in water (20ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (100ml). The precipitate formed was filtered off and recrystallized from ethanol. The product was then oven dried at 60°C . Yield 2.64g, 66%.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (16H, m, $8 \times \text{CH}_2$), 2.3 (8H, t, $4 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (4H, t, $2 \times \text{CH}_2\text{NH}$), 3.6 (6H, s, $2 \times \text{CH}_3$). IR (KBr disc) 1740 (C=O ester), 1690 (C=O weak), 1640 (C=O amide), 3310 (NH) cm^{-1} . The IR band at 1690 cm^{-1} is thought to be the disproportionation product.

c) A solution of methyl hydrogen adipate (3.2g; 0.02mol) in dry tetrahydrofuran (100ml) was prepared at -10°C in a 250ml two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (5ml) was added and the solution stirred at -10°C for twenty minutes prior to treatment with ethyl chloroformate (2.2g; 0.02mol). The solution was again allowed to react under stirring for twenty minutes at -10°C . Freshly distilled hexamethylene diamine (1.16g; 0.01mol) in water (20ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (100ml). The precipitate formed was filtered off and recrystallized from ethanol. The product was then oven dried at 60°C . Yield 2.72g, 68%.

^1H NMR (CDCl_3) δ_{H} 1.3-1.8 (16H, m, $8 \times \text{CH}_2$), 2.3 (8H, t, $4 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (4H, t, $2 \times \text{CH}_2\text{NH}$), 3.6 (6H, s, $2 \times \text{CH}_3$).
IR (KBr disc) 1740 (C=O ester), 1640 (C=O amide), 3310 (NH) cm^{-1} .

BIS-C-ESTER OLIGOMER / D.O.P. = 1.5 (35)

Via mixed anhydride reaction with *n*-butyl chloroformate

a) A solution of methyl hydrogen adipate (3.2g; 0.02mol) in dry tetrahydrofuran (100ml) was prepared at -10°C in

a 250ml two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (5ml) was added and the solution stirred at -10°C for forty minutes prior to treatment with *n*-butyl chloroformate (2.7g; 0.02mol). The solution was again allowed to react under stirring for forty minutes at -10°C . Freshly distilled hexamethylene diamine (1.16g; 0.01mol) in water (20ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (100ml). The precipitate formed was filtered off and recrystallized from ethanol. The product was then oven dried at 60°C . Yield 3.28g, 82%.

^1H NMR (CD_3OD) δ_{H} 1.3-1.8 (16H, m, $8 \times \text{CH}_2$), 2.3 (8H, t, $4 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (4H, t, $2 \times \text{CH}_2\text{NH}$), 3.6 (6H, s, $2 \times \text{CH}_3$).
IR (KBr disc) 1740 (C=O ester), 1640 (C=O amide), 3310 (NH) cm^{-1} .

b) A solution of methyl hydrogen adipate (16g; 0.1mol) in dry tetrahydrofuran (500ml) was prepared at -10°C in a one litre two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (25ml) was added and the solution stirred at -10°C for twenty minutes prior to treatment with *n*-butyl chloroformate (13.5g; 0.1mol). The solution was

again allowed to react under stirring for twenty minutes at -10°C . Freshly distilled hexamethylene diamine (11.6g; 0.05mol) in water (100ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (500ml). The precipitate formed was filtered off and recrystallized from ethanol. The product was then oven dried at 60°C . Yield 18g, 90%.

^1H NMR (CD_3OD) δ_{H} 1.3-1.8 (16H, m, $8\times\text{CH}_2$), 2.3 (8H, t, $4\times\text{CH}_2\text{C}=\text{O}$), 3.2 (4H, t, $2\times\text{CH}_2\text{NH}$), 3.6 (6H, s, $2\times\text{CH}_3$).
IR (KBr disc) 1740 (C=O ester), 1640 (C=O amide), 3310 (NH) cm^{-1} .

DICARBOXYLIC ACID OLIGOMER / D. O. P. = 1.5 (37)

Potassium hydroxide (15g;) was dissolved in warm, dry methanol (500ml). The bis-C-ester oligomer D. O. P. 1.5 (20g; 0.05mol) was introduced with stirring, a condenser was attached, and the solution refluxed for one hour. The methanol was removed on a rotary evaporator and the residue dissolved in a minimal amount of warm water and filtered. The solution was cooled in an ice bath and sulphuric acid (2M) was added dropwise under stirring until no more product is precipitated out. The product was filtered and washed with water (2x20ml). The product

was recrystallized from ethanol. Yield 17.7g, 95%. Mpt. 195-197°C.

¹H NMR (CD₃OD) δ_H 1.3-1.8 (16H, m, 8xCH₂), 2.2-2.4 (8H, t, 4xCH₂C=O), 3.2 (4H, t, 2xCH₂NH) 11 (s, COOH). IR (KBr disc) 3310 (NHstr), 3300-2500 (OHstr), 1700 (C=O acid), 1640 (C=O amide).

BIS-N-CARBOBENZOXY OLIGOMER / D. O. P. = 1.5 (34)
Via mixed anhydride reaction

A solution of adipic acid (7.3g; 0.05mol) in dry tetrahydrofuran (500ml) was prepared at -10°C in a one litre two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (25ml) was added and the solution stirred at -10°C for twenty minutes prior to treatment with *n*-butyl chloroformate (13.5g; 0.1mol). The solution was again allowed to react under stirring for twenty minutes at -10°C. N-carbobenzoxy monomer (25g; 0.1mol) in water (100ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (500ml). The precipitate formed was filtered off and recrystallized from ethanol. The product was then oven dried at 60°C. Yield 28g, 92%.

¹H NMR (CD₃OD) δ_H 1.3-1.8 (20H, m, 10xCH₂), 2.2 (4H, t, 2xCH₂C=O), 3.3 (8H, t, 4xCH₂NH), 5.0 (4H, s, 2xPhCH₂), 7.1 (10H, s, 10xArH). IR (KBr disc) 1685(C=O carbamate), 1640(C=O amide), 3310(NH)cm⁻¹.

DIAMINE OLIGOMER / D. O. P. = 1.5 (36)
Via catalytic hydrogenation / Pd(C)

a) A 50ml flame dried round bottomed flask was charged with dry methanol (20ml), the bis-carbobenzoxy oligomer D. O. P. 1.5 (4.9g; 8x10⁻³mol) and palladium black (0.6g). The solution was attached to hydrogenation equipment for twelve hours (carbon dioxide evolution could not be observed). The solution was filtered and the product oven dried at 40°C before recrystallization in ethanol.

The "product" that was obtained was the bis-N-carbobenzoxy starting material. IR (KBr disc) 1685(C=O carbamate), 1640(C=O amide), 3310(NH)cm⁻¹.

b) A 50ml flame dried round bottomed flask was charged with dry methanol (20ml), acetic acid (5ml), carbobenzoxy methyl ester monomer (4.9g; 8x10⁻³mol) and palladium black (0.6g). The solution was attached to hydrogenation equipment for twelve hours (carbon dioxide evolution could not be observed). The solution was

filtered and the product oven dried at 40°C before recrystallization in methanol.

The "product" that was obtained was the bis-N-carbobenzoxy starting material. IR (KBr disc) 1685 (C=O carbamate), 1640 (C=O amide), 3310 (NH) cm^{-1} .

DIAMINE OLIGOMER / D. O. P. = 1.5 (36)
Via hydrobromic acid in acetic acid

The bis-carbobenzoxy oligomer D. O. P. (5g; 8×10^{-3} mol) was dissolved in a solution of hydrogen bromide in acetic acid (37%; 25ml) in a 100ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was left stirring gently at 40°C for two hours. The mixture was evaporated to an oil which was dissolved in water (25ml). The solution was washed with ether (4x20ml), and then evaporated to dryness. The residue was dried completely in a desiccator under vacuum overnight. The product was crystallized repeatedly from methanol and ether.

No diamine was produced.

DIAMINE OLIGOMER / D. O. P. =1.5 (36)
Via concentrated hydrochloric acid

A solution of the bis-N-carbobenzoxy product D. O. P. 1.5 (20g; 0.033mol) in concentrated hydrochloric acid (250ml) was prepared in a 500ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was heated to 40°C for three hours (carbon dioxide evolution), then cooled, mixed with water (600ml) and extracted with ether (3x100ml) to remove the benzyl chloride. The filtrate of the hydrochloride solution was taken down on a rotary evaporator and the residue dissolved in a minimal amount of glacial acetic acid. This solution was purified by warming with activated charcoal and then filtered. The hydrochloride was precipitated with dry ether. The resulting oil was again taken down on a rotary evaporator and the residue was mixed with water and ether. The aqueous layer was separated and after neutralization with sodium hydroxide (2M) evaporated to near dryness, on cooling the solid precipitate was recrystallized from ethanol. Yield 9.8g, 87%. Mpt. 141°C.

¹H NMR (CDCl₃) δ_H 1.3-1.8 (20H, m, 10xCH₂), 2.2 (4H, t, 2xCH₂C=O), 2.7 (4H, t, 2xCH₂NH₂), 3.3 (4H, t, 2xCH₂NH). IR (KBr disc) 1645 (C=O amide), 3315 (NH) cm⁻¹.

DINITRILE OLIGOMER / D. O. P. =1.5 (42)
Via the mixed anhydride reaction

A solution of adipic acid (9.1g; 0.05mol) in dry tetrahydrofuran (500ml) was prepared at -10°C in a one litre two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (25ml) was added from the dropping funnel and the solution stirred at -10°C for twenty minutes prior to treatment with *n*-butyl chloroformate (13.5g; 0.1mol). The solution was again allowed to react under stirring for twenty minutes at -10°C . 6-aminocaproic nitrile (11.2g; 0.1mol) in water (100ml) was added and the reaction mixture was left stirring at room temperature in a fume cupboard overnight. The resulting layers were then separated and the upper layer mixed vigorously with water (500ml). The precipitate that formed was filtered off and recrystallized from ethanol. The product was then oven dried at 60°C . Yield 13.4g, 80%.

^1H NMR (CD_3OD) δ_{H} 1.3-1.8 (16H, m, $8\times\text{CH}_2$), 2.2-2.4 (8H, t, $2\times\text{CH}_2\text{C}=\text{O}$, $2\times\text{CH}_2\text{CN}$), 3.4 (4H, t, $2\times\text{CH}_2\text{NH}$). IR (KBr disc) 1640 ($\text{C}=\text{O}$ amide), 2250 (CN), 3300 (NH) cm^{-1} .

DIAMINE OLIGOMER / D. O. P. =1.5 (36)
Using catalytic hydrogenation / Pd(C)

A 50ml flame dried round bottomed flask was charged with dry methanol (20ml), the dinitrile oligomer D.O.P. 1.5 (4.5g; 8×10^{-3} mol) and palladium black (0.6g). The solution was attached to hydrogenation equipment for twelve hours. The solution was filtered and the product oven dried at 40°C before recrystallization in methanol.

The product recovered was the starting bis-nitrile. IR (KBr disc) 1640 (C=O amide), 2250 (CN), 3310 (NH) cm^{-1} .

DIAMINE OLIGOMER / D. O. P. =1.5 (36)
Via lithium aluminium tetrahydride

A solution of lithium aluminium hydride (0.76g; 0.02mol) in dry dry tetrahydrofuran (50ml) was placed in a 150ml two-necked flask equipped with a condenser and a magnetic stirrer. The solution was gently refluxed while the dinitrile oligomer D.O.P. 1.5 (5.6g; 0.01mol) was slowly added over a period of 30 minutes. The mixture was refluxed for an additional 2 hours. The reaction mixture was worked up by the addition of water (10ml). After filtration to remove the solid aluminium and lithium salts, the dry tetrahydrofuran was evaporated. The product was recrystallized from ethanol.

The product recovered was the unchanged bis-nitrile. IR (KBr disc) 1640(C=O amide), 2250(CN), 3315(NH)cm⁻¹.

DIAMINE OLIGOMER / D. O. P. =1.5 (36)

Via sodium and ethanol

In a 250ml two necked round bottomed flask fitted with a dropping funnel and reflux condenser was added clean sodium (2g) and sodium dried toluene (50ml). The mixture was stirred and heated until boiling forming an emulsion. A solution of the dinitrile oligomer D. O. P. 1.5 (10; 0.017mol) in ethanol (30ml) was introduced dropwise through the funnel over a period of one hour. Once the ethanol solution had been added further ethanol was added to destroy any residual sodium. The solution was cooled and then shaken with hydrochloric acid (2M; 25ml). The aqueous layer was then separated and neutralized with sodium hydroxide (2M). The solution was taken down on a rotary evaporator and the residue recrystallized from methanol.

The product recovered was unreduced bis-nitrile. IR (KBr disc) 1640(C=O amide), 2250(CN), 3310(NH)cm⁻¹.

BIS-N-CARBOBENZOXY OLIGOMER / D. O. P. =2.5 (38)

Via mixed anhydride reaction

A solution of the dicarboxylic acid oligomer D.O.P. 1.5 (9.7g; 0.025mol) in dry tetrahydrofuran (500ml) was prepared at -10°C in a one litre two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (14ml) was added from the dropping funnel and the solution stirred at -10°C for twenty minutes prior to treatment with *n*-butyl chloroformate (7.4g; 0.05mol). The solution was again allowed to react under stirring for twenty minutes at -10°C . Mono-N-carbobenzoxy hexamethylenediamine (12.5g; 0.05mol) in water (100ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (500ml). The precipitate formed was filtered off and recrystallized from water. The product was then oven dried at 60°C . Yield 16g, 77%.

^1H NMR (CD_3OD) δ_{H} 1.3-1.9 (32H, m, $16 \times \text{CH}_2$), 2.3 (8H, t, $4 \times \text{CH}_2\text{C}=\text{O}$), 3.3 (12H, t, $6 \times \text{CH}_2\text{NH}$), 5.0 (4H, s, $2 \times \text{PhCH}_2$), 7.1 (10H, s, $10 \times \text{ArH}$). IR (KBr disc) 1685 (C=O carbamate), 1640 (C=O amide), 3310 (NH) cm^{-1} .

DIAMINE OLIGOMER / D. O. P. =2.5 (43)

A solution of the bis-N-carbobenzoxy product D.O.P. 2.5 (10g; 0.012mol) in concentrated hydrochloric acid (150ml) was prepared in a 250ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was heated to 40°C for three hours (carbon dioxide evolution), then cooled, mixed with water (500ml) and extracted with ether (3x50ml) to remove the benzyl chloride. The filtrate of the hydrochloride solution was taken down on a rotary evaporator and the residue dissolved in a minimal amount of glacial acetic acid. This solution was purified by warming with activated charcoal and then filtered. The hydrochloride was precipitated with dry ether. The resulting oil was again taken down on a rotary evaporator and the residue was mixed with water and ether. The aqueous layer was separated and after neutralization with sodium hydroxide (2M) evaporated to near dryness, on cooling the solid precipitate was recrystallized from water. Yield 5.5g, 80%. Mpt. 227-229°C.

¹H NMR (CD₃OD) δ_H 1.3-1.8 (32H, m, 16xCH₂), 2.2 (8H, t, 4xCH₂C=O), 2.7 (4H, t, 2xCH₂NH₂), 3.3 (8H, t, 4xCH₂NH). IR (KBr disc) 3315 (NH), 1645 (C=O amide), 1530 (NHb) cm⁻¹.

BIS-C-ESTER OLIGOMER / D. O. P. =2.5 (39)
Via mixed anhydride reaction

A solution of methyl hydrogen adipate (3.2g; 0.02mol) in dry tetrahydrofuran (100ml) was prepared at -10°C in a 250ml two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (5ml) was added and the solution stirred at -10°C for twenty minutes prior to treatment with *n*-butyl chloroformate (2.7g; 0.02mol). The solution was again allowed to react under stirring for twenty minutes at -10°C . The diamine oligomer D. O. P. 1.5 (3.4g; 0.01mol) in water (40ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (100ml). The precipitate formed was filtered off and recrystallized from water. The product was then oven dried at 60°C . Yield 4.4g, 70%.

^1H NMR (CF_3COOD) δ_{H} 1.3-1.8 (28H, m, $14 \times \text{CH}_2$), 2.3 (12H, t, $6 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (8H, t, $4 \times \text{CH}_2\text{NH}$), 3.6 (6H, s, $2 \times \text{CH}_3$).
IR (KBr disc) 1740 (C=O ester), 1640 (C=O amide), 3310 (NH) cm^{-1} .

DICARBOXYLIC ACID OLIGOMER / D. O. P. =2.5 (44)

Potassium hydroxide (4g) was dissolved in warm, dry methanol (200ml) added. The bis-C-ester oligomer D. O. P. 2.5 (6.26g; 0.01mol) was introduced with stirring. A reflux condenser was attached and the solution refluxed for one hour. The methanol was removed on a rotary evaporator and the residue dissolved in warm water and filtered. The solution was cooled in an ice bath and sulphuric acid (2M) was added dropwise under stirring until no more product precipitated. The product was filtered and washed with water (2x50ml), then recrystallized from water. Yield 5.7g, 95%. Mpt. 203-205°C.

^1H NMR (CF_3COOD) δ_{H} 1.3-1.8 (28H, m, 14x CH_2), 2.2-2.4 (12H, t, 6x $\text{CH}_2\text{C=O}$), 3.2 (8H, t, 4x CH_2NH). IR (KBr disc) 3310 (NHstr), 3300-2500 (OHstr), 1700 (C=O carboxylic acid), 1640 (C=O amide).

BIS-N-CARBOBENZOXY OLIGOMER / D. O. P. =3.5
Via mixed anhydride reaction

A suspension of the dicarboxylic acid D. O. P. 2.5 (3.0g; 5×10^{-3} mol) in dry tetrahydrofuran (100ml) was prepared at -10°C in a 250ml two necked round bottomed flask fitted with a calcium chloride guard tube and a

dropping funnel. Triethylamine (6ml) was added and the solution stirred at -10°C for twenty minutes prior to treatment with *n*-butyl chloroformate (1.4g; 0.01mol). The solution was again allowed to react under stirring for twenty minutes at -10°C . Mono-N-carbobenzoxy hexamethylenediamine (2.5g; 0.01mol) in water (30ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (100ml). The precipitate formed was filtered off and recrystallized from dimethylformamide. The product was then oven dried at 60°C . Yield 3.2g, 60%.

^1H NMR (CF_3COOD) δ_{H} 1.3-1.9 (44H, m, $22 \times \text{CH}_2$), 2.2 (12H, t, $6 \times \text{CH}_2\text{C}=\text{O}$), 3.3 (16H, t, $8 \times \text{CH}_2\text{NH}$), 5.0 (4H, s, $2 \times \text{PhCH}_2$), 7.1 (10H, s, $10 \times \text{ArH}$). IR (KBr disc) 1685 ($\text{C}=\text{O}$ carbamate), 1640 ($\text{C}=\text{O}$ amide), $3310 (\text{NH}) \text{cm}^{-1}$.

DIAMINE OLIGOMER / D. O. P. = 3.5

A solution of the bis-N-carbobenzoxy product D. O. P. 3.5 (3g; 3×10^{-3} mol) in concentrated hydrochloric acid (75ml) was prepared in a 250ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was heated to 40°C for three hours (carbon dioxide evolution). The solution was then cooled, mixed with water (200ml) and extracted with ether ($3 \times 50\text{ml}$) to

remove the benzyl chloride. The filtrate of the hydrochloride solution was taken down on a rotary evaporator and the residue dissolved in a minimal amount of glacial acetic acid. This solution was purified by warming with activated charcoal and was then filtered. The hydrochloride was precipitated with dry ether. The resulting solid was dissolved in a minimum amount of water. After neutralization with sodium hydroxide (2M) the solid precipitate was recrystallized from dimethylformamide. Yield 2.3g, 95%. Mpt. 239-241°C.

¹H NMR (CD₃OD) δ_H 1.3-1.8 (44H, m, 16xCH₂), 2.2 (8H, t, 4xCH₂C=O), 2.8 (4H, t, 2xCH₂NH₂), 3.3 (12H, t, 6xCH₂NH). IR (KBr disc) 3315 (NHstr), 1645 (C=O amide)cm⁻¹.

BIS-C-ESTER OLIGOMER / D. O. P. =3.5
Via mixed anhydride reaction

A solution of methyl hydrogen adipate (3.0g; 0.02mol) in dry tetrahydrofuran (100ml) was prepared at -10°C in a 250ml two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (6ml) was added and the solution stirred at -10°C for twenty minutes prior to treatment with *n*-butyl chloroformate (2.8g; 0.02mol). The solution was again allowed to react under stirring for twenty minutes

at -10°C . The diamine oligomer D.O.P. 2.5 (5.7g; 0.01mol) in water (30ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (100ml). The precipitate formed was filtered off and recrystallized from dimethylformamide. The product was then oven dried at 60°C . Yield 5.45g, 64%.

^1H NMR (CF_3COOD) δ_{H} 1.3-1.8 (40H, m, $20 \times \text{CH}_2$), 2.3 (16H, t, $8 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (12H, t, $6 \times \text{CH}_2\text{NH}$), 3.6 (6H, s, $2 \times \text{CH}_3$).
IR (KBr disc) 1740 (C=O ester), 1640 (C=O amide), 3310 (NH) cm^{-1} .

DICARBOXYLIC ACID OLIGOMER / D.O.P.=3.5

Potassium hydroxide (5g) was dissolved in warm, dry methanol (150ml) added. The bis-C-ester oligomer D.O.P. 3.5 (15g; 0.018mol) was introduced with stirring. A condenser was attached and the solution refluxed for one hour. The methanol was removed on a rotary evaporator and the residue dissolved in warm water and filtered. The solution was cooled in an ice bath and sulphuric acid (2M) was added dropwise under stirring until no more product precipitated out. The product was filtered and washed with water ($3 \times 50\text{ml}$), then recrystallized from dimethylformamide. Yield 14g, 95%. Mpt. $213-215^{\circ}\text{C}$.

^1H NMR (CF_3COOD) δ_{H} 1.3-1.8 (40H, m, $20 \times \text{CH}_2$), 2.2-2.4 (16H, t, $8 \times \text{CH}_2\text{C}=\text{O}$), 3.2 (12H, t, $6 \times \text{CH}_2\text{NH}$). IR (KBr disc) 3310 (NHstr), 3300-2500 (OHstr), 1700 (C=O carboxylic acid), 1640 (C=O amide).

BIS-N-CARBOBENZOXY OLIGOMER / D. O. P. = 8.5 (51)
Via mixed anhydride reaction

A suspension of the N-carbobenzoxy tetramer (see 4.3.2. Integer Oligomers) ($2.0\text{g}; 1.9 \times 10^{-3}\text{mol}$) in dry tetrahydrofuran (100ml) was prepared at -5°C in a 250ml two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (1ml) was added and the solution stirred at -5°C for twenty minutes prior to treatment with *n*-butyl chloroformate ($0.26\text{g}; 1.9 \times 10^{-3}\text{mol}$). The solution was again allowed to react under stirring for twenty minutes at -5°C . Freshly distilled hexamethylenediamine ($0.36\text{g}; 9.5 \times 10^{-3}\text{mol}$) in water (20ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting solid was filtered off and added to boiling glacial acetic acid. On cooling the product crystallized out. The crystals were washed in methanol and oven dried at 80°C . Yield 0.75g, 36%. Mpt. $229-232^\circ\text{C}$.

From the GPC chromatogram the presence of contaminant oligomers, mainly tetrameric, was evident. IR (KBr disc) 1690 (C=O carbamate), 1640 (C=O amide), 3310 (NH) cm^{-1} .

4.3.2. INTEGER OLIGOMERS.

CARBOBENZOXY METHYL ESTER MONOMER (17)

Via mixed anhydride reaction

A solution of methyl hydrogen adipate (16g; 0.1mol) in dry tetrahydrofuran (500ml) was prepared at -10°C in a one litre two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (31ml). was added and the solution stirred at -10°C for twenty minutes prior to treatment with *n*-butyl chloroformate (13.6g; 0.1mol). The solution was again allowed to react under stirring for twenty minutes at -10°C . Mono-N-carbobenzoxyhexamethylenediamine (25g; 0.1mol) in water (100ml) was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (400ml). The precipitate formed was filtered off and recrystallized from acetone and water. The product was then oven dried at 60°C . Yield 33.3g, 85%. Mpt. $103-4^{\circ}\text{C}$.

^1H NMR (CD_3OD) δ_{H} 1.3-1.8 (12H, m, $6\times\text{CH}_2$), 2.2 (4H, t, $2\times\text{CH}_2\text{C}=\text{O}$), 3.3 (4H, t, $2\times\text{CH}_2\text{NH}$), 3.6 (3H, s, CH_3), 5.0 (2H, s, PhCH_2), 7.1 (5H, s, $5\times\text{ArH}$). IR (KBr disc) 1730 (C=O ester), 1680 (C=O carbamate), 1640 (C=O amide) $3300(\text{NH})\text{cm}^{-1}$. EIMS 392 (M^+)

UNPROTECTED MONOMER (28)
Using concentrated hydrochloric acid

A solution of carbobenzoxy methyl ester monomer (15g; 0.04mol) in concentrated hydrochloric acid (100ml) was prepared in a 250ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was heated to 40°C for three hours (carbon dioxide evolution). The solution was then cooled, mixed with water (200ml) and extracted with ether (200ml) to remove the benzyl chloride. The filtrate of the hydrochloride solution was taken down on a rotary evaporator and the residue dissolved in a minimal amount of glacial acetic acid. This solution was purified by warming with activated charcoal and was then filtered. The hydrochloride was precipitated with dry ether. The resulting oil was again taken down on a rotary evaporator and the residue was mixed with water and ether. The aqueous layer was separated and after neutralization with sodium hydroxide (2M) evaporated to near dryness, on cooling the solid precipitate was recrystallized from methanol and ether. Yield 9.0g, 96%. Mpt. 189-190°C.

¹H NMR (CDCl₃) δ_H 1.4-1.7 (12H, m, 6xCH₂), 2.0 (2H, t, CH₂C=O), 2.4 (2H, t, CH₂COO⁻), 3.3-3.4

(4H, t, CH_2NH , CH_2NH_3^+). IR (KBr disc) 1640 (C=O amide), 1400 (COO^-), 3300 (NH) cm^{-1} .

N-CARBOBENZOXY MONOMER (21)

Using potassium hydroxide and methanol

Potassium hydroxide (5.3g;) was dissolved in warm, dry methanol (200ml) . Carbobenzoxy methyl ester monomer (15.0g; 0.04mol) was introduced with stirring. A reflux condenser was attached and the solution refluxed for one hour. The solution was cooled and left in a fridge where the potassium salt precipitated and was filtered off and recrystallized from ethanol. This intermediate was dissolved in a minimal amount of water and filtered. Sulphuric acid (2M) was added dropwise under stirring until no more of the free carboxylic acid precipitated out. The product was filtered off and washed with cold water (3x20ml). Yield 13.6g, 94%. Mpt 139-140°C.

^1H NMR (CD_3OD) δ_{H} 1.3-1.8 (12H, m, $6 \times \text{CH}_2$), 2.1 (2H, t, $\text{CH}_2\text{C}=\text{O}$), 2.4 (2H, t, CH_2COOH), 3.3 (4H, t, $2 \times \text{CH}_2\text{NH}$), 5.0 (2H, s, PhCH_2), 7.1 (5H, s, $5 \times \text{ArH}$). IR (KBr disc) 3300 (NHstr), 3300-2500 (OHstr), 1680 (C=O carbamate, carboxylic acid), 1635 (C=O amide) cm^{-1} . EIMS 378 (M^+).

C-METHYL ESTER MONOMER (19)

Using hydrobromic acid and acetic acid

Carbobenzoxy methyl ester monomer (1g; 3×10^{-3} mol) was dissolved in a solution of hydrogen bromide in acetic acid (37%; 10ml) in a 50ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was left stirring gently at 40°C for two hours. The mixture was evaporated to an oil which was dissolved in water (25ml). The solution was washed with ether (4x20ml), and then evaporated to dryness. The residue was dried completely in a desiccator under vacuum overnight. The product was crystallized repeatedly from methanol and ether.

No deprotected product could be isolated.

C-METHYL ESTER MONOMER (19)

Using catalytic hydrogenation / Pd(C)

A 50ml flame dried round bottomed flask was charged with dry methanol (20ml), acetic acid (5ml), carbobenzoxy methyl ester monomer (3g; 8×10^{-3} mol) and palladium black (0.3g). The solution was attached to hydrogenation equipment for twelve hours (carbon dioxide evolution could not be observed). The solution was filtered and the product oven dried at 40°C before recrystallization in methanol.

The product obtained was unchanged carbobenzoxy methyl ester monomer. IR (KBr disc) 1730 (C=O ester), 1680 (C=O carbamate), 1640 (C=O amide), 3300 (NH) cm^{-1} . EIMS 392 (M^+)

C-METHYL ESTER MONOMER (19)

Using trimethylsilyl iodide

A solution of carbobenzoxy methyl ester monomer (0.5g; 1.3×10^{-3} mol) in dry chloroform (20ml) was prepared in a 50ml three necked round bottomed flask fitted with a calcium chloride guard tube, a nitrogen tap and a septum. The solution was flushed with nitrogen and trimethylsilyl iodide (0.43ml; 1.5×10^{-3} mol) introduced via a dry syringe. The solution was stirred for fifteen minutes before quenching with methanol (20ml). The solvent was removed under vacuum and the residue recrystallized from methanol.

The product obtained was unchanged carbobenzoxy methyl ester monomer. IR (KBr disc) 1730 (C=O ester), 1680 (C=O carbamate), 1640 (C=O amide), 3300 (NH) cm^{-1} . EIMS 392 (M^+)

N-CARBOBENZOXY DIMER (46)

Via mixed anhydride reaction

a) A solution of N-carbobenzoxy monomer (2g; 5×10^{-3} mol) in dry tetrahydrofuran (100ml) was prepared at -10°C in a one litre two necked round bottomed flask fitted with

a calcium chloride guard tube and a dropping funnel. Triethylamine (2ml). was added and the solution stirred at -10°C for twenty minutes prior to treatment with *n*-butyl chloroformate (0.72g; 5×10^{-3} mol). The solution was again allowed to react under stirring for twenty minutes at -10°C . Unprotected monomer (1.3g; 5×10^{-3} mol) in water was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (30ml). The precipitate formed was filtered off and recrystallized from methanol and acetic acid (3:1). The product was then oven dried at 60°C . Yield 1.96g, 65%. Mpt. $183-187^{\circ}\text{C}$.

^1H NMR (CD_3OD) δ_{H} 1.3-1.8 (24H, m, $12 \times \text{CH}_2$), 2.1 (6H, t, $3 \times \text{CH}_2\text{C}=\text{O}$), 2.4 (2H, t, CH_2COOH), 3.3 (8H, t, $4 \times \text{CH}_2\text{NH}$), 5.0 (2H, s, PhCH_2), 7.1 (5H, s, $5 \times \text{ArH}$). IR (KBr disc) 3305 (NHstr), 3300-2500 (OHstr), 1685 (C=O carbamate, carboxylic acid), 1630 (C=O amide) cm^{-1} .

b) A solution of *N*-carboboxy monomer (9g; 0.024mol) in dry tetrahydrofuran (500ml) was prepared at -5°C in a one litre two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (8ml). was added and the solution stirred at -5°C for twenty minutes prior to treatment with *n*-butyl chloroformate (3.32g; 0.024mol). The solution was

again allowed to react under stirring for twenty minutes at -5°C . Unprotected monomer (5.82g; 0.024mol) in water was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (100ml). The precipitate formed was filtered off and recrystallized from methanol and acetic acid (3:1). The product was then oven dried at 60°C . Yield 10.6g, 73%. Mpt. $183-184^{\circ}\text{C}$.

^1H NMR (CD_3OD) δ_{H} 1.3-1.8 (24H, m, $12 \times \text{CH}_2$), 2.1 (6H, t, $3 \times \text{CH}_2\text{C}=\text{O}$), 2.4 (2H, t, CH_2COOH), 3.3 (8H, t, $4 \times \text{CH}_2\text{NH}$), 5.0 (2H, s, PhCH_2), 7.1 (5H, s, $5 \times \text{ArH}$). IR (KBr disc) 3305 (NHstr), 3300-2500 (OHstr), 1685 (C=O carbamate, carboxylic acid), 1630 (C=O amide) cm^{-1} .

c) A solution of N-carbobenzoxy monomer (2g; 5×10^{-3} mol) in dry tetrahydrofuran (100ml) was prepared at -0°C in a one litre two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (2ml). was added and the solution stirred at 0°C for twenty minutes prior to treatment with *n*-butyl chloroformate (0.72g; 5×10^{-3} mol). The solution was again allowed to react under stirring for twenty minutes at -0°C . Unprotected monomer (1.3g; 5×10^{-3} mol) in water was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were

separated and the upper layer mixed vigorously with water (30ml). The precipitate formed was filtered off and recrystallized from methanol and acetic acid (3:1). The product was then oven dried at 60°C. Yield 2.24g, 74%. Mpt. 183-185°C.

¹H NMR (CD₃OD) δ_H 1.3-1.8 (24H, m, 12xCH₂), 2.1 (6H, t, 3xCH₂C=O), 2.4 (2H, t, CH₂COOH), 3.3 (8H, t, 4xCH₂NH), 5.0 (2H, s, PhCH₂), 7.1 (5H, s, 5xArH). IR (KBr disc) 3305 (NHstr), 3300-2500 (OHstr), 1685 (C=O carbamate, carboxylic acid), 1630 (C=O amide) cm⁻¹.

UNPROTECTED DIMER (47)

Using concentrated hydrochloric acid

A solution of N-carbobenzoxy dimer (5g; 8.3x10⁻³mol) in concentrated hydrochloric acid (20ml) was prepared in a 100ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was heated to 40°C for three hours (carbon dioxide evolution). The solution was then cooled, mixed with water (300ml) and extracted with ether (2x100ml) to remove the benzyl chloride. The filtrate of the hydrochloride solution was taken down on a rotary evaporator and the residue dissolved in a minimal amount of glacial acetic acid. This solution was purified by warming with activated charcoal and was then filtered.

The hydrochloride was precipitated with dry ether and filtered off.

The free amino acid was then obtained from a solution of the hydrogen chloride salt in a minimal amount of water after neutralization with sodium hydroxide (2M). The precipitate was filtered off and recrystallized twice from methanol and water due to the appearance of acetic acid in the initial product. Yield 3.6g, 92%. Mpt. 221-224°C.

^1H NMR (CD_3OD) δ_{H} 1.4-1.7 (24H, m, $12 \times \text{CH}_2$), 2.0-2.4 (8H, t, $3 \times \text{CH}_2\text{C}=\text{O}$, CH_2COO^-), 3.3-3.4 (8H, t, $3 \times \text{CH}_2\text{NH}$, CH_2NH_3^+).
IR (KBr disc) 1640 (C=O amide), 1400 (COO^-), 3300 (NH) cm^{-1} .

N-CARBOBENZOXY TETRAMER (48)

Via mixed anhydride reaction

a) A solution of N-carbobenzoxy dimer (4g; 6.6×10^{-3}) in dry tetrahydrofuran (200ml) was prepared at -5°C in a 500ml two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel. Triethylamine (2.5ml). was added and the solution stirred at -5°C for twenty minutes prior to treatment with *n*-butyl chloroformate (0.9g; 6.6×10^{-3}). The solution was again allowed to react under stirring for twenty minutes at -5°C . Unprotected dimer (3.1g; 6.6×10^{-3}) in

water was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (35ml). The precipitate formed was filtered off and recrystallized from glacial acetic acid and methanol (3:1). The product was then oven dried at 80°C. Yield 3.0g, 45%. Mpt. 203-210°C.

$^1\text{H NMR}$ ($\text{CF}_3\text{CD}(\text{OD})\text{CF}_3$) δ_{H} 1.3-1.8 (48H, m, 24x CH_2), 2.1-2.5 (16H, t, 7x $\text{CH}_2\text{C}=\text{O}$, CH_2COOH), 3.2 (16H, t, 8x CH_2NH), 4.9 (2H, s, PhCH_2), 7.0 (5H, s, 5xArH). IR (KBr disc) 3310 (NHstr), 3300-2500 (OHstr), 1690 (C=O carbamate, carboxylic acid), 1635 (C=O amide) cm^{-1} .

b) Repeat using 5.8g of dimer with appropriate scale up elsewhere gave 6.6g (61%) product, Mpt. 207-211°C. Spectra as for a).

UNPROTECTED TETRAMER (49)

Using concentrated hydrochloric acid

A solution of N-carbobenzoxy tetramer (4g; 4×10^{-3} mol) in concentrated hydrochloric acid (50ml) was prepared in a 100ml round bottomed flask fitted with a reflux condenser and a calcium carbonate drying tube. The solution was heated to 60°C for three and a half hours (carbon dioxide evolution), then cooled, mixed with

water (150ml) and extracted with ether (2x40ml) to remove the benzyl chloride. The hydrochloride solution was left to stand overnight in a fridge and the fine white precipitate that resulted was filtered off. This precipitate was dissolved in a minimal amount of hot glacial acetic acid. This solution was purified by warming with activated charcoal and then filtered. The hydrochloride was precipitated with dry ether and filtered off.

The free amino acid was then obtained from a solution of the hydrogen chloride salt in a minimal amount of boiling water after neutralization with sodium hydroxide (2M). The precipitate was filtered off and recrystallized from dimethylformamide and water. The final product was repeatedly washed with water and then oven dried at 80°C. Yield 1.99, 57%. Mpt. 237-243°C.

IR (KBr disc) 1640 (C=O amide), 1400 (COO⁻), 3300 (NH) cm⁻¹.

N-CARBOBENZOXY OCTAMER (50)
Via mixed anhydride reaction

A solution of N-carbobenzoxy tetramer (2g; 1.8×10^{-3} mol) in dry tetrahydrofuran (100ml) was prepared at -5°C in a 250ml two necked round bottomed flask fitted with a calcium chloride guard tube and a dropping funnel.

Triethylamine (2ml) was added and the solution stirred at -5°C for thirty minutes prior to treatment with *n*-butyl chloroformate (0.25g; 1.8×10^{-3} mol). The solution was again allowed to react under stirring for thirty minutes at -5°C . Unprotected tetramer (1.66g; 1.8×10^{-3} mol) in water was added and the reaction mixture was left stirring at room temperature overnight. The resulting layers were separated and the upper layer mixed vigorously with water (30ml). The precipitate formed was filtered off and recrystallized from glacial acetic acid and dimethylformamide (3:1). The product was then oven dried at 80°C . Yield 1.5g, 43%. Mpt. 223-225 $^{\circ}\text{C}$.

From the GPC chromatogram the majority of the product was found to be tetrameric. IR (KBr disc) 3300(NH), 3300-2500(OHstr) 1690(C=O carbamate, carboxylic acid), 1635(C=O amide), 3305(NH) cm^{-1} .

5. REFERENCES.

- 1) J.H. de Bussy, *Material and Technology*; 6, 321-325, Longman, (1973).
- 2) Van Nostrand's Scientific Encyclopedia; 7th Ed., Consideine, 1, 1137, Van Nostrand Reinhold, N.Y., (1989).
- 3) B.C. Cox, R.P. Kendall, ICI paper; FP/2418/B, Oligomers in Nylon-6.6: Re-equilibrium rate and effect of polymerization temperature. (1966).
- 4) ICI paper; FH/17034/B, Oligomers in Nylon-6.6: A review of past work and current knowledge, (1987).
- 5) D.A. Eden, G.W. Follows, B. Smithies, G. Tonika, ICI paper; FP/7753/B, Nylon-6.6: The formation of oligomers and their effects upon polymer properties. (1970).
- 6) A. Ballistreri et al; Macromol., 20, 2991-2997, (1970).
- 7) I. Luderwald, F. Merz; Ang. Makromol. Chem. 74, 165-185, (1978).
- 8) D.C. Bassett, Principles of Polymer Morphology; Cambridge University Press, (1981).
- 9) P.H. Geil; J. Polym. Sci., 44, 449, (1960).
- 10) V.F. Holland; Makromol. Chem., 71, 204, (1964)
- 11) J.L.Koenig, M.C. Agboatwalla; J. Makromol. Sci. - Phys., B2(3), 391-420, (1968).
- 12) P. Dreyfuss, A. Keller; J. Makromol. Sci. - Phys., B4(4), 811-836 (1970).
- 13) A. Keller, F.M. Willmouth; J. Polym. Sci., A-2 V10, 857-861, (1972).
- 13a) E.D.T. Atkins, A. Keller, D.M. Sadler; J. Polym. Sci., A-2 V10, 863-875, (1972).
- 14) S.J. Spells, D.M. Sadler, A. Keller; Polymer, 32(3), 387-392, (1991).
119, (1967).
- 15) P. Kusch; Kolloid-Z., 208, 138, (1966).
- 16) M. Rothe, W. Dunkel; Polym. Lett., 5, 589-593, (1967).

- 17) H. Zahn, W. Lauer; Makromol. Chem., 23, 85, (1957).
- 18) H. Zahn, F. Schmidt; Makromol. Chem., 36 1, (1959).
- 19) H. Zahn, P. Kusch, J. Shah; Z. Polym., 216-217, 298, (1967).
- 20) Lancaster Synthesis Catalogue 1991/92; Catalogue Number 9061.
- 21) A.K. Bose, F. Greer, C.C. Price; Org. Chem., 23, 1335, (1958).
- 22) G.H.L. Nefkens; Nature., 185, 309, (1960).
- 23) ICI paper; NB9197.
- 24) Authur I. Vogel, Practical Organic Chemistry; Vogel, 3rd Ed., 361, Longmans, (1962).
- 25) H. Ing, R. Manske; J. Chem. Soc., 2348, (1926).
- 26) B.R. Baker, J.P. Joseph, R.E. Schaub; J. Am. Chem. Soc., 5905, (1955).
- 27) E. Schröder, K. Lübke, The Peptides; Vol. 1, 108, Academic Press, (1965).
- 28) Jerry March, Advanced Organic Chemistry; 3rd Ed., page 372
- 29) E. Schröder, K. Lübke, The Peptides; Vol. 1, 73, Academic Press, (1965).
- 30) M.E. Jung, M.A. Lyster; J. Chem. Soc., 315, (1978).
- 31) R.S. Lott et al; J. Chem. Soc., 495, (1979).
- 32) Ben-Ishai Berger; J. Org. Chem., 17, 1564-1570, (1952).
- 33) Ben-Ishai Berger; J. Org. Chem., 19, 62-66, (1954).
- 34) G.W. Anderson, J. Blodinger, A.D. Welcher; J. Am. Chem. Soc., 74, 5309, (1952).
- 35) R.A. Boissonnas et al; Helv. Chim. Acta., 38, 1491, (1955).
- 36) R.A. Boissonnas; Adv. Org. Chem., 3, 164-169; (1963).
- 37) E. Schröder, K. Lübke, The Peptides; Vol. 1, 22-30, Academic Press, (1965).

- 38) O. Gawron, F. Draus; J. Org. Chem., 23, 1040, (1957).
- 39) N.F. Albertson, F.C. McKay; J. Am. Chem. Soc., 75, 5323, (1953).
- 40) Z. Naturforsch; 14B, 472, (1959).
- 41) Helv. Chim. Acta., 46, 870, (1963).
- 42) R.B. Merrifield, D.W. Woolley; J. Am. Chem. Soc., 78, 4646, (1956).
- 43) J. White; J. Biol. Chem., 106, 141, (1934).
- 44) E. Schröder, K. Lübke, The Peptides; Vol.1, 52-57, Academic Press, (1965).
- 45) H. Aigner, D. Marquarding; Tetrahedron letters, 36, 3325-3326, (1978).
- 46) Tetrahedron; 36, 2409, (1980).
- 45) Chemistry and Biochemistry of the Amino Acids; G.C. Barrett, 313, Chapman and Hill.
- 48a) D. Rehn, I. Ugi; J. Chem. Research(S), 119, (1977).
- 48b) D. Rehn, I. Ugi; J. Chem. Research(M), 1501-1506, (1977).
- 49) Org. Synth. Coll. Vol.; 7, 93, (1986).
- 50) Shimura, Ikeda; J. Polym. Sci., 11, 1271, (1973).
- 51) Introduction to Organic Chemistry; Strietwieser, Heathcock, 2nd Ed., 746-747, Collier Macmillan.
- 52) Practical Organic Chemistry; Vogel, 3rd Ed., 411-418.
- 53) C.G. Cannon; Mikrochim Acta[Wien], 555, (1955).
- 54) H. Mitomo; Polymer, 29, 1636, (1988).