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Cyclic oligo(undecanamide)s (nylon 11 s) and cyclic alternating oligo(undecanamide–undecanoate)s: their synthesis using high dilution conditions and their analysis

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A sample of cyclic oligo(undecanamide)s (**1**) (nylon 11 s), containing from the cyclic monomer to at least the cyclic hexamer, was conveniently prepared (57% yield) by the cyclo-oligomerization of 11-aminoundecanoic acid *p*-nitrophenyl ester under high dilution conditions. The cyclics, obtained free of linear oligomers by virtue of their greater solubilities in chloroform, were analysed by fast atom bombardment mass spectrometry (FABMS), high pressure liquid chromatography (HPLC), gel permeation chromatography (g.p.c.) and ^{1}H nuclear magnetic resonance (n.m.r.) spectroscopy. The latter, which displayed a series of N–H signals reflecting the proportions of the various cyclics, was the most convenient method for analysing the cyclic oligo(undecanamide)s. A sample of cyclic alternating oligo(undecanamide–undecanoate)s (**2**), containing from the cyclic monomer to at least the cyclic undecamer, was conveniently prepared (57% yield) from (11-aminoundecanoyl)-11-oxyundecanoic acid *p*-nitrophenyl ester in a similar manner. Linear oligo(undecanamide–undecanoate)s (**4**) were prepared from the appropriate ω-bromo acid using a phase transfer catalysed reaction. These cyclic and linear oligomers, which were much more soluble than the corresponding oligo(undecananide)s, were analysed by FABMS, g.p.c., and ^{1}H n.m.r. spectroscopy. For these oligomers g.p.c. was the most convenient method of analysis. © 1997 Elsevier Science Ltd.

(Keywords: cyclic oligo(undecanamide)s; cyclic alternating oligo(undecanamide–undecanoate)s)

INTRODUCTION

Cyclic oligomers are of interest for a variety of reasons. Thus, they are present as minor components in, and influence the properties of, many step-growth polymers[1], they can serve as starting materials for entropy-driven ring-opening polymerizations[2], and, if they contain moieties that allow them to take part in, for example, hydrogen-bonding and/or π-donor–acceptor interactions, they can have useful recognition properties[3]. This paper describes the synthesis under high dilution conditions and the characterization of cyclic oligo(undecanamide)s (**1**) (nylon11s) and of alternating cyclic oligo(undecanamide–undecanoate)s (**2**). The corresponding linear oligomers (**3** and **4**) were also synthesized in order to facilitate identification of the cyclic oligomers. The use of high dilution conditions for the synthesis of cyclic compounds, by condensation reactions of α,ω-difunctional compounds, is based on the fact that intramolecular cyclizations, being first-order reactions, are favoured at low concentrations over second-order intermolecular condensations which give linear products[4]. This principle was first exploited by Ruggli in 1912 in connection with the syntheses of a series of cyclic diamides[5]. It has been used extensively since and has been reviewed[6,7]. Theoretical treatments have been reported[4,8–10]. Usually the aim is the synthesis of cyclized monomer, but the formation of higher oligomers has been noted on numerous occasions[11].

In the present work cyclic oligo(undecanamide)s (**1**) were selected for study mainly because cyclizations of activated derivatives of 11-aminoundecanoic acid (**5**) are unlikely to give simply the cyclized monomer, i.e. lactam **6**, as the major product[4]. Thus, the lactam **6** is a 'medium-sized' ring and so has strain resulting from numerous transannular interactions. In contrast analogous cyclizations of 6-aminohexanoic acid (**7**) for example, would be expected[4] to give the cyclized monomer, i.e. caprolactam (**8**), as the major product. The main objective of the present study was to identify analytical methods that would allow other syntheses of these, and related cyclics, to be monitored easily.

EXPERIMENTAL

General experimental details

Organic solutions were dried using magnesium sulfate. Petroleum ether refers to the fraction b.p. 40–60°C. Abbreviations: dicyclohexylcarbodiimide (DCC); tetrahydrofuran (THF); trifluoroacetic acid (TFA); dimethylformamide (DMF); di-isopropylethylamine (DIEA); dimethyl sulfoxide (DMSO). Melting points were measured using a Gallenkamp Melting Point Apparatus and are uncorrected. Infra-red (i.r.) spectra were recorded on a Perkin-Elmer 1710 Fourier transform (*FT*) i.r. instrument for, unless indicated otherwise, KBr discs. ^{1}H nuclear magnetic resonance (n.m.r.) spectra were recorded at 500 Mz using a Varian Unity Spectrometer for, unless indicated otherwise,

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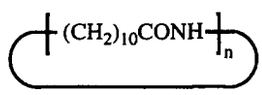
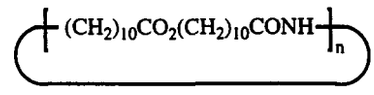


(1)



(2)

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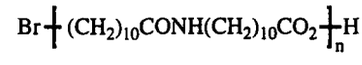
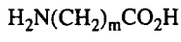


(4)

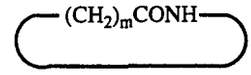
(**a**) : X = NH_2; Y = $-CO_2^-Na^+$

(**b**) : X = $CF_3CO_2^-\overset{+}{N}H_3-$; Y = $-CO_2H$



(**5**) : m = 10

(**7**) : m = 5



(**6**) : m = 10

(**8**) : m = 5

solutions in deuteriochloroform. Fast atom bombardment mass spectrometry (FABMS) were obtained using a Kratos Concept 1 S Spectrometer: ionization was achieved by xenon atoms bombarding the sample in a matrix of *m*-nitrobenzyl alcohol. Gel permeation chromatography (g.p.c.) analyses were carried out using a series of four PLgel 30 cm mixed E columns or a 10 μm–500 Å column. The eluant was chloroform at 20°C and the detector a Polymer Laboratories GPC LC1240 RI detector. It was calibrated using a series of polystyrene standards.

*N-t-butoxycarbonyl-11-aminoundecanoic acid (**9**)*

A three-necked flask (1 l) equipped with a mechanical stirrer, thermometer and dropping funnel was charged with a solution of sodium hydroxide (6.80 g, 0.17 mol) in water (150 ml) and 11-aminoundecanoic acid (30.00 g, 0.15 mol). The clear solution was diluted with *t*-butyl alcohol (100 ml). To this well-stirred mixture di-*t*-butyl dicarbonate (33.80 g, 0.16 mol) was added dropwise over 1 h. A white precipitate formed. Additional sodium hydroxide (3.20 g, 0.08 mol) in water (10 ml) was added carefully. The solution became clear again. The pH was between 7 and 8. This solution was left overnight, then acidified (to Congo Red indicator) with 2 N hydrochloric acid, and extracted with diethyl ether. The extracts were washed with water, and dried. The solvent was evaporated off and the residue dissolved in a minimum volume of ethyl acetate–petroleum ether (equal volumes). On storage at 5°C needle-like crystals formed. These were collected, washed and dried. Compound **9** (38.0 g, 84% yield) had m.p. 69–70°C (lit.[12], 67–68°C) and ν_{max} (film cast from chloroform) 1710 (CO_2H) and 1683 cm^{-1} (t-Boc carbonyl).

*N-t-butoxycarbonyl-11-aminoundecanoic acid p-nitrophenyl ester (**10**)*

Into a well-stirred solution of acid **9** (6.02 g, 20 mmol), *p*-nitrophenol (4.17 g, 30 mmol) and 4-dimethylaminopyridine (0.10 g) in THF (30 ml) at 0–10°C, DCC (6.18 g, 30 mmol) in THF (20 ml) was added dropwise over 30 min. Stirring was continued at 20°C for 24 h, then the THF was evaporated off. Recrystallization of the residue, initially from methanol (2 ×) then from cyclohexane, gave the desired ester (**10**) (5.80 g, 69%) as pale yellow crystals m.p. 57–58°C; ν_{max} (film cast from chloroform) 1754 (aryl ester) and 1683 cm^{-1} (t-Boc carbonyl); δ 1.30 (*br*; 14H; $7CH_2$), 1.45 (*s*; 9H; t-Boc), 1.76 (*m*; 2H; $NHCH_2\underline{CH_2}$), 2.55 (*t*, J = 7.45 Hz; 2H; CH_2CO), 3.10 (*br.m*; 2H; $NH\underline{CH_2}$), 4.50 (*br*; 1H; NH), 7.28 (*m*; 2H; aromatic H) and 8.28 ppm (m; 2H, aromatic H). Found C 62.5, H 8.2, N 6.8; $C_{22}H_{34}N_2O_6$ requires C 62.6, H 8.1 and N 6.6%.

*Linear oligomers (**3a** and **3b**) of 11-aminoundecanoic acid*

The above ester (**10**) (850 mg, 2.0 mmol) was dissolved in TFA (7.5 ml) and chloroform (7.5 ml) and the mixture stirred at 0–10°C for 60 min. The mixture was then evaporated to dryness to leave salt **11**. The salt **11** was dissolved in DMF (20 ml), then DIEA (1.5 ml, 11 mmol) was added. The mixture was stirred at 20°C for 5 h. The product was isolated by adding the reaction mixture to ether (300 ml). A precipitate formed and this was collected, washed with copious amounts of 1 N hydrochloric acid, saturated aqueous sodium bicarbonate and water, then dried. Product **3a** (299 mg, 75%), a white powder, was insoluble in chloroform, DMF, ethyl acetate and methanol.

Product **3a** was dissolved in a mixture of TFA (10 ml) and chloroform (10 ml) and reprecipitated from methanol. This gave product **3b** (290 mg, 72% overall yield). It had ν_{max} 3299 (N–H), 1643 (amide I) and 1555 cm^{-1} (amide II); δ (equal volumes of d^1-TFA and d^6-DMSO) 1.10 (*br.s*; 12H; $6CH_2$), 1.38 (*br*; 4H; $2CH_2$), 2.22(*m*; 2H; CH_2CO), 2.80 (*br*; 0.2H; $CH_2N^+H_3$) and 3.12 ppm (*br*; 2H; $CONHCH_2$): $\overline{DP}$ = integration of $\delta_{2.22}$/integration of $\delta_{2.80}$ = 10.2. Elemental analysis: Found C 66.6, H 10.7, N 7.5 and F 3.3%: $\overline{DP}$ = 3 × 19 × N%/14 × F% = 9.2.

*Cyclic oligomers (**1**) of 11-aminoundecanoic acid*

The reaction procedure was exactly the same (including the quantities of reagents) as that described above for the synthesis of the linear oligomers (**3a**), except that a much larger volume of DMF (500 ml) was used and the reaction time was extended to 96 h. Reprecipitation of the crude product from chloroform into petroleum ether gave pure cyclic product (**1**) (210 mg, 57%). It had ν_{max} 3295 (N–H), 1642 (amide I) and 1553 cm^{-1} (amide II); δ 1.33(*br.s*; 12H; $6CH_2$), 1.55(*br.s*; 2H; $CH_2\underline{CH_2}CO$), 1.72 (*m*; 2H; $NHCH_2\underline{CH_2}$), 2.20 (*m*; 2H; CH_2CO), 3.30 (*m*; 2H; $CONHCH_2$) and 5.30–6.00 ppm (*m*; 1H; NH). Found: C 71.9, H 11.4 and N 7.75%; $(C_{11}H_{21}NO)_n$ requires C 72.1, H 11.5 and N 7.65%. FABMS: 184($M_1 + H^+$, 25%), 367($M_2 + H^+$, 100%), 550($M_3 + H^+$, 82%), 734($M_4 + H^+$, 1.0%),

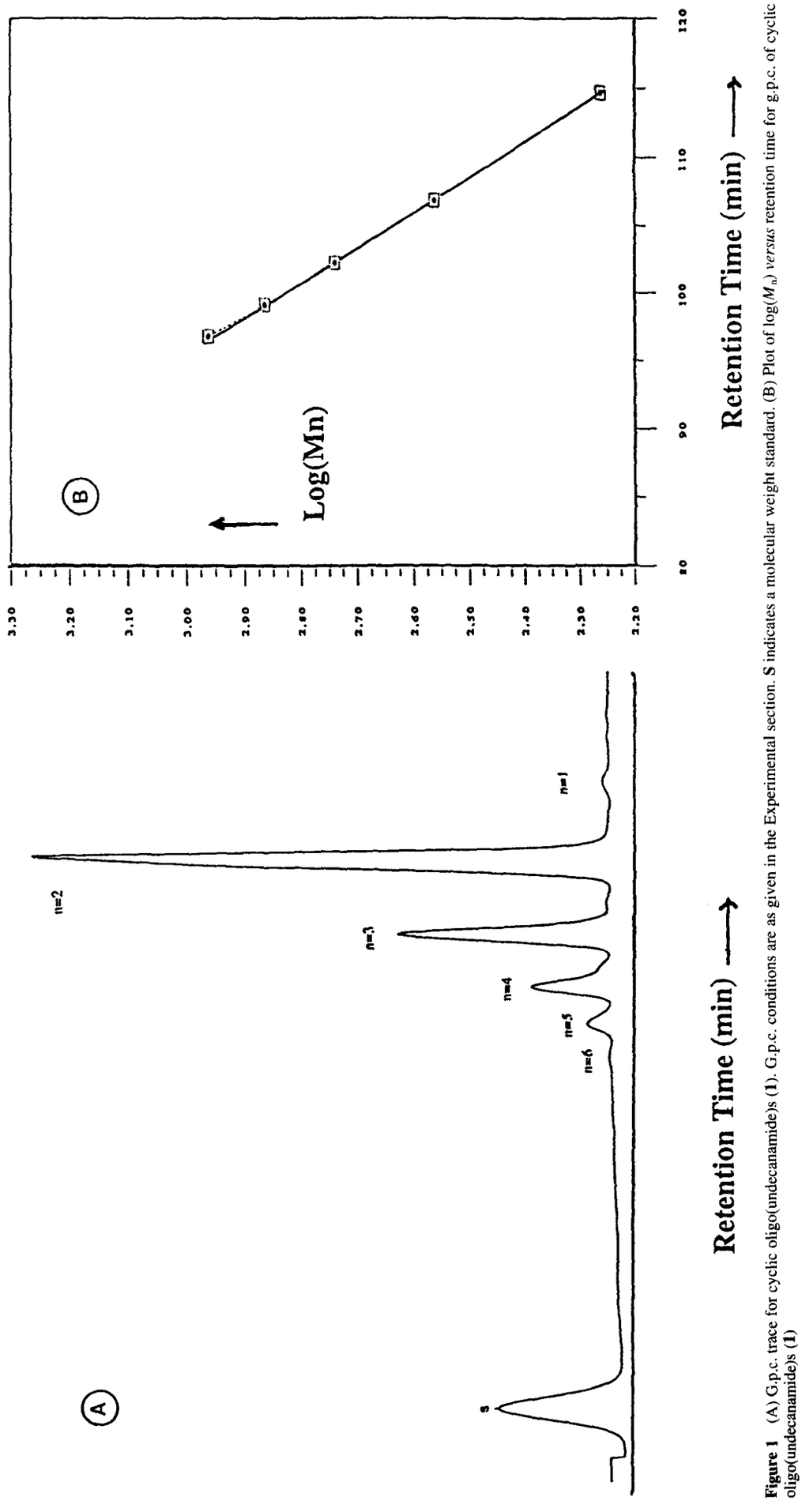


Figure 1 (A) G.p.c. trace for cyclic oligo(undecanamide)s (1). G.p.c. conditions are as given in the Experimental section. S indicates a molecular weight standard. (B) Plot of $\log(M_n)$ *versus* retention time for g.p.c. of cyclic oligo(undecanamide)s (1)

Table 1 Analysis of cyclic(undecanamide)s (**1**) by various methods

Analytical method	Amount of each component[a]					
	Unimer	Dimer	Trimer	Tetramer	Pentame	Hexamer
^{1}H n.m.r.	3	100	34	13	3	–
HPLC	3	100	38	7	–	–
G.p.c.	2	100	30	5	2	0.3

[a]Mole ratios relative to the dimer. The latter is arbitarily assigned to be 100. The mole ratios are signal areas divided by the relevant DP

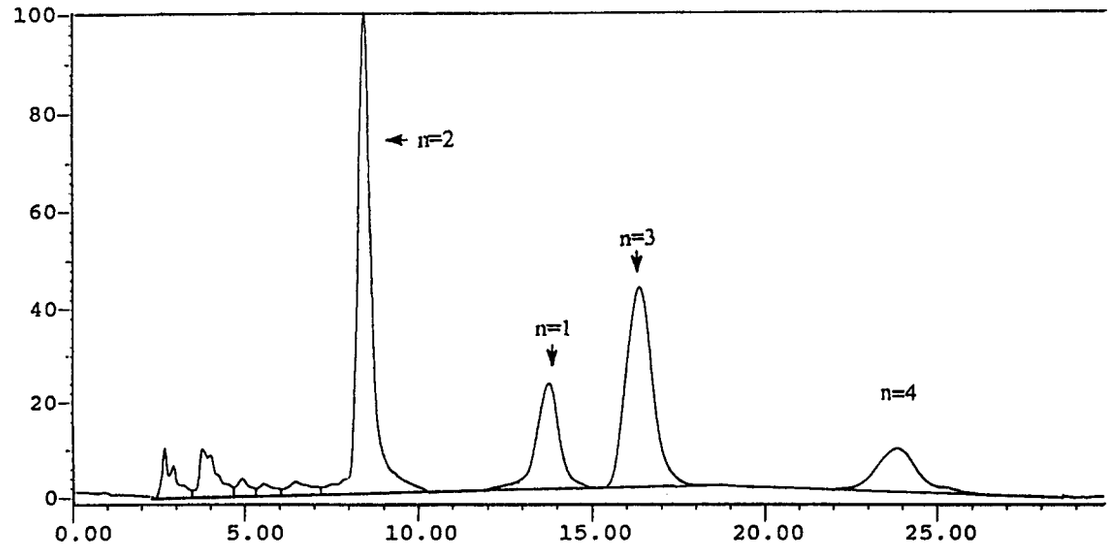


Figure 2 HPLC trace of a cyclic oligo(undecanamide)s (**1**) fraction chosen to show the resolution achieved. HPLC conditions are as given in the Experimental section

917($M_5 + H^+$, 0.4%) and 1100($M_6 + H^+$, 0.3%). For g.p.c. see *Figure 1* and *Table 1*. For high pressure liquid chromatography (HPLC) analysis see below.

HPLC analysis and preparative HPLC of cyclic oligo(undecanamide)s (1)

Analytical HPLC was carried out at 25°C using a Waters ODS RP-18 silica column (100 mm × 8 mm), methanol/water (80 vols/20 vols) as the mobile phase at a flow rate of 2 ml min^{-1}, and a Perkin-Elmer LC-480 diode array detector set at 210 nm. The results obtained from a chloroform solution of the cyclic oligomers (**1**) described above are given in *Figure 2* and *Table 1*.

Preparative HPLC was carried out using the above conditions except that the column (250 mm × 21 mm) and the flow rate (15 ml min^{-1}) were larger. The fractions eluting at 8.5 min and 16.5 min were collected. The fractions were identified as the dimer (**1**, $n = 2$) and trimer (**1**, $n = 3$) respectively.

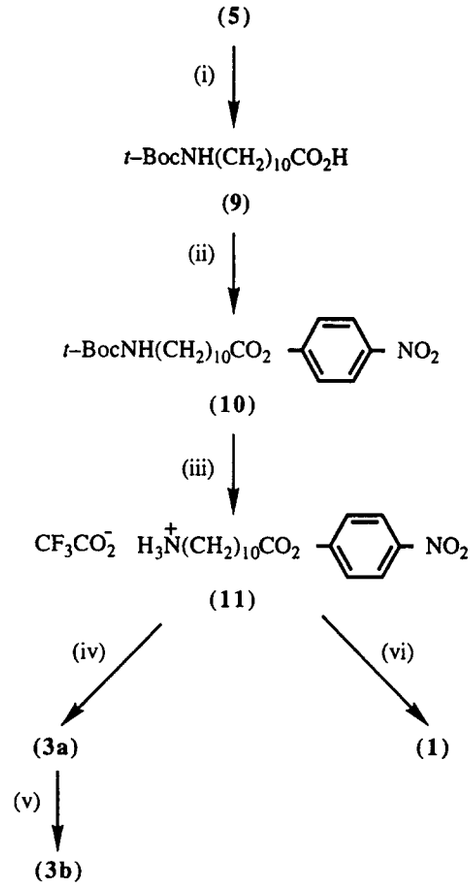
The dimer (**1**, $n = 2$) had m.p. 178–180°C (lit.[13], 186–187°C); ν_{max} 3292 (N–H), 1641 (amide I) and 1554 cm^{-1} (amide II); δ as for the cyclic product (**1**) above except that the NH signal appeared at 5.56 ppm. Found: C 71.8, H 11.2 and N 7.5%. FABMS 367 ($M_2 + H^+$, 100%). Analytical HPLC indicated the sample consisted of the dimer, trimer and tetramer in the ratio 96/2/2.

The trimer (**1**, $n = 3$) had m.p. 169–170°C; ν_{max} 3295 (N–H), 1640 (amide I), and 1552 cm^{-1} (amide II); δ as for the cyclic product (**1**) above except that the NH signal appeared at 5.74 ppm. Found: C 72.0, H 11.8, and N 7.9%. FABMS 550 ($M_3 + H^+$, 100%). Analytical HPLC indicated the sample consisted of the dimer and trimer in the ratio 1.5/98.5.

Synthesis of N(11-bromoundecanoyl)-11-aminoundecanoic acid (**14**). This acid was synthesized as outlined in *Scheme 1*.

(a) 11-Aminoundecanoic acid benzyl ester (12). 11-Aminoundecanoic acid (20.1 g, 0.10 mol), *p*-toluenesulfonic acid monohydrate (20.9 g, 0.11 mol), benzyl alcohol (11.8 g, 0.11 mol), and toluene (150 ml) were heated together under reflux in an apparatus equipped with a Dean–Stark trap. When no more water was produced the mixture was cooled and the white syrup added, with vigorous stirring, to petroleum ether (200 ml). The solid obtained was filtered off, air dried, and recrystallized from ethyl acetate. This gave the salt (38.7 g, 83% yield) of the desired ester. A portion (22.3 g, 0.05 mol) of the salt was dissolved in chloroform (200 ml) and the solution washed successively with saturated aqueous sodium bicarbonate and water, then dried.

(b) N(11-bromoundecanoyl)-11-aminoundecanoic acid benzyl ester (13). The solution prepared in (a) above was diluted with chloroform (20 ml) and the mixture added dropwise over 30 min to a stirred solution of 11-bromoundecanoyl chloride [freshly prepared from the commerical acid (13.3 g, 0.05 mol) using thionyl chloride] in chloroform (10 ml). Triethylamine (7.0 ml, 0.055 mol) was added and the mixture stirred for 24 h at 23°C. The reaction mixture was then washed successively with 5% aqueous sodium bicarbonate, 1 N hydrochloric acid, water and dried. Evaporation of the solvent gave a white solid (16.5 g). Recrystallization from ethanol gave the desired product (**13**) as white needles (15.0 g, 56%), m.p. 82–84°C; ν_{max} 1737 (ester), 1633 (amide I) and 1547 cm^{-1} (amide II). Found: C 64.9, H 8.9, N 2.7 and Br 15.0. $C_{29}H_{48}BrNO_3$ requires C 64.7, H 8.9, N 2.6 and Br 14.8.



Scheme 1 *Reaction conditions:* (i) (t-BuO_2C_2O, NaOH, t-butanol at 20°C; (ii) p-nitrophenol, DCC in THF at 20°C; (iii) TFA, chloroform at 10°C; (iv) DIEA, DMF at 20°C; (v) TFA, chloroform at 20°C; (vi) DIEA, DMF at 20°C under high dilution conditions.

*(c) Acid **14**.* The product (**13**) (11.0 g) prepared in (b) above, palladium hydroxide (10% on charcoal, 2.00 g) and cyclohexene (80 ml) in THF (200 ml) was stirred and heated at reflux temperature for 6 h. The solution was then filtered and evaporated to dryness. Recrystallization of the crude product (9.0 g) from chloroform gave acid (**14**) as white crystals (6.88 g, 75% yield), m.p. 97–98°C (lit.[14], 87–89°C); ν_{max} 1694 (CO_2H), 1632 (amide I), and 1563 cm^{-1} (amide II).

*Synthesis of linear alternating oligo(undecanamide–undecanoate)s (**4**)*

A mixture of acid **14** (449 mg, 1.0 mmol) in chloroform (6 ml) and a solution of tetra-n-butylammonium hydroxide in water (649 mg of 40%, 1.0 mmol) was vigorously stirred and heated under reflux for 2 h. The mixture was then cooled and added to acetone (100 ml) containing 2% of acetic acid. The product (**4**) was filtered off and dried (280 mg, 78% yield). It had ν_{max} 1728 (ester), 1638 (amide I) and 1541 cm^{-1} (amide II); δ 1.25 (*br.s*; 24H; $12CH_2$), 1.50 (*m*; 2H; CH_2), 1.60 (*br*; 6H; $3CH_2$), 2.13 (*t*, $J = 7.3$ Hz; 2H; CH_2CONH), 2.28 (*t*, $J = 7.2$ Hz; 2H; CH_2CO_2), 3.20 (*m*, 2H, $CONHCH_2$), 3.40 (*t*, $J = 7.4$ Hz; $BrCH_2$ of end groups), 4.08 (*t*, $J = 7.1$ Hz; 2H; CO_2CH_2) and 5.5–5.8 ppm (*m*; 1H; CONH). Found: C 68.7, H 10.5, N 3.8, and Br 4.2%: this corresponds to DP = 4.9. FABMS: There were two series of peaks due to the *linear* oligomers, one corresponding to ^{79}Br end groups and one due to ^{81}Br end groups. Only the former series are recorded here: 816 ($M_2 + H^+$, 24%), 1183 ($M_3 + H^+$, 24%), 1550 ($M_4 + H^+$, 8%), 1917 ($M_5 + H^+$, 3%) and 2284 ($M_6 + H^+$, 1%). In addition there was a series of peaks due to *cyclic* oligomers: 368 ($M_1 + H^+$, 16%), 736 ($M_2 + H^+$, 100%), 1103($M_3 + H^+$, 9%) and 1472 ($M_4 + H^+$, 2%). For g.p.c. analysis see text and *Figure 3a*.

*Synthesis of (N-t-butoxycarbonyl-11-aminoundecanoyl)-11-oxyundecanoic acid (**16**)*

This acid was synthesized as outlined in *Scheme 2*.

(a) 11-bromoundecanoic acid benzyl ester. 11-Bromoundecanoyl chloride (14.0 g, 0.05 mol) in chloroform (10 ml) was added dropwise over 1 h to a vigorously stirred solution of benzyl alcohol (6.00 g, 0.055 mol) and DIEA (7.5 g) in chloroform (10 ml) at 0°C. The reaction mixture was left at 20°C for 18 h, then diluted with chloroform (100 ml) and the solution washed successively with hydrochloric acid (1 N), 5% aqueous sodium bicarbonate, and brine. Evaporation of the solvent from the dried solution gave the product (15.0 g, 84% yield) as a clear oil with ν_{max} (film cast from a solution in chloroform) 1737 cm^{-1} (ester).

*(b) (N-t-butoxycarbonyl-11-aminoundecanoyl)-11-oxyundecanoic acid benzyl ester (**15**).* The oily product (15.0 g, 0.042 mol) prepared in (a) above and N-t-butoxycarbonyl-11-aminoundecanoic acid (**9**) (13.0 g, 0.043 mol) were dissolved in ethyl acetate (15 ml), then DIEA (5.6 g, 0.043 mol) was added to the solution. The mixture was stirred vigorously and heated at reflux temperature for 24 h. The cold reaction mixture was diluted with more ethyl acetate and the resulting solution washed successively with saturated aqueous sodium bicarbonate and water, then dried. Evaporation of the solvent gave an oil (16.0 g) which was purified by chromatography using a silica column and a mixture of ethyl acetate–cyclohexane (1 vol/4 vols) as the eluant. Recrystallization from petroleum ether gave ester **15** (9.5 g, 39%) as white plates, m.p. 44–45°C; ν_{max} 1731 (ester), 1683 (amide I) and 1536 cm^{-1} (amide II); δ 1.30 (*br.s*; 28H; $14CH_2$), 1.44 (*s*; 9H t-Boc), 1.45 (*m*; 2H; CH_2), 1.65 (*m*; 2H; CH_2), 2.30 (*m*; 4H; $2CH_2CO$), 3.08 (*m*; 2H; $CONHCH_2$), 4.05 (*t*, $J = 6.5$ Hz; 2H; CO_2CH_2), 5.11 (*s*; 2H; $C_6H_5CH_2$) and 7.35 ppm (*s*; 5H; aromatic H). Found: C 71.0, H 9.8, N 2.5; $C_{34}H_{57}NO_6$ requires C 71.0, H 10.0, and N 2.4%.

*(c) Acid **16**.* The product (**15**) (4.20 g) described in (b) above was dissolved in ethanol (100 ml). Palladium on charcoal (20%, 0.5 g) was added and the mixture was shaken for 4 h under 1 atmosphere of hydrogen. The catalyst was then filtered off and the filtrate diluted with water (20 ml). The small white needles of acid (**16**) that formed were collected (3.30 g, 94% yield). They had m.p. 64–65°C; ν_{max}, 1725 (ester), 1703 (CO_2H) 1681 (amide I) and 1529 cm^{-1} (amide II); δ 1.28 (*br.s*; 26H, $13CH_2$), 1.60 (*m*; 6H; $3CH_2$), 2.32 (*m*; 4H; $2CH_2CO$), 3.09 (m; 2H; $NHCH_2$); 4.05 (*m*; 2H; CH_2CO) and 4.54 ppm (br; 1H; BocNH). Found: C 66.9, H 10.5, N 2.9; $C_{27}H_{51}NO_6$ requires C 66.8, H 10.5, and N 2.9%.

*Synthesis of p-nitrophenyl ester (**17**) from acid **16***

The acid (**16**) (4.90 g, 10 mmol), p-nitrophenol (1.54 g, 11 mmol) and 4-dimethylaminopyridine (0.15 g) were dissolved in THF (40 ml) at 0°C. To the vigorously stirred solution DCC (2.25 g, 11 mmol) in THF (10 ml) was added dropwise. The mixture was stirred for 24 h at 20°C, then

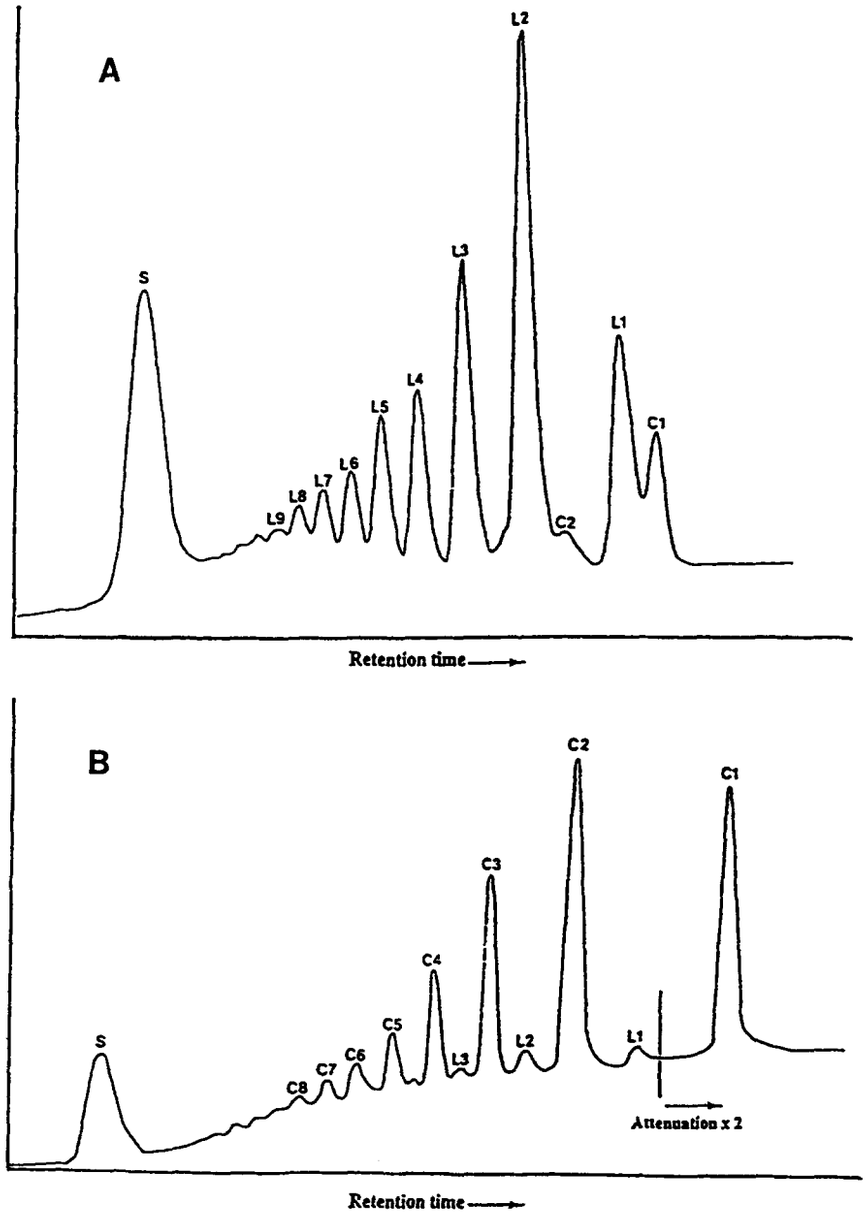
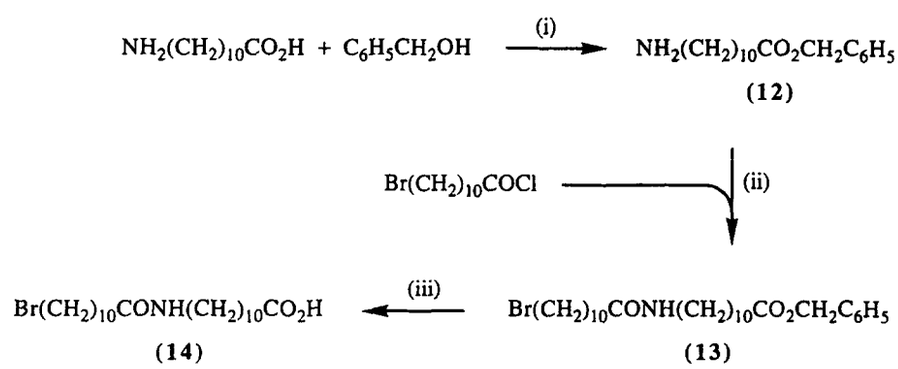


Figure 3 (A) G.p.c. trace for linear alternating oligo(undecanamide–undecanoate)s (**4**). (B) G.p.c. trace for cyclic alternating oligo(undecanamide–undecanoate)s (**2**). In both cases G.p.c. conditions are as given in the Experimental section. S indicates a molecular weight standard



Scheme 2 *Reaction conditions:* (i) PTSA, toluene, 110 °C; (ii) $(C_2H_5)_3N$, in $CHCl_3$ at 23 °C; (ii) $Pd(OH)_3$cat., cyclohexene in THF at 65 °C.

filtered and the filtrate evaporated to dryness. The residue was recrystallized twice from ethanol–petroleum ether (1 vol/2 vols). The product (**17**) (4.0 g, 66% yield) was pale yellow crystals, m.p. 102–105°C; ν_{max} 1752 (active ester), 1725 (ester), 1691 (amide I) and 1536 cm^{-1} (amide II); δ 1.31 (*br.s*; 26H; $13CH_2$), 1.49 (*s*; 9H; *t*-Boc), 1.65 (*m*; 4H; $2CH_2$), 1.76 (*m*; 2H; CH_2), 2.28 (*t*, J = 7.4 Hz; 2H; CH_2CO), 2.60 (*t*, J = 7.4 Hz; 2H; CH_2CO), 3.08 (*m*; 2H; $CONHCH_2$), 4.05 (*t*, J = 6.8 Hz; 2H; CO_2CH_2), 4.50 (*b*; 2H; CONH), 7.26 (*m*; 2H; aromatic H) and 8.26 ppm (*m*;

2H; aromatic H). Found: C 65.25, H 9.2, N 4.7: $C_{33}H_{55}N_2O_8$ requires C 65.2, H 9.1, and N 4.6%.

Cyclic oligomers of alternating oligo(undecanamide–undecanoate)s (2) via compound ***18***

The ester (**17**) (610 mg, 1.0 mmol), prepared as described above, was deprotected by treatment with a mixture of TFA (4 ml) and dichloromethane (4 ml) at 23°C for 1 h. The solvent was then removed under vacuum. The residue was dissolved in chloroform (300 ml) and treated with DIEA (5 ml). This gave compound **18**. It was allowed to react for 100 h at 20°C. The solvent was then evaporated off and the residue recrystallized twice from methanol. This afforded the cyclic oligomers (**2**) as white crystals (210 mg, 57% yield), m.p. 97–100°C; ν_{max} 1727 (ester), 1640 (amide I) and 1535 cm^{-1} (amide II); δ 1.35 (*s*; 24H; $12CH_2$), 1.50 (*m*; 2H; CH_2), 1.60 (*m*; 6H; $3CH_2$), 2.15 (*m*; 2H; CH_2CO), 2.30 (*m*; 2H; CH_2CO), 3.25 (*m*; 2H; $CONHCH_2$), 4.10 (*m*; 2H; CO_2CH_2), and 5.78 and 5.43 ppm (*br.ms*; 1H; CONH). Found: C 70.9, H 11.1, N 3.6; ($C_{22}H_{41}NO_3$) requires C 71.9, H 11.2, and N 3.8%. For FABMS: 368 ($M_1 + H^+$, 100%), 736 ($M_2 + H^+$, 25%) and 1103 ($M_3 + H^+$, 8%). For g.p.c. analysis see *Figure 3b*.

RESULTS AND DISCUSSION

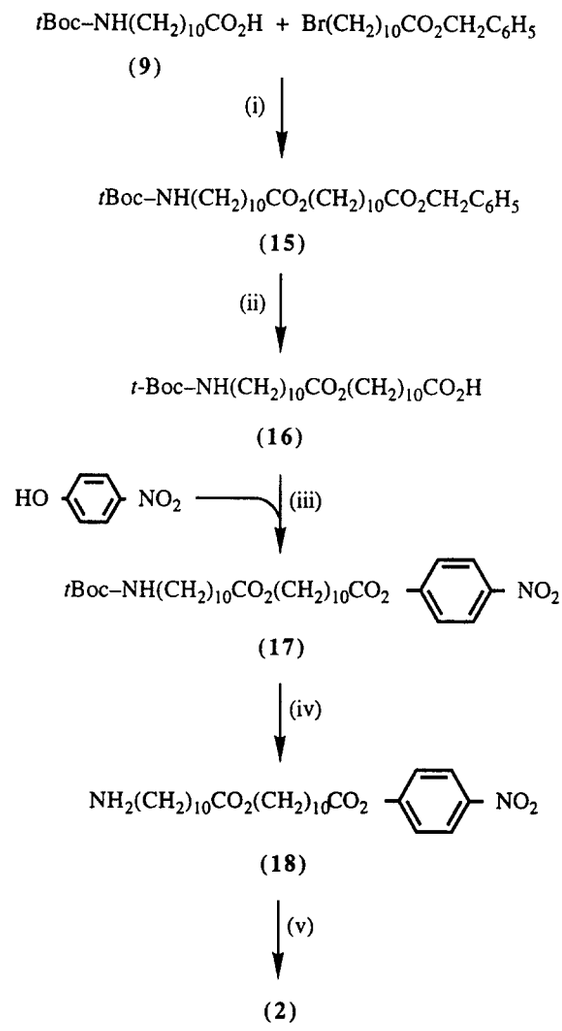
Synthesis and characterization of linear and cyclic oligo(undecanamide)s

11-Aminoundecanoic acid (**5**) was converted, *via* compounds **9** and **10**, into the trifluoroacetic acid salt (**11**) of 11-aminoundecanoic acid *p*-nitrophenylester. Both the linear and cyclic oligo(undecanamide)s were synthesized from this salt: see *Scheme 3*.

Treatment of the salt (**11**) with DIEA in DMF at 20°C for 5 h gave linear oligomers (**3a**) in 75% yield. The product was essentially insoluble in chloroform, methanol and other common solvents and it was neither possible to measure the ^1H n.m.r. spectrum nor to carry out HPLC or g.p.c. analyses under the conditions used successfully with the cyclic oligomers (see below). In order to estimate the average degree of polymerization ($\overline{DP}$) of the linear product it was dissolved in a mixture of TFA and chloroform, then recovered by precipitation into methanol. This converted the original amine end-groups into salt end-groups: see (**3b**). The elemental analysis for fluorine and the ^1H n.m.r. spectrum indicated the linears had a $\overline{DP}$ *ca* 9.

Treatment of the salt (**11**) with DIEA in DMF at 20°C under high dilution conditions (4×10^{-3} M) for 96 h followed by precipitation into ether, then reprecipitation from chloroform into petroleum ether, gave cyclic oligomers (**1**) in 57% yield. FABMS has been used before to identify cyclic nylons[15] and a FABMS on the present product clearly showed the presence of cyclics from at least $n = 1$ to $n = 6$. The cyclic product had significant solubility in chloroform, and methanol so several further types of analysis were possible. The results of these analyses are summarized in *Table 1*.

HPLC has been used successfully to analyse the smaller oligomers present in samples of various cyclic nylons, for example, nylon 6[16,17] and nylon 12[18]. Analysis of the present cyclics (nylon 11s) on a Waters CDS RP 18 silica column using methanol–water (4 vols, 1 vol) as the eluant and an ultra-violet (u.v.) detector showed four peaks: see *Figure 2*. Samples of the two major peaks were isolated by preparative HPLC and identified by FABMS as the cyclic



Scheme 3 *Reaction conditions:* (i) DIEA in ethyl acetate at 78°C; (ii) H_2, Pd/C in ethanol at 20°C; (iii) DCC, DMAP, in THF at 20°C; (iv) TFA in dichloromethane at 23°C, then DIEA in chloroform at 20°C; (v) dilute solution in chloroform, 100 h at 20°C.

dimer (**1**: $n = 2$) and the cyclic trimer (**1**: $n = 3$). With these and a sample of undecanelactam (**6**) in hand the main HPLC peaks could be assigned unambiguously. Here, as with the cyclic nylon 6s[16,17] and nylon 12s[18], for reasons which are not clear the cyclic monomer elutes after the cyclic dimer. Due to the poor solubility of the linear samples (**3a** and **3b**) they could not be analysed under the HPLC conditions successfully used here with the cyclics.

G.p.c. analysis using chloroform as the eluant showed a series of peaks due to cyclics from the unimer (**6**) to the hexamer (**1**: $n = 6$): see *Figure 1a*. Using the authentic samples available (see above) the first three peaks could be assigned unambiguously. A plot of $\log\overline{M}_n$ *versus* the retention time was a straight line, see *Figure 1b*, confirming that all the peaks were due to the cyclic family. The linear samples could not be analysed by g.p.c. under the conditions used successfully with the cyclics.

The ^1H n.m.r. spectrum of the cyclics in deuteriochloroform solution proved most interesting. All the signals were as anticipated except that there was a series of signals due to the N–H protons: see *Figure 4*. Use of the three standard samples available allowed these signals to be confidently assigned to the different cyclics. Comparison of the signal areas with the results obtained from the HPLC and g.p.c. analyses, see *Table 1*, shows reasonably close agreement given that in each analytical method the use of different

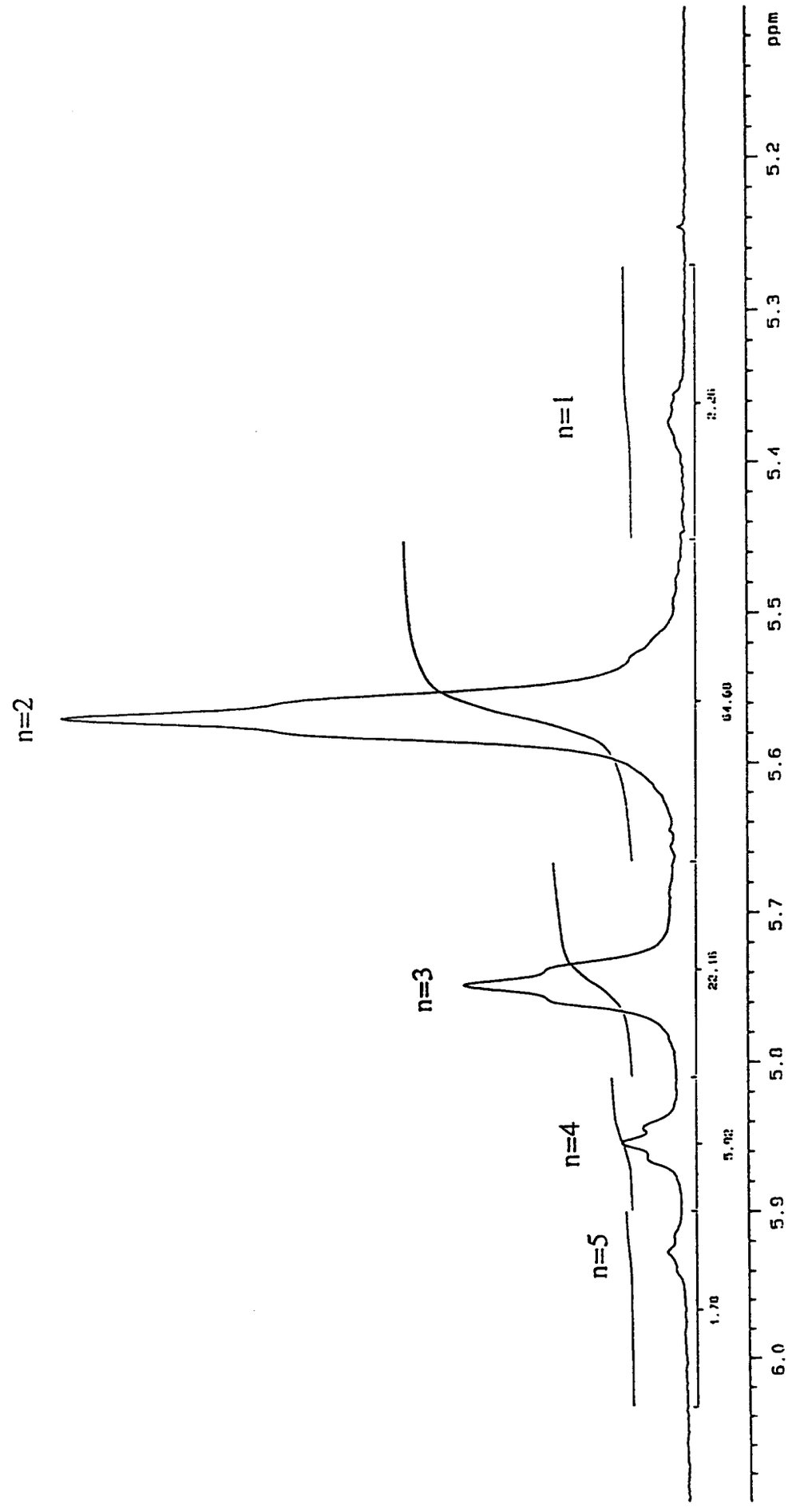


Figure 4 The N–H signal region of the ^{1}H n.m.r. spectrum of the cyclic oligo(undecanamide)s (1). The experimental conditions are as given in the Experimental section

solvents and/or concentrations means that the cyclics, which have only modest solubilities in the solvents used (especially the larger rings) may be present in slightly different proportions. It also has to be borne in mind that in the HPLC analyses no allowance has been made for the fact that different cyclics may have different extinction coefficients[17]. Similarly in the g.p.c. analyses it is assumed that all the cyclics produce a similar response at the refractive index detector. It is clear that analysis by ^{1}H n.m.r. spectroscopy is the most satisfactory, especially as no calibration of the signal intensities is required. ^{13}C n.m.r.[19] and ^{29}Si n.m.r.[20] have previously been used for the identification and analysis of families of cyclic oligomers.

Synthesis and characterization of linear and cyclic alternating oligo(undecanamide–undecanoate)s.

The poor solubilities in organic solvents of the linear oligo(undecanamide)s (**3a** and **3b**) and the modest solubilities of the cyclic oligo(undecanamide)s (**1**) is due to the extensive hydrogen-bonding possibilities with these molecules. This prompted a study of the cyclic alternating oligo(undecanamide–undecanoate)s (**2**) and their linear analogues (**4**). As expected, replacing half of the amide links with ester links greatly improves the solubilities.

Linear oligomers (**4**) were conveniently synthesized by treating ω-bromo acid (**14**) with aqueous tetra-*n*-butylammonium hydroxide under phase transfer conditions[21]. The ω-bromo acid was prepared *via* compounds **12** and **13** as outlined in *Scheme 1*. The linear product (**4**), obtained in 78% yield, was soluble in chloroform. End-group analysis by elemental analysis for bromine and by ^{1}H n.m.r. spectroscopy (bromomethyl groups) indicated $\bar{M}_n$ values of 1500 and 1300 respectively, corresponding to a $\overline{DP}$ of *ca* 3.8. It should be noted here that, since the molecular weight of the repeat unit in this linear polymer is approximately twice that of the repeat unit in the oligo(undecanamide)s discussed above, for a given oligomer molecular weight $\overline{DP}$ values for the former will be about half those for the latter. G.p.c. analysis showed a series of peaks (85% of the mass of the sample) due to linear oligomers from DP 2–12 and cyclics (see below) (15% of the sample) from DP 1–4. FABMS indicated the presence of linears from DP 2–6 and cyclics from DP 1–4. It is interesting to note that, for example, the peak due to the cyclic dimer was four times as intense as that due to the linear dimer, even though the former was present at only *ca* 1/5 th the concentration. Thus, FABMS detects the cyclics far more easily than the linears. The presence of such a high percentage of cyclics in the 'linear' sample may be a result of hydrogen-bonding in the linears bringing the reactive end-groups into proximity.

Cyclic oligo(undecanamide–undecanoate)s (**2**) were prepared from ω-amino *p*-nitrophenyl ester (**18**) in chloroform in 57% yield by reaction of the amine groups with the active ester groups under high dilution conditions (3.3×10^{-3} M). The ester (**18**) was prepared *via* compounds **15–17** as outlined in *Scheme 2*. No end-group signals were apparent in the ^{1}H n.m.r. spectrum of the cyclics and g.p.c. analysis showed a series of peaks due to the cyclics of DP 1–11 in proportions corresponding to an $\bar{M}_n$ value of 525 and $\overline{DP}$ = 1.4. FABMS confirmed the presence of cyclics from DP 1–3. As expected plots of log DP *versus* the g.p.c. elution volumes for the linear and cyclic oligomers produced two lines which are almost parallel: see *Figure 5*. The spacing of the lines is such that at a given elution volume the DP cyclic/DP linear ratio is *ca* 1.20. Examination of the ^{1}H n.m.r. spectrum of the cyclics revealed N–H signals at δ 5.43 and 5.78. By analogy with the results obtained with the cyclic oligo(undecanamide)s (**1**) and given the relative areas of the signals, these can be assigned respectively to the cyclic monomer and cyclic dimer.

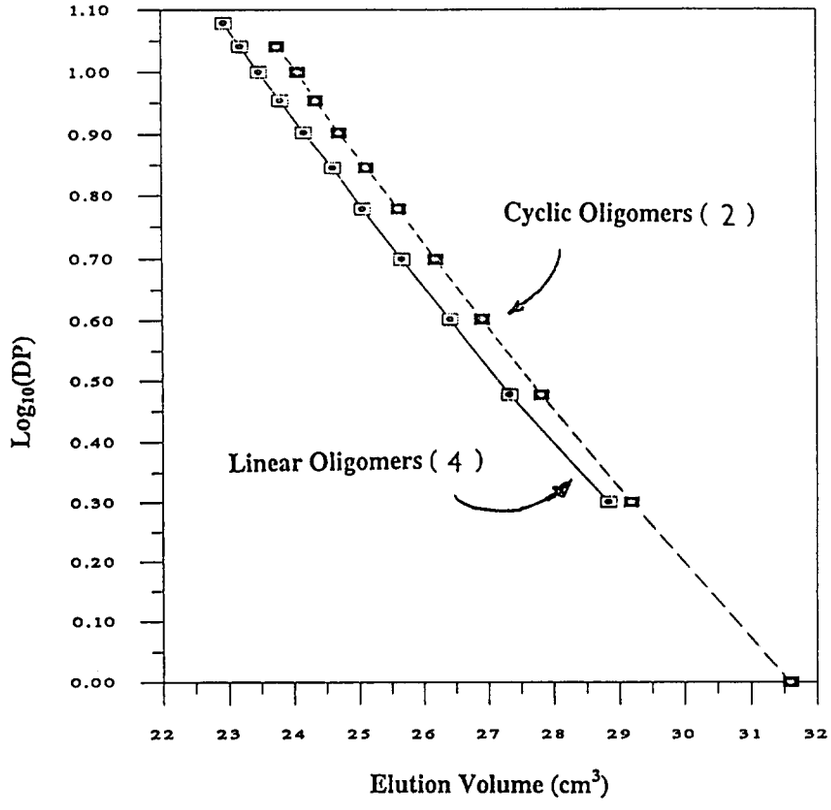


Figure 5 Plots of logDP *versus* elution volumes for cyclic oligomers (**2**) and linear oligomers (**4**). G.p.c. conditions are as given in the Experimental section

CONCLUSIONS

Although cyclic oligo(undecanamide)s (**1**) are not very soluble in organic solvents they are significantly more soluble than the analogous linear oligomers and this facilitates isolation of the cyclics free of linears. The cyclics can be analysed by HPLC (for DP 1–4) and g.p.c. (for DP 1–6) but to a significant extent the proportions of the higher oligomers estimated by these chromatographic techniques is determined by their solubility. The simplest method of analysis, and one that requires no calibration, is the range of N–H signals observed in the ^{1}H n.m.r. spectrum.

Cyclic alternating oligo(undecanamide–undecanoate)s (**2**) and their linear analogues (**4**) are much more soluble in organic solvents than the oligo(undecanamide)s (**1** and **3**) and they are easily analysed by g.p.c. for DPs up to at least 11. However, the good solubilities makes the separation of the cyclics from the linears a problem. The ^{1}H n.m.r. spectrum of the cyclics (**2**) again shows N–H signals that vary with ring size.

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