Synthesis of oligomers related to nylon 6

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A series of end-capped oligomers 13 (2*n* = 1, 2, 4, 8 and 16) related to nylon 6, have been prepared from a fully protected derivative of 6-aminohexanoic acid 4 using the reactions of polypeptide chemistry. The formation of *N*-protected *secondary* amide bonds bearing the *N*-(*p*-methoxybenzyl) group ensured the solubility of all intermediates in common organic solvents and enabled purification by chromatography; boiling trifluoroacetic acid removed the protecting group in the final stage of the synthesis.

The best science is carried out on *pure compounds*. Consequently, the interpretation of physical data obtained from the study of synthetic polymers is blunted by their polydispersity: the materials are not pure in the chemical sense. Recently the preparation of some monodisperse linear long-chain alkanes was described.[1] These compounds are of interest for relating their crystallisation processes and crystal morphology to that of commercial polythene; the folding of the molecular chains in these alkanes is of particular interest.[2] It can be argued that the study of oligoamides (short chain 'nylons') will provide important insights into the chain-folding of polymethylene segments because of the presence of hydrogen-bonding effects between amide groups. The present work concerns the syntheses of pure nylon 6 oligomers.

The inter-chain hydrogen-bonding factor of the amide functionality is fundamental for conferring on nylons those properties which make them so useful in their practical applications: tough, hard materials, insoluble in common solvents *etc.* However, in his pioneering work on polyamides, Carothers also described the first use of a *di*secondary diamine to make poly(*N*,*N*′-dimethylpentamethylenesuccinamide), −[N-(Me)(CH₂)₅N(Me)(C=O)(CH₂)₂(C=O)]ₙ−, a material which exhibited rubbery properties.[3] Soon afterwards, nylon 6,6 derivatives containing different levels of *N*-methyl groups were prepared from appropriate diamines,[4] the fully methylated material being a viscous liquid/gum at room temperature, with increased solubility in organic solvents; other dialkyl groups incorporated were ethyl, 2-methylpropyl and benzyl.[5] Recently, *N*-allylated aromatic polyamides, highly soluble in chlorinated solvents, have been prepared from the parent polymer *via* treatment with various bases followed by reaction with allyl bromide.[6]

German workers first described the preparation of a variety of *oligo*amides over 30 years ago by methods which would seem to present no problems to the modern synthetic organic chemist.[7] The measurement of molecular weights by end-group titration methods was given as evidence for the integrity of the materials, but their very poor solubility in common organic solvents render their purification by preparative-scale chromatography (and hence the monitoring of their purity by analytical chromatography) impossible so that the precise degree of purity of the compounds made by this method will be unknown. In the present work, we required soluble *secondary amide intermediates* −NR(C=O)− capable of purification by chromatography and from which the group R could be replaced by hydrogen in the last stage of the procedure.
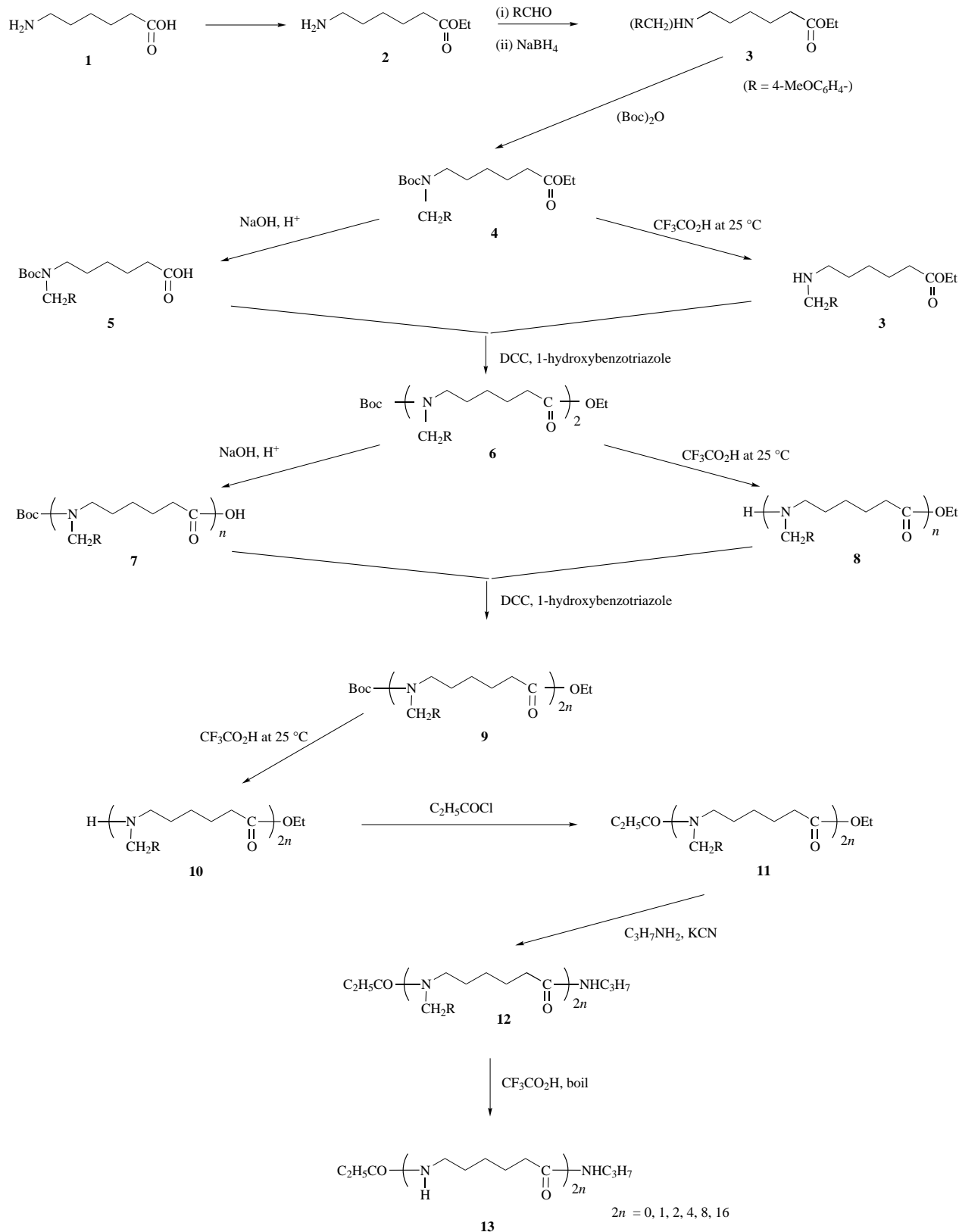
Relatively little work has been carried out on amide protecting groups,[8] but we have discovered that the *p*-methoxybenzyl group in a secondary amide −N(CH₂C₆H₄OMe-4)(C=O)−, is an excellent protecting group,[9] conferring solubility in common solvents on all host derivatives, and being readily removed by *boiling* trifluoroacetic acid (TFA). The procedure for the syntheses of end-capped oligomers of nylon 6 (prepared originally by Zahn and Gleitsman[7]) shown in Scheme 1 exploits reactions developed for the polypeptide work. Our strategy also involved the principle of molecular multiplication:[10] a compound a−b with two separately removable end groups gave molecules a−B and A−b capable of reacting together to reproduce the original functionality with a doubled chain length a−L−b.

6-Aminohexanoic acid 1 was first converted into the ethyl ester 2 which was then reacted with *p*-methoxybenzaldehyde. The crude intermediate imine was reduced to the secondary amine derivative 3 with sodium borohydride and the residual N−H bond in *half* of this compound was protected with the Boc group[11] to give 4—which is effectively the primary building block for the synthesis of the oligoamides. A small-scale experiment of 4 with trifluoroacetic acid at room temperature[12] was shown to remove the Boc group but leave the *p*-methoxybenzyl group intact. The ester protecting group on 4 was removed with hot aqueous alkali and the resultant carboxylic acid 5 coupled with the secondary amine 3 using dicyclohexylcarbodiimide and 1-hydroxybenzotriazole[13] to form the first secondary amide bond in the fully protected dimer 6. A further chain-doubling reaction to the fully protected tetramer 9 (2*n* = 4) was carried out *via* 6 by deprotecting the terminal carboxylic acid end as before to give 7 (*n* = 2), and coupling this with 8 (*n* = 2), the product of deprotection of the terminal nitrogen with TFA at room temperature. The procedure was repeated two more times to form the octamer and hexadecamer, 9 (2*n* = 8 and 16, respectively).

Terminal end-capped amides 13 (2*n* = 1, 2, 4, 8 and 16) were required for polymer physics work and were obtained in a four stage procedure: (i) deprotection of N-terminus of 9 with TFA at room temperature to yield 10; (ii) propanoylation of the nitrogen to 11; (iii) amide formation at the ester-protected carboxylic acid terminus with *n*-propylamine, catalysed with KCN,[14] to give 12; and finally (iv) removal of the *p*-methoxybenzyl-protecting group from the secondary amide functionality with TFA at reflux temperature. During this latter reaction, an unidentified solid was precipitated. Removal of the excess TFA *in vacuo* and addition of dichloromethane however, gave homogeneous solutions which, on treatment with dilute aqueous sodium hydrogen carbonate, immediately caused the precipitation of the amides; presumably traces of TFA rendered the protonated amides *soluble* in the CH₂Cl₂.

Prior to this final reaction, *all* compounds were purified by chromatography on silica to give viscous liquids/gums, and purity assessed by HPLC and by ¹H NMR spectroscopy. Terminal NH compounds 8 (or 10) could not be obtained free from residual solvent since heating *in vacuo* led to decomposition

Scheme 1

(i) RCHO
(ii) NaBH$_4$

(R = 4-MeOC$_6$H$_4$-)

(Boc)$_2$O

NaOH, H$^+$

CF$_3$CO$_2$H at 25 °C

DCC, 1-hydroxybenzotriazole

DCC, 1-hydroxybenzotriazole

CF$_3$CO$_2$H at 25 °C

C$_2$H$_5$COCl

C$_3$H$_7$NH$_2$, KCN

CF$_3$CO$_2$H, boil

$2n = 0, 1, 2, 4, 8, 16$

(presumably polymerisation); consequently, no elemental analysis data are given. The end-capped monomeric, dimeric and tetrameric amides **13** ($2n$ = 1, 2 and 4, respectively) were recrystallised from ethanol, but the octameric and hexadecameric amides were simply washed and dried.

The structures of *all* the intermediate compounds were established by ^{1}H NMR spectroscopy. Data for the fully protected oligomers are shown in Table 1; for oligomers deprotected at the terminal carboxylic acid in Table 2; for oligomers depro-

tected at the terminal nitrogen in Table 3; for terminally *N*-propanoylated fully protected oligomers in Table 4; and for terminally *N*-propanoylated terminal *n*-propylamide fully protected oligomers, in Table 5. The most significant data concerning *chain lengths* are found in Table 1 for the fully protected oligomers from the chain-doubling reactions. Very conveniently, the chemical shift of the −CH$_2$− group (*ca.* 4.1 ppm) in the *terminal* −CO$_2$CH$_2$CH$_3$ functionality is adjacent to the signals due to the *p*-CH$_3$O− substituent(s) on the protecting group on

Table 1 ^1H NMR spectra of compound **9** (in $CDCl_3$); chemical shifts at 500 MHz (^{a} at 400 MHz)

	$-C_6H_4-$	$-CH_2CONCH_2Ar$ (internal)	$BocNCH_2Ar$ (terminal)	$-CO_2CH_2CH_3$	$-OCH_3$	$-CH_2CON(CH_2Ar)CH_2-$; $BocN(CH_2Ar)CH_2-$	$-CH_2CO-$	$NCH_2(CH_2)_3CH_2CO$ $(CH_3)_3C$ $-CO_2CH_2CH_3$
4^a [≡**9** (2n = 1)]	7.14 (bs) 6.83 (d)		4.35 (bs)	4.10 (q)	3.78 (s)	3.08 (bs), 3.16 (bs) (overlapping)	2.25 (t)	1.2–1.7
Integrations (required)	2.0 (2) 1.9 (2)		2.0 (2)	1.9 (2)	3.000 (3)	2.0 (2)	2.0 (2)	18.8 (18)
6^a [≡**9** (2n = 2)]	6.7–7.15	4.44 (s), 4.36 (s)	4.27 (b)	4.04 (overlapping q)	3.7–3.73 (overlapping singlets)	3.24 (t), 3.07 (b); 3.05 (b)	2.17–2.27 (m)	1.1–1.7
Integrations (required)	8.1 (8)	4.0 (4)		2.0 (2)	6.000 (6)	4.1 (4)	4.1 (4)	25.1 (24)
9^a (2n = 4)	6.7–7.2	4.2–4.5		4.04 (overlapping q)	3.7–3.73 (overlapping singlets)	3.12 (b), 3.30 (b)	2.18–2.26 (m)	1.1–1.8
Integrations (required)	15.6 (16)	8.0 (8)		2.0 (2)	12.000 (12)	8.6 (8)	8.0 (8)	36.6 (36)
9 (2n = 8)	6.7–7.2	4.2–4.5		4.04 (overlapping q)	3.7–3.72 (overlapping singlets)	3.04 (b), 3.25 (b)	2.18–2.26 (m)	1.1–1.7
Integrations (required)	32.2 (32)	16.0 (16)		2.0 (2)	24.000 (24)	16.1 (16)	16.0 (16)	61.7 (60)
9 (2n = 16)	6.7–7.2	4.2–4.6		4.11 (overlapping q)	3.7–3.8 (overlapping singlets)	3.12 (b), 3.30 (b)	2.2–2.4 (m)	1.1–1.7
Integrations (required)	64.5 (64)	32.1 (32)		1.92 (2)	48.000 (48)	32.2 (32)	32.1 (32)	111 (108)

Table 2 ^1H NMR spectra of compound **7** (in $CDCl_3$); chemical shifts at 500 MHz (^{a} at 400 MHz)

	$-C_6H_4-$	$-CH_2CONCH_2Ar$ (internal)	$BocNCH_2Ar$ (terminal)	$-OCH_3$	$-CH_2CON(CH_2Ar)CH_2-$	$BocN(CH_2Ar)CH_2-$	$-CH_2CO-$	$NCH_2(CH_2)_3CH_2CO$ + $(CH_3)_3COCO$
5 [≡**7**^{a} (n = 1)]	7.14 (bs) 6.84 (d)		4.36 (bs)	3.79 (bs)		3.09 (bs), 3.17 (bs) (overlapping)	2.31 (t)	1.29 (b) 1.46 (Bu^t) 1.60 (m)
Integrations (required)	4.0 (4)		2.1 (2)	3.000 (3)		2.0 (2)	2.0 (2)	15.7 (15)
7^a (n = 2)	6.75–7.2	4.43 (s) 4.51 (s)	4.33 (bs)	3.77–3.79 (overlapping singlets)	3.14 (t) 3.33 (t)	3.0–3.2 (bm)	2.31 (m)	1.1–1.75
Integrations (required)	8.3 (8)	2.0 (2)	2.0 (2)	6.000 (6)		4.1 (4)	4.1 (4)	21.6 (21)
7 (n = 4)	6.7–7.2	4.42 (m) 4.48 (m)	4.33 (bs)	3.76–3.78 (overlapping singlets)	3.32 (bm) 3.13 (bm)	3.0–3.2 (bm)	2.31 (m)	1.1–1.75
Integrations (required)	15.9 (16)	6.0 (6)	2.0 (2)	12.000 (12)		8.0 (8)	8.0 (8)	33.7 (33)
7 (n = 8)	6.7–7.25	4.41 (m) 4.48 (m)	4.34 (bs)	3.76–3.8 (overlapping singlets)	3.14 (bm) 3.31 (bm)	3.0–3.2 (bm)	2.29 (m)	1.1–1.75
Integrations (required)	31.7 (32)	14.0 (14)	1.7 (2)	24.000 (24)		15.4 (16)	15.9 (16)	57.0 (57)

Table 3 ^{1}H NMR spectra of compound **8** (in CDCl$_3$); chemical shifts at 500 MHz

	−C$_6$H$_4$−	−CH$_2$CONCH$_2$Ar	HNCH$_2$Ar	−CO$_2$CH$_2$CH$_3$	−OCH$_3$	−CON(CH$_2$Ar)-CH$_2$−	HN(CH$_2$Ar)CH$_2$−	−CH$_2$CO−	NCH$_2$(CH$_2$)$_3$-CH$_2$CO	−CO$_2$CH$_2$CH$_3$
3 [≡**8** (n = 1)]	7.21 (d); 6.84 (d)		3.70 (s)	4.10 (q)	3.79 (s)		2.60 (t)	2.28 (t)	1.3–1.7	1.23 (t)
Integrations (required)	4.03 (4)		2.000 (2)	2.0 (2)	3.1 (3)		2.0 (2)	2.0 (2)	7.1 (6 + 1 from NH broad)	
8 (n = 2)	6.8–7.3	4.42 (s) 4.48 (s)	3.81 (s) 3.84 (s)	4.10 (overlapping q)	3.74–3.79 (overlapping singlets)	3.13 (t), 3.30 (t)	2.69 (t) 2.65 (t)	2.2–2.36 (m)		1.2–1.72
Integrations (required)	Solvent interference (8)	2.0 (2)	2.0 (2)	2.0 (2)	6.0 (6)	2.0 (2)	2.0 (2)	4.1 (4)		14.7 (15)
8 (n = 4)	6.76–7.25	4.36–4.54 (m)	3.69 (s) 3.71 (s)	4.10 (overlapping q) 2.0 (2)	3.76–3.79 (overlapping singlets)	3.13 (m) 3.30 (m)	2.60 (m)	2.2–2.38 (m)		1.2–1.8
Integrations (required)	13.9 (two H's overlapped by CHCl$_3$) (14)	6.000 (6)	(2 overlapping)		13.7 (12 + 2 from HNCH$_2$Ar)	7.6 (6 + NH)	1.9 (2)	8.4 (8)		27.9 (27)
8 (n = 8)	6.7–7.4	4.36–4.54 (m)		4.09 (overlapping q)	3.7–3.88 (overlapping singlets)	3.12 (m) 3.29 (m)	2.69 (m) 2.76 (m)	2.28 (m)		1.14–1.73
Integrations (required)	31.2 (32)	14.000 (14)	(2 overlapping)	1.9 (2)	26.2 (24 + 2 from HNCH$_2$Ar)	14.0 (14)	1.9 (2)	16.0 (16)		52.3 (51)
8 (n = 16)	6.6–7.3	4.3–4.5	3.67	4.03 (m) (overlapping q)	3.69–3.72 (overlapping singlets)	3.06 (m) 3.22 (m)	2.6–2.8 (m)	2.15–2.3 (m)		1.1–1.8
Integrations (required)	62.8 (64)	30.000 (30)	(2 overlapping)	1.9 (20)	50.9 (48 + 2 from HNCH$_2$Ar)	30.0 (30)	1.6 (2)	32.4 (32)		99.2 (99)

Table 4 ^{1}H NMR spectra of compound **11** (in CDCl$_3$); chemical shifts at 500 MHz (^{a} at 400 MHz)

	−C$_6$H$_4$−	CH$_2$CONCH$_2$Ar	−COOCH$_2$CH$_3$	−OCH$_3$	−CH$_2$CON(CH$_2$Ar)CH$_2$−	−CH$_2$CO$_2$Et −CH$_2$CON(CH$_2$Ar)− CH$_3$CH$_2$CON	NCH$_2$(CH$_2$)$_3$CH$_2$CO	CH$_3$CH$_2$CO CH$_3$CH$_2$OCO
11 (2n = 1)	6.7–7.3	4.4–4.6	4.12 (overlapping q)	3.7–3.9 (overlapping singlets)	3.0–3.4	2.2–2.5		1.0–1.8
Integrations (required)	4.01 (4)	2.0 (2)	2.0 (2)	3.000 (3)	1.9 (2)	4.1 (4)		12.1 (12)
11 (2n = 2)	6.7–7.2	4.42 (m?) 4.49 (m?)	4.10 (m) (overlapping q)	3.77–3.79 (overlapping singlets)	3.32 (m), 3.14 (m)	2.22–2.42 (m)		1.08–1.73
Integrations (required)	8.0 (8)	4.0 (4)	2.0 (2)	6.000 (6)	4.0 (4)	6.0 (6)		18.3 (18)
11 (2n = 4)	6.7–7.2	4.42 (m) 4.49 (m)	4.10 (m) (overlapping q)	3.77–3.79 (overlapping singlets)	3.14 (bm), 3.30 (bm)	2.22–2.42 (m)		1.08–1.74
Integrations (required)	15.5 (16)	7.6 (8)	1.8 (2)	12.000 (12)	7.5 (8)	9.8 (10)		30.1 (30)
11^a (2n = 8)	6.7–7.2	4.42 (m) 4.49 (m)	4.10 (m) (overlapping q)	3.72–3.78 (overlapping singlets)	3.12 (bm), 3.30 (bm)	2.2–2.4 (m)		1.05–1.75
Integrations (required)	32.4 (32)	15.8 (16)	1.8 (2)	24.000 (24)	15.4 (16)	16.8 (18)		47 (54)
11 (2n = 16)	6.7–7.2	4.41 (m) 4.48 (m)	4.10 (m) (overlapping q)	3.76–3.78 (overlapping singlets)	3.13 (bm), 3.31 (bm)	2.2–2.4 (m)		1.05–1.75
Integrations (required)	62.8 (64)	31.0 (32)	1.9 (2)	48.000 (48)	31.3 (32)	32.9 (34)		101 (102)

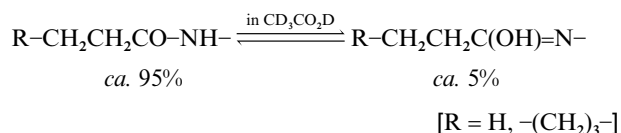**Table 5** ^{1}H NMR spectra of compound **12** (in CDCl$_3$); chemical shifts at 500 MHz

	–(C$_6$H$_4$)–	–CONH–	CH$_2$CONCH_2Ar	–OCH$_3$	–CON(CH$_2$Ar)CH_2 + CONHCH_2	–CH_2CO	CH$_3$CH_2CO	NCH$_2$(CH_2)$_3$-CH$_2$CO,	NH–CH$_2$CH_2CH$_3$	CH_3CH$_2$CO	NHCH_2CH$_2$CH_3
12 (2n = 0)	—	6.8 (bs)	—	—	2.98 (CONHCH_2) (overlapping t)	—	2.04 (overlapping t)	—	1.33 (m)	0.95 (t)	0.72 (t)
Integrations (required)		1.0 (1)			2.0 (2)		2.000(2)		2.0 (2)	3.0 (3)	3.0 (3)
12 (2n = 1)	6.8–7.2	5.57 (bs) 5.72 (bs)	4.43 (s) 4.50 (s)	3.77 (s) 3.79 (s)	3.1–3.35 (m)	2.3–2.4 (m)	2.08–2.17 (m)		1.27 (m); 1.44–1.67 (m)	1.11 (t), 1.17 (t)	0.90 (overlapping t)
Integrations (required)	4.0 (4)	0.9 (1)	2.0 (2)	3.000 (3)	4.0 (4)	2.0 (2)	2.0 (2)		8.0 (8)	3.0 (3)	2.9 (3)
12 (2n = 2)	6.7–7.16	5.5–5.84	4.3–4.5 (m)	3.65–3.8 (overlapping singlets)	3.0–3.34 (m)	2.18–2.36 (m)	2.0–2.12 (m)		1.0–1.66 (m)		0.83 (overlapping t)
Integrations (required)	8.0 (8)	0.95 (1)	4.0 (4)	6.000 (6)	6.0 (6)	5.7 (4 + 2)			17.0 (17)		2.9 (3)
12 (2n = 4)	6.7–7.15	5.6–6.0 (b)	4.3–4.5 (m)	3.6–3.8 (overlapping singlets)	3.0–3.32 (m)	2.14–2.36 (m)	2.0–2.21 (m)		1.0–1.66 (m)		0.83 (overlapping t)
Integrations (required)	16.0 (16)	0.95 (1)	7.9 (8)	12.000 (12)	10.0 (10)	9.9 (8 + 2)			29.2 (29)		2.9 (3)
12 (2n = 8)	6.7–7.2	5.6–5.9 (b)	4.3–4.6 (m)	3.6–3.8 (overlapping singlets)	3.0–3.4 (m)	2.2–2.4 (m)	2.05–2.15 (m)		1.0–1.8 (m)		0.89 (overlapping t)
Integrations (required)	32.3 (32)	0.92 (1)	15.9 (16)	24.000 (24)	18.3 (18)	18.4 (16 + 2)			54.7 (53)		2.9 (3)
12 (2n = 16)	6.7–7.2	5.6–5.9 (b)	4.3–4.6 (m)	3.7–3.9 (overlapping singlets)	3.0–3.4 (m)	2.2–2.4 (m)	2.05–2.15 (m)		1.0–1.8 (m)		0.90 (overlapping t)
Integrations (required)	63.7 (64)	0.9 (1)	31.4 (32)	48.000 (48)	33.7 (34)	31.9 (32)	2.2 (2)		102 (101)		2.9 (3)

Table 6 ^{1}H NMR spectra of compound **13** (in CD$_3$CO$_2$D) at 500 MHz

	−CONHCH_2−		CH_2CONH	CH_2CH$_2$CONH	NHCH_2CH$_2$	NH(CH$_2$)$_2$CH_2-(CH$_2$)$_2$CO	CH_3CH$_2$-CONH	−NHCH$_2$CH$_2$-CH_3
13 ($2n = 0$)	3.18 (t)	2.35 (m)	2.27 (q)		1.51 (m)		1.12 (t)	0.90 (t)
Integrations (required)	2.000 (2)	0.094	1.93 (2)		2.0 (2)		3.0 (3)	3.1 (3)
13 ($2n = 1$)	3.2 (m)	2.37 (m)	2.27(m)	1.65 (m)	1.50 (m)	1.34 (m)	1.12 (t)	0.90 (t)
Integrations (required)	4.000 (4)	0.182	3.8 (4)	2.1 (2)	3.9 (4)	2.0 (2)	2.9 (3)	3.0 (3)
13 ($2n = 2$)	3.2 (m)	2.37 (m)	2.27 (m)	1.65	1.50 (m)	1.34 (m)	1.12 (t)	0.91 (t)
Integrations (required)	6.000 (6)	0.290	5.8 (6)	4.2 (4)	6.0 (6)	4.0 (4)	3.0 (3)	2.9 (3)
13 ($2n = 4$)	3.2 (m)	2.37 (m)	2.27 (m)	1.63 (m)	1.51 (m)	1.33 (m)	1.12 (t)	0.90 (t)
Integrations (required)	10.000 (10)	0.48	9.4 (10)	8.2(8)	9.7 (10)	7.9 (8)	2.9 (3)	2.9 (3)
13 ($2n = 8$)	3.2 (m)	2.36 (m)	2.27 (m)	1.63 (m)	1.51 (m)	1.34 (m)	1.12 (t)	0.90 (t)
Integrations (required)	18.000 (18)	0.86	17.4 (18)	16.6 (16)	18.0 (18)	16.3 (16)	3.0 (3)	2.9 (3)
13 ($2n = 16$)	3.2 (m)	2.37 (m)	2.26 (m)	1.64 (m)	1.53 (m)	1.35 (m)	1.12 (t)	0.90 (t)
Integrations (required)	34.000 (34)	1.56	32.9 (34)	32.8 (32)	34.5 (34)	32.5 (32)	3.0 (3)	2.9 (3)

the secondary amide in the *repeating* group. This ratio increases with the degree of oligomerisation: 2:3 [monomer **4** ≡ **9** ($2n = 1$)]; 2:6 [dimer **6** ≡ **9** ($2n = 2$)]; 2:12 [tetramer **9** ($2n = 4$)]; 2:24 [octamer **9** ($2n = 8$)]; and 2:48 [hexadecamer **9** ($2n = 16$)]; clearly the integral ratios for these signals are in complete agreement with the proposed structural lengths. The monomeric compounds **4** and **3** both display the expected quartet for the −CH$_2$− signal from the −CO$_2$CH$_2$CH$_3$ group; however, in the dimers **6** and **8** ($n = 2$), which contain one amide bond (as distinct from a urethane bond), the corresponding −CH$_2$− signals consist of two overlapping quartets giving five absorptions overall; moreover, duplication (though not 50:50) of benzylic CH$_2$, CH$_2$N and CH$_3$O signals is also apparent in these compounds and also in the dimer **7**; the presence of additional amide bonds in higher oligomers increases the complexities of these absorptions. This plurality of signals is accounted for on the basis of *E*/*Z* isomerism in amides which occurs because of partial double bond character between the C−N bond.[15]

The structures of all the target end-capped amides **13** ($2n = 1, 2, 4, 8, 16$), and also the 'zeromer' [**13** ($2n = 0$)] (*i.e. N*-propylpropanamide) were determined by ^{1}H NMR spectroscopy in perdeuteroacetic acid, the higher oligomers being run at 80 °C to ensure solubility; data are given in Table 6. The most notable feature in these spectra is the presence of an extra multiplet at 2.37 ppm close to the −CH$_2$CO-protons at 2.27 ppm, *consistently* present in each oligomer in the proportions *ca.* 5:95, respectively. The *combined* integral values of these two absorptions fit extremely well into the patterns required for the expected structures. However, for the two compounds which were soluble in CDCl$_3$, the 'zeromer' and monomer, **13** ($2n = 0$ and 1) respectively, the ^{1}H NMR spectra showed only 2% of the extra multiplet relative to the −CH$_2$CO-protons. The proton COSY spectrum of the end-capped monomer **13** ($2n = 1$) in CD$_3$CO$_2$D showed clearly coupling of the extra multiplet absorption at 2.37 ppm with *both* the CH$_3$ (1.11 ppm) of the CH$_3$CH$_2$CO group (the absorption coinciding with the main triplet due to coupling of the CH$_2$ group with the CH$_3$ of the CH$_3$CH$_2$CONH group) *and* with the β-CH$_2$ group of the (CH$_2$)$_3$CH_2CH$_2$CONH group (hidden under the main multiplet structure at 1.65 ppm): clearly, the integrity of both CH$_2$ groups α to the CONH group are retained, a situation which must also prevail in the higher oligomers. The explanation for the behaviour of the amides in the weak acid solvent probably lies in the known protonation of the oxygen and the formation of iminol tautomers[16] which result in the hydrogens in the α-CH$_2$ groups having slightly different chemical shifts.

$$\text{R–CH}_2\text{CH}_2\text{CO–NH–} \xrightleftharpoons{\text{in CD}_3\text{CO}_2\text{D}} \text{R–CH}_2\text{CH}_2\text{C(OH)=N–}$$

ca. 95%　　　　　　　　　　　*ca.* 5%

[R = H, −(CH$_2$)$_3$−]

Experimental

Preparative chromatography and HPLC analysis

After each reaction, the product was generally purified by preparative chromatography on silica. The effectiveness of the separation of the fully protected oligomers **6** and **9**, the terminal *N*-propanoylated esters **11** and the *N*-propanoylated propylamides **12** were assessed by HPLC.

Ethyl 6-(*p*-methoxybenzylamino)hexanoate 3

6-Aminohexanoic acid **1** was esterified with ethanol in toluene using conc. sulfuric acid as catalyst. Because of its instability, the crude ethyl ester **2** (100 g, 0.63 mol) was immediately dissolved in a mixture of ethanol (100 ml), toluene (50 ml) and toluene-*p*-sulfonic acid monohydrate (1 g) and *p*-methoxybenzaldehyde (85.6 g, 0.63 mol) added. The mixture was heated under reflux for 18 h, the solvents were removed *in vacuo* and the residue was dissolved in methanol (500 ml) in a three-necked 5 l round-bottomed flask. The solution of the imine was stirred and sodium borohydride (23.8 g, 0.63 mol) was added in small portions over 2.5 h, the internal temperature of the mixture being maintained at 40–50 °C by external cooling. The solvent was removed *in vacuo*, water added to the residue and the mixture extracted with dichloromethane. The extracts were dried (Na$_2$SO$_4$), the solvent evaporated and the residue fractionated using a Vigreux column to give *ethyl 6-(p-methoxybenzylamino)hexanoate* **3** (91 g, 53%), bp 148–151 °C/0.01 mmHg (Found: C, 68.64; H, 9.08; N, 5.02. C$_{16}$H$_{25}$NO$_3$ requires C, 68.79; H, 9.02; N, 5.01%); ^{1}H NMR data in Table 3.

1-*tert*-Butyl 8-ethyl 2-(*p*-methoxybenzyl)-2-azaoctanedioate 4

A solution of compound **3** (88.7 g, 0.32 mol) in dichloromethane (300 ml) containing triethylamine (53.2 ml, *d* 0.726, 0.38 mol) was cooled to 0–5 °C, and di-*tert*-butyl dicarbonate (76.3 g, 0.35 mol) in dichloromethane (50 ml) was added at such a rate to ensure the internal temperature of the mixture did not rise above 10 °C. After a further 1 h at room temperature, volatile solvents were removed *in vacuo* at 25 °C. The residue was dissolved in dichloromethane (250 ml), the solution washed

consecutively with HCl (1 M, 100 ml), aqueous sodium hydrogen carbonate (1 M, 100 ml) and brine (100 ml) and dried (Na$_2$SO$_4$). Removal of the solvent *in vacuo* followed by careful chromatography of the residue on silica using light petroleum (bp 40–60 °C)–diethyl ether (70:30 v/v) gave 1-tert-*butyl* 8-*ethyl* 2-(p-*methoxybenzyl*)-2-*azaoctanedioate* **4** (85.2 g, 71%), a viscous liquid (Found: C, 66.13; H, 8.83; N, 4.02. C$_{21}$H$_{33}$NO$_5$ requires C, 66.47; H, 8.76; N, 3.69%); ^{1}H NMR data in Table 1.

Three stage process for formation of chain-doubled oligomers from fully protected derivatives

A (i) Selective removal of the Boc group from monomer 4. Compound **4** (0.5 g) in dichloromethane (5 ml), was treated with trifluoroacetic acid (1 ml) at room temperature for 1 h. The solution was diluted with water (10 ml), extracted with dichloromethane, the extracts washed with aqueous sodium hydrogen carbonate (0.1 M, 2 × 20 ml) and brine and dried (Na$_2$SO$_4$). Evaporation of the solvent *in vacuo* gave a viscous oil (0.31 g, 95%), pure by TLC, and having a ^{1}H NMR spectrum identical with **3**.

(ii) Selective hydrolysis of the ethyl ester in monomer 4. Compound **4** (77.3 g, 0.20 mol) was stirred with NaOH (10.0 g, 0.25 mol) in water (120 ml) and heated in an oil bath at 120 °C. The reaction was stopped after the initial cloudiness had disappeared (35 min), and extracted with ether. The aqueous layer was cooled to *ca.* 0 °C and carefully acidified with sulfuric acid (2 M), and extracted with diethyl ether, the extracts dried (Na$_2$SO$_4$) and the solvent removed *in vacuo* initially at water pump pressure, then under high vacuum (0.01 mmHg) for 1 h, to give 1-tert-*butyl* 8-*hydrogen* 2-(p-*methoxybenzyl*)-2-*azaoctanedioate* **5** (70.2 g, 98%), a viscous liquid (Found: C, 64.69; H, 8.34; N, 4.39. C$_{19}$H$_{29}$NO$_5$ requires C, 64.93; H, 8.32; N, 3.99%); ^{1}H NMR data in Table 2.

(iii) Chain-doubling reaction to form the dimer 6. The carboxylic acid **5** (69.69 g, 0.199 mol) in dichloromethane (250 ml) was treated with dicyclohexylcarbodiimide (DCC) (41.08 g, 0.199 mol) in dichloromethane (30 ml), a white solid appearing immediately. 1-Hydoxybenzotriazole (26.90 g, 0.199 mol) was added, the mixture stirred at room temperature for 40 min, and after being cooled to 5 °C, the secondary amine **3** (55.55 g, 0.199 mol) in dichloromethane (50 ml) was added and stirring continued for 18 h. The white precipitate was filtered, washed with dichloromethane (2 × 50 ml) and the filtrate washed with water (100 ml). Further precipitation of a white solid occurred into the aqueous phase, whereupon the organic phase was separated, and further washed with HCl (1 M, 3 × 100 ml). Finally the organic phase was washed with aqueous sodium hydrogen carbonate (1 M, 100 ml), water (100 ml) and brine (100 ml) and dried (Na$_2$SO$_4$). Evaporation of the solvent *in vacuo* gave a viscous oil which contained a fine precipitate; TLC on silica in diethyl ether–light petroleum (bp 40–60 °C) (80:20, v/v) revealed the presence of very small amounts of other components which were removed from the main component by preparative column chromatography on silica (1 kg loaded with 20 g portions of impure product using the same solvent system). Removal of the final traces of solvents under high vacuum at 80–100 °C gave α-tert-*butoxy*-ω-(*ethoxycarbonyl*)*di*[*carbonyl*-(p-*methoxybenzylimino*)*pentamethylene*] **6**, a highly viscous liquid (90.6 g, 75%) (Found: C, 68.62; H, 8.63; N, 4.74. C$_{35}$H$_{52}$N$_2$O$_7$ requires C, 68.60; H, 8.55; N, 4.57%); ^{1}H NMR data in Table 1.

B (i) Selective removal of Boc group from dimer 6. Compound **6** (33.6 g) in dichloromethane (50 ml) was treated with trifluoroacetic acid (40 ml) at room temperature for 5 h and worked up as in **A (i)**. The crude product was purified by chromatography on silica using dichloromethane–methanol (95:5, v/v) and removal of most of the solvents under high vacuum at 25 °C gave ω-*ethoxydi*[(p-*methoxybenzylimino*)(6-*oxohexamethylene*)] **8** (*n* = 2) a highly viscous liquid (21.6 g, 77%); ^{1}H NMR data in Table 3.

(ii) Selective hydrolysis of the ethyl ester in dimer 6. Compound **6** (22.0 g, 3.59 × 10^{-3} mol) was stirred with NaOH (1.72 g, 4.3 × 10^{-2} mol) in water (25 ml) and heated in an oil bath at 120 °C. The reaction was stopped after the initial cloudiness had disappeared (35 min), and worked up as in **A (ii)** to give α-tert-*butoxy*-ω-*carboxydi*[*carbonyl*(p-*methoxybenzylimino*)-*pentamethylene*] **7** (*n* = 2) (18.21 g, 87%) a viscous liquid (Found: C, 67.62; H, 8.22; N, 4.76. C$_{33}$H$_{48}$N$_2$O$_7$ requires C, 67.78; H, 8.27; N, 4.79%); ^{1}H NMR data in Table 2.

(iii) Chain-doubling reaction to form the tetramer 9 (2*n* = 4). The carboxylic acid **7** (*n* = 2) (18.0 g, 3.08 × 10^{-2} mol) in dichloromethane (190 ml) was treated with dicyclohexylcarbodiimide (DCC) (6.37 g, 3.08 × 10^{-2} mol) in dichloromethane (10 ml), followed by 1-hydroxybenzotriazole (4.37 g, 3.23 × 10^{-2} mol) and the mixture stirred at room temperature for 1 h. The secondary amine **8** (*n* = 2) (15.78 g, 3.08 × 10^{-2} mol) in dichloromethane (20 ml) was added and the mixture stirred for 18 h at room temperature. The crude product was isolated as in **A (iii)** and purified by chromatography on silica using diethyl ether–methanol (96:4, v/v) to give α-tert-*butoxy*-ω-(*ethoxycarbonyl*)*tetra*[*carbonyl*(p-*methoxybenzylimino*)*pentamethylene*] **9** (2*n* = 4) a viscous oil (28.9 g, 87%) (Found: C, 70.01; H, 8.44; N, 5.15. C$_{63}$H$_{90}$N$_4$O$_{11}$ requires C, 70.10; H, 8.40; N, 5.19%); ^{1}H NMR data in Table 1.

C (i) Selective removal of the Boc group from tetramer 9 (2*n* = 4). Compound **9** (2*n* = 4) (4.8 g), cooled to 0 °C was treated with trifluoroacetic acid (5 ml) for 4 h and worked up as in **A (i)**. The crude product was purified by chromatography on silica using dichloromethane–methanol (95:5, v/v) and removal of most of the solvents under high vacuum at 25 °C gave ω-*exthoxytetra*[(p-*methoxybenzylimino*)(6-*oxohexamethylene*)] **8** (*n* = 4), a highly viscous liquid (4.1 g, 94%); ^{1}H NMR data in Table 3.

(ii) Selective hydrolysis of the ethyl ester in tetramer 9 (2*n* = 4). Compound **9** (2*n* = 4) (2.4 g, 2.22 × 10^{-3} mol) was stirred with NaOH (0.24 g, 6 × 10^{-3} mol) in water (3 ml) and heated in an oil bath at 120 °C. The initial cloudiness had not disappeared after 4 h; nevertheless, the experiment was worked up as in **A (ii)** to give α-tert-*butoxy*-ω-*carboxytetra*[*carbonyl*(p-*methoxybenzylimino*)*pentamethylene*] **7** (*n* = 4) (2.17 g, 93%), a viscous liquid (Found: C, 69.60; H, 8.14; N, 5.28. C$_{61}$H$_{86}$N$_4$O$_{11}$ requires C, 69.69; H, 8.24; N, 5.33%); ^{1}H NMR data in Table 2.

(iii) Chain-doubling reaction to form the octamer 9 (2*n* = 8). The carboxylic acid **7** (*n* = 4) (4.63 g, 4.41 × 10^{-3} mol) in dichloromethane (50 ml) was treated with dicyclohexylcarbodiimide (DCC) (0.96 g, 4.65 × 10^{-3} mol) in dichloromethane (10 ml), followed by 1-hydroxybenzotriazole (0.63 g, 4.66 × 10^{-3} mol) and the mixture stirred at room temperature for 1.5 h. The secondary amine **8** (*n* = 4) (4.34 g, 4.43 × 10^{-3} mol) in dichloromethane (35 ml) was added and the mixture stirred for 48 h at room temperature. The crude product was isolated as in **A (iii)** and purified by chromatography on silica using ethyl acetate–methanol (96:4, v/v) to give α-tert-*butoxy*-ω-(*ethoxycarbonyl*)-*octa*[*carbonyl*(p-*methoxybenzylimino*)*pentamethylene*] **9** (2*n* = 8), a viscous oil (7.57 g, 85%) (Found: C, 71.01; H, 8.54; N, 5.69. C$_{119}$H$_{166}$N$_8$O$_{19}$ requires C, 71.02; H, 8.31; N, 5.57%); ^{1}H NMR data in Table 1.

D (i) Selective removal of the Boc group from octamer 9 (2*n* = 8). Compound **9** (2*n* = 8) (7.57 g) in dichloromethane (4 ml) was treated with trifluoroacetic acid (6 ml) at room temperature for 5 h and worked up as in **A (i)**. The crude product was purified by chromatography on silica using dichloromethane–methanol (94:6, v/v) and removal of most of the solvents under high vacuum at 25 °C gave ω-*ethoxyocta*[(p-*methoxybenzylimino*)(6-*oxohexamethylene*)] **8** (*n* = 8), a highly viscous liquid (6.57 g, 91%); ^{1}H NMR data in Table 3.

(ii) Selective hydrolysis of the ethyl ester in octamer 9 (2*n* = 8). Compound **9** (2*n* = 8) (13.0 g, 6.46 × 10^{-3} mol) was stirred with NaOH (0.3 g, 7.5 × 10^{-3} mol) in water (5 ml) and ethanol (10 ml) and heated in an oil bath at 120 °C. The initial cloudiness

disappeared after 10 min and the experiment was worked up as in **A (ii)** and the crude product purified by chromatography on silica using dichloromethane–methanol (95:5, v/v→50:50, v/v) to give α-tert-*butoxy*-ω-*carboxyocta*[*carbonyl*(p-*methoxybenzylimino*)*pentamethylene*] **7** (*n* = 8) (8.571 g, 67%), a viscous liquid (Found: C, 70.74; H, 8.24; N, 5.60. $C_{117}H_{162}N_8O_{19}$ requires C, 70.81; H, 8.23; N, 5.65%); ^{1}H NMR data in Table 2.

(iii) Chain-doubling reaction to form the hexadecamer 9 (2*n* = 16). The carboxylic acid **7** (*n* = 8) (8.31 g, 4.19×10^{-3} mol) in dichloromethane (80 ml) was treated with dicyclohexylcarbodiimide (DCC) (0.90 g, 4.36×10^{-3} mol) in dichloromethane (5 ml), followed by 1-hydroxybenzotriazole (0.58 g, 4.29×10^{-3} mol), and the mixture stirred at room temperature for 1 h. The secondary amine **8** (*n* = 8) (8.28 g, 4.33×10^{-3} mol) in dichloromethane (15 ml) was added and the mixture stirred for 48 h at room temperature. The crude product was isolated as in **A (iii)** and purified by chromatography on silica using ethyl acetate–methanol (90:10, v/v→85:15 v/v) to give α-tert-*butoxy*-ω-(*ethoxycarbonyl*)*hexadeca*[*carbonyl*(p-*methoxybenzylimino*)*pentamethylene*] **9** (2*n* = 16), a viscous oil (12.297 g, 76%) (Found: C, 71.27; H, 8.24; N, 5.76. $C_{231}H_{318}N_{16}O_{35}$ requires C, 71.52; H, 8.26; N, 5.78%); ^{1}H NMR data in Table 1.

Three stage process leading to the formation of 'end-capped' oligomers of nylon 6

E (i) Propanoylation of terminal NH of monomer 3. Compound **3** (10.0 g, 3.58×10^{-2} mol) in a mixture of dichloromethane (60 ml) and triethylamine (12 ml, *d* 0.726, 8.61×10^{-2} mol) was treated dropwise at −5 °C with propionyl chloride (7.7 ml, *d* 1.065, 8.86×10^{-2} mol), and after stirring for 2 h, the solvent was removed *in vacuo* and the residue dissolved in dichloromethane (150 ml). The solution was washed in turn with HCl (1 M, 2×25 ml) and brine (30 ml) and dried (Na$_2$SO$_4$). The solvent was removed *in vacuo* and the crude residue purified by chromatography on silica using diethyl ether–light petroleum (bp 40–60 °C) (65:35, v/v) to give *ethyl* 6-[N-(p-*methoxybenzyl*)*propanamido*]*hexanoate* **11** (2*n* = 1), an oil (9.12 g, 76%) (Found: C, 68.07; H, 8.90; N, 4.47. $C_{19}H_{29}NO_4$ requires C, 68.03; H, 8.71; N, 4.18%); ^{1}H NMR data in Table 4.

(ii) *n*-Propylamide formation from monomer 11 (2*n* = 1). Compound **11** (2*n* = 1) (1.64 g), methanol (6 ml), *n*-propylamine (8 ml) and a catalytic amount of KCN (20 mg) were heated together under reflux for 48 h, and the solvents removed *in vacuo*. The residue was dissolved in dichloromethane (50 ml) and the solution washed with water and dried (Na$_2$SO$_4$). Removal of the solvent *in vacuo* gave the crude product which was purified by chromatography on silica using dichloromethane–methanol (96:4, v/v); removal of the final traces of solvents under high vacuum at 80–100 °C gave 6-[N-(p-*methoxybenzyl*)*propanamido*]-N-*propylhexanamide* **12** (2*n* = 1) a viscous liquid (Found: C, 68.57; H, 9.35; N, 8.12. $C_{20}H_{32}N_2O_3$ requires C, 68.93; H, 9.26; N, 8.04%); ^{1}H NMR data in Table 5.

(iii) Final deprotection of secondary amide to give end-capped monomer of nylon 6, 13 (2*n* = 1). The end-capped monomer **12** (2*n* = 1) (1.0 g) and trifluoroacetic acid (3 ml) were heated under reflux for 1 h, during which an unidentified solid precipitated. The excess reagent was removed *in vacuo* and the residue was washed through a short column of silica with ethanol to remove unidentified insoluble material. Evaporation of the solvent and addition of dichloromethane gave a solution which was washed with saturated aqueous sodium hydrogen carbonate to remove traces of trifluoroacetic acid, dried (Na$_2$SO$_4$) and the solvent removed *in vacuo* to give 6-*propanamido*-N-*propylhexanamide* **13** (2*n* = 1) mp 101–102 °C (from ethanol) (lit.,[7] mp 106 °C) (Found: C, 63.03; H, 10.86; N, 12.32. $C_{12}H_{24}N_2O_2$ requires C, 63.12; H, 10.59; N, 12.27%); ^{1}H NMR data in Table 6.

F (i) Propanoylation of terminal NH of dimer 8 (*n* = 2). Compound **8** (*n* = 2) (3.5 g, 6.83×10^{-3} mol) in a mixture of di-

chloromethane (20 ml) and triethylamine (3.0 ml, *d* 0.726, 2.15×10^{-2} mol) was treated dropwise at 0–5 °C with propionyl chloride (3.0 ml, *d* 1.065, 3.45×10^{-2} mol), and the reaction worked up as in **E (i)**. The crude product was purified by chromatography on silica using diethyl ether–methanol (98:2→94:6, v/v) to give α-*ethyl*-ω-(*ethoxycarbonyl*)*di*[*carbonyl*(p-*methoxybenzylimino*)*pentamethylene*] **11** (2*n* = 2), a viscous liquid (3.2 g, 82%) (Found: C, 69.42; H, 8.48; N, 5.08. $C_{33}H_{48}N_2O_6$ requires C, 69.69; H, 8.51; N, 4.93%); ^{1}H NMR data in Table 4.

(ii) *n*-Propylamide formation from dimer 11 (2*n* = 2). Compound **11** (2*n* = 2) (1.90 g), methanol (10 ml), *n*-propylamide (15 ml) and a catalytic amount of KCN (20 mg) were heated together under reflux for 72 h, and the reaction worked up as in **E (ii)**. The crude product which was purified by chromatography on silica using diethyl ether–methanol (95:5, v/v) and removal of the final traces of solvents under high vacuum at 80–100 °C gave α-*ethyl*-ω-(N-n-*propylcarbamoyl*)*di*[*carbonyl*-(p-*methoxybenzylimino*)*pentamethylene*] **12** (2*n* = 2), a viscous liquid (1.76 g, 91%) (Found: C, 70.05; H, 8.92; N, 7.41. $C_{34}H_{51}N_3O_5$ requires C, 70.19; H, 8.84; N, 7.22%); ^{1}H NMR data in Table 5.

(iii) Final deprotection of secondary amide to give end-capped dimer of nylon 6, 13 (2*n* = 2). The end-capped monomer **12** (2*n* = 2) (1.55 g) and trifluoroacetic acid (3 ml) were heated under reflux for 0.5 h, and the reaction worked up as in **E (iii)** to give α-*ethyl*-ω-(N-n-*propylcarbamoyl*)*di*(*carbonyliminopentamethylene*) **13** (2*n* = 2), mp 153–154 °C (from ethanol) (lit.,[7] mp 149 °C) (Found: C, 63.18; H, 10.47; N, 12.48. $C_{18}H_{35}N_3O_3$ requires C, 63.31; H, 10.33; N, 12.30%); ^{1}H NMR data in Table 6.

G (i) Propanoylation of terminal NH of tetramer 8 (*n* = 4). Compound **8** (*n* = 4) (18.0 g, 1.84×10^{-2} mol) in a mixture of dichloromethane (100 ml) and triethylamine (4.7 ml, *d* 0.726, 3.37×10^{-2} mol) was treated dropwise at 0–5 °C with propionyl chloride (3.0 ml, *d* 1.065, 3.45×10^{-2} mol), and the reaction worked up as in **E (i)**. The crude product was purified by chromatography on silica using diethyl ether–methanol (95:5→90:10, v/v) to give α-*ethyl*-ω-(*ethoxycarbonyl*)*tetra*-[*carbonyl*(p-*methoxybenzylimino*)*pentamethylene*] **11** (2*n* = 4), a viscous liquid (15.98 g, 84%) (Found: C, 70.63; H, 8.38; N, 5.36. $C_{61}H_{86}N_4O_{10}$ requires C, 70.76; H, 8.37; N, 5.41%); ^{1}H NMR data in Table 4.

(ii) *n*-Propylamide formation from tetramer 11 (2*n* = 4). Compound **11** (2*n* = 4) (14.53 g), methanol (20 ml), *n*-propylamine (30 ml) and a catalytic amount of KCN (20 mg) were heated together under reflux for 60 h, and the reaction worked up as in **E (ii)**. The crude product, which was purified by chromatography on silica using diethyl ether–methanol (95:5→90:10, v/v) and by removal of the final traces of solvents under high vacuum at 80–100 °C gave α-*ethyl*-ω-(N-n-*propylcarbamoyl*)*tetra*[*carbonyl*(p-*methoxybenzylimino*)-*pentamethylene*] **12** (2*n* = 4), a viscous liquid (14.0 g, 95%) (Found: C, 70.91; H, 8.53; N, 6.51. $C_{62}H_{89}N_5O_9$ requires C, 71.03; H, 8.56; N, 6.68%); ^{1}H NMR data in Table 5.

(iii) Final deprotection of secondary amide to give end-capped tetramer of nylon 6, 13 (2*n* = 4). The end-capped monomer **12** (2*n* = 4) (1.19 g) and trifluoroacetic acid (3 ml) were heated under reflux for 40 min, and the excess reagent removed *in vacuo*. The residue dissolved in dichloromethane (50 ml) and the solution was shaken with saturated aqueous sodium hydrogen carbonate (5 ml) which precipitated a solid: this was washed with water, then dichloromethane, and dried *in vacuo* to give α-*ethyl*-ω-(N-n-*propylcarbamoyl*)*tetra*(*carbonyliminopenta-methylene*) **13** (2*n* = 4) (0.54 g, 84%), mp 194–195.5 °C (from ethanol), (lit.,[7] mp 181 °C) (Found: C, 63.51; H, 10.23; N, 12.26. $C_{30}H_{57}N_5O_5$ requires C, 63.46; H, 10.12; N, 12.33%); ^{1}H NMR data in Table 6.

H (i) Propanoylation of terminal NH of octamer 8 (*n* = 8). Compound **8** (*n* = 8) (6.57 g, 3.43×10^{-3} mol) in a mixture of

dichloromethane (100 ml) and triethylamine (1 ml, d 0.726, 7.17×10^{-3} mol) was treated dropwise at 0–5 °C with propionyl chloride (1.5 ml, d 1.065, 17.3×10^{-3} mol), and the reaction worked up as in **E (i)**. The crude product was purified twice by chromatography on silica using first ethyl acetate–methanol (94:6, v/v), then on alumina using dichloromethane followed by dichloromethane–methanol (98:2, v/v) to give α-*ethyl-*ω-*(ethoxycarbonyl)octa*[*carbonyl*(p-*methoxybenzylimino)penta-methylene*] **11** (2*n* = 8), a viscous liquid (6.02 g, 89%) (Found: C, 71.22; H, 8.39; N, 5.69. $C_{117}H_{162}N_8O_{18}$ requires C, 71.38; H, 8.29; N, 5.69%); ^{1}H NMR data in Table 4.

(ii) *n*-Propylamide formation from octamer 11 (2*n* = 8). Compound **11** (2*n* = 8) (6.02 g), methanol (10 ml), *n*-propylamine (15 ml) and a catalytic amount of KCN (20 mg) were heated together under reflux for 67 h, and the reaction worked up as in **E (ii)**. The crude product was purified three times by chromatography on silica, twice using ethyl acetate–methanol (90:10, v/v), and then using pure dichloromethane→dichloromethane–methanol (98:2, v/v) and removal of the final traces of solvents under high vacuum at 80–100 °C to give α-*ethyl-*ω-(N-*n*-*propylcarbamoyl)octa*[*carbonyl*(p-*methoxybenzylimino)*-*pentamethylene*] **12** (2*n* = 8) (5.8 g, 96%), a viscous liquid (Found: C, 71.43; H, 8.47; N, 6.46. $C_{118}H_{165}N_9O_{17}$ requires C, 71.52; H, 8.39; N, 6.36%); ^{1}H NMR data in Table 5.

(iii) Final deprotection of secondary amide to give end-capped octamer of nylon 6, 13 (2*n* = 8). The end-capped monomer **12** (2*n* = 8) (2.24 g) and trifluoroacetic acid (6 ml) were heated under reflux for 40 min, and the excess reagent was removed *in vacuo*. The residue dissolved in dichloromethane (50 ml) and the solution was shaken with saturated aqueous sodium hydrogen carbonate (5 ml) which precipitated a solid: this was washed with water, then dichloromethane, and dried *in vacuo* to give α-*ethyl-*ω-(N-*n*-*propylcarbamoyl)octa*(*carbonyliminopenta-methylene*) **13** (2*n* = 8) (0.98 g, 85%), mp 208.5–212 °C (from acetic acid) (lit.,[7] mp 200 °C) (Found: C, 63.43; H, 10.15; N, 12.45. $C_{54}H_{101}N_9O_9$ requires C, 63.56; H, 9.98; N, 12.35%); ^{1}H NMR data in Table 6.

I (i) Selective removal of the Boc group from hexadecamer 9 (2*n* = 16). A solution of compound **9** (2*n* = 8) (11.68 g) in dichloromethane (50 ml) was evaporated to a soft gum consistency, capable of being stirred with a magnetic stirrer bar. The mixture was treated with trifluoroacetic acid (11 ml) at room temperature for 18 h and worked up as in **A (i)**. The crude product was purified by chromatography on silica using dichloromethane–methanol (95:5→80:20 v/v) and removal of most of the solvents under high vacuum at 25 °C gave ω-*ethoxyhexadeca*[(p-*methoxybenzylimino)*(6-*oxohexamethylene)*] **8** (*n* = 16), a highly viscous liquid (10.19 g, 90%); ^{1}H NMR data in Table 3.

(ii) Propanoylation of terminal NH of hexadecamer 8 (*n* = 16). Compound **8** (*n* = 16) (9.97 g, 2.64×10^{-3} mol) in a mixture of dichloromethane (60 ml) and triethylamine (0.55 ml, d 0.726, 3.95×10^{-3} mol) was treated dropwise at −5 °C with propionyl chloride (0.34 ml, d 1.065, 3.91×10^{-3} mol), and the reaction worked up as in **E (i)**. The crude product was purified by chromatography on silica using ethyl acetate–methanol (88:12, v/v), to give α-*ethyl-*ω-(*ethoxycarbonyl)hexadeca*[*carbonyl*(p-*methoxybenzylimino)pentamethylene*] **11** (2*n* = 16), a viscous liquid (7.409 g, 73%) (Found: C, 71.74; H, 8.34; N, 5.89. $C_{229}H_{314}N_{16}O_{34}$ requires C, 71.72; H, 8.25; N, 5.84%); ^{1}H NMR data in Table 4.

(iii) *n*-Propylamide formation from hexadecamer 11 (2*n* = 16). Compound **11** (2*n* = 16) (6.75 g), methanol (10 ml), *n*-propylamine (15 ml) and a catalytic amount of KCN (20 mg)

were heated together under reflux for 72 h, and the reaction worked up as in **E (ii)**. The crude product was purified by chromatography on silica using ethyl acetate–methanol (88:12, v/v) and removal of the final traces of solvents under high vacuum at 80–100 °C to give α-*ethyl-*ω-(N-*n*-*propylcarbamoyl)hexa-deca*[*carbonyl*(p-*methylbenzylimino)pentamethylene*] **12** (2*n* = 16) (5.00 g, 74%), a viscous liquid (Found: C, 71.62; H, 8.32; N, 6.06. $C_{230}H_{317}N_{17}O_{33}$ requires C, 71.79; H, 8.30; N, 6.19%); ^{1}H NMR data in Table 5.

(iv) Final deprotection of secondary amide to give end-capped hexadecamer of nylon 6, 13 (2*n* = 16). The end-capped mono-mer **12** (2*n* = 16) (2.50 g) and trifluoroacetic acid (8 ml) were heated under reflux for 45 min, and the reaction worked up as in **H (iii)** to give α-*ethyl-*ω-(N-*n*-*propylcarbamoyl)hexadeca*-(*carbonyliminopentamethylene*) **13** (2*n* = 16) (1.10 g, 88%) mp 205.5–206 °C (from acetic acid) (lit.,[7] mp 206 °C) (Found: C, 62.88; H, 9.78; N, 12.21. $C_{102}H_{189}N_{17}O_{17}$ requires C, 63.62; H, 9.89; N, 12.36%); ^{1}H NMR data in Table 6.

Synthesis of *n*-propyl propanamide ['zeromer' 13 (2*n* = 0)]
This compound was prepared as a model for the ^{1}H NMR work, from *n*-propylamine and propanoyl chloride–triethyl-amine, but a purer product resulted from propanoylation of N-(p-methoxybenzy)propylamine followed by deprotection with boiling trifluoroacetic acid. ^{1}H NMR data in CDCl[3] are given in Table 5, and in CD[3]CO[2]D in Table 6.

References

1 G. M. Brooke, S. Burnett, S. Mohammed, D. Proctor and M. Whiting, *J. Chem. Soc.*, *Perkin Trans. 1*, 1996, 1635.
2 D. C. Bassett, R. H. Holley, S. J. Sutton and A. S. Vaughan, *Macromolecules*, 1996, **29**, 1852.
3 W. H. Carothers, US Pat. 2 130 523 (September 20th, 1938).
4 W. O. Baker and C. S. Fuller, *J. Am. Chem. Soc.*, 1943, **65**, 1120.
5 E. L. Wittbecker, R. C. Houtz and W. W. Watkins, *Ind. Eng. Chem.*, 1948, **40**, 875; B. S. Briggs, C. J. Frosch and R. H. Erickson, *Ind. Eng. Chem.*, 1946, **38**, 1016; and J. R. Lewis and R. J. W. Reynold, *Chem. Ind.* (*London*), 1951, 958.
6 Y. H. Kim and J. C. Calabrese, *Macromolecules*, 1991, **41**, 2951.
7 H. Zahn and G. B. Gleitsman, *Angew. Chem.*, *Int. Ed. Engl.*, 1963, **2**, 410.
8 T. W. Greene and P. G. M. Wutts, *Protective Groups in Organic Synthesis*, Wiley, New York, 2nd edn., 1991, p. 397.
9 G. M. Brooke, S. Mohammed and M. C. Whiting, *Chem. Commun.*, 1997, 1511.
10 E. Igner, O. I. Paynter, D. J. Simmonds and M. C. Whiting, *J. Chem. Soc.*, *Perkin Trans. 1*, 1987, 2447.
11 M. Bodanszky and A. Bodanszky, *The Practice of Peptide Synthesis*, Springer-Verlag, Berlin, Heidelberg, 1994, 2nd edn., p. 15.
12 Ref. 11, p. 142.
13 Ref. 11, p. 119.
14 T. Hogberg, P. Storm, M. Ebner and S. Ramsby, *J. Org. Chem.*, 1987, **52**, 2033.
15 J. March, *Advanced Organic Chemistry*, Wiley, New York, 4th edn., 1992, p. 129.
16 H. Sigel and R. B. Martin, *Chem. Rev.*, 1982, **82**, 385.