Tetrahedron Vol. 43, No. 1, pp. 115 to 122, 1987
Printed in Great Britain.

0040-4020/87 $5.00+.00

SYNTHESIS OF FOUR n-ALKANES WITH TERMINAL DIPOLAR SUBSTITUENTS

T.A. AINSCOW[1]* M.R. BELMONT[1] J.L. HENSHALL[1] R.M. HOOPER[1]
and D.J. SIMMONDS[2]

1) Department of Engineering Science, University of Exeter, Exeter, Devon, EX4 4QF.
2) Department of Chemistry, Sheffield City Polytechnic, Pond Street, Sheffield, S1 1WB.

(*Received in UK* 24 *October* 1986)

Abstract - 12-Nitrododecanol, 1,12-dinitrododecane, 1,24-dinitrotetracontane and 2,15-diaminohexadecan-1,16-dioic acid were prepared from the common intermediate 12-bromododecanol. This bromoalcohol, being prepared from cyclododecanone, is free of homologous bifunctional impurities. The functionalised 24 carbon chain was prepared by a Wittig reaction of 12-bromododecanal with the triphenylphosphonium salt of 12-bromododecanal ethylene acetal using 'naked' carbonate anion to provide the base. The resulting bromoacetal was converted to 24-bromotetracont-12-enol, both this and the 12-bromododecanol were converted to the corresponding α,ω-di-iodides and then to the desired α,ω-dinitro compounds. The α-amino acid functionality can be introduced on an α,ω-dihalide with the anion of either diethyl 2-acetylaminopropan-1,3-dioate or benzylidene glycine ethyl ester. Also detailed is the previously unreported reduction of a carboxylic acid to an alcohol by borane-dimethyl sulphide in dichloromethane.

INTRODUCTION

This paper presents the synthesis of two previously unreported linear alkanes, and their intermediaries, carrying terminal nitro groups, 1,12-dinitrododecane 7 and 1,24-dinitrotetracontane 18. Also prepared was 12-nitrododecanol 9, which has been reported [1] but has not been described in literature, and the previously unreported 2,15-diamino-1,16-hexadecandioic acid 21, a linear alkane carrying terminal amino acid groups. These compounds were desired to extend the previous studies of the electrical and mechanical properties of alkanes of known crystal structures [2]. The synthesis of functionalised linear alkanes has been much simplified by the reported procedures to prepare non-symmetrical bifunctional C_{12}-acyclic compounds [3]. The synthesis of these compounds is based on the ring opening of cyclododecanone. The cyclododecanone is prepared from the trimerisation of butadiene and is subsequently free of homologous cyclic ketones. Thus the α,ω-bifunctional dodecane derivatives available will be free of homologous impurities. Homologous impurities in alkanes are known [4] to cause unwanted phase changes in the crystals of those alkanes when under study. Non-homologous impurities would be expected to be readily removed by zone refining techniques.

The nitro group was chosen as a substituent because of the highly polarised nature which should introduce significant changes in the properties of these

compounds when compared with the unsubstituted alkanes. The amino acid was chosen to attempt to prepare an ionic lattice separated by covalent sheets which could be expected to have unusual properties when compared to either an ionic lattice or an alkane crystal. The dielectric properties of the two dinitro compounds are currently being studied. Conformational studies by numerical techniques are being performed on the solution behaviour of 1,12-dinitrododecane 7 as well as by experimental observation. Preliminary studies on single crystals of 1,12-dinitrododecane 7 show that they are much harder and more brittle than single crystals of n-alkanes such as eicosane. The crystal structure of 1,12-dinitrododecane 7 [5] shows a novel orientation of molecules when compared with that observed in analagous alkanes [4,6].

RESULTS AND DISCUSSION

1,12-Dinitrodocedane 7

The route to the bifunctional C_{12} compounds starts from cyclododecanone which undergoes the Baeyer-Villiger reaction to give the lactone of 12-hydroxydodecanoic acid. Hydrolysis of this lactone followed by recrystallisation yielded pure 12-hydroxydodecanoic acid 1. Initially it had been proposed to convert this hydroxy acid 1 to dodecan-1,12-diol 2 by the use of borane–dimethyl sulphide, the dihydroxy compound 2 would then have been converted to the required 1,12-dibromododecane 5. However as the borane-dimethyl sulphide was added to the reaction mixture, 12-hydroxydodecanoic acid 1 in diethyl ether, the viscosity increased until the contents of the reaction flask virtually solidified. Very cautious addition of water to the reaction vessel, with manual stirring, was performed and the recovered product was the desired dodecan-1, 12-diol 2. The problems encountered in accomplishing this reaction prompted the authors to adopt the slightly longer but more tractable route to the desired dibromide 5 as follows. 12-Hydroxydodecanoic acid 1 was readily converted to 12-bromododecanoic acid 3 by hydrogen bromide in glacial acetic acid, decolourisation with activated charcoal and recrystallisation provided the pure 12-bromododecanoic acid 3. Reduction with borane-dimethyl sulphide proceeded readily to give the required 12-bromododecanol 4. This reaction usually proceeded without event except on one occasion when a large quantity (circa one third) of the contents of the reaction vessel was ejected. This anomalous behaviour cannot at present be satisfactorily explained.

Consequently different solvent systems in which the reaction would proceed readily but also potentially more safely were considered. Borane-dimethyl sulphide reductions of carboxylic acids had previously been reported only in diethyl ether [3,7,8], tetrahydrofuran [9] and some non-halogenated solvents [7]. The hydroboration of alkanes had been reported in dichloromethane [10], amongst other solvents, and no anomalous reaction had occurred, but on the other hand borane–dimethyl sulphide had been reported to react with tetrachloromethane [11]. Dichloromethane is non-inflammable and of low boiling point and therefore a suitable substitute for diethyl ether. Trial experiments were successful and a large scale reduction of 12-bromododecanoic acid 3 to the 12-bromododecanol 4 was performed in dichloromethane. The reaction proceeded smoothly, product recovery presented no problems and the desired 12-bromododecanol 4 was isolated pure in good yield.

The next stage in the synthesis of 1,12-dinitrododecane 7 was the bromination of the alcohol 4 to 1,12-dibromododecane 5 which was accomplished by the use of hydrogen bromide in glacial acetic acid. Initially to achieve the transformation to the desired dinitro compound 7 the dibromide 5 was reacted with sodium nitrite in N,N-dimethylformamide [12], whence 1,12-dinitrododecane 7 was isolated but in

low (20%) yield. Repeating the reaction with a longer reaction time resulted in a complex reaction mixture which did not contain 1,12-dinitrododecane 7, and using a shorter reaction time gave an incomplete reaction. To resolve this problem the dibromide 5 was converted to 1,12-di-iododododecane 6 by the action of sodium iodide in butanone [13]. The reaction proceeding smoothly in high yield and subsequent reaction of the di-iodide 6 with silver nitrite in diethyl ether suspension [14] produced the desired 1,12-dinitrododecane 7 in good (60%) yield. As the nitrite can act as an ambifunctional nucleophile some of the iodide would be replaced by the NO_2 group in the nitrito form. This could well have decomposed, as nitrito compounds are known to be labile [15], during isolation to the hydroxy compound which accounted for the recovery of small quantities of 12-nitrododecanol 9.

12-Nitrododecanol 9

The nitroalcohol 9 was synthesised to observe the change in properties introduced by substitution of one nitro group for a group which would be capable of hydrogen bonding to other polar groups in the molecule. The synthesis proceeded readily by the conversion of the bromoalcohol 4 to the iodoalcohol 8 which was then reacted with silver nitrite in diethyl ether to yield the desired 12-nitrododecanol 9. This was also shown to be identical with the nitroalcohol isolated from the synthesis of the dinitro compound 7.

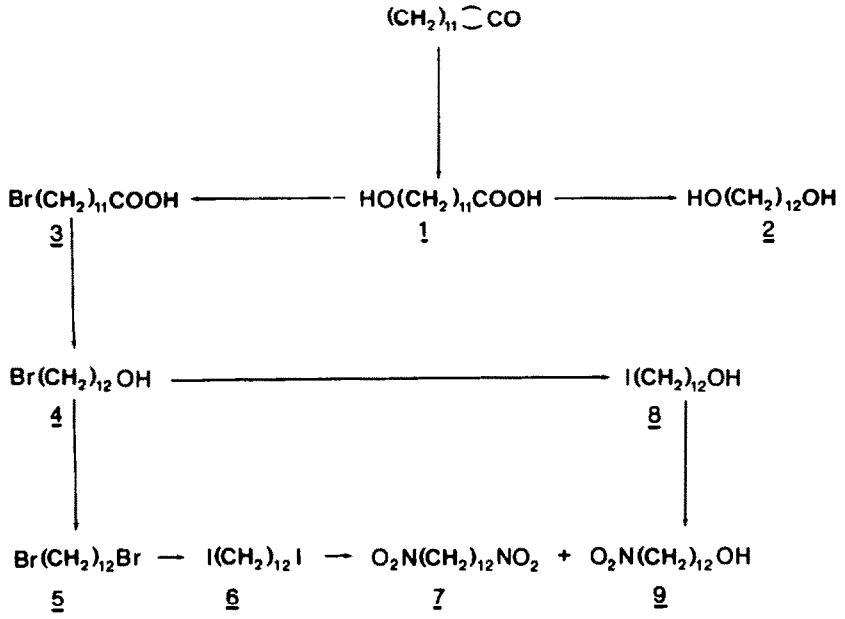

Figure 1. Synthesis of 1,12-dinitrododecane and 12-nitrododecanol.

1,24-Dinitrotetracontane

The synthesis of the 24 carbon chain homologue involved the doubling of the 12 carbon chain. To accomplish this transformation 12-bromododecanol 4 was oxidised to 12-bromododecanal 10 by the use of activated dimethyl sulphoxide [3,16], the crude aldehyde was then transformed to the ethylene acetal by reaction with a mixture of ethane-1,2-diol and triethylorthoformate (previously refluxed together in the presence of p-toluenesulphonic acid) [3], the product was then

fractionally distilled followed by recrystallisation to purify the 12-bromododecanal ethylene acetal 11. This ethylene acetal 11 was the basic repeat unit for chain growing. Reaction of the ethylene acetal 11 with triphenylphosphine in acetonitrile solution gave the corresponding triphenylphosphonium bromide salt 12 [17]. To provide the aldehyde 10 for the Wittig reaction, the ethylene acetal 11 was percolated through a silica gel column impregnated with p-toluenesulphonic acid and eluted with dichloromethane [17]. The 12-bromododecanal 10 so produced was used immediately in a Wittig reaction in tetrahydrofuran using potassium carbonate and 18-crown-6 to act as the base to generate the ylid from the triphenylphosphonium bromide salt 12 [18]. This reaction produced 24-bromotetracont-12-enal ethylene acetal 13, a 24 carbon chain with the correct substituents for further chain doubling steps, or as we require in this case terminal substituents that can readily be transformed to other functionalities. This ethylene acetal 13 was firstly transformed to the corresponding aldehyde 14 and then immediately reduced to 24-bromotetracont-12-enol 15 by the action of sodium borohydride in ethanol [19]. Tosylation by standard methods [20] proceeded smoothly and reaction with sodium iodide in butanone yielded 1,24-di-iodotetracont-12-ene 16. This reacted with silver nitrite in diethyl ether to yield 1,24-dinitrotetracont-12-ene 17. Hydrogenation in ethyl acetate solution with palladium (5%) on carbon [21] gave the desired 1,24-dinitrotetracontane 18.

Attempted hydrogenation of the di-iodido-alkene 16 using the same conditions as with the dinitro-alkene 17 failed. This was attributed to a slight contamination by sulphur containing impurities despite the compound being pure by spectroscopic techniques and having a satisfactory elemental analysis. As both the di-iodo- and dinitro-alkenes 16 and 17 were purified by column chromatography then, if the failure to hydrogenate is caused by sulphur containing impurities, these impurities are relatively non-polar and difficult to remove from the relatively non-polar di-iodo-alkene 16 but easier to remove from the much more polar dinitro-alkene 17.

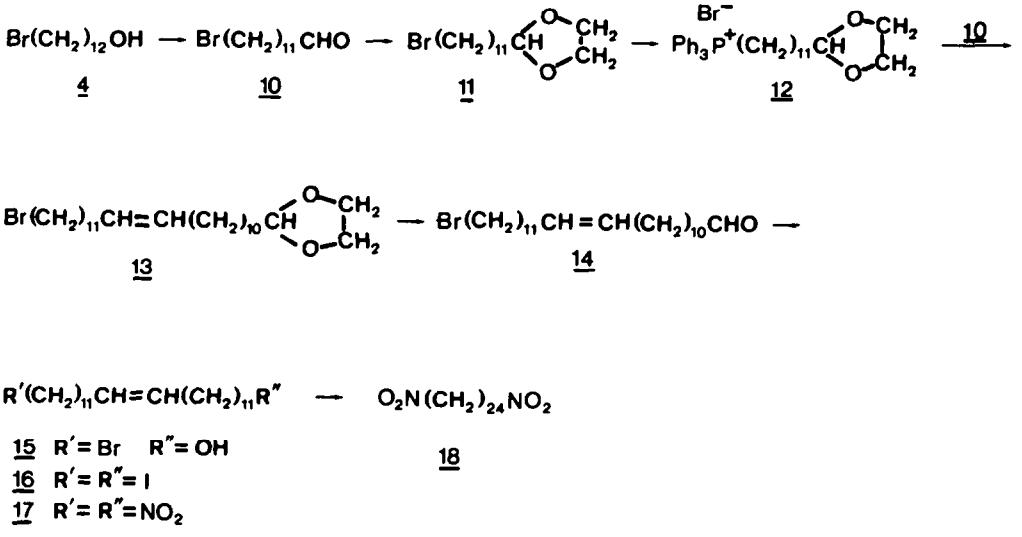

Figure 2. Synthesis of 1,24-dinitrotetracontane

2,15-Diaminohexadecan-1,16-dioic acid 21

Of the many available methods for the synthesis of an α-amino acid [22,23,24, 25,26,27,28] only two were chosen for study. Both of these methods were chosen as they were likely to accomplish the desired transformation (alkyl halide to α-amino acid) readily and are reported to work on similar halo-alkanes [22,23]. The first method involved the use of diethyl 2-acetylaminopropan-1,3-dioate which is readily available as a crystalline material. This also will only undergo monoalkylation unlike the second reagent - benzylidene glycine ethyl ester - which could potentially undergo bisalkylation.

All of the following reactions were conducted in freshly dried solvents in an atmosphere of dry nitrogen. Initially the alkylation of diethyl 2-acetylaminopropan-1,3-dioate by the dibromide 5 was attempted under literature conditions [22] (Na/EtOH) and surprisingly no alkylation occurred. However an activated alkyl bromide such as benzyl bromide did give the expected alkylation product under these conditions. Other methods to generate the anion of diethyl 2-acetylaminopropan-1,3-dioate and then alkylate the anion with the dibromide 5 were as follows. LDA in THF at 0°C for two hours followed by stirring at room temperature with the dibromide 5. Reacting diethyl 2-acetylaminopropan-1,3-dioate with excess NaH in DMF [25] at room temperature followed by filtration from solid residues, a solution of the dibromide 5 was then slowly added and the mixture warmed to 80°C for 24 hours. Other methods attempted to generate the anion in-situ were as follows. Stirring with potassium hydroxide in DMSO [29] at room temperature, a 1:1 mixture of DMSO and toluene [29] with potassium hydroxide at 50°C - after 24 hours significant decomposition was observed. Potassium carbonate and 18-crown-6 in refluxing acetonitrile again failed to yield a substitution product. Eventually it was found that substitution of the dibromide 5 by the di-diodide 6 in the alkylation conditions first attempted (Na/EtOH) did yield the desired protected amino acid 19.

The second method of preparing the α-amino acid was by alkylation of the anion prepared from benzylidene glycine ethyl ester [23]. Benzylidene glycine ethyl ester was readily prepared from glycine ethyl ester hydrochloride and benzaldehyde under basic conditions [23] and obtained as a pale yellow oil. The anion of benzylidene glycine ethyl ester was formed by using LDA in THF at -70°C. HMPA was used in the literature method and trial experiments showed that the presence of HMPA was necessary and that it could not be replaced by N,N,N',N'-tetramethylethane-1,2-diamine. The alkylation of the anion formed in this way proceeded smoothly with the dibromide 5 to give the protected amino acid 20 as a viscous amber oil.

The hydrolysis of both of these protected amino acids 19 and 20 was accomplished using refluxing aqueous acid, the resulting solution was taken to pH 6 (universal indicator paper) with aqueous base and the desired amino acid 21 precipitated [22].

In conclusion the authors have shown that a range of novel compounds uncontaminated by homologous impurities can be readily prepared, in good yield, starting from the readily available cyclic ketone dodecanone.

EXPERIMENTAL

M.ps. were measured on an electrothermal melting point apparatus and are uncorrected. IR. spectra were recorded on a Perkin-Elmer 398 infrared spectrophotometer. ^{1}H N.M.R. spectra were recorded on a Hitachi Perkin-Elmer R600 instrument. Petroleum ether (40-60°C fraction) is referred to as light petroleum and diethyl ether is referred to as ether. Column chromatography was performed using silica gel 60-120 mesh, flash chromatography [30] was accomplished using silica gel 230-400 mesh.

12-Bromododecanol 4

The apparatus was assembled and flame dried whilst being purged with

nitrogen. Borane-dimethyl sulphide (92 ml) was added to a mechanically stirred solution of 12-bromododecanoic acid 3 (200g, 0.717 mol) in dry dichloromethane (1000 ml) at room temperature, in an atmosphere of nitrogen. The addition proceeded over 1.5 hours and apparently proceeded in two stages. During the first 30 minutes the temperature of the reaction mixture rose to 24°C and vigorous gas evolution was observed. After 30 minutes the vigorous gas evolution ceased and the reaction mixture gradually rose to reflux temperature. At no time was the reaction exothermic enough to warrant a cooling bath being used, although it is advisable to have one on hand.

After the addition of the borane-dimethyl sulphide was complete the reaction mixture was refluxed under nitrogen for a further 2 hours. The reaction mixture was cooled to room temperature and water (750 ml) was added cautiously. Vigorous gas evolution occurred and the mixture was stirred for 15 minutes. A white precipitate was observed and addition of small quantities of 10% aqueous sodium carbonate aided the dissolution of this precipitate. The phases were separated and the aqueous phase was extracted with dichloromethane (150 ml). The combined organic phases were washed with water (300 ml), 10% aqueous sodium carbonate (2x200 ml), water and then dried over anhydrous sodium sulphate containing some anhydrous sodium carbonate. The solvents were removed by evaporation under reduced pressure and the residue dissolved in light petroleum. A fine suspension of white powder was observed which was removed by filtration, and subsequent cooling of the solution to -5°C yielded the desired 12-bromododecanol 3 (169.5g, 0.640 mol 89.2%) as a white powdery solid identical to that produced by the reduction of 12-bromododecanoic acid in diethyl ether.

1,12-Dibromododecane 5

To a solution of bromoalcohol 3 (43.00g, 0.16 mol) in glacial AcOH (70 ml) was added 47% hydrogen bromide in glacial AcOH (70 ml) and the mixture brought to reflux. After 18 hours the mixture was cooled and the solvent evaporated under reduced pressure with warming. The dark brown mixture was dissolved in hot light petroleum (200 ml), activated charcoal was added and the mixture refluxed for 10 minutes and filtered whilst hot. On cooling (ice-salt) the dibromide 5 (35.60g, 0.11 mol, 67%) crystallised as white platelets recrystallised from light petroleum m.p. 37-8°C (lit., [31] 37-38°C), δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.25 (16 H, br s), 1.60 (4 H, br quintet, J 9 Hz), 3.35 (4 H, t, J 8 Hz).

1,12-Di-iododododecane 6

To a solution of dibromide 5 (26.67g, 81.3 mmol) in butanone (200 ml) was added NaI (31.74g, 212 mmol) and the mixture refluxed for 1 hour. The mixture was cooled to room temperature, filtered and the solvent removed by evaporation under reduced pressure. The residue was treated with light petroleum (200 ml), filtered and the solvent removed under reduced pressure. Recrystallisation from EtOAc gave the di-iodide 6 (32.68 g, 77.4 mmol, 95%) as white platelets m.p. 38-39°C (Found: C, 34.2; H, 5.7 $C_{12}H_{24}I_2$ requires C 34.14, H 5.73%); δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1,15 (16 H, br s), 1.75 (4 H, br quintet, J 7 Hz), 3.10 (4 H, t, J 7 Hz).

1,12-Dinitrododecane 7

A solution of di-iodide 6 (8.18 g, 19.4 mmol) in ether (25 ml) was slowly added to a stirred suspension of $AgNO_2$ (6.38 g, 41.5 mmol) in ether (80 ml) at 5°C in the dark. After the addition was complete the mixture was stirred for 18 hours at room temperature, filtered and the solvent removed by evaporation under reduced pressure. Flash chromatography on silica gel with light petroleum-EtOAc (9:1) yielded the dinitro compound 7. Recrystallisation from MeOH yielded 7 (3.54 g, 13.6 mmol, 70%) as white crystals m.p. 59-60°C (Found: C 55.2, H 9.4, N 10.9. $C_{12}H_{24}N_2O_4$ requires C 55.36, H 9.29, N 10.76%); ν max(CH_2Cl_2) 1550, 1385 (NO_2); δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.30 (16 H, br s), 2.05 (4 H, br m), 4.40 (4 H, br t, J 7 Hz).

Also isolated by chromatography was 12-nitrododecanol 9 (0.45 g, 1.9 mmol, 9.8%).

12-Iododododecanol 8

Using the procedure detailed for the synthesis of 1,12-di-iododododecane 6, 12-bromododecanol 3, (21.4 g, 80.7 mmol) was converted to the iodoalcohol 8 (17.5 g, 56.0 mmol, 70.0%). M.p. 38-9°C (light petroleum) ν max(KBr) 3600-3100 (O-H); δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.30 (20 H, br s), 3.20 (2 H, t, J 7 Hz), 3.65 (2 H, br t, J 7 Hz).

12-Nitrododecanol 9

Using the procedure detailed for the synthesis of the dinitro compound 7, 12-iododecanol 8 (16.0 g, 51.2 mmol) was converted to 12-nitrododecanol 9. Recrystallisation from light petroleum yielded white needles 9 (9.4 g, 40.7 mmol, 79.5%), m.p. 42-3°C ν max (nujol) 3600-3100 (O-H), 1555, 1380 (NO_2), 1025 (C-O); δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.30 (16 H, br s), 2.10 (4 H, m), 3.70 (2 H, br t, J 6 Hz), 4.40 (2 H, t, J 7 Hz).

24-Bromotetracont-12-enal ethylene acetal 13

Acetal 11 (30.0g, 97.7mmol) was converted to aldehyde 10 and then to acetal 13 by the procedure described in Whiting et al [17].

The acetal 13 (32.1 g, 83%) was recrystallised from EtOH (-10°C) m.p. 24-25°C (lit., [3] 25°C), ν max (CCl_4) 3060 (C=C-H), 1140, 1120; δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.35 (34 H, br s), 2.00 (6 H, m), 3.40 (2 H, t, J 7 Hz), 3.90 (4 H, m), 4.85 (1 H, t, J 7 Hz), 5.35 (2 H, m).

24-Bromotetracont-12-enol 15

Acetal 13 (16.5 g, 34.9 mmol) was converted to aldehyde 14 by the procedure utilised in the preparation of 13 and this aldehyde was then reduced, in EtOH solution, by $NaBH_4$ to the bromoalcohol 15. Recrystallisation from MeOH (0°C) yielded white crystals (11.25 g, 26.1 mmol, 75%) m.p. 32-3°C, ν max (KBr) 3450-3200 (O-H), 3005 (C=C-H), 1060 (O-H), 720 (cis-olefinic protons); δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.25 (34 H, br s), 1.95 (6 H, m), 3.40 (2 H, t, J 6 Hz), 3.65 (2 H, t, J 7 Hz), 5.40 (2 H, m).

1,24-Di-iodotetracont-12-ene 16

p-Toluenesulphonyl chloride (2.07 g, 10.9 mmol) was added, in small portions, to a stirred solution of the alcohol 15 (3.75 g, 8.7 mmol) in dry pyridine (60 ml) at 5°C, after the addition was complete the solution was stirred for a further 3 hours at room temperature, poured on to ice cold water (65 ml) containing concentrated hydrochloric acid (5 ml) and extracted with ether (3x50 ml), the organic solution was washed with hydrochloric acid (50 ml, 2M), water and then dried Na_2SO_4 containing some K_2CO_3). This crude tosylate was used immediately without further purification in the preparation of the di-iodide 16 by the reaction with NaI (5 g) in butanone (50 ml) at room temperature for 16 hours followed by removal of the solid residues by filtration. The solvent was removed by evaporation under reduced pressure, the residue was treated with light petroleum (80 ml) and then filtered and the solvent removed by evaporation under reduced pressure. Flash chromatography (silica, light petroleum) followed by recrystallisation yielded the di-iodide 16 (2.68 g, 4.6 mmol, 53%) m.p. 37-38°C (light petroleum), (Found: C 49.1, H 8.0. $C_{24}H_{48}I_2$ requires C 48.98, H 7.82). δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.30 (36 H, br s), 1.90 (4 H, br m), 3.18 (4 H, t, J 7 Hz), 5.40 (2 H, m).

1,24-Dinitrotetracont-12-ene 17

By the method outlined in the preparation of the dinitro-alkane 7 the di-iodide 16 (0.54 g, 0.92 mmol) was converted to the required dinitro-alkene 17 using $AgNO_2$ (0.30 g, 1.95 mmol). Purification by flash chromatography (light petroleum-ether 9:1) followed by recrystallisation gave white crystalline 17 (0.25 g, 0.59 mmol, 64%) m.p. 68-70°C (MeOH), ν max (KBr) 1565, 1385 (NO_2) δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.30 (32 H, br s), 2.00 (8 H, m), 4.40 (4 H, t, J 8 Hz), 5.40 (2 H, m).

1,24-Dinitrotetracontane 18

Hydrogenation of the alkene 17 (0.043 g, 0.1 mmol) was accomplished in EtOAc (10 ml) with 5% palladium on carbon (0.01 g). The suspension was shaken under an atmosphere of hydrogen, for 12 hours, filtered, the solvent removed under reduced pressure and the resulting solid purified by flash chromatography (silica, light petroleum-EtOAc 9:1) to give the desired dinitro compound 18 (0.016 g, 0.04 mmol, 37%) m.p. 88-9°C, ν max (CCl_4) 1550, 1385 (NO_2); δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.20 (40 H, br s), 2.00 (4 H, m), 4.30 (4 H, t, J 7 Hz).

Diethyl N,N'-diacetyl-2,15-diamino-2,15-diethoxycarbonylhexadecan-1,16-dioate 19

Sodium (0.19 g, 8.2 mmol) was dissolved in anhydrous ethanol (50 ml) under an atmosphere of dry nitrogen. Diethyl 2-acetylaminopropan-1,3-dioate (1.78 g, 8.2 mmol) was added in one portion and the mixture stirred until a clear solution was obtained. A solution of the di-iodide 6 (1.48 g, 3.5 mmol) in anhydrous ethanol (50 ml) was then rapidly added. The solution was then heated at reflux for 16 hours, cooled to room temperature and made acidic by the slow addition of glacial acetic acid. Water (200 ml) was added and the solution extracted with ether (3x200 ml). The organic phase was dried (Na_2SO_4) and the solvent removed by evaporation under reduced pressure to leave a yellow oily solid. Trituration with light petroleum yielded a white crystalline solid - 19 (1.05 g, 1.8 mmol, 50.0%). δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.20 (32 H, br s + t), 2.05 (6 H, s), 2.10-2.55 (4 H, br t, J 10 Hz), 4.25 (8 H, q, J 8 Hz), 6.85 (2 H, br s, exchanges with D_2O).

Diethyl (N,N'-dibenzylidene)-2,15-diaminohexadecan-1,16-dioate 20

Butyl lithium solution in hexane (1.88 ml, 3.0 mmol) was added to di-isopropylamine (0.42 ml, 3.0 mmol) in anhydrous THF (40 ml) at -78°C under an atmosphere of dry nitrogen. After five minutes stirring benzylidene glycine ethyl ester (0.58 g, 3.0 mmol) was added dropwise to the LDA solution followed by a solution of the dibromide 5 (0.50 g, 1.5 mmol) in THF (5 ml). The mixture was stirred for a further 5 minutes then the cooling bath was removed and the deep red solution stirred for 12 hours and allowed to warm to ambient temperature.

The colour of the solution slowly faded. The mixture was then poured onto ice cold aqueous ammonium chloride solution and the resulting mixture extracted with ether (3x100 ml). The ethereal solution was dried (Na_2SO_4) and the solvent removed by evaporation under reduced pressure. The resulting amber oil was purified by chromatography using light petroleum-ether (9:1) to give the desired protected amino acid 20 as an amber oil (0.60 g, 1.1 mmol, 72%). δ^1H (60 MHz, $CDCl_3$, Me_4Si) 1.20 (26 H, br s), 1.95 (4 H, br s), 4.00 (2 H, t, J 8 Hz), 4.20 (4 H, t, J 7 Hz), 7.35 (6 H, m), 7.75 (4 H, m), 8.30 (2 H, s).

2,15-Diaminohexadecan-1,16-dioic acid 21

The protected amino acid 20 (0.55 g, 1.0 mmol) was refluxed with conc. hydrochloric acid (100 ml) for 6 hours and then the mixture was evaporated under reduced pressure. Water (40 ml) and ethanol (120 ml) was added and the solution was filtered. Slow addition of aqueous Na_2CO_3 solution adjusted the pH to 6 when a brown precipitate appeared. This was filtered and washed copiously with warm water to yield a pale brown solid 2,15-diaminohexadecan-1,16-dioic acid 21 (0.25 g, 0.8 mmol, 79%). This solid is readily soluble in cold trifluoroacetic and formic acids but is insoluble in both cold and hot acetic acid, water, methanol, butanol, DMSO and DMF. M.p. >310°C (goes brown >240°C), ν max (KBr) 3800-2400, 1730 (w), 1580; δ^1H (60 MHz, CF_3COOD, Me_4Si) 1.4 (20 H, br s), 2.2 (4 H, br m), 4.4 (2 H, br t, J 8 Hz).

ACKNOWLEDGEMENTS

One of us (T.A. Ainscow wishes to thank the S.E.R.C. for the provision of a postdoctoral research fellowship. We also express our thanks to Professor E.W. Abel, University of Exeter, and to Dr. D.J. Mowthorpe, Sheffield City Polytechnic, for the provision of research facilities.

REFERENCES

1. Morio Asaoka, Masayoshi Abe, Takashi Mukuta and Hisashi Takei, Chem. Lett., 215 (1982).
2. Belmont, M.R., J. Phys. Chem. Solids, 46, 595 (1985);
Belmont, M.R., Hooper, R.M. and Amechi, P.A.C., J.Phys. Chem. Solids, 46, 607 (1985).
3. Bidd, I., Kelly, D.J., Ottley, P.M., Paynter, O.I., Simmonds, D.J. and Whiting, M.C., J. Chem. Soc., Perkin Trans. 1, 1369 (1983).
4. Broadhurst, J., Res. Nat. Bur. Stand., Sect. A, 66A, 241 (1962).
5. Hooper, R.M., Ainscow, T.A., Belmont, M.R., Henshall, J.L., Hursthouse, M.B. and Short, J.M., in submission.
6. Mathisen. J., Norman, N. and Pedersen, B.F., Acta. Chem. Scand., 21, 127 (1967);
Nyburg, S.C. and Luth, H., Acta. Crystallogr., B28, 2992 (1972).
7. Lane, C.F., Aldrichimica Acta, 8, 20 (1975).
8. Brown, H.C,, Rao, C.G. and Kulkarni, S.U., Synthesis, 704 (1979).
9. Brown, H.C. and Choi, Y.M., Synthesis, 439 (1981).
10. Lane, C.F., J.Org. Chem., 39, 1437 (1974).
11. Paget, W.E. and Smith, K., J.C.S. Chem. Comm., 1169 (1980).
12. Kornblum, N., Org. React., 12, 30;
Kornblum, N., Larsen, H.O., Blackwood, R.K., Mooberry, D.D., Oliveto, E.P. and Graham, G.E., J. Am. Chem. Soc., 78, 1497 (1956).
13. Blatt, A.H., Org. Synth., Coll. Vol. 2, 476, J. Wiley and Sons, New York (1959).
14. Johnson, W.S., Org. Synth., 34, 37, J. Wiley and Sons, New York (1954).
15. Barton, D. and Ollis, W.D., Comprehensive Organic Chemistry, Vol. 2, p. 357, Pergammon, Oxford (1979).
16. Omura, K. and Swern, D., Tetrahedron, 34, 1651 (1978).
17. Paynter, O.I., Simmonds, D.J. and Whiting, M.C., J. Chem. Soc. Chem. Commun., 1165 (1982);
Iguar, E., Paynter, O.I., Simmonds, D.J. and Whiting, M.C., in submission.
18. Boden, R.M., Synthesis, 784 (1975);
Bidd, I. and Whiting, M.C., J. Chem. Soc. Chem Commun., 543 (1985).
19. Chaikin, S.W. and Brown, W.G., J. Am. Chem. Soc., 71, 122 (1949).
20. Vogel, A.I., A Textbook of Practical Organic Chemistry, 3rd Edn., p. 825, Longmans, London (1964).
21. Rylander, P.N., Catalytic Hydrogenation Over Platinum Metals, Academic Press, London (1969).
22. Richards, J.C. and Spenser, I.D., Can. J. Chem., 60, 2810 (1982);
Simmonds, D.H., Biochem. J., 520 (1954).
23. Stork, G., Leong, A.Y.W. and Touzin, A.M., J. Org. Chem., 41, 3491 (1976).
24. Berger, A., Smolarsky, M., Kurn, N. and Bosshard, H.R., J. Org. Chem., 38, 457 (1978).
25. Ablewhite, A.J. and Wooldridge, K.R.H., J. Chem. Soc. 'C', 2488 (1967).
26. O'Donnell, M.J., Bruder, W.A., Eckrich, T.M., Shullenbureger, D.F. and Staten, G.S., Synthesis, 127 (1984).
27. Strecker, A., Ann., 75, 27 (1850).
28. Marvel, C.S., Org. Synth. Coll. Vol. 3, 848, J. Willey and Sons, New York (1955).
29. Johnstone, R.A.W. and Rose, M.E., Tetrahedron, 35, 2169 (1979);
Johnstone, R.A.W., Deepak Tuli and Rose, M.E., J. Chem. Res. (M), 3591 (1980).
30. Still, W.C., Kahn, M. and Mitra, A. J. Org. Chem., 43, 2923 (1978).
31. Salmon-Legangneur, F. and Neveu, C., Bull. Soc.Chem. Fr., 2270 (1965).