The synthesis of monodisperse alkanes with long chains

Burnett, Simon

The Synthesis of Monodisperse Alkanes with Long Chains

by

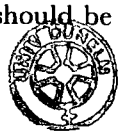
Simon Burnett B.Sc.

University of Durham

Department of Chemistry

A Thesis submitted for the degree of Master of Science

September 1995



Declaration

The work described in this Thesis was carried out in the Department of Chemistry at the University of Durham between October 1993 and September 1995. All the work is my own, unless stated to the contrary and it has not been submitted previously for a degree at this or any other University.

Acknowledgements

I would like to thank Dr. Gerald M. Brooke, my supervisor, for his great help and encouragement throughout the last two years. Thanks also to Dr. Dave Proctor and Dr. S 'Mo' Mohammed for their continual advice, friendship and good humour. I am also grateful to Professor Mark Whiting for his consultancy.

I am indebted to many others in the chemistry department for the high level of service and friendship provided : Lenny Lauchlin for HPLC analysis, Julia Say and Alan Kenwright for help with NMR, Jarka Dostall for micro analysis and all the technical staff. Also many thanks to Dr. Chris Drury and all the occupants, past and present of lab 27 for a very enjoyable two years.

Abstract

The Synthesis of Monodisperse Alkanes with Long Chains.

This thesis discusses reasons for the interest in monodisperse long chain alkanes and describes attempts, past and present, to synthesise such molecules.

Chapter 1 discusses why the synthesis of such molecules are important and the objectives of this project.

Chapter 2 reviews the methods previous groups have devised to prepare pure samples of long chain alkanes. In particular, work carried out by Whiting et al. at Bristol, whose scheme formed the basis of the early work in Durham.

Chapter 3 describes the work in Durham and improvements which were made to Whiting's method, allowing the synthesis of longer chain lengths and greater quantities of materials to be achieved.

Chapter 4 provides a summary of the practical work carried out by the author.

Chapter 5 gives experimental details of the work described in Chapter 4.

Simon Burnett (September 1995)

Contents

page

Chapter 1

Monodisperse Long Chain Alkanes

Chapter 1

Monodisperse Long Chain Alkanes

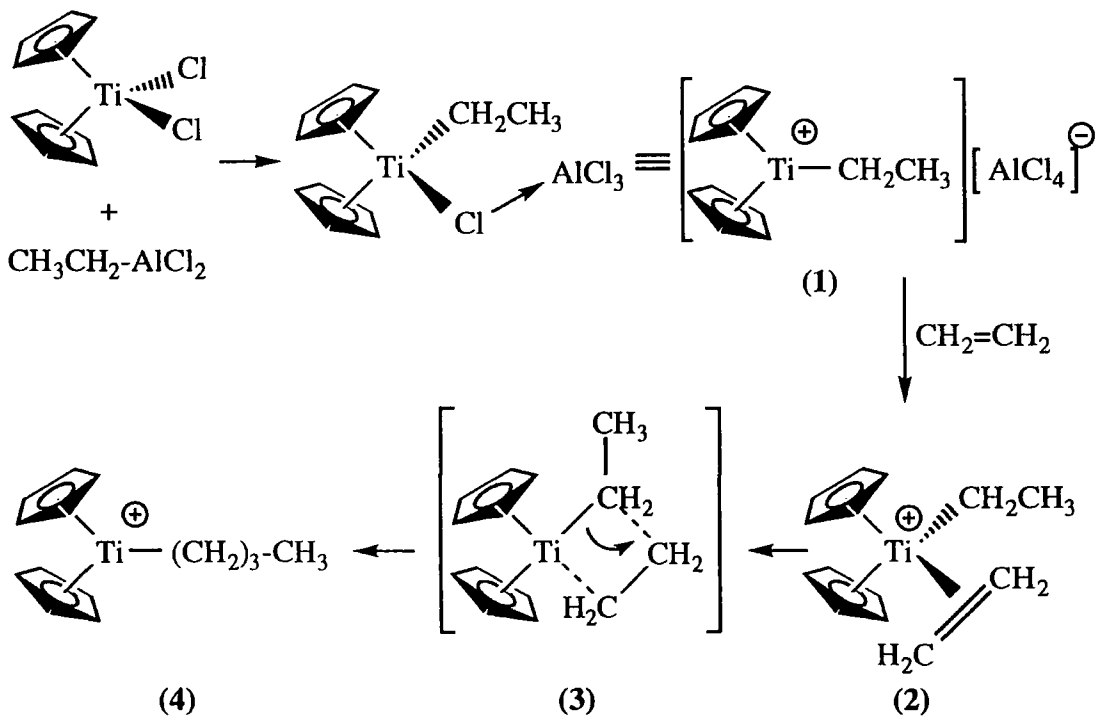
1.1 Production of Polyethylene

No other group of synthetic organic compounds has had as greater impact on our day to day living as synthetic polymers. Polyethylene, one of the first alkene chain growth polymers to be manufactured commercially, has been produced since 1943 and has a current annual US production of nearly 16 billion lb (1986).

Chemically, polyethylene is one of the simplest of the synthetic polymers, with the repeating unit -(CH_2-CH_2)- ; it can be prepared in a number of different ways leading to products with various properties. Three grades of polyethylene are available commercially : high density polyethylene (HDPE) ; low density polyethylene (LDPE) ; and linear low density polyethylene (LLDPE).

1.1.1 High Density Polyethylene [1]

HDPE is prepared by the Ziegler-Natta process which uses an organometallic catalyst. Majority opinion now favours a mechanism where chain growth occurs at the titanium-alkyl bond, as shown in Scheme 1.

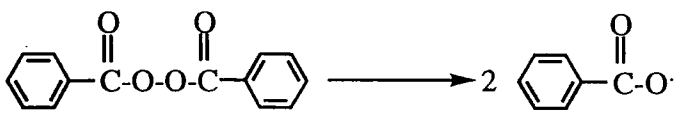


Scheme 1 *Production of HDPE by the Ziegler Natta process.*

The formation of a tricoordinate alkyl cation (1) forms an active site, which can accommodate an incoming monomer unit (2). A four membered transition state (3) is thought to occur which allows insertion of the monomer between the alkyl - titanium bond. This leads to the polymeric chain being extended whilst at the same time a new active site is produced (4) so the process can be repeated. HDPE is a structurally regular material with very few branch points (less than 7 per 1000 carbon atoms). The regularity allows the chain to pack efficiently resulting in a highly crystalline material with a correspondingly high density. HDPE has the greatest strength and heat resistance of the three grades and is used to manufacture bottles, crates and pipes. Polymeric materials have been of increasing use in the medicinal field. HDPE is used as a replacement part for damaged hip joints, forming the socket, which accommodates a steel ball cemented to the femur with polymethylmethacrylate.

1.1.2 Low Density Polyethylene [1]

LDPE is produced by a radical process, carried out at high pressure (1000-3000atm) and high temperature (100-125°C). The process, outlined in Scheme 2, proceeds in three distinct phases : (i) initiation : a small concentration of radicals, generated by a catalyst, react with an ethylene molecule generating an active centre ; (ii) propagation : growth of the macromolecular chain by repeated addition of the monomer ; and (iii) termination : the growth of the chain is brought to a halt by self condensation or transfer of the active centre.



(i) (In ·)

$$In\cdot + H_2C{=}CH_2 \longrightarrow In\text{-}CH_2\text{-}CH_2\cdot$$

(ii) $$In\text{-}CH_2\text{-}CH_2\cdot + H_2C{=}CH_2 \longrightarrow In\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}CH_2\cdot$$

$$\Longrightarrow In\text{-}(CH_2\text{-}CH_2)_nCH_2CH_2\cdot$$

(iii) $$2\ In\text{-}(CH_2\text{-}CH_2)_nCH_2CH_2\cdot \longrightarrow In\text{-}(CH_2\text{-}CH_2)_n\text{-}(CH_2)_4\text{-}(CH_2\text{-}CH_2)_n\text{-}In$$

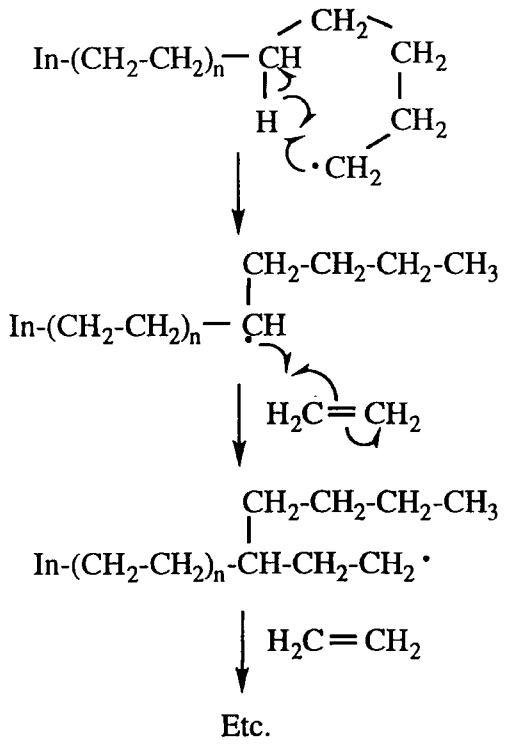
combination

$$In\text{-}(CH_2\text{-}CH_2)_nCH{=}CH_2 + In\text{-}(CH_2\text{-}CH_2)_n\text{-}CH_2\text{-}CH_3$$

disproportionation

Scheme 2 *Production of LDPE by a radical process.*

LDPE is a highly branched polymer (approximately 60 branch points per 1000 carbon atoms). The branches are formed by hydrogen abstraction (Scheme 3).



Scheme 3 *Chain branching in LDPE.*

LDPE has a much lower crystalline content and density than HDPE, but has good film forming properties; therefore its largest application is as film for packaging and cable coatings.

1.1.3 Linear Low Density Polyethylene [1]

The production of linear low density polyethylene (LLDPE) has filled the property gap between HDPE and LDPE. It is actually a copolymer of ethylene with 8-10% of an alkene such as but-1-ene, pent-1-ene, hex-1-ene or oct-1-ene. This produces a polymer with a controlled number of short chain branches and densities between HDPE and LDPE. The density can be varied by changing the copolymer. Oct-1-ene gives a lower density product than but-1-ene since the longer hexyl branch of the former pushes the chains further apart than the ethyl branch of the latter, thereby lowering the packing density of the chains. LLDPE is beginning to compete with LDPE in film blowing and casting as it has superior resistance to puncture by hard particles. It also has better

qualities of toughness and lower brittle temperatures than LDPE and is used to replace blends of LDPE and HDPE.

1.2 Distributions In Chain Lengths

In all the preparations of polyethylene and indeed all polymers, the monomers combine in more or less statistical fashion to form the chains, leading to a distribution in the size of the resulting chain. This distribution depends on the polymerisation process used ; for example, radical induced polymerisation, described above, gives a very wide distribution with between a few hundred and a few thousand monomer units in the chain. The Ziegler Natta process gives a narrower distribution with between 500-1000 monomer units. By polymer standards the latter is narrow but by the standards of precise molecular science, this distribution is still very appreciable. For most applications the width in distribution is not of serious consequence ; however, this factor has led to a barrier between the essentially statistical science of polymers and the exact science of simple molecules.

Overcoming this barrier by controlled, stepwise building up of polymers has always proved difficult. This situation has changed in the last ten years as work by Professor Whiting, motivated by the interest of groups in polymer physics, produced small amounts of n-alkanes of precise chain length, which bridge the gap between small molecules (alkanes up to $C_{20}H_{42}$) and polymers (polyethylene). This work and other syntheses of long chain alkanes are described in Chapter 2.

1.3 Physical Properties of Interest

The physical properties of interest in these pure hydrocarbons include the crystallisation process, crystallinity and the morphology of crystalline entities.

1.3.1 The Crystallisation Process [1]

The occurrence of significant crystallinity in a polymer is of considerable consequence to a materials' scientist. The polymer is no longer subject to the rules which apply when in the amorphous state, consequently, the properties of the polymer change. The extent of this change is dependant upon the proportion of crystallinity, since a polymer is rarely completely crystalline.

The creation of a three dimensional ordered phase from a disordered state is a two stage process:

(i) The first step is the creation of a stable nucleus. This requires an ordering of the chains and therefore results in a large negative entropy of activation. In order to achieve a favourable free energy change for crystallisation, the entropy term has to be offset by a large negative energy contribution. This occurs when strong intermolecular forces are present between the closely aligned chains which form the crystalline nucleus. The greater this interaction between chains, the more favourable will be the energy parameter. Therefore, for a polymer to form significant levels of crystallinity, the chains should: (i) allow regular close packing ; and (ii) possess groups which will form strong intermolecular interactions, thereby providing a favourable free energy contribution. Polyethylene possess a suitable symmetry for crystalline formation as the chains pack closely together allowing van der Waals forces to provide additional stability. If the chain is substantially branched then the packing efficiency deteriorates and the crystalline content is lowered. As discussed earlier, polyethylene provides a good example of this, as extensive branching in LDPE lowers the density and crystallinity of the polymer.

(ii) The second step is the growth of the crystalline region, the size of which is governed by the rate of addition of other chains to the nucleus. The growth rate is dependant on the thermal motion of the polymer chains. At higher temperatures (close to the melting point of the crystal (T_M)) the motion of the chains is too great to allow significant formation of stable nuclei. As the temperature decreases to the glass transition temperature (T_G), the melt viscosity increases and the motion of the chains is too slow for significant growth. Therefore, a maximum growth rate occurs in the range between (T_M -10°C) and (T_G +30°C). However, a further factor must be considered, since the melt viscosity is a function of the molar mass, so the optimum temperature of crystallisation depends not only on the interval T_M to T_G, but also on the molar mass of the sample.

1.3.2 Chain-Folding

Using a dilute solution of a polymer, it is possible to obtain well defined single crystals. Studies using an electron microscope reveal the crystals to be made up of thin lamellae, about 20-30 nm thick depending on the temperature of crystallisation, yet surprisingly, the polymer chains, which may be as long as 1000nm, are oriented across the lamellae. This means that the chain must be folded many times to be accommodated in the crystal. For a polymer such as polyethylene, the fold is completed using only 3-4 monomer units with the bonds in the gauche conformation, while the bonds of the extended portions, in between the folds, are in the trans position.

Conventional n-alkanes, with short chain lengths ($C_{20}H_{42}$ and below), crystallise by forming layers of fully extended chains, the layer thickness corresponding to the chain length. The question which immediately arises is at what length does the extended chain (n-alkanes) give way to the folded chain behaviour (polyethylene)? The n-alkanes of uniform length produced by Whiting span the two modes of crystallisation. As such they serve as models for exploring the origin and nature of chain-folding, as well as the potential to solve many other problems and controversies in the field of chain-folded polymer crystallisation. Work carried out by Keller et al at Bristol,[2] using the n-alkanes produced by Whiting, showed that in both melt and solution crystallisation, the chains start to fold at lengths between 100 and 150 carbon atoms. The fold length, l, increases

Chain Conform.	E	F2	F3	F4	F5
n-Alkane					
$C_{102}H_{206}$	*				
$C_{150}H_{302}$	*	*			
$C_{198}H_{398}$	*	*	*		
$C_{246}H_{494}$	*	*	*	*	
$C_{294}H_{590}$	*	*	*	*	
$C_{390}H_{782}$	*	*	*	*	*

Table 1 *Chain conformations observed in n-alkanes with the chain lengths shown.*

with temperature of crystallisation (T_c). The conformations taken up in the final stage of crystallisation by the materials studied are outlined in Table 1.

It was initially thought that the fold length of the monodisperse long chain alkanes was always an integer fraction of the chain length, giving a layer with a sharp, well ordered fold structure (IF state, Figure 1).

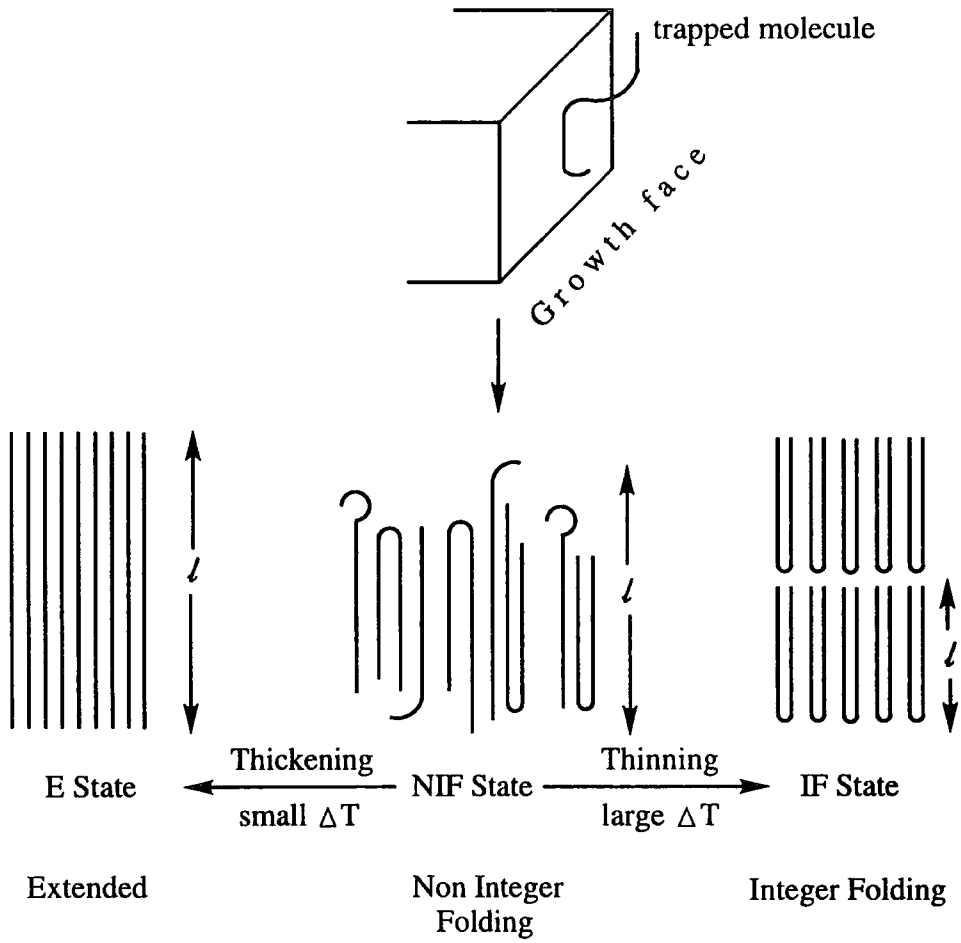


Figure 1 *The two possible methods of chain rearrangement subsequent to growth.*

However, it was later noted that the primary l values depart from this strict quantisation and display a continuity with T_c, somewhat in the manner of polyethylene, with higher T_c yielding larger l. This gives a more disordered structure, known as the non integer fraction (NIF) state as shown in Figure 1. Nevertheless, this is only a transient state, transforming into the integer fraction (IF) state during crystallisation and / or cooling. The transformation can occur by thickening or by thinning into the nearest IF state (Figure 1).

An explanation for these observations appears to hinge on two competing criteria; the state of maximum stability of the crystal and the fastest kinetic pathway of its formation. It is accepted that the state of maximum stability for polymers is the fully extended chain. However, chain folding arises because it is the fastest way for the crystal to grow. Therefore, the crystal formed has a lower than maximum state of stability. However, when mobility conditions permit, the crystal will tend to the state of maximum stability by refolding (isothermal thickening).

The same applies to the short uniform chains, but in this case local minima of free energy arise when l is an integer fraction of the chain length and all the chain ends are at the layer surface. As in polymer crystallisation, the crystal grows fastest by forming NIF transient states. This can be seen by considering a chain depositing along the crystal face as in Figure 1. The particular chain, as shown, will obviously not be able to complete an IF structure without translation. It is apparent therefore that for an IF structure to form, the first attachment of the chain has to satisfy particular conditions, with corresponding low attachment probability. Therefore the probability of an attaching chain leading to a NIF structure is much greater than leading to an IF state, so NIF will be the pathway for faster growth.

The primary NIF structures formed by the n-alkanes also tend towards the more stable, extended structures, just as conventional chain folded structures do ; however, the nearby IF structures offer stations of increased stability along the road. This allows the possibility of not only isothermal thickening, but also a lowering of the l value (isothermal thinning) to reach a more stable structure.

The nature of the fold, whether loose or sharp, has been a major issue in high polymers, studied most closely in polyethylene. These studies show that the folds in alkanes must have appreciable looseness when forming (NIF state) but become sharper after refolding and cooling (IF state). Therefore the particular state observed depends on the stage of crystallisation and / or transformation at which the system is examined and no categorical statement can be made from examination of any one specimen.

The fold surface disorder which occurs in the NIF state of the alkanes is confined to loops which span nearby, if not adjacent stems. In the case of high polymers a further

kind of disorder occurs where the loop is made of large portions of the chain, allowing extensive meandering of the chains between the lamellae, forming interfacial amorphous regions. This form of disorder would not be easily removed by isothermal refolding.

1.3.3 Rates of Crystallisation [3]

Although in the first instance the work was undertaken to elucidate such issues relating to chain folding in high polymers, at the same time new effects have been uncovered. Rates of crystallisation of the alkanes have been followed by differential scanning calorimetery (DSC) and in situ synchrotron X-ray diffraction. These studies reveal a very sharply defined minimum in both the rate of nucleation and crystal growth with decreasing T_c. Figure 2 shows the minimum in the crystallisation rate, R, of $C_{198}H_{398}$ grown from a 3.85% solution in toluene, as a function of T_c. This minimum is very surprising as all current crystallisation theories predict an increased rate with supercooling, provided the temperatures are well above those of glass transition.

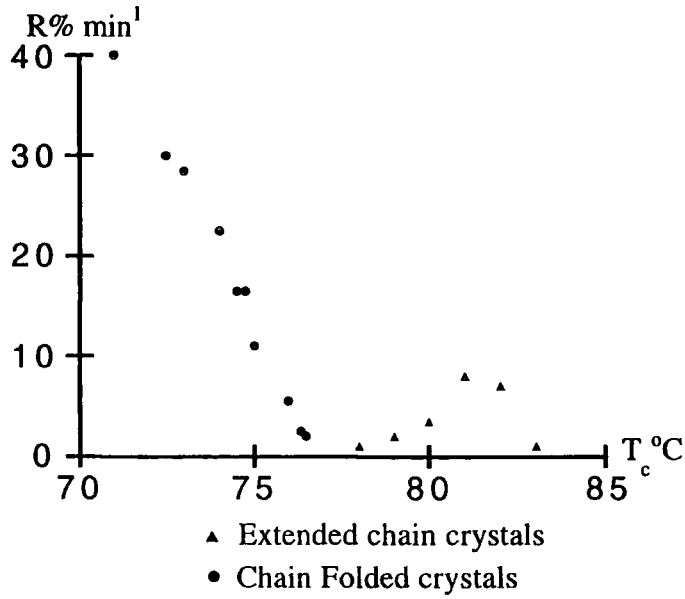


Figure 2 *Crystallisation rate, R, of $C_{198}H_{398}$ grown from a 3.85% solution in toluene, as a function of crystallisation temperature T_c.*

This minimum is interpreted through a new concept of self poisoning during crystal growth. The first expected increase and subsequent unexpected decrease correspond to the formation of extended chain crystals. The renewed increase beyond the minimum

corresponds to folded chain crystallisation. The minimum is thought to arise through competition between extended and folded chain deposition. This can be understood more clearly by considering how the crystal grows as the temperature drops. When the temperature drops below the melting point of the extended chain state (T_m^E), only extended chain nuclei can lead to stable crystals. However as the temperature continues to drop and the melting point of the folded chain state (T_m^F) is approached , another process appears to interfere with extended chain crystallisation, decreasing its rate. The retardation becomes increasingly significant as T_m^F is approached. It appears that the retardation of crystal growth is caused by temporarily attached folded molecules reducing the growth surface available for productive extended growth (Fig. 3).

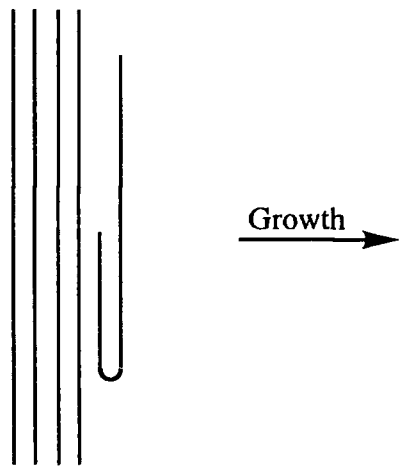


Figure 3 *The temporary attachment of a chain folded molecule retards the rate of productive extended growth.*

Although at temperatures greater than T_m^F the lifetime of each individual folded configuration is bound to be very short, the large number of possible folded molecular conformations, multiplied by the number of positions along the chain growth surfaces makes the partial coverage of these sites by folded molecules a viable possibility. As the temperature drops towards T_m^F the lifetime of the folded conformations increases and the obstruction becomes enhanced. A similar retardation mechanism occurs in primary nucleation. Only extended chain nuclei can lead to productive growth above T_m^F. However, as the temperature approaches T_m^F, an increasing number of chains will form unproductive chain folded conformations, which involve a significantly lower free energy barrier than do extended chains, thereby slowing the rate of primary nucleation.

It is thought that a minimum in crystallisation rate with supercooling is unprecedented not only for polymers, but for crystallisation in general. This is one of several hitherto hidden features of polymer crystallisation which has become accessible through the availability of strictly uniform long chain alkanes.

1.4 Aims Of The Current Work

The results described above were achieved despite the difficulties imposed by only having milligram quantities of the materials available. The purpose of the present work is to provide further quantities of these materials to allow a continuation of the physical work. Using a method based on that developed by Whiting it was aimed to ;

(i) increase the quantities compared with those that Whiting achieved.

(ii) produce alkanes with chain lengths up to C_{390} and beyond, thereby bridging the gap to low molecular weight polymers.

(iii) prepare special chemically modified materials to suit particular investigations.

A number of groups of polymer physicists have met to discuss the continued physical work to be carried out on the new samples produced. Some of the major ideas are as follows.

- Morphological studies to elicit the basic mechanisms promoting spherulite growth.

- Structural studies on precise IF systems by a variety of techniques offer the possibility of obtaining definitive information on the nature and the packing of the folds.

- Kinetic and morphological studies of the NIF to IF and onto other IF states and comparison with the various theories available.

- Studies on the minima in crystallisation rate of a range of alkanes. Is there a minimum in the rate associated with the transition from once folded to twice folded?

- Investigations on mixtures of alkanes. In order to form links with 'real' polymers it would be essential to quantify the precise effect of non uniformity. The alkanes would be mixed in pre-designed proportions and the effects on crystallisation and thermodynamics studied.

- High resolution, solid state and carbon-13 nmr are to be used on a wide range of polyethylenes with linear, branched and linear low density structures, to study various

structural regions (crystalline, amorphous, interfacial / chain folds). The ultimate aim is to correlate structural features with physical and mechanical properties. The use of the n-alkanes in technique development and calibration would, because of their precise structures, be very appropriate.

These and other physical studies will contribute significantly to our understanding of the fundamentals of crystallisation processes and the structure of crystallinity in long chain molecules, particularly those associated with chain folding. Such understanding is basic to much of polymer science.

Chapter 2

Previous Attempts to Form Monodisperse Long Chain Alkanes

Chapter 2

Previous Attempts to Form Monodisperse Long Chain Alkanes

2.1 Nomenclature

When dealing with long carbon chains the nomenclature used to describe the number of carbon atoms can become confusing. The stem is split into a prefix and a suffix which describe the units and number of tens respectively.

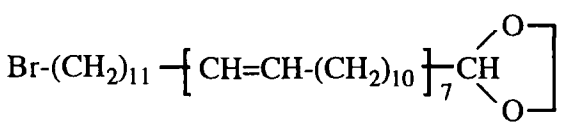
	Units		Tens		Hundreds
* 1	hen-	1	-deca- (ne)	1	hectane
2	do-	2	-cosa- (ne)	2	dictane
3	tria-	3	-triaconta- (ne)	3	trictane
4	tetra-	4	-tetraconta- (ne)		
5	penta-	5	-pentaconta- (ne)		
6	hexa-	6	-hexaconta- (ne)		
7	hepta-	7	-heptaconta- (ne)		
8	octa-	8	-octaconta- (ne)		
9	nona-	9	nonaconta- (ne)		

* The only exception to this is $C_{11}H_{24}$, which is called undecane rather than hendecane which the rules above suggest.

Examples

$Br\text{-}(CH_2)_{12}\text{-}OH$ 12-bromododecan-1-ol

$Br\text{-}(CH_2)_{11}\text{-}CH{=}CH\text{-}(CH_2)_{10}\text{-}CHO$ 24-bromotetracos-12-en-1-al



96-bromohexanonaconta-12,24,36,48,60,72,84-heptaenal ethylene acetal

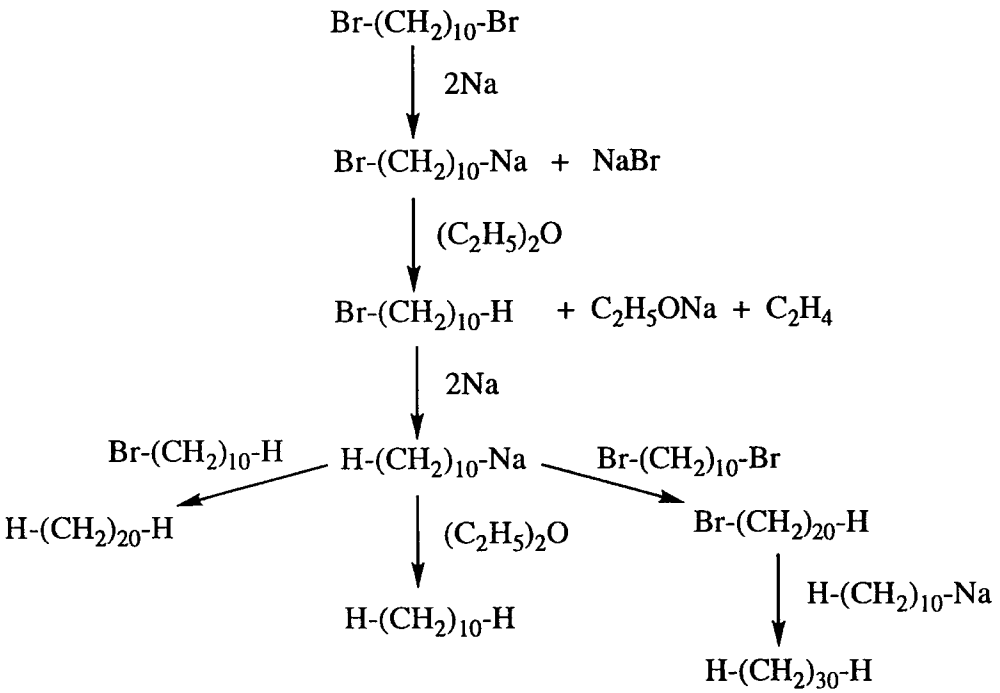
2.2 Review Of Early Work

Previous workers have used one of two strategies in the preparation of pure samples of long chain alkanes : (i) polymer chemistry, where a single reaction produces a series of oligomers which must then be separated ; and (ii) synthetic organic chemistry, where a scheme is devised which leads specifically to the desired molecule.

2.2.1 The Strategy of Polymerisation

2.2.1.1 Carothers, Hill, Kirby and Jacobson, 1930 [4]

This strategy was first attempted by Carothers in 1930. He carried out a bifunctional Wurtz reaction using 1,10-dibromodecane to give oligomers of the form $H[(CH_2)_{10}]_nH$. The reaction involved heating 1,10-dibromodecane with sodium in diethyl ether, the solvent participating in the reaction as shown in Scheme 4. As well as the desired oligomers it is likely that similar chains terminated at one or both ends with bromine would be formed.



Scheme 4 *The bifunctional Wurtz reaction used by Carothers.*

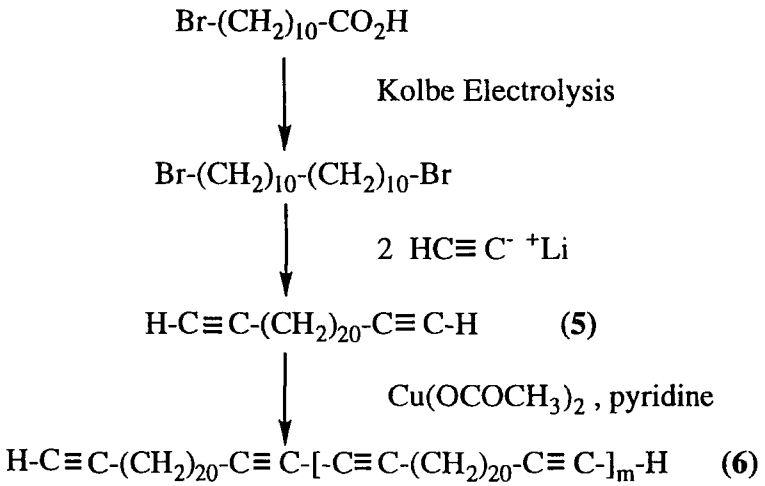
The hydrocarbon mixture from the reaction was separated in a molecular still. A number of fractions were collected and redistilled, leaving a solid residue. The distillates were recrystallised to constant melting point and assigned to the alkanes C_{20}-

C_{70}. All apart from C_{20} and C_{30} were new compounds and C_{70} was longer than any hydrocarbon previously described.

There are two sources of impurity which may have been present in the samples. Due to the great difficulties involved in separation of members of an oligomeric series, it is likely that any n-mer would contain some of the (n-1) and (n+1)mers. Any impurity present in the starting material in x% would form nx% of a near homologue in the final product.

2.2.1.2. Schill, Zurcher and Fritz, 1977 [5]

Schill, Zurcher and Fritz were the next to attempt the polymer chemistry approach in 1977. They carried out stepwise oxidative oligomerisation of 1,23-tetracosadiyne (Scheme 5) (5) with cupric acetate in pyridine, thereby producing oligomers up to the nonamer (6, m=8), which then underwent hydrogenation to form the alkanes. A major advantage of oxidative coupling is that no side products are formed ; however, a mixture of oligomers is formed which requires careful separation.



Scheme 5 *Stepwise oxidative oligomerisation of 1,23-tetracosadiyne.*

2.2.1.3 Lee and Wegner, 1985 [6]

Schill's method was developed further by Lee and Wegner in 1985. They similarly coupled 1,23-tetracosadiyne (5) to form the dimer in good yield. Other homologues up to the heptamer were isolated in reasonable yields. The oligomers were separated by adsorption chromatography using alumina, then hydrogenated over a Pd/C catalyst. The purity of the resulting alkanes was determined by GPC, elemental and end group

analysis and NMR spectroscopy. This strategy was used to prepare linear alkanes up to $C_{384}H_{770}$.

Separation of the higher oligomers were eased slightly by using the dimer and trimer as starting materials for the oxidative coupling, so members of the resulting homologous series differed by 48 and 72 carbon atoms respectively. However, there remains a possibility of contamination. The only way to avoid this is to use the approach of synthetic organic chemistry.

2.2.2 The Strategy of Stepwise Synthesis

2.2.2.1 Doolittle and Peterson, 1951 [7]

In 1951 Doolittle and Peterson used the Wurtz reaction to synthesise n-hexatriacontane ($C_{36}H_{74}$) and n-tetrahexacontane ($C_{64}H_{130}$) from 1-bromooctadecane ($C_{18}H_{37}Br$) and 1-bromodotriacontane ($C_{32}H_{65}Br$) respectively. The use of starting materials with longer chain length is advantageous since the oligomers formed in the Wurtz reaction will differ by more carbon atoms making separation slightly easier.

The bromoalkane was refluxed with sodium sand in ether and the products purified by recrystallisation. However, measurements of the melting points and densities of the hydrocarbons suggested that they were impure. This was probably due to impurities in the starting materials. The 1-bromodotriacontane ($C_{32}H_{65}Br$) used was prepared from dotriacontanol ($C_{32}H_{65}OH$) isolated from carnauba wax. It is likely that higher alcohols present in carnauba wax were not completely separated, leading to the presence of higher homologues in the final product.

2.2.2.2 Ställberg, Ställberg-Stenhagen and Stenhagen 1952 [8]

Ställberg saw the need to carry out a synthesis which used a homologue-free starting material and chain lengthening methods which would not give rise to by-products of similar chain lengths to that of the desired product. This would minimise problems of purification of the final alkanes.

A long chain β-keto ester derivative (Scheme 6) (8) and a long chain iodoalkane (7) were used to give a mono-alkylation product (9). The β-keto ester used was the

relatively easily accessible dimethyl 3-oxocosan-1,20-dicarboxylate (8, C_{20}) , derived from the mono ester of decane-1,10-dicarboxylic acid (Scheme 6) (15). It was reacted with 1-iododododecane (7, n=11, C_{12}) and with 1-iododocosane (7, n=21, C_{22}) to give, after hydrolysis and decarboxylation, 18-oxohentriacontanoic acid (10, n=11, C_{31}) and 18-oxohentetracosanoic acid (10, n=21, C_{41}) in yields of 69% and 64% respectively.

$CH_3\text{-}(CH_2)_n\text{-}I$ **(7)** + $CH_3O\text{-}CO\text{-}CH_2\text{-}CO\text{-}(CH_2)_{16}\text{-}CO\text{-}OCH_3$ **(8)**

↓ K_2CO_3 , methyl-n-propyl ketone

$CH_3\text{-}(CH_2)_n\text{-}CH(CO_2CH_3)\text{-}CO\text{-}(CH_2)_{16}\text{-}CO\text{-}OCH_3$ **(9)**

↓ KOH , H_2O , CH_3OH , benzene ; H^+

$CH_3\text{-}(CH_2)_n\text{-}CH_2\text{-}CO\text{-}(CH_2)_{16}\text{-}CO\text{-}OH$ **(10)**

↓ $ZnHg_x$; HCl ; $CH_3CH_2CH_2OH$

$CH_3\text{-}(CH_2)_n\text{-}CH_2CH_2\text{-}(CH_2)_{16}\text{-}CO\text{-}O\text{-}CH_2CH_2CH_3$ **(11)**

↓ H_2 (250 atms)

$CH_3\text{-}(CH_2)_n\text{-}CH_2CH_2\text{-}(CH_2)_{16}\text{-}CH_2\text{-}OH$ **(12)**

↓ P , I_2

$CH_3\text{-}(CH_2)_n\text{-}(CH_2)_2\text{-}(CH_2)_{16}\text{-}CH_2\text{-}I$ **(13)**

$2\ CH_3\text{-}(CH_2)_n\text{-}(CH_2)_2\text{-}(CH_2)_{16}\text{-}CH_2\text{-}I$ **(13)**

↓ Na

$CH_3\text{-}(CH_2)_{(2n+38)}\text{-}CH_3$ **(14)**

Scheme 6 *Synthesis of long chain hydrocarbons attempted by Stallenberg et al.*

$2\ HOOC\text{-}(CH_2)_8\text{-}CO\text{-}OCH_3$ **(15)**

↓

$CH_3O\text{-}CO\text{-}(CH_2)_{16}\text{-}CO\text{-}OCH_3 + 2CO_2$

↓

$CH_3O\text{-}CO\text{-}CH_2\text{-}CO\text{-}(CH_2)_{16}\text{-}CO\text{-}OCH_3$ **(8)**

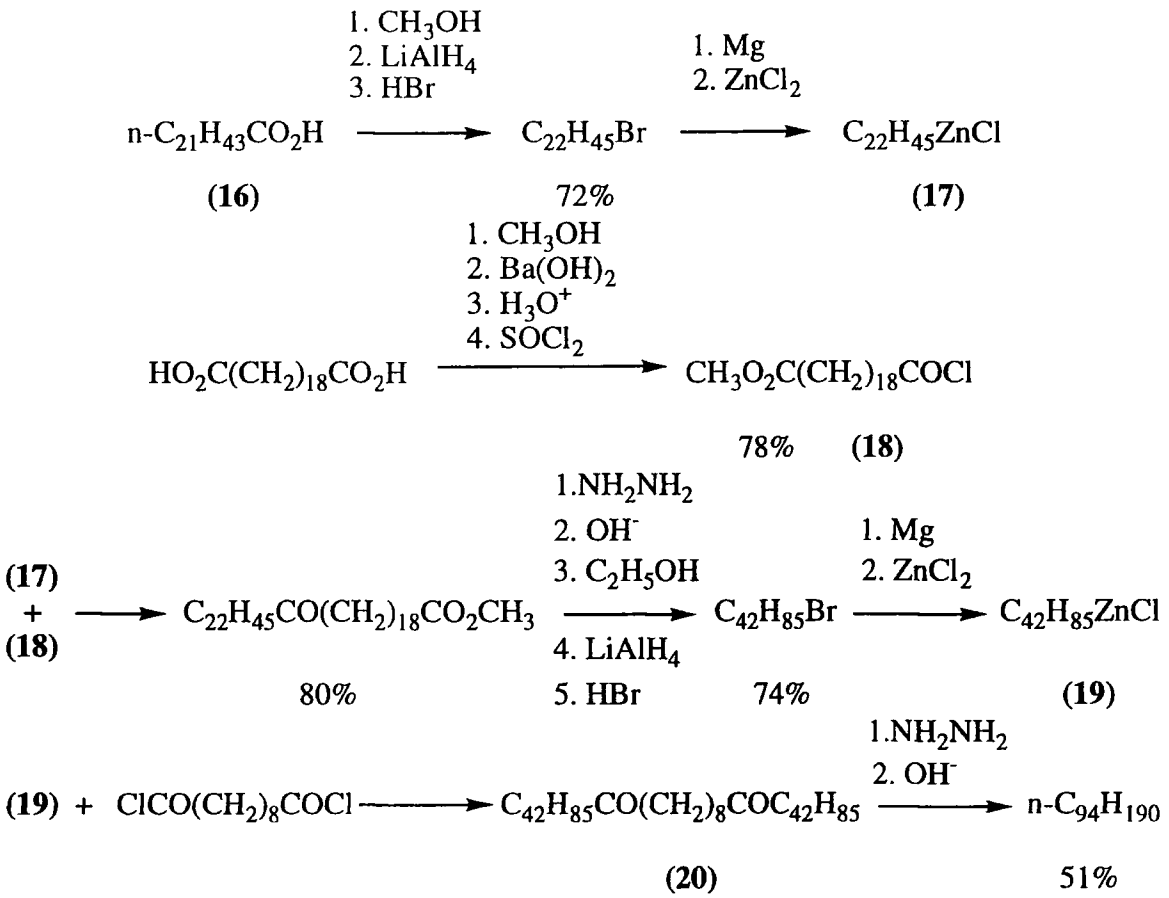
Scheme 7 *Synthesis of dimethyl 3-oxocosan-1,20-dicarboxylate (8).*

Similarly, reaction of the β-keto ester (8) with 1-iodononacosane (7, n=28, C_{29}) and 1-iodohentriacontane (7, n=30, C_{31}) gave 18-oxooctatetracontanoic acid (10, n=28, C_{48}) and 18-oxopentacontanoic acid (10, n=30, C_{50}) respectively, in yields of 75-80%. Various methods of the Wolf-Kischner and Clemmenson reactions were attempted to reduce the keto acid (10) to the n-acid. The selected method involved carrying out the reduction in n-propanol saturated in dry HCl to give the n-propylester (11) , in yields of 70% and 73% for C_{48} and C_{50} respectively. The ester (11) was further reduced to the n-alcohol (12) by high pressure hydrogenation over a copper chromite catalyst in a yield of 87% for n-pentacontanol (12, n=30, C_{50}). Reaction with phosphorus and iodine gave the iodide (13) in good yields (88% for C_{50}) which was then purified by molecular distillation. Wurtz coupling was carried out without solvent (the hydrocarbon chain acts to dilute the halide) using sodium at 150°, to form the alkanes in yields of 60-70%. However, considerable losses occurred in the final purification, carried out by treatment with hot sulphuric acid, which acted to protonate the carbonyl or alcohol groups of any precursors present, making their removal from the product straightforward. Molecular distillation was not possible due to the high molecular weights involved.

The Wurtz reaction is thought to occur via a free radical mechanism and side reactions (rearrangement and elimination) are common, making it likely that the samples of n-hectane ($C_{100}H_{202}$) contained some pentacontane ($C_{50}H_{102}$) and branched chain isomers of hectane. Near homologues may also be present due to minor impurities in the starting materials, which would be undetectable by techniques used at the time. Thus, 0.3% of a C_{12} compound in the C_{10} diacid (15), a precursor to the β-keto-acid would lead to 2.4% of a C_{102} homologue of the final product. Both of these impurities would be very difficult to remove.

2.2.2.3 Reinhard and Dixon, 1965 [9]

In 1965 Reinhard and Dixon developed a synthesis of tetranonacontane ($C_{94}H_{190}$) which avoided the use of the Wurtz reaction as they had observed the formation of undesirable branched chain products. Their synthesis, shown in Scheme 8, was based on an alkylzinc reagent (17), initially formed from docosanoic acid (16).

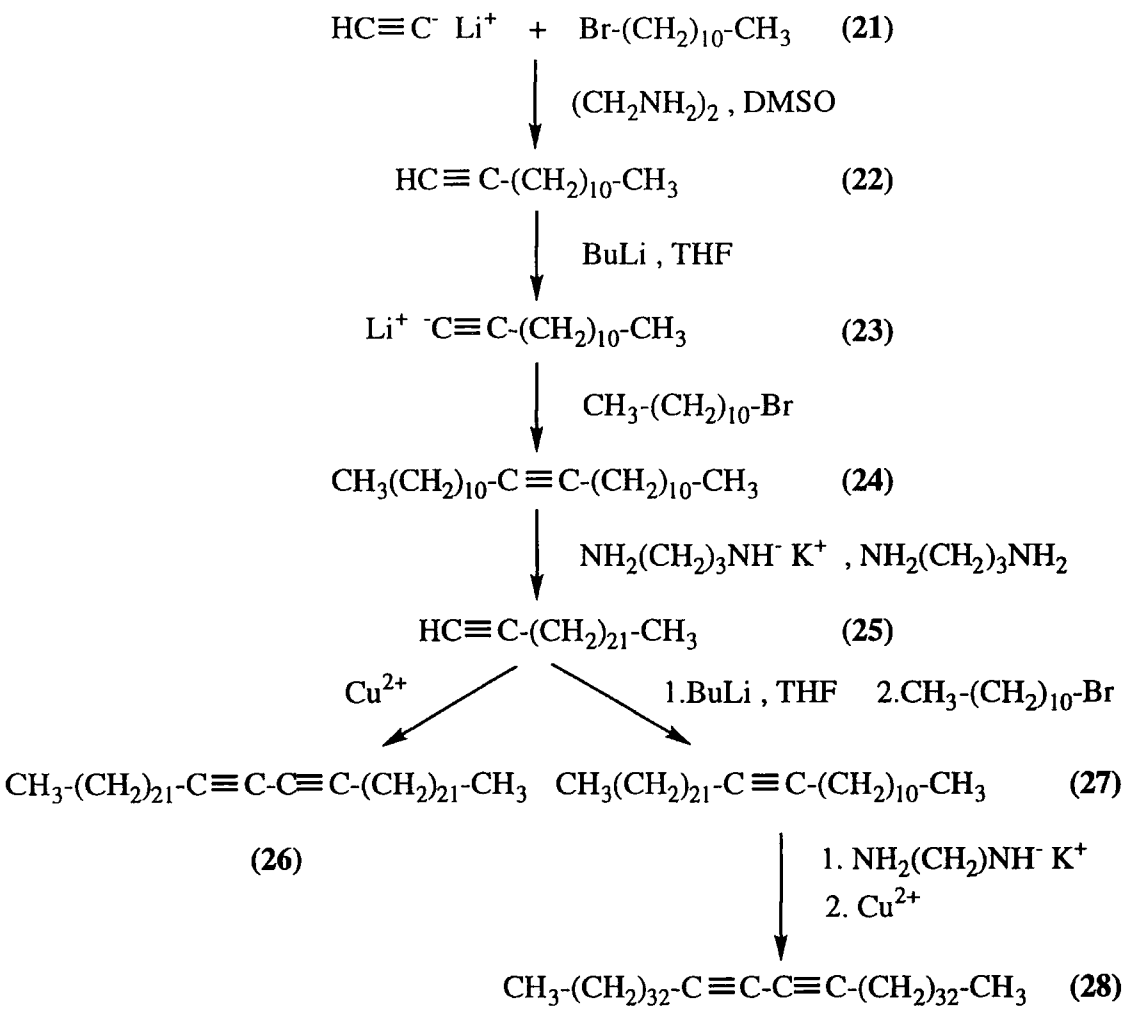


Scheme 8 *Synthesis of tetranonacontane.*

All attempts to remove traces of the preceding diketone (20) from the final product by chromatography and recrystallisation failed, so they resorted to treatment with concentrated sulphuric acid at 125°C. This was an improvement on Ställberg's synthesis since the final product was probably free from compounds of considerably different chain length ; however, there remains the possibility of the presence of near homologues caused by impurities in the docosanoic acid (16).

2.2.2.4 Bidd, Holdup and Whiting, 1987 [10 11]

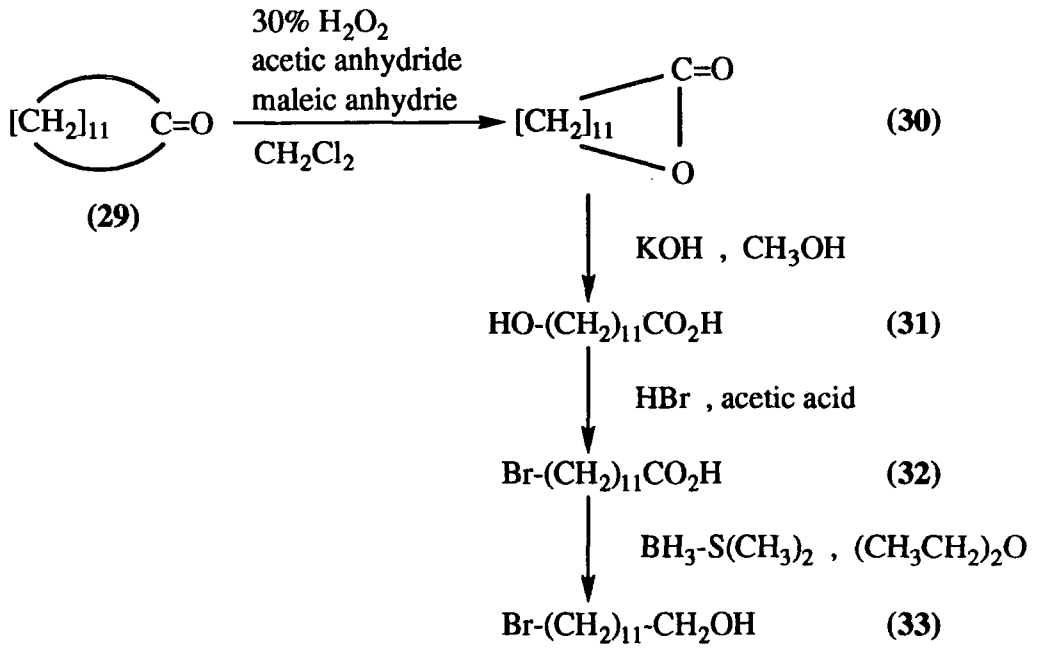
In 1987 Whiting published work on the synthesis of long chain hydrocarbons. His earliest work was based on alkylation of a lithium alkyne with a bromoalkane (Scheme 9).



Scheme 9 *Alkylation of a lithium alkyne with a bromoalkane as a means of building long chain alkanes.*

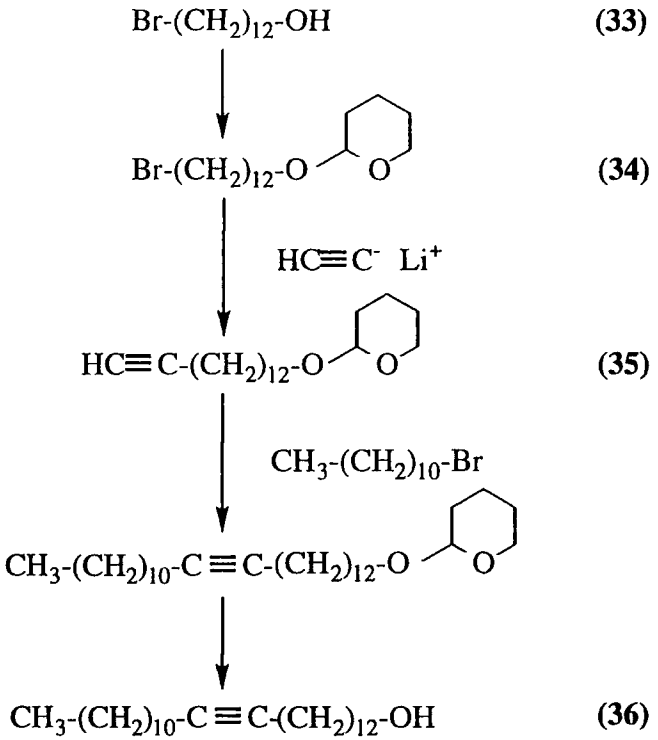
Undec-10-enoic acid, derived from ricinoleic acid, was used as a starting material in preliminary work. Derivatives, such as 1-bromoundecane (21), were available in apparently good purity. Reaction of (21) with lithium acetylide gave tridec-1-yne (22) which in turn was converted to its lithium derivative (23) and alkylated to form tetracos-12-yne (24). This undergoes rearrangement to tetracos-1-yne (25) using potassium-3-aminopropylamide in propane-1,3-diamine. Oxidative coupling of the tetracos-1-yne gave the C_{48} diyne (26). Alternatively, further alkylation of the tetracos-1-yne with 1-bromoundecane gave pentatriacont-12-yne (27), a procedure which required the addition of hexamethylphosphoramide (HMPA). Similarly, the pentatriacont-12-yne (27) was rearranged to form pentatriacont-1-yne, which was oxidatively coupled to give the C_{70} diyne (28) ; however, it was considered unlikely that hydrocarbons of a desired chain length would be achievable by this method.

A related approach used 12-bromododecanol, produced from cyclododecanone (29) (Scheme 10)[12]. The cyclododecanone is derived from a cyclic trimer of butadiene, giving a pure, inexpensive starting material, free from near homologues. Baeyer-Villiger oxidation of the cyclododecanone (29), followed by hydrolysis gave the hydroxy acid (31), which was then converted into the bromo acid (32). Borane-dimethyl sulphide was used to reduce this to the alcohol, since other reducing agents such as $LiAlH_4$ and $NaBH_4$ had attacked the terminal bromine forming dodecanol.



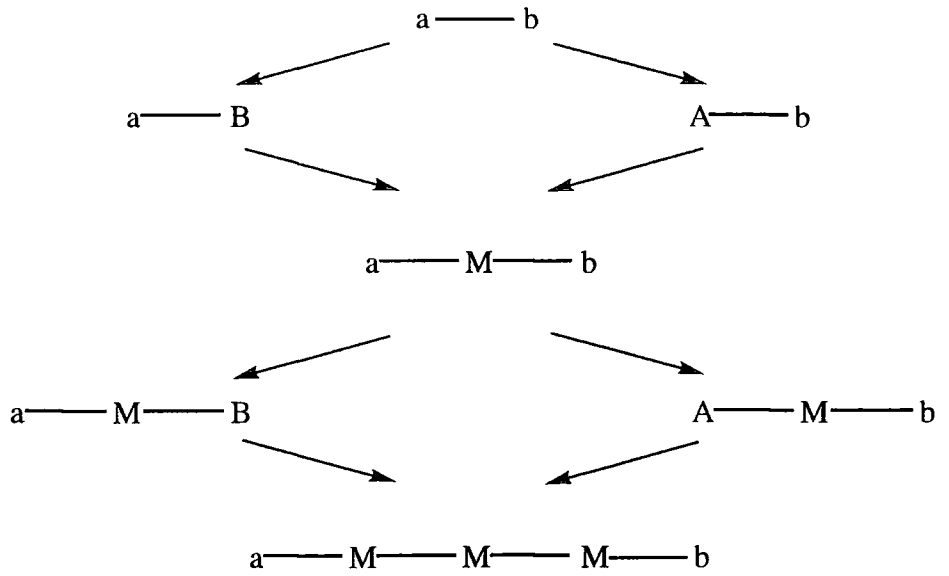
Scheme 10 *Synthesis of 12-bromododecanol (33).*

In the new approach, shown in Scheme 11, 12-bromododecanol (33) was converted into its tetrahydropyranyl ether (34) and reacted with lithium acetylide to form tetradec-13-ynyl tetrahydropyranyl ether (35). A further alkylation, with 1-bromoundecane in HMPA, followed by deprotection gave pentacos-13-yl-1-ol (36). Attempts to rearrange this to pentacos-24-yl-1-ol were unsuccessful, probably due to the very long reaction times required. This problem combined with the accumulating evidence of the carcinogenic properties of HMPA necessitated a change in strategy.



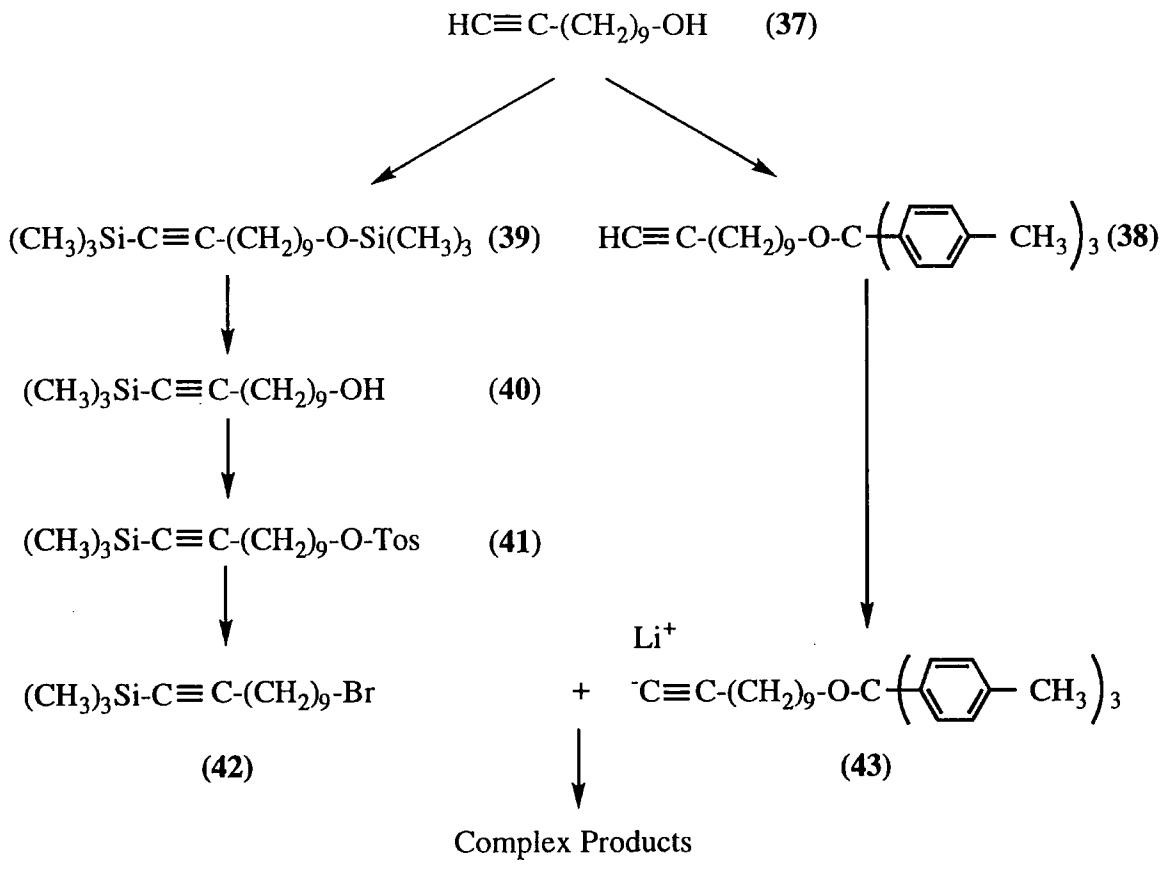
Scheme 11 *Alkylation of a lithium alkyne with a 12-bromododecanol derivative as a means of building long chain hydrocarbons.*

In order to obtain very long chain lengths with minimal labour the chain length should be doubled at each addition. This could be achieved using a chain with an electrophilic group (A) at one end and nucleophilic group (B) at the other, in conjunction with effective, yet easily removed protecting groups (a and b) (Scheme 12); when brought together, A and B double the chain length by forming a grouping M. Typically M would contain a carbon to carbon double or triple bond, which could be hydrogenated in the final stage. The presence of unsaturated groups is advantageous since a prolonged sequence of methylene groups renders the material highly crystalline and insoluble. This would undoubtedly have been a handicap in the previous Schemes 9 and 11. It is preferable that the double bond is *cis*, as it has been shown that the introduction of *cis* >C=C< lowers the melting point more than the corresponding *trans* >C=C<.



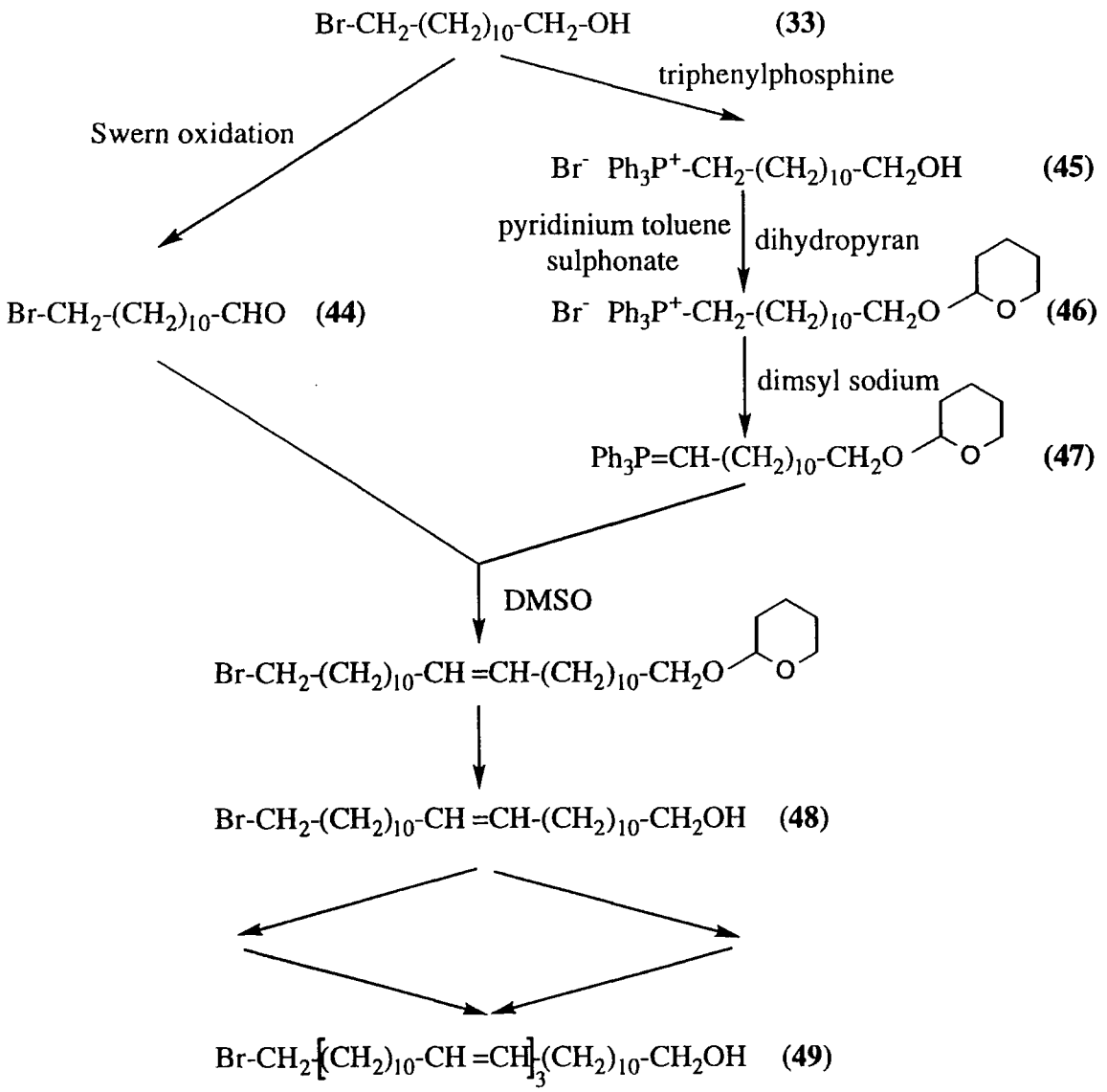
Scheme 12 *A potential method for forming long chains; doubling the chain length at each addition.*

This strategy was first attempted using undec-10-yn-1-ol (37) shown in Scheme 13. The alcohol functionality could be either protected as the tri-p-tolylmethyl ether (38) (trimtyl ether) or converted to the bromide to form the electrophilic group. An attempt was made to protect the proton of the terminal acetylene group as the trimethylsilyl derivative. Treatment of undec-10-yn-1-ol with butyl lithium and chlorotrimethylsilane formed the C, O bis trimethylsilyl derivative (39). Hydrolysis of the O-trimethylsilyl group regenerated the alcohol (40) which was then converted into the tosyl derivative (41) from which the bromide (42) was easily accessible. However, when 1-bromoundec-10-yltrimethylsilane (42) was treated with the lithium derivative of undec-10-ynyl trimtyl ether (43), a complex mixture was produced. This was caused by rapid distribution of the $-SiMe_3$ group between the two acetylenes. Other protecting groups, including more hindered silanes were tried but satisfactory protection of the acetylene group under reaction conditions was not achieved.



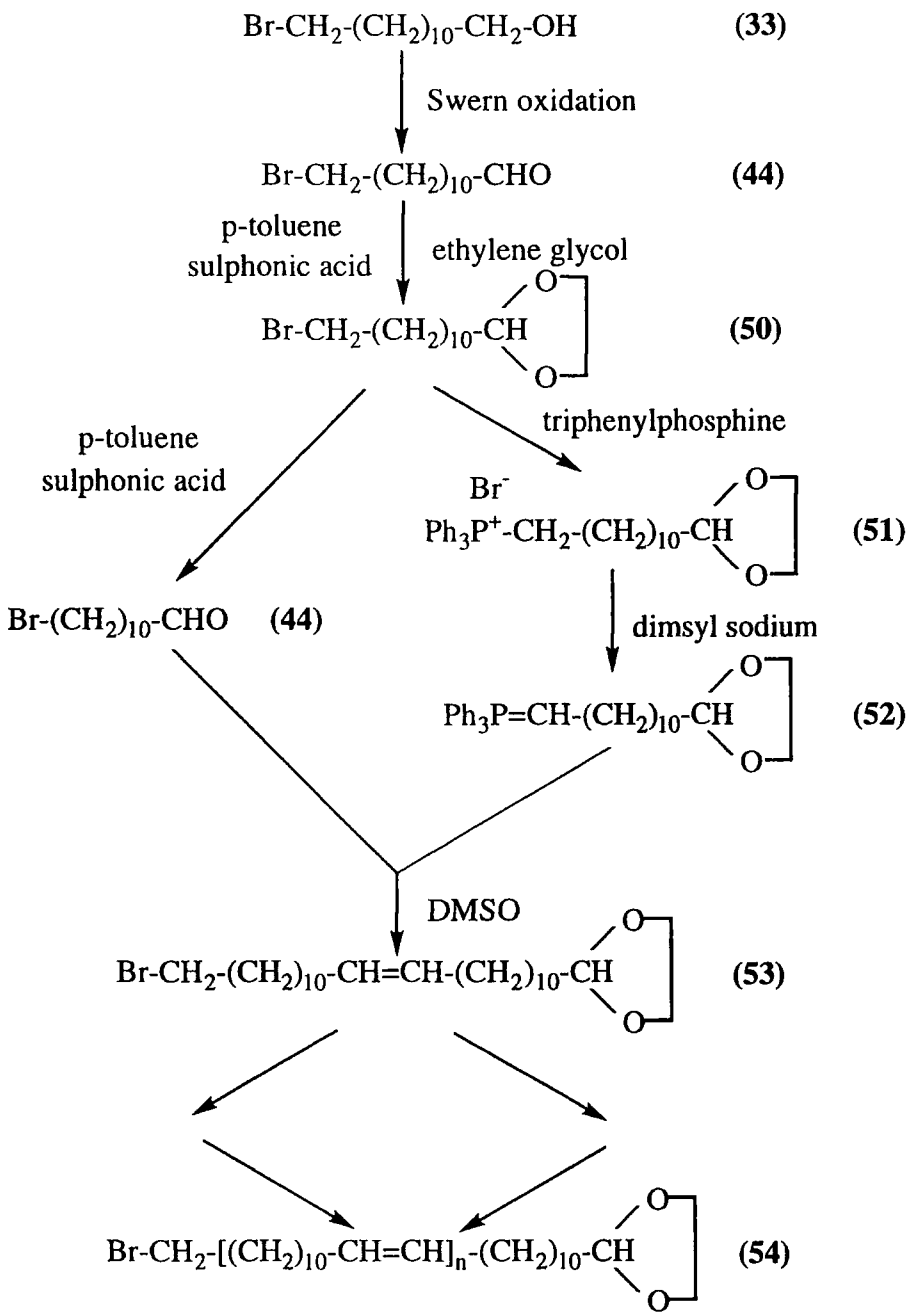
Scheme 13 *An attempt at chain doubling; alkylation of a lithium alkyne derivative with an alkyl bromide derivative.*

A new scheme was developed using the Wittig reaction as the method for the chain-doubling reaction (Scheme 14). 12-Bromododecan-1-ol (33) was used as a starting material. This underwent either a Swern oxidation to form the corresponding aldehyde (44) or treatment with triphenylphosphine, forming 12-hydroxydodecyltriphenylphosphonium bromide (45), a crystalline salt. The alcohol functionality was protected as the tetrahydropyranyl ether (46) by reaction with dihydropyran and a trace of pyridinium toluene sulphonate. Treatment of the resulting 12-(tetrahydropyran-2-yl)oxydodecyltriphenylphosphonium bromide (46) with dimsylsodium formed the ylide (47) which was reacted with 12-bromododecanal (44) in DMSO to give some 24-bromotetracos-12-enol (48)(the Wittig reaction), although the yields were low. Change to a less polar solvent increased the yield. The resulting 24-bromotetracos-12-enol (48) underwent a Swern oxidation to form the corresponding C_{24} aldehyde, and repetition of the above procedure gave the desired 48-bromooctatetraconta-12,24,36-trienol tetrahydropyranyl ether (49).



Scheme 14 *The Wittig reaction as a means of chain doubling.*

The need for a Swern oxidation at each stage was undesirable, so the strategy was further developed by oxidising the 12-bromododecanol (33) to the corresponding aldehyde (44), by the Swern technique, and protecting the aldehyde group as the ethylene acetal (50) (Scheme 15). This was done by heating the aldehyde with ethylene glycol, trimethyl orthoformate and p-toluene sulphonic acid. Repeated Swern oxidations were now unnecessary as removal of the protecting group directly formed the aldehyde. This deprotection was achieved by carrying out the reaction on a chromatographic column, the silica being impregnated with an aqueous solution of p-toluene sulphonic acid. The reaction is driven to completion by the cascade process which occurs in the column.



Scheme 15 *Protection of the aldehyde functionality as the ethylene acetal, thereby removing the need for repeated Swern Oxidations.*

24-Bromotetracosa-12-enal ethylene acetal (53) was made by this method in ~40% yield and recrystallised to remove residual 12-bromododecanal ethylene acetal (50). Removal of the C_{24} ethylene acetal protecting group was attempted under the conditions used for the C_{12} compound but this led to some unreacted material being eluted. Addition of tetrahydrothiophene, chosen to maintain acidity whilst improving solubility of the substrate in the aqueous phase, to the p-toluene sulphonic acid / silica gel mixture led to complete hydrolysis. Treatment of the 24-bromotetracos-12-enal

ethylene acetal (53) with triphenylphosphine formed a non-crystalline salt. This was reacted with dimsylsodium to give the ylide, which was extracted in hexane and reacted with 24-bromotetracos-12-enal to give a 30% yield of 48-bromooctatetraconta-12,24,36-trienal ethylene acetal (54, n=3). Removal of the ethylene acetal protecting group and formation of the triphenylphosphonium salt of the C_{48} compound were achieved in a manner analogous to that of the C_{24} material. The Wittig reaction between the C_{48} aldehyde and C_{48} ylide gave an 8% yield of 96-bromohexanonaconta-12,24,36,48,60,72,84-heptaenal ethylene acetal (54, n=7), which was purified by chromatography on alumina to remove residual C_{48} aldehyde. A further chain doubling produced a small amount of the C_{192} homologue (54, n=15), although this was probably impure and deteriorated on storage. Wittig reactions were also carried out between aldehydes and triphenylphosphonium salts of different chain lengths: for example, C_{48} aldehyde and C_{12} triphenylphosphonium bromide readily gave 60-bromohexaconta-12,24,48-trienal ethylene acetal (54, n=4).

In order to form the n-alkane the terminal functionalities had to be removed. The aldehyde functionality was removed by treatment with the ylide derived from a salt such as n-octyltriphenylphosphonium bromide. This particular ylide was reacted with the aldehyde of the C_{48} and C_{96} homologues in hexane to give 1-bromohexapentaconta-12,24,36,48-tetraene (C_{56}) and 1-bromotetrahecta-12,24,36,48,60,72,84,96,-octaene (C_{104}) respectively. The bromine was removed by reduction with lithium triethylborohydride to form the poly-alkene which was then hydrogenated at 150°C in ethyl palmitate to form the alkane hexapentacontane ($C_{56}H_{114}$).

In order to reach compounds with 100 plus carbon atoms it was vital that the yields were maximised and that the purity of the starting material and the intermediates was very high.

There are potentially two major sources of impurity present at each doubling :

1. Incomplete removal of the ethylene acetal protecting group during formation of the aldehyde. At the C_{12} doubling stage this would lead to the presence of residual 12-bromododecanal ethylene acetal (50) in the 24-bromotetracosa-12-enal ethylene acetal (53). Whiting was able to remove this by recrystallisation.

2. Inadvertent removal of some of the ethylene acetal protecting group during the formation of the triphenylphosphonium bromide (51) would give a chain with a free aldehyde at one end and the potential to form an ylide at the other. With this material present at the C_{12} doubling stage, the Wittig product would contain the impurity 36-bromohexatriaconta-12,24,-dienal ethylene acetal (54, n=2). Whiting found this difficult to remove from (53) so the triphenylphosphonium bromide (51) derived from 12-bromododecanal ethylene acetal was itself recrystallised. (The triphenylphosphonium salts of the longer chain homologues were non-crystalline so the ethylene acetal group was regenerated, by heating the salt with ethylene glycol and p-toluene sulphonic acid in dichloromethane).

It is particularly important that these impurities are removed at the C_{24} stage since subsequently their presence would lead to products of n carbon atoms containing homologues with (n+12) and (n-12) carbons, which would be increasingly difficult to remove as the chain length grew longer.

The use of ether and hexane in Wittig reactions proved unreliable so a different variation was used whereby the triphenylphosphonium salt was heated with the aldehyde, potassium carbonate and 18-crown-6 in THF under nitrogen. This gave better yields than the previous method, particularly at higher chain lengths.

This new Wittig method, combined with further modification allowed a pure batch of the C_{96} material (54, n=7) to be prepared. Two further doublings were achieved, forming C_{192} (54, n=15) and C_{384} (54, n=31), as well as compounds of intermediate chain length. These were converted into the polyenes as described above and hydrogenated in ethyl palmitate to form n-alkanes with 102, 150, 198, 246, 294 and 390 carbon atoms. The most probable impurity would be the (n+12) or (n-12) homologues ; however, these are only likely to be present in 0.5% - 5% in the 246 carbon paraffin for example.

Chapter 3

The Development of New Methodology for the Synthesis of Monodisperse Long Chain Alkanes

CHAPTER 3

The Development of New Methodology for the Synthesis of Monodisperse Long Chain Alkanes

3.1 Nomenclature

Due to the complicated IUPAC nomenclature used for the long chain hydrocarbons and their precursors, a shorthand system has been used in the following two chapters. This is outlined below.

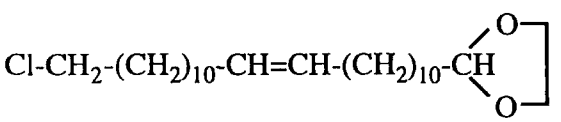
The Carbon Chain

This is simply described by stating the number of carbon atoms in the longest chain, e.g.: C_{12}, C_{24}, C_{48} etc. For clarity the position and number of double bonds is omitted, though in each case the double bonds are present at regular intervals, every 12 carbon atoms, along the chain.

The Terminal Functional Groups

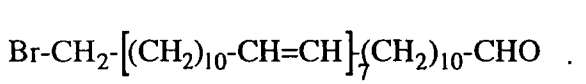
Five terminal functional groups are referred to throughout the syntheses. The product of each Wittig reaction has either a chlorine or a bromine at one terminus and an ethylene acetal group at the other. Therefore such a compound is described as a chloro / bromo acetal.

For example, C_{24} chloro acetal :



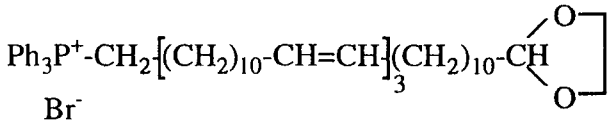
In order to double the chain length, the ethylene acetal group is removed to form an aldehyde group, which is described as a chloro / bromo aldehyde. The removal of the ethylene acetal group is referred to as "deprotection".

For example, C_{96} bromo aldehyde :



Alternatively, treatment with triphenylphosphine transforms the halogen into the triphenylphosphonium halide.

For example, C_{48} triphenylphosphonium bromide acetal :



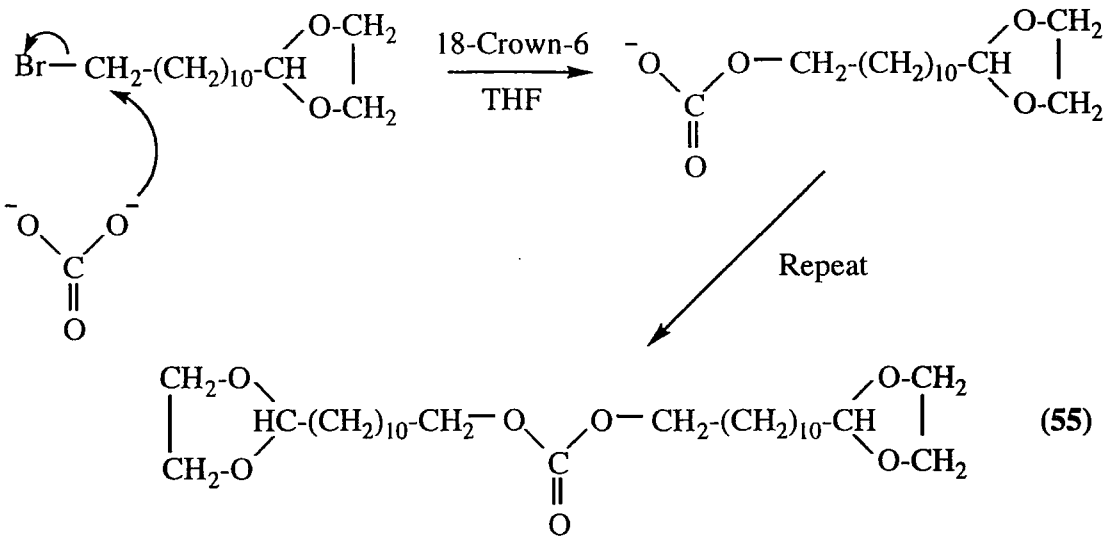
The nomenclature used for any further functional groups will be described as they are encountered.

3.2 Chain Doubling Using 12-Chlorododecanol as Starting Material

The first attempts to synthesise long chain hydrocarbons in Durham began in November 1991. The work was carried out by Dr GM Brooke and Dr DG Proctor, who attempted a method of chain doubling similar to that developed by Professor Whiting in Bristol. After consultation with Whiting, it was decide that 12-chlorododecanol would be used as the starting material as opposed to the bromo analogue used extensively in Bristol. It was hoped that this change would prevent the occurrence of two sources of impurity that Whiting had encountered:

(i) Throughout the synthesis, the bromo compound had been frequently contaminated with the corresponding chloro analogue. The problem had been caused by the use of chlorinated solvents, particularly dichloromethane, in the presence of adventitious phase transfer catalysts. Indeed it is possible that such catalysts may have included the triphenylphosphonium salts themselves.

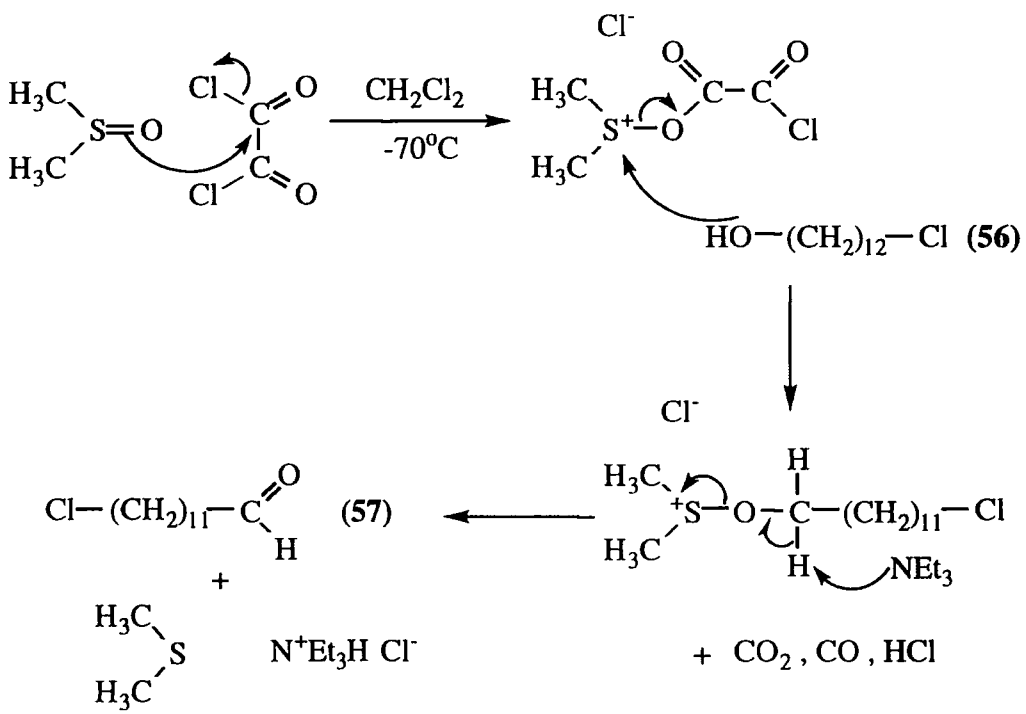
(ii) The reactivity of the $-CH_2Br$ group towards nucleophiles led to the formation of side products. In particular, reaction between the $-CH_2Br$ group and potassium carbonate / 18-crown-6 ether used in the Wittig reaction led to the formation of a carbonate ester (55) (Scheme 16). This was unlikely to be a problem when using the chloro analogue, since Cl^- is much less readily removed than Br^-.



Scheme 16 *Formation of the carbonate ester (55).*

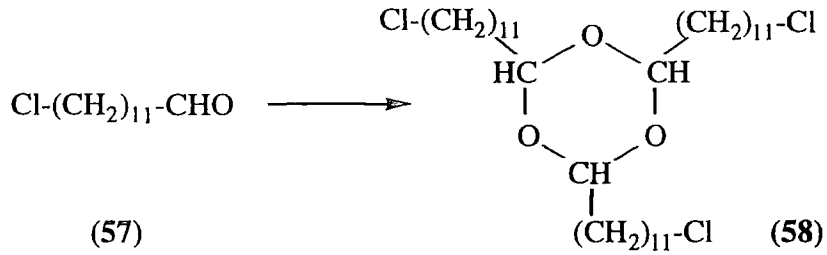
3.2.1 Preparation of C_{12} Chloro Acetal (59) [14]

The 12-chlorododecanol (56)[15] was oxidised to the corresponding aldehyde (57) using the Swern technique (Scheme 17).



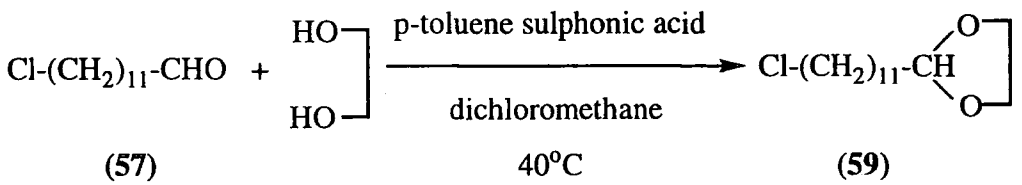
Scheme 17 *Swern oxidation of C_{12} chloro alcohol (56) to give C_{12} chloro aldehyde (57).*

The aldehyde (57) was analysed by ^1H nmr to show the reaction had gone to completion. Care had to be taken not to heat the aldehyde (57) above room temperature as it is prone to form the trimer (58) (Scheme 18).



Scheme 18 *Formation of C_{12} chloro aldehyde trimer (58).*

The ethylene acetal protecting group was added by heating the C_{12} chloro aldehyde (57) with ethylene glycol and p-toluenesulphonic acid in dichloromethane (Scheme 19).

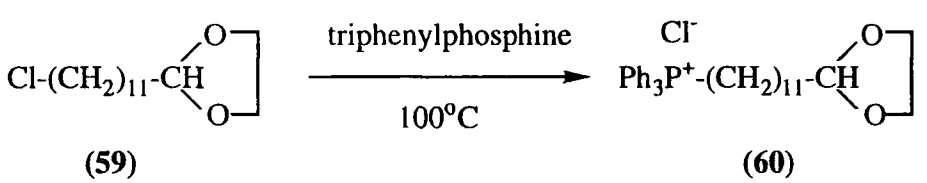


Scheme 19 *Preparation of C_{12} chloro acetal (59).*

The product was purified using the short path distillation unit (KDL-1) manufactured by U.I.C. GmbH Alzenau, Germany. The product was recrystallised from light petroleum bp 40-60°C and the material produced was passed through the KDL-1 once more to give anhydrous material. At each stage the residues from the KDL-1 were combined with the mother liquors from the recrystallisations and reworked in order to maximise yields. An overall yield of 71% was achieved in converting the C_{12} chloro alcohol (56) to the chloro acetal (59).

3.2.2 Preparation of C_{12} Triphenylphosphonium Chloride Acetal (60) [16]

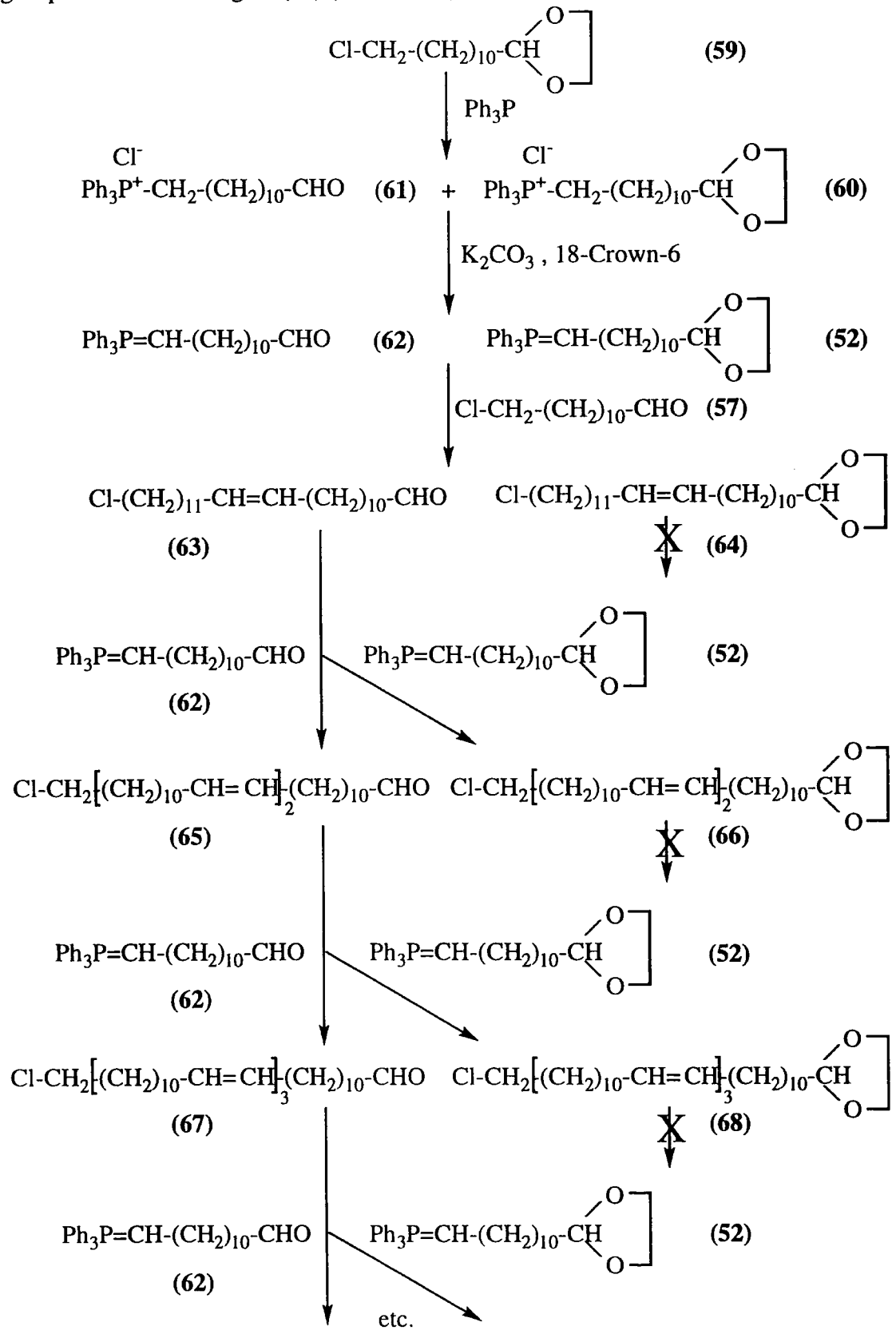
The C_{12} triphenylphosphonium chloride acetal (60) was prepared by heating the 12-chloro acetal (59) with four equivalents of triphenylphosphine at 100°C (Scheme 20).



Scheme 20 *Preparation of C_{12} triphenylphosphonium chloride acetal (60).*

No solvent was used and the reagents were stirred for 3 weeks, after which ^{1}H nmr showed the reaction to be complete. Removal of the excess triphenylphosphine from the salt was achieved using an acetonitrile / light petroleum bp 40-60°C extraction, the

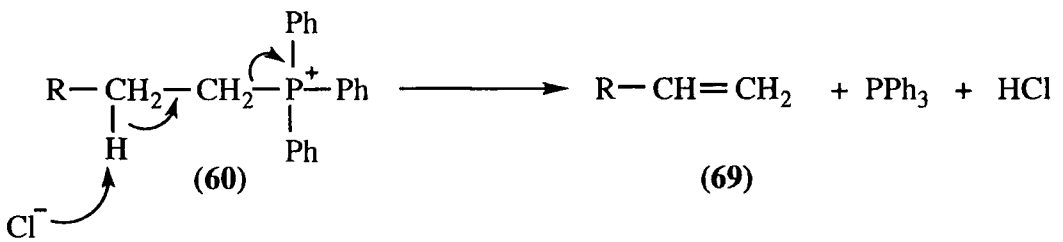
triphenylphosphine being soluble in the petrol layer while the salt remained in the acetonitrile. ^1H nmr analysis of the salt showed that some deprotection of the aldehyde group had occurred to give (61) (Scheme 21).



Scheme 21 *Formation of C_{36} and C_{48} impurities as a result of using material containing deprotected triphenylphosphonium salt (61) in a C_{12}+C_{12} Wittig reaction.*

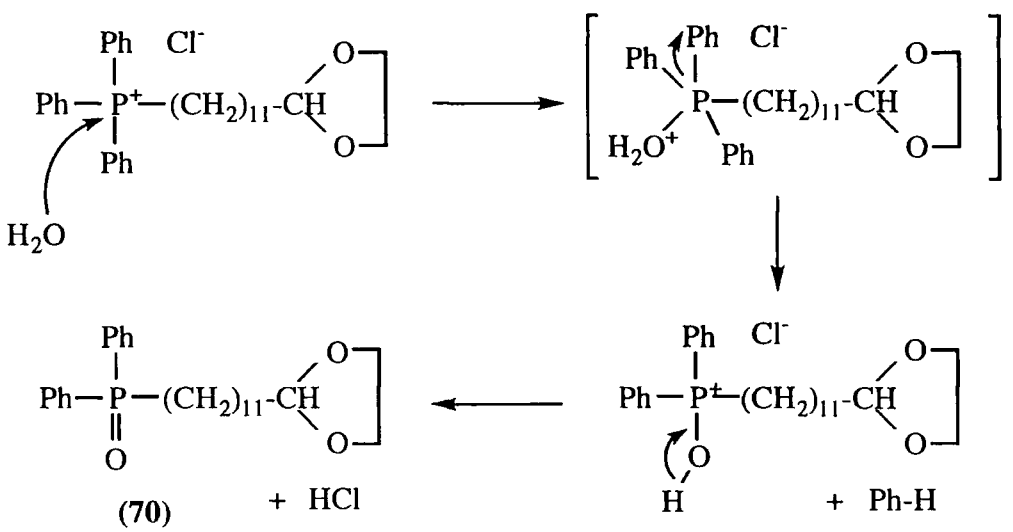
If this deprotected material were to be used in a Wittig reaction it would lead to the formation of a C_{36} impurity (65, 66). The C_{36} chloro aldehyde (65) could couple with further C_{12} ylide (62, 52) forming a C_{48} chain (67, 68), which could likewise form longer chains. It was therefore necessary to regenerate all of the ethylene acetal protecting group. This was achieved by dissolving the salt in dichloromethane and heating the solution with ethylene glycol and p-toluenesulphonic acid.

The salt was formed in good yields, yet two side products were observed in the petrol layers from the extractions. A vinylic species was identified (69) (Scheme 22) possibly formed due to the chloride ion acting as a base and extracting a proton from the carbon in the β position to the triphenylphosphine in the salt (60), leading to elimination of triphenylphosphine and consequently formation of a double bond.



Scheme 22 *Formation of vinylic impurity (69) during the preparation of C_{12} triphenylphosphonium chloride acetal (60).*

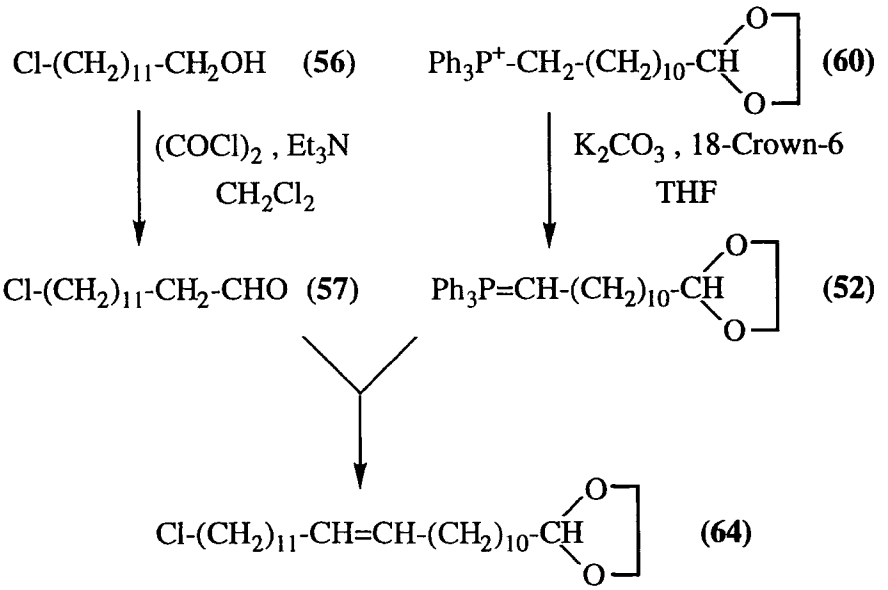
The salt proved to be very hygroscopic and the water led to slow decomposition to form the second side product, the diphenylphosphine oxide compound (70) (Scheme 23).



Scheme 23 *Formation of the diphenylphosphonium oxide (70) of C_{12} triphenylphosphonium chloride acetal (60).*

3.2.3 The $C_{12} + C_{12}$ Wittig Reaction → C_{24} Chloro Acetal (64) [14]

The first Wittig reaction was attempted using the method developed by Whiting. The C_{12} chloro aldehyde (57) [formed directly by Swern oxidation of the alcohol (56)(Scheme 17) and purified using the KDL-1] and the C_{12} triphenylphosphonium chloride acetal (60) were heated under reflux in THF, with potassium carbonate and 18-crown-6 ether, under nitrogen (Scheme 24).



Scheme 24 *Preparation of C_{24} chloro acetal (64).*

After 88 hours the reaction was stopped and the crude product filtered to remove excess K_2CO_3. The remaining solution was dissolved in acetonitrile and the C_{24} material was extracted with light petroleum bp 40-60°C, leaving the polar triphenylphosphine oxide and other polar side products in the acetonitrile. The resulting solid was chromatographed on silica using 10% diethyl ether / 90% light petroleum bp 40-60°C, to remove any remaining phosphorus side products. ^1H nmr analysis of one Wittig reaction showed that these included the C_{12} diphenylphosphine oxide (70) (Scheme 23). Infra-red analysis showed the presence of carbonate ester (55) (Scheme 16), as Whiting had found in his synthesis when using the bromine analogues, so it became standard practice to carry out a $LiAlH_4$ reduction of the product. This would reduce any of the carbonate ester (55) to 12-hydroxydodecanal ethylene acetal. All C_{12} materials were removed from the higher boiling C_{24} product and C_{36} impurities by distillation at 80°C using the KDL-1. Increasing the temperature to 140°C allowed the

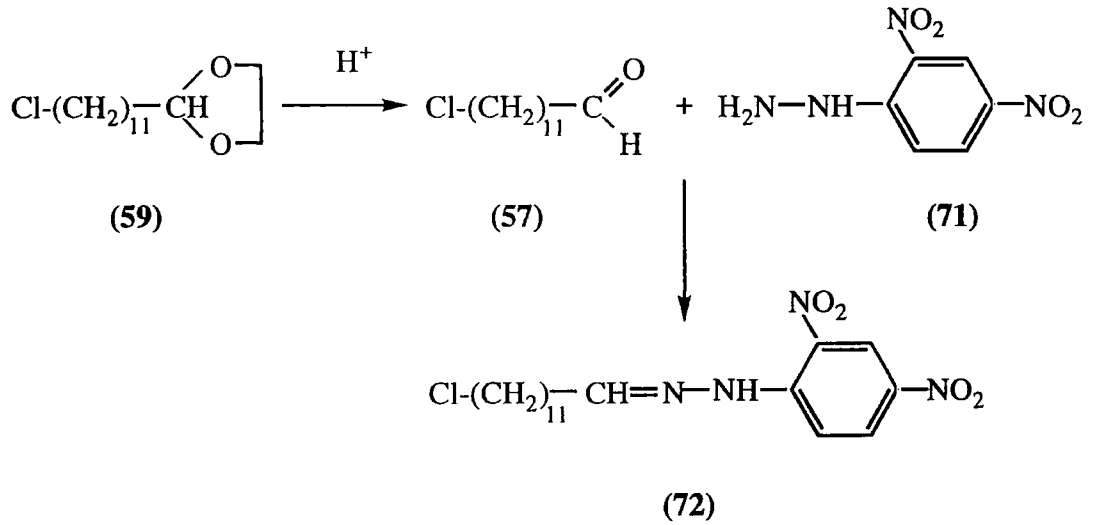
C_{24} material to be distilled from the higher boiling C_{36}, C_{48} and C_{60} compounds, which remained in the residue.

Interestingly, the ^1H nmr analysis of the C_{12} impurities removed from the C_{24} chloro acetal (64) using the KDL-1, showed them to contain a large amount of C_{12} chloro acetal (59). This was not present in any of the reagents, since the C_{12} chloro aldehyde (57) used was formed directly from the alcohol (56) by Swern oxidation, whilst the C_{12} triphenylphosphine chloride acetal (60) had been extensively washed with light petroleum bp 40-60°C, which would have removed any unreacted C_{12} chloro acetal (59). Also, ^1H nmr of both reactants had shown no C_{12} chloro acetal (59) to be present, so this compound must have formed during the Wittig reaction by an unusual trans-acetalation reaction, whereby the ethylene acetal protecting group of the C_{12} triphenylphosphonium chloride acetal (60) transfers to the C_{12} chloro aldehyde (57). This would leave some of the C_{12} triphenylphosphonium chloride with an unprotected aldehyde group (61). On forming the ylide, a C_{12} chain with reactive groups at each end would be produced (62), accounting for the presence of the C_{36} material (Scheme 21). Using this method 365g of pure C_{24} chloro acetal (64) was formed with an overall yield of 47%.[14]

3.2.4 Preparation of the 2,4-Dinitrophenylhydrazone Derivatives

Analysis of the resulting material from the first chain doubling reaction was initially attempted by GLC, as used by Whiting; however, this proved difficult since temperatures between 200°C-330°C were required. It was therefore was decided to prepare the 2,4-dinitrophenylhydrazone (2,4-DNP) derivatives of the aldehydes, (72) (Scheme 25), which could be monitored using reverse phase high performance liquid chromatography (HPLC). The 2,4-DNP derivatives were prepared directly from the purified Wittig products by stirring overnight with 2,4-dinitrophenylhydrazine (71) and concentrated sulphuric acid (which removed the ethylene acetal protecting group in the process) in methanol. 2,4-DNP derivatives of C_{12}, C_{24} and C_{36} were formed and used as standards (a sample of C_{36} chloro acetal was produced from a Wittig reaction using C_{12} triphenylphosphine chloride acetal and C_{24} chloro aldehyde[16]). Various HPLC conditions were tried, the best results being achieved using a C_1 reverse phase column

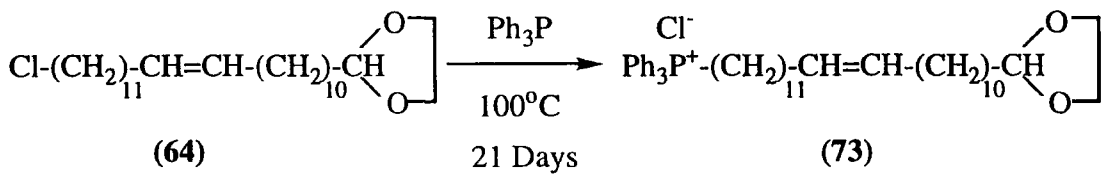
(Hypersil 5 SAS 25cm x 4.6mm) and 70% THF / 30% H_2O mobile phase. The C_{24} chloro acetal (64) was shown to contain no C_{12} nor C_{36} impurities.



Scheme 25 *Preparation of C_{12} 2,4-DNP derivative (72).*

3.2.5 Preparation of C_{24} Triphenylphosphonium Chloride Acetal (73) [16]

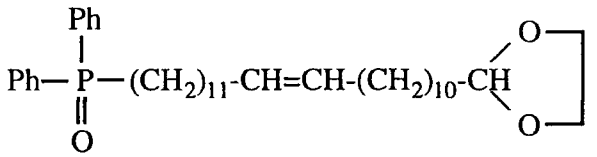
This was attempted under similar conditions to those used for the C_{12} analogue. The C_{24} chloro acetal (64) was heated at 100°C with 6 equivalents of triphenylphosphine under nitrogen (no solvent) for 21 days, when a sample studied by ^1H nmr showed the reaction to be complete (Scheme 26).



Scheme 26 *Preparation of C_{24} triphenylphosphonium chloride acetal (73).*

The salt (73) was separated from excess triphenylphosphine by stirring for a short time with light petroleum bp 100-120°C at 85°C, followed by decantation of the petrol. (Care had to be taken when heating the triphenylphosphonium chloride salts, following one occasion when C_{12} triphenylphosphonium chloride acetal (60) was heated in boiling light petroleum bp 100-120°C causing decomposition back to C_{12} chloro acetal (59) and triphenylphosphine). This was repeated six times and ^1H nmr showed it to be an effective way of removing the excess triphenylphosphine. It was also observed that some removal of the ethylene glycol protecting group had taken place during the salt preparation. The aldehyde group was reprotected by heating overnight with ethylene

glycol and p-toluenesulphonic acid in dichloromethane. The resulting solution was washed twice with aqueous potassium carbonate solution, the aqueous layer being extracted with dichloromethane. ^{1}H nmr of the resulting salt showed it to contain some C_{24} diphenylphosphine oxide derivative (74), as the C_{12} analogue had done.

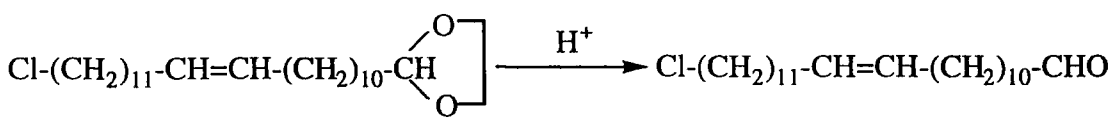


(74)

The C_{24} triphenylphosphonium chloride acetal (73) was very hygroscopic and a broad signal at 2.5ppm representing water was present in the ^{1}H nmr spectrum. Consequently, the salt was dried by azeotropic distillation with benzene in a Dean and Stark apparatus and was stored as a solution in freshly dried THF under nitrogen. Aliquots of the solution could then be taken for use in the Wittig reaction as required. However, this precaution proved unsatisfactory as one batch of salt stored in this manner was shown to contain water when analysed by ^{1}H nmr five months later and so had to be redried.

3.2.6 Deprotection of C_{24} Chloro Acetal (64) → C_{24} Chloro Aldehyde (63) [14]

Removal of the ethylene acetal protecting group from C_{24} chloro acetal (64) was successfully achieved using the method developed by Whiting[11] : the C_{24} chloro acetal (64) was passed through a silica column impregnated with an aqueous solution of p-toluenesulphonic acid, using 25% dichloromethane / 75% light petroleum bp 40-60°C (Scheme 27). The resulting material was analysed by ^{1}H nmr to ensure complete deprotection.



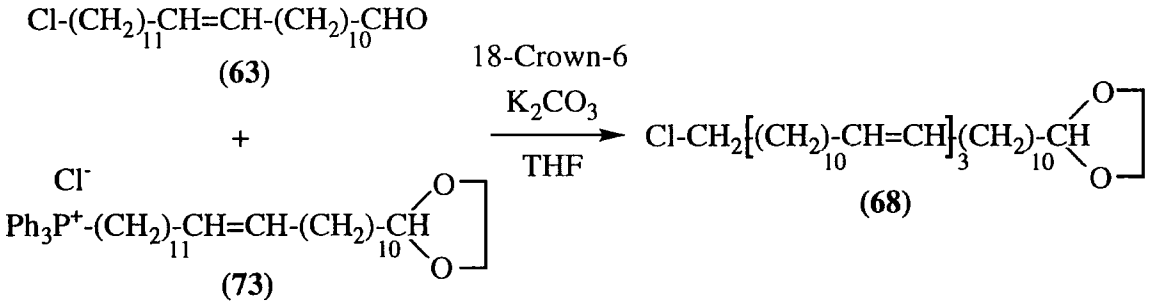
(64) **(63)**

Scheme 27 *Deprotection of C_{24} chloro acetal (64).*

3.2.7 The C_{24} + C_{24} Wittig Reaction → C_{48} Chloro Acetal (68). [15]

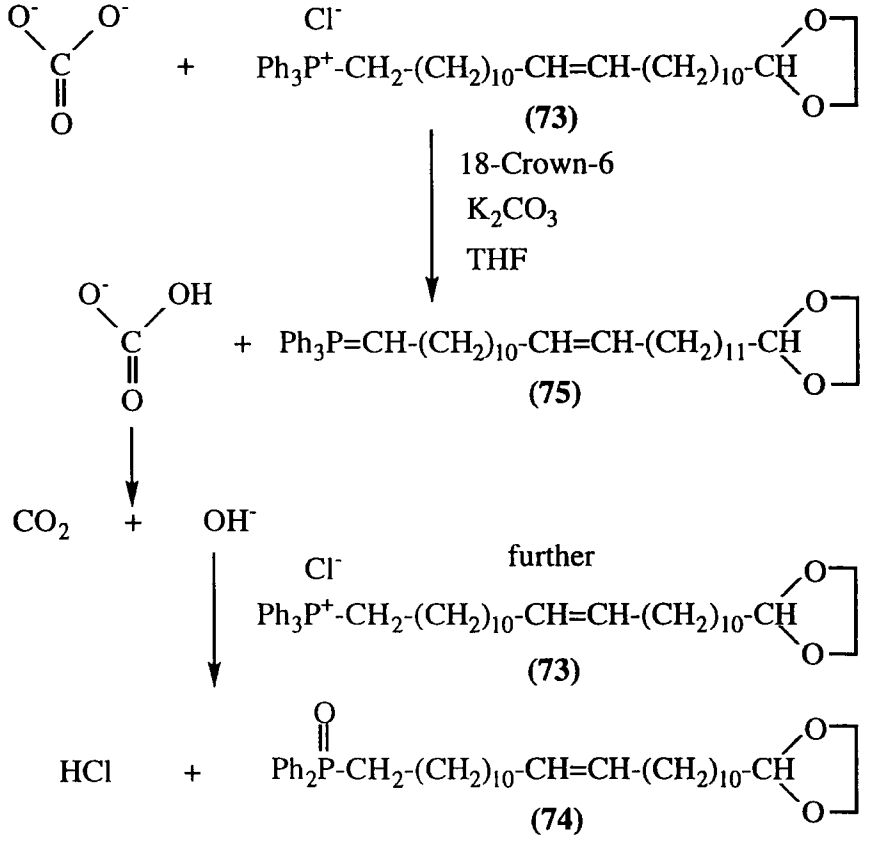
The C_{24} coupling reaction was first attempted using the method which had proved successful with the C_{12} analogue. A solution of the C_{24} triphenylphosphonium chloride

acetal (73), in THF, was heated under reflux with C_{24} chloro aldehyde (63), potassium carbonate and 18-crown-6 ether under nitrogen.



Scheme 28 *Preparation of C_{48} chloro acetal (68).*

After 7 days a sample was analysed by ^1H nmr, revealing the presence of a large amount of unreacted aldehyde (63). The reaction was continued for a further 10 days, when a small amount of the desired C_{48} chloro acetal (68) was detected. However, a large proportion of C_{24} chloro aldehyde (63) was still present so the reaction was abandoned. It seemed that the C_{24} coupling reactions were failing due to problems in forming the ylide (75). When potassium carbonate is used as the base, hydrogen carbonate is formed (Scheme 29).



Scheme 29 *Decomposition of hydrogen carbonate to water and consequently formation of the diphenylphosphine oxide derivative (74).*

Once formed, the hydrogen carbonate must decompose to form carbon dioxide and hydroxide ion, which would convert further triphenylphosphonium salts to the diphenylphosphine oxide derivative (74)

3.2.7.1 A New Base for Wittig Reactions : Potassium Hydride

In order to avoid hydrolysis of the triphenylphosphonium salts, the C_{24} coupling was attempted using a new base, potassium hydride. A solution of C_{24} triphenylphosphonium chloride acetal (73) was added to the potassium hydride in THF which had been freshly distilled from $LiAlH_4$. 18-crown-6 ether was again used to complex the potassium cation and the mixture was stirred at 40°C overnight to form the orange / red ylide. Addition of C_{24} chloro aldehyde (63) instantly formed a cream coloured suspension, which was stirred under reflux. A number of small scale doublings were attempted, using slight excesses of base and salt, designed to give a slight excess of the ylide. However, ^1H nmr routinely showed 20-30% unreacted aldehyde (63) to be present after 2-3 hours, and leaving overnight led to little change. It was concluded that this was due to low levels of ylide formation, which had two potential causes :

(i) The KH was not reacting quantitatively with the salt (73).

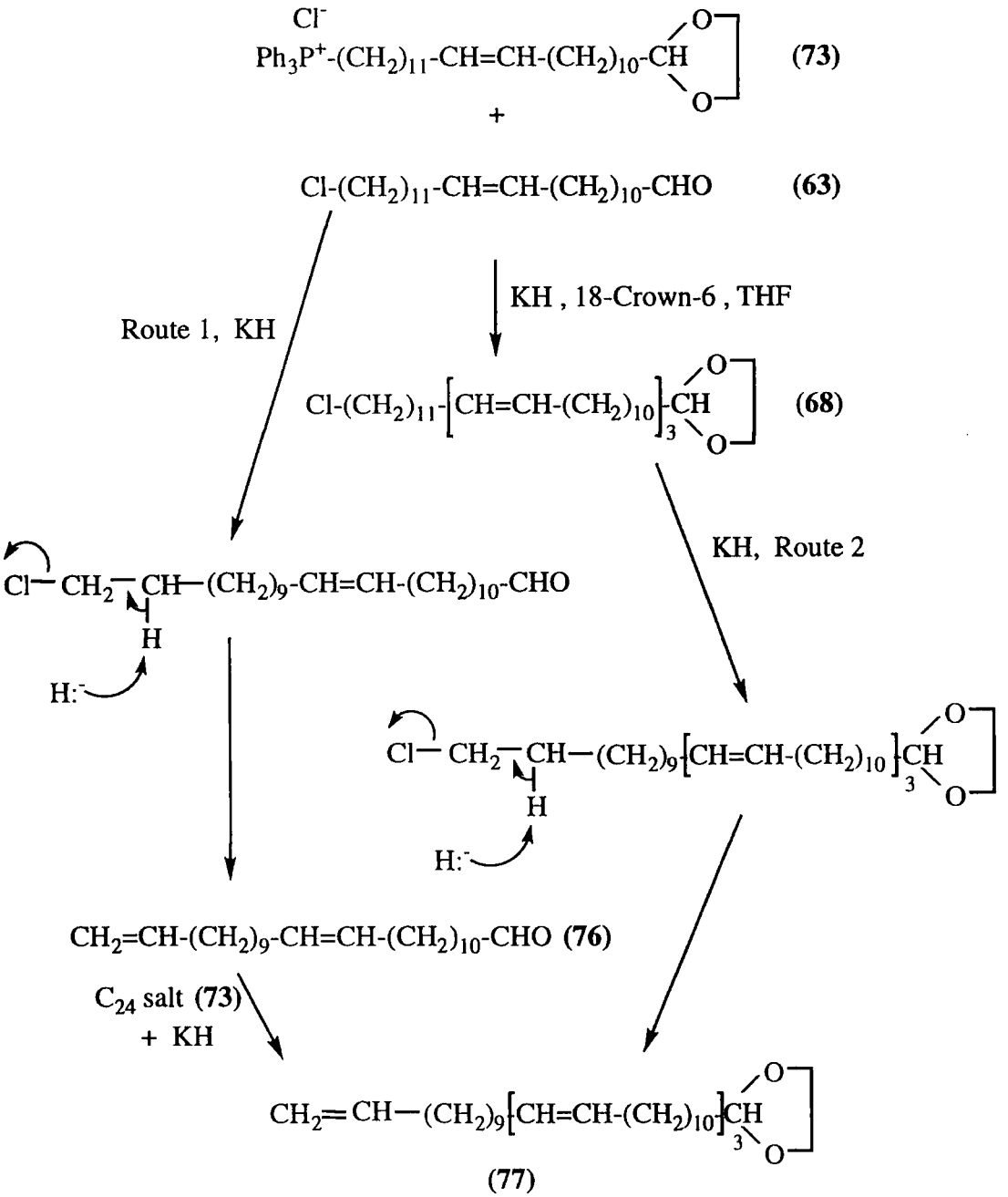
(ii) The ylide (75) formed effectively, but was destroyed in a further reaction.

It was decided that the first of these was the most likely scenario, since the latter would lead to production of another species, which was never detected. Therefore, the reaction was next attempted using two equivalents of KH to one equivalent of aldehyde (63) and salt (73). This was more successful, ^1H nmr showing only 3% of unreacted aldehyde to be present.

A further improvement to the method was achieved using ^{31}P nmr to monitor the levels of ylide formation. Knowing the exact amount of ylide formed made it possible to add the precise amount of aldehyde, thereby reducing waste of precious material and lowering the probability of side reactions occurring. Using this method the C_{24} doubling was scaled up, the largest reaction undertaken used 17.76g (25.7mmol) of C_{24} triphenylphosphonium chloride acetal (73)[14]. After 48 hours, a sample of this, monitored by ^{31}P nmr, showed no unreacted salt and an 85% yield of ylide (75). 8.4g (21.8mmol) of C_{24} chloro aldehyde (63) were added, ultimately producing 14.33g of

C_{48} chloro acetal (68) in 85% yield. In order to achieve such yields it was crucial that the solvent and all the reagents were thoroughly dry.

The resulting material was purified by chromatography on silica, using 10% diethyl ether / 90% light petroleum bp 40-60°C and was recrystallised from light petroleum bp 40-60°C. However, ^1H nmr analysis showed a C_{48} vinylic impurity (77) to be present (Scheme 30).

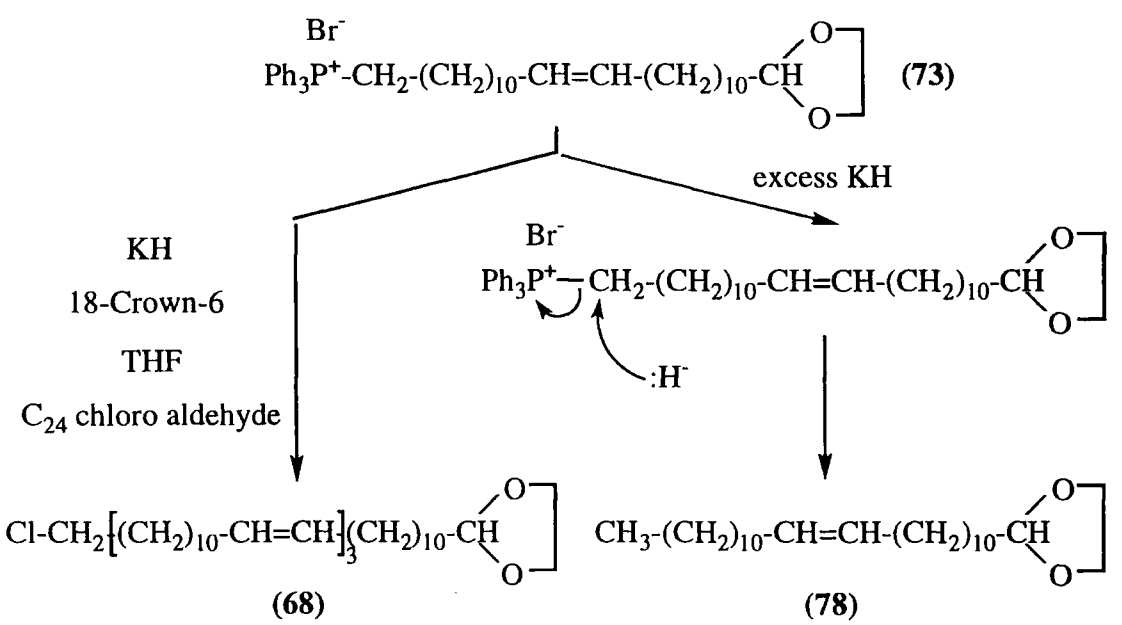


Scheme 30 *Formation of a C_{48} vinylic impurity (77) during a C_{24} coupling reaction.*

This must be caused by excess potassium hydride extracting a proton from the carbon β to the chlorine (Scheme 30), either by reacting with the C_{24} chloro aldehyde (63) to

give C_{24} vinyl aldehyde (76), which ultimately forms the C_{48} vinyl acetal (77) (Scheme 30, Route 1) and / or by reacting with the newly formed C_{48} chloro acetal (68), (Route 2). The vinylic impurity proved very difficult to remove by either chromatography or recrystallisation; however, its presence would not ultimately cause a problem in the final hydrocarbon. If treated with triphenylphosphine the vinyl compound (77) would not react and would be easily separated from the resulting triphenylphosphonium bromide. If deprotected it would form C_{48} vinyl aldehyde which would react with C_{48} triphenylphosphonium bromide to give C_{96} vinyl acetal; consequently the vinyl group would remain in the chain. It would however, be removed in any final hydrogenation stage, forming the desired hydrocarbon.

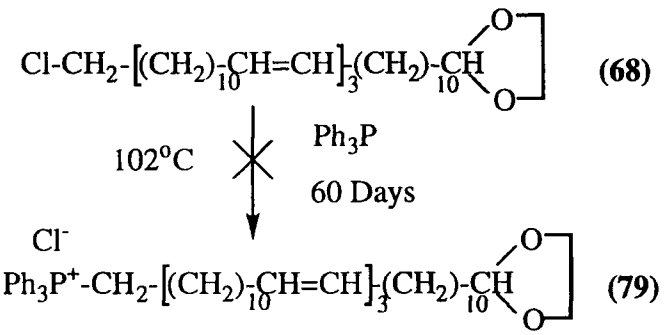
A more serious C_{24} impurity (78), containing a terminal $-CH_3$ group rather than a $-CH_2Br$ group, was observed in the C_{48} product (Scheme 31). This was formed by the hydride ion acting as a nucleophile and displacing triphenylphosphine, which had been observed by ^{31}P nmr, during the ylide formation. It proved virtually impossible to remove this impurity (78) by chromatography [the R_f values of (68) and (78) were very close], though it was achieved by sublimation at 150-180°C, 0.001mm Hg. These problems forewarned of insuperable difficulties in the subsequent $C_{48} + C_{48}$ chain doubling reaction.



Scheme 31 *Formation of a C_{24} impurity with a terminal $-CH_3$ group (78), during a C_{24} coupling reaction.*

3.2.8 Formation of C_{48} Triphenylphosphonium Chloride Acetal (79) [16]

Preparation of the C_{48} triphenylphosphonium chloride acetal (79) was first attempted by the method used for the C_{24} analogue (73). C_{48} chloro acetal (68) was stirred with 4.2 equivalents of triphenylphosphine at 102°C (Scheme 32). The reaction was sampled after 26 days but ^1H nmr showed 38% of unreacted C_{48} chloro acetal to be present. After a further 34 days the ^1H nmr was very complex in the region where the $-CH_2Cl$ and $-CH_2P^+Ph_3Cl^-$ signals are normally found. Clearly the duration of the experiment and the nature of the reaction products were totally unsatisfactory and the procedure was abandoned.

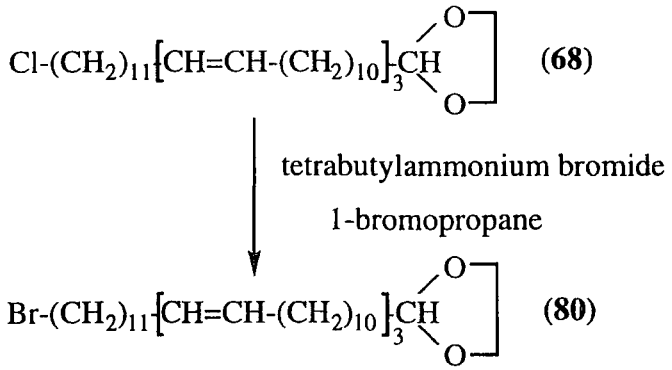


Scheme 32 *Failed preparation of C_{48} triphenylphosphonium chloride (79).*

3.3 The Mixed Halogen Wittig Reaction : Chloro Aldehyde + Triphenylphosphonium Bromide Acetal

3.3.1 Halogen Exchange : C_{48} Chloro Acetal (68) → C_{48} Bromo Acetal (80) [16]

The triphenylphosphine chloride salts had been problematical throughout the synthesis due to their hygroscopic nature, so it was decided to revert back to using the C_{48} triphenylphosphonium bromide, as in the original procedure by Whiting. A halogen exchange reaction was undertaken on some of the C_{48} chloro acetal by refluxing in a freshly dried solution of tetrabutylammonium bromide in 1-bromopropane for 48 hours (Scheme 33). Analysis of a sample by ^1H nmr showed the presence of unreacted chloro compound and slight deprotection of the aldehyde group. Therefore, p-toluenesulphonic acid and ethylene glycol were added and the mixture was refluxed for a further 24 hours. This proved effective, as ^1H nmr showed <0.5% of the chloro analogue (68) and complete regeneration of the ethylene acetal protecting group.



Scheme 33 *Halogen exchange reaction to prepare C_{48} bromo acetal (80).*

3.3.2 The Use of Lithium Diisopropylamide as a Base for the Wittig Reaction

During the C_{24} doubling reaction, a C_{24} impurity with a terminal -CH_3 group (78) had formed, due to displacement of triphenylphosphine by hydride ion (Scheme 31) and had been removed by sublimation. If an analogous impurity formed during the C_{48} doubling reaction it would prove extremely difficult to remove, since the temperature required for sublimation would be prohibitively high. It was therefore decided to use lithium diisopropylamide (LDA) as the base for Wittig reactions, replacing potassium hydride and 18-crown-6 ether. The presence of the two bulky isopropyl groups should prevent the LDA displacing triphenylphosphine in an S_N2 reaction as the hydride had done. However, even if this did occur, the product would be a tertiary amine, which would show up clearly on ^1H nmr and could be removed by an acid wash (although this may lead to removal of the ethylene acetal protecting group).

The new base was first used for a C_{12} coupling to test its effectiveness. Addition of LDA to a solution of C_{12} triphenylphosphonium bromide acetal (51) in THF instantly produced the characteristic orange / red colour of the ylide (52), ^{31}P nmr showing a yield of 85%. This had taken up to 24 hours to achieve using potassium hydride. The ylide (52) was stirred for an hour, when addition of C_{12} chloro aldehyde (57) caused the colour to disappear, leaving a creamy suspension. Early yields of C_{24} chloro acetal (64) were lower than had been hoped (~50%), although this may have been due to an inefficient work up scheme. This had involved removing the THF and passing the remaining material down a silica column in 10% diethyl ether / 90% light petroleum bp 40-60°C. However, on loading the column a sticky mass tended to form, which may have caused a loss in yield. This was improved by first filtering the crude Wittig

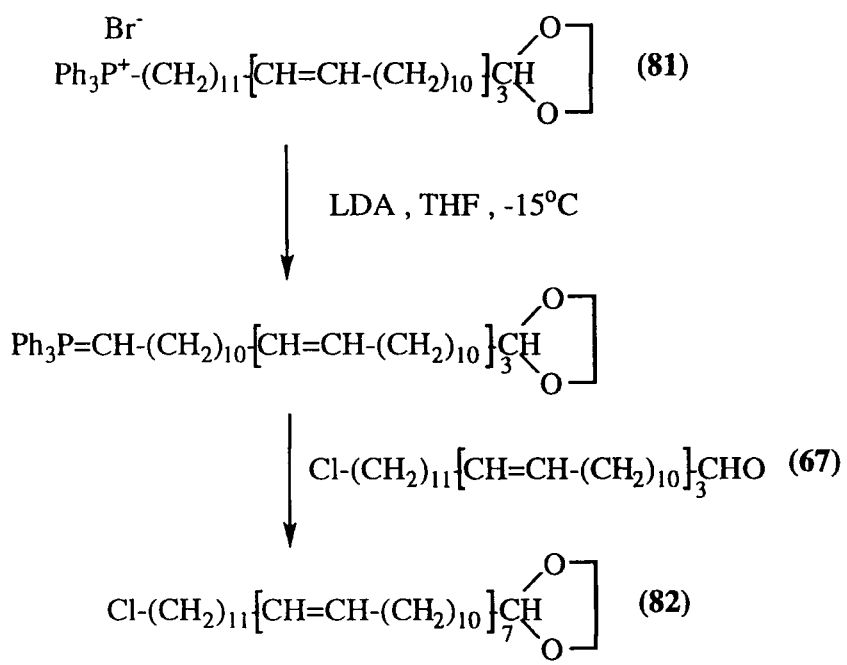
product through a silica plug, using THF as the eluent. Removal of the THF then gave a finely dispersed solid, which was straightforward to chromatograph, using silica and 10% diethyl ether / 90% light petroleum bp 40-60°C to remove polar phosphorus products. The 2,4-DNP derivatives were prepared and analysis by HPLC showed successful removal of any C_{12} impurities.

It was important to determine the *cis / trans* ratio of the carbon to carbon double bonds formed when using this new base, since a high proportion of *trans* double bonds would lower the solubility and melting points of the chains, which may cause problems later in the synthesis. Analysis of the resulting C_{24} chloro acetal (64) by ^{13}C nmr showed the *cis / trans* ratio to be 4. This was identical to that found when using potassium carbonate as the base for Wittig reactions, suggesting few problems would arise in terms of solubility.

Similarly a C_{24} coupling reaction was carried out using LDA, giving an overall yield of C_{48} chloro acetal (68) of 50%[14].

3.3.3 The C_{48} + C_{48} Wittig Reaction → C_{96} Chloro Acetal (82) [16]

The C_{48} triphenylphosphonium bromide acetal (81) obtained from the bromo acetal (80) was treated with LDA and reacted with the C_{48} chloro aldehyde (67) to give C_{96} chloro acetal (82), in a yield of 76%.



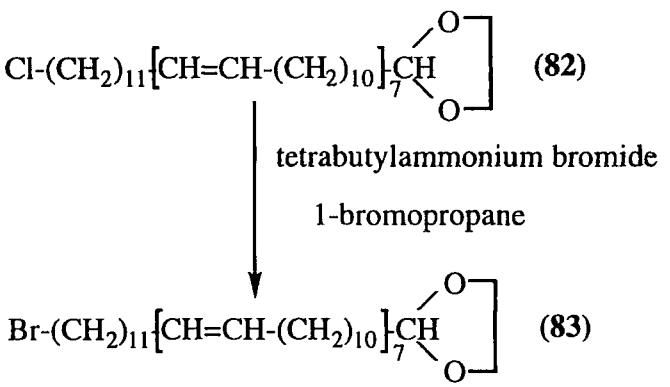
Scheme 34 *Preparation of C_{96} chloro acetal (82), using LDA.*

3.4 Reversion to the Single Halogen Wittig Reaction : Bromo Aldehyde + Triphenylphosphonium Bromide Acetal

A problem with the mixed halogen Wittig reaction, illustrated in Scheme 34, was the need for a halogen exchange after each coupling, since some of the resulting chloro acetal had to be converted to the bromo analogue, in order to form the C_{96} triphenylphosphonium bromide acetal for the next chain doubling reaction. It was therefore decided to revert back to using both the triphenylphosphonium bromide and the bromo aldehyde for the coupling reaction, thereby removing the need for any further halogen reactions.

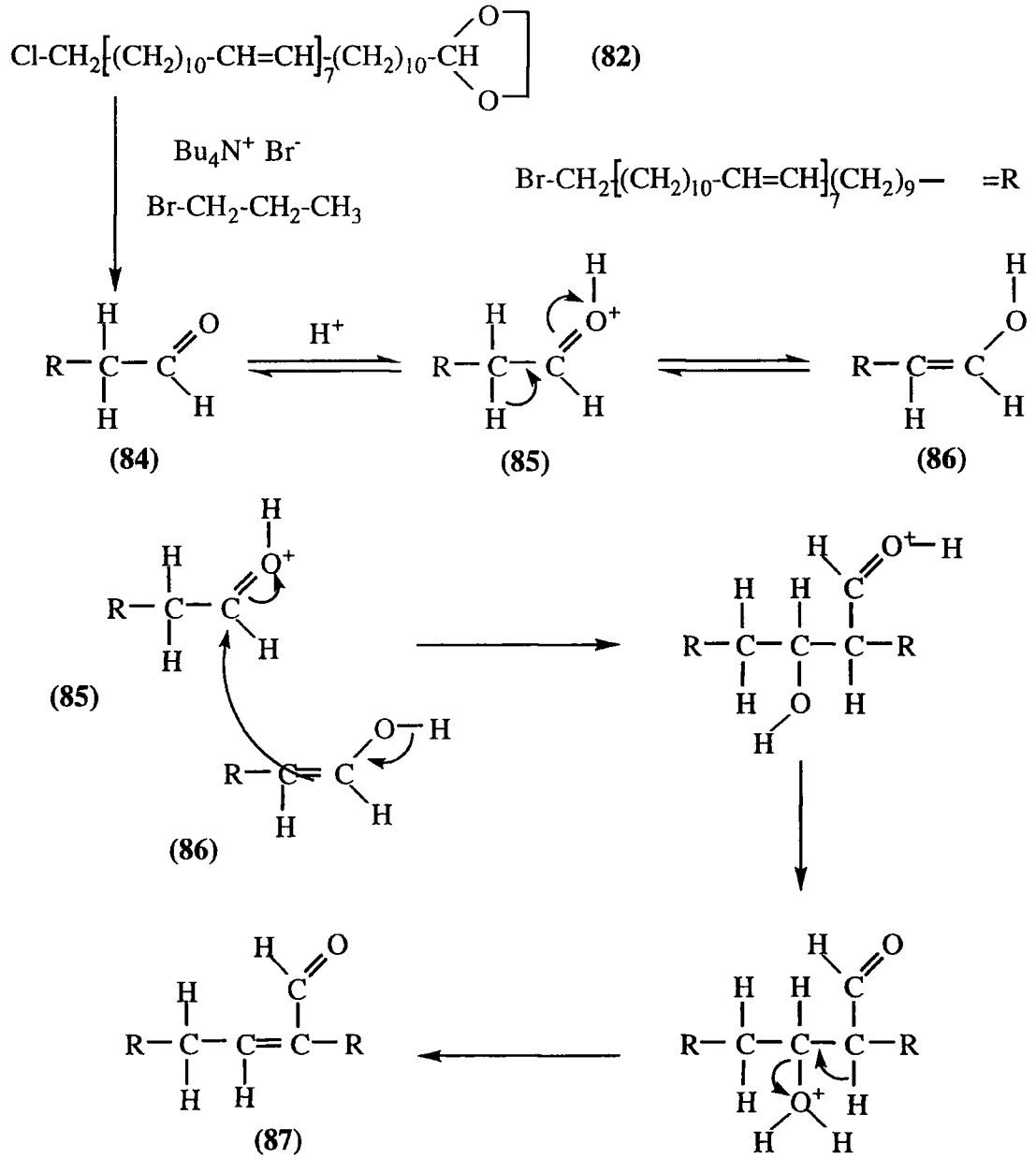
3.4.1 Halogen Exchange : C_{96} Chloro Acetal (82) → C_{96} Bromo Acetal (83) [16]

The halogen exchange reaction was carried out by refluxing C_{96} chloro acetal (82) with a solution of tetrabutylammonium bromide in 1-bromopropane (Scheme 35).



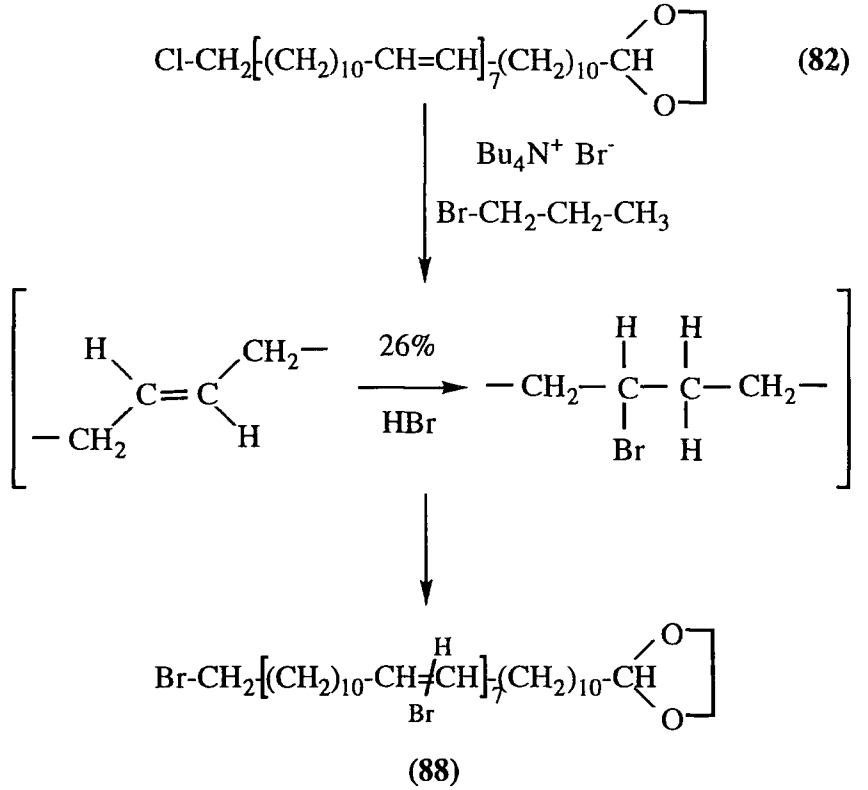
Scheme 35 *Halogen exchange reaction to prepare C_{96} bromo acetal (83).*

After 5 days the sample was analysed by ^1H nmr, which showed 10% chloro compound (82) was still present, along with significant deprotection of the aldehyde group. The reaction was allowed to continue for a further 4 days when it was sampled again by ^1H nmr. This revealed no chloro compound (82) to be present though 85% of the ethylene glycol protecting group had been removed and 40% of the product was the aldol condensation product (87) (Scheme 36) (characteristic absorptions in ^1H nmr ; 6.45δ, triplet C<u>H</u>=C-CHO; 9.4δ singlet -CHO), presumed to have formed by the presence / formation of HBr during the reaction. The mixture was worked up and the C_{96} aldehyde group reprotected. ^1H nmr showed that the aldehyde group in the $C_{191}CHO$ aldol condensation product did not form an ethylene acetal protecting group.



Scheme 36 *Formation of the C_{19}CHO aldol condensation product (86).*

A further impurity was also apparent in the ^{1}H nmr, a secondary bromide (88) (>CHBr at ca. δ 4.0 in the ^{1}H nmr spectrum) caused by the actual addition of HBr across a double bond to the extent of 26% of the product (Scheme 37). After extensive chromatography on silica using 10% diethyl ether / 90% light petroleum bp 40-60°C, the C_{96} bromo acetal (83) and the C_{192} aldol condensation product (87) were separated, although the secondary bromide was still present. A further attempt to remove it, by recrystallisation from light petroleum bp 40-60°C failed.



(88)

Scheme 37 *Adventitious formation of secondary bromide (88) during a halogen exchange reaction.*

The presence of the secondary bromide would be problematical if it formed a secondary triphenylphosphonium salt. If this was present in a Wittig reaction, a branched chain product could be formed which would have to be removed by chromatography. If the secondary bromide was unaffected by the conditions used to form the terminal triphenylphosphonium bromide then it would remain in the chain, until the end of the synthesis when it could be removed.

3.4.2 Preparation of C_{96} Triphenylphosphonium Bromide Acetal (89) [16]

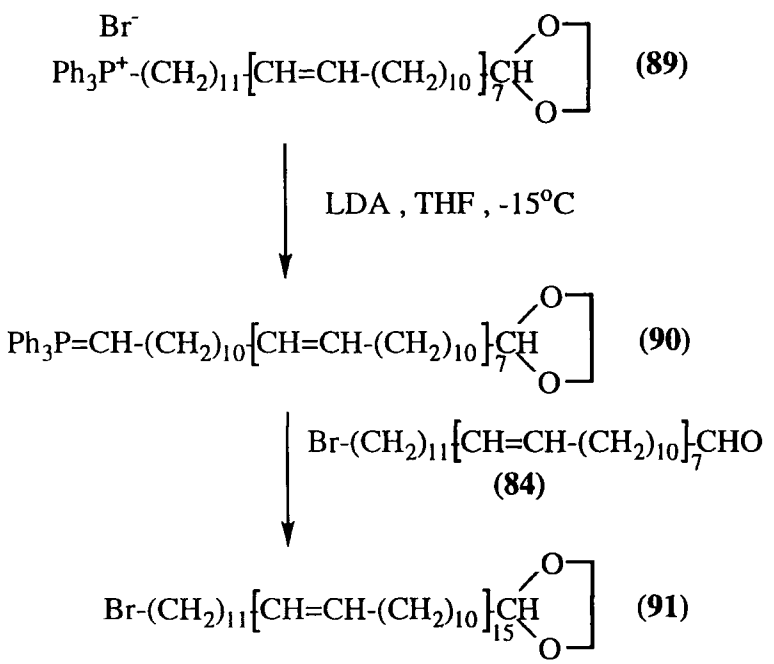
The C_{96} triphenylphosphonium bromide (89) was prepared by refluxing the C_{96} bromo acetal, containing secondary bromide (88), with 5 equivalents of triphenylphosphine in acetonitrile containing 2,2-dimethyl-1,3-dioxolane to ensure anhydrous conditions. After 95 hours a sample studied by ^1H nmr showed the reaction had gone to completion. The product was separated from unchanged triphenylphosphine by chromatography on silica using 2.5% methanol / 97.5% dichloromethane.

Model experiments have shown that secondary bromides react very slowly with triphenylphosphine compared with primary bromides and the proton in $>C\underline{H}P^+Ph_3Br^-$ occurs at δ 4.48ppm. The triphenylphosphonium bromide (89) from the C_{96} bromo acetal containing secondary bromide, described here had no signal at δ 4.48ppm ; only the signal at δ 3.78ppm due to $-CH_2P^+Ph_3Br^-$ was present. Consequently no complications could occur in future Wittig reactions.

3.4.3 The C_{96} + C_{96} Wittig Reaction → C_{192} Bromo Acetal (91) [16]

The C_{96} bromo acetal (83) was deprotected to form the C_{96} bromo aldehyde (84) using the same technique employed at the C_{48} stage. Complete deprotection was determined by ^1H nmr, which also showed the secondary bromide to be present, formed during the halogen exchange reaction. The C_{96} bromo aldehyde (84) was routinely left overnight at 38°C under high vacuum but on one occasion this led to partial trimerisation of the aldehyde. The trimer was removed from the free aldehyde by chromatography on silica, using 5% diethyl ether / 95% light petroleum bp 40-60°C.

The C_{96} ylide (90) was formed by adding LDA to the triphenylphosphonium bromide (89) in THF at -15°C (Scheme 38).



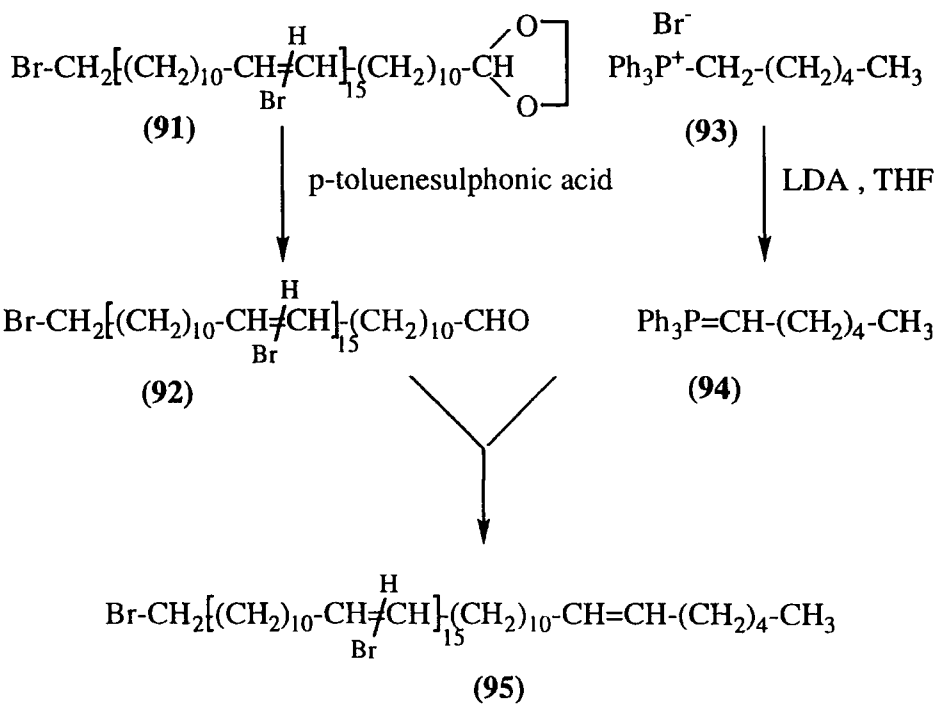
Scheme 38 *Preparation of C_{192} bromo acetal (91).*

At this temperature the salt did not fully dissolve in the THF, but on adding LDA the characteristic orange colour appeared. The aldehyde (84) was added at the same

temperature giving a pale yellow suspension and the reaction was allowed to warm up slowly and then worked up by passing through silica in 10% diethyl ether / 90% light petroleum bp 40-60°C. The resulting C_{192} bromo acetal (91) was then purified by extensive chromatography on silica using 5% diethyl ether / 95% light petroleum bp 40-60°C, giving an overall yield of 77%. The 2,4-DNP derivative of the product was formed although HPLC analysis proved unsuccessful, due to problems in resolving a well defined signal for the C_{192} material.

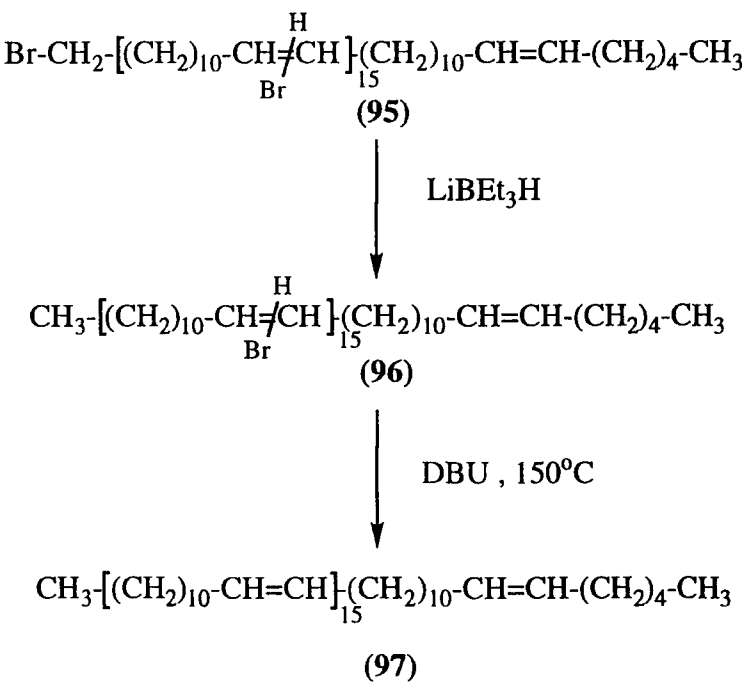
3.5 Formation of Hydrocarbons : Removal of Functionality

To form the final hydrocarbons, the functionality at each end of the chain and the internal double bonds must be removed. In the case of the acetal group, this was deprotected to the aldehyde and subjected to a Wittig reaction using the ylide (94) from n-hexyltriphenylphosphonium bromide (Scheme 39). (The C_6 triphenylphosphonium bromide (93) had been prepared from 1-bromohexane, which had been purified by fractional distillation and analysed by GC.) Thus the C_{192} bromo acetal (91) gave a 75% yield of C_{198} unsaturated primary bromide, containing secondary bromide (95). ^1H nmr analysis of the product, showed a triplet at 0.9ppm representing the terminal $-CH_3$ group.



Scheme 39 *Capping C_{192} bromo acetal (91) with C_6 ylide (94) to remove the acetal functionality.*

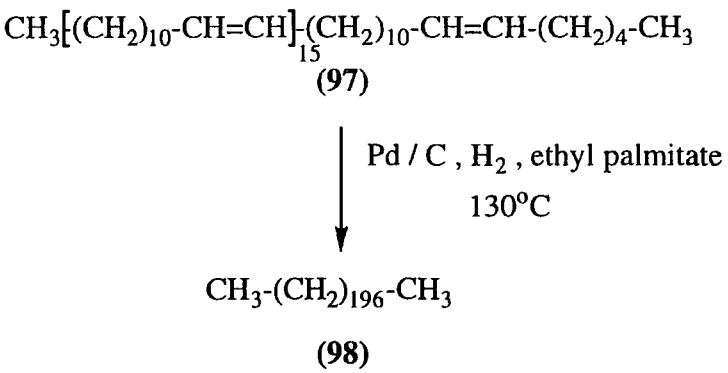
The terminal bromine was removed by treatment with $LiBEt_3H$ ("Superhydride"). It was hoped that this would also remove the secondary bromide. The C_{198} bromide (95) was stirred with a solution of "Superhydride" in THF, for four hours at room temperature (Scheme 40) and was worked up by dissolving in diethyl ether and washing with water. The product (96) was analysed by ^1H nmr which showed complete removal of the terminal bromine although the secondary bromide was still present. In an attempt to remove this functionality the product was heated under reflux with further superhydride for 15 hours, but these conditions proved to be too vigorous and the material polymerised. The secondary bromide (96) was eventually removed in a dehydrobromination reaction, by heating with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) at 140-150°C for 3 hours [structure (97) written for convenience though isomers will be present.]



Scheme 40 *Removal of primary and secondary bromide*

Removal of the internal carbon to carbon double bonds was achieved by hydrogenation. The polyene (97) was heated with hydrogen at 130°C, with 5% Pd / C catalyst in ethyl palmitate at atmospheric pressure for 24 hours (Scheme 41) [the high temperature ensured complete solubility of all hydrocarbon materials]. The reaction was worked up by filtering the solid from the mixture at room temperature, washing with light petroleum bp 40-60°C to remove any ethyl palmitate and extracting the

hydrocarbon from the catalyst with boiling light petroleum bp 100-120°C. A final purification was carried out, which involved heating the alkanes just below their melting points, under high vacuum. This led to a mist forming at the top of the vessel, which was found to be a mixture of dibutyl and dioctyl phthalate, contaminants which are thought to have originated from the petroleum solvents used.



Scheme 41 *Hydrogenation of the carbon to carbon double bonds.*

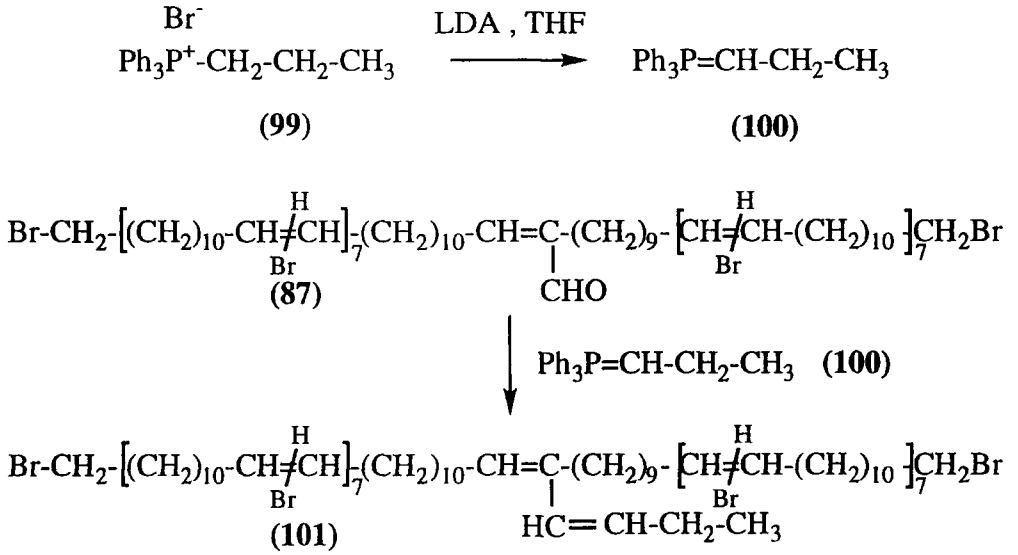
This general method was used to make two further hydrocarbons. Coupling the C_{192} bromo aldehyde (92) with the C_{96} triphenylphosphonium bromide (89) gave C_{288} bromo acetal. The aldehyde group was deprotected and reacted with the ylide formed from C_6 triphenylphosphonium bromide (94) to give the C_{294} bromide, from which $C_{294}H_{590}$ was formed. The C_{240} bromo acetal was produced by coupling the C_{192} bromo aldehyde (92) with the C_{48} triphenylphosphonium bromide (81). This was then capped with the C_6 unit to form the C_{246} bromide, from which $C_{246}H_{498}$ hydrocarbon was produced.

3.6 Synthesis of Long Chain Alkanes with Chain Branching

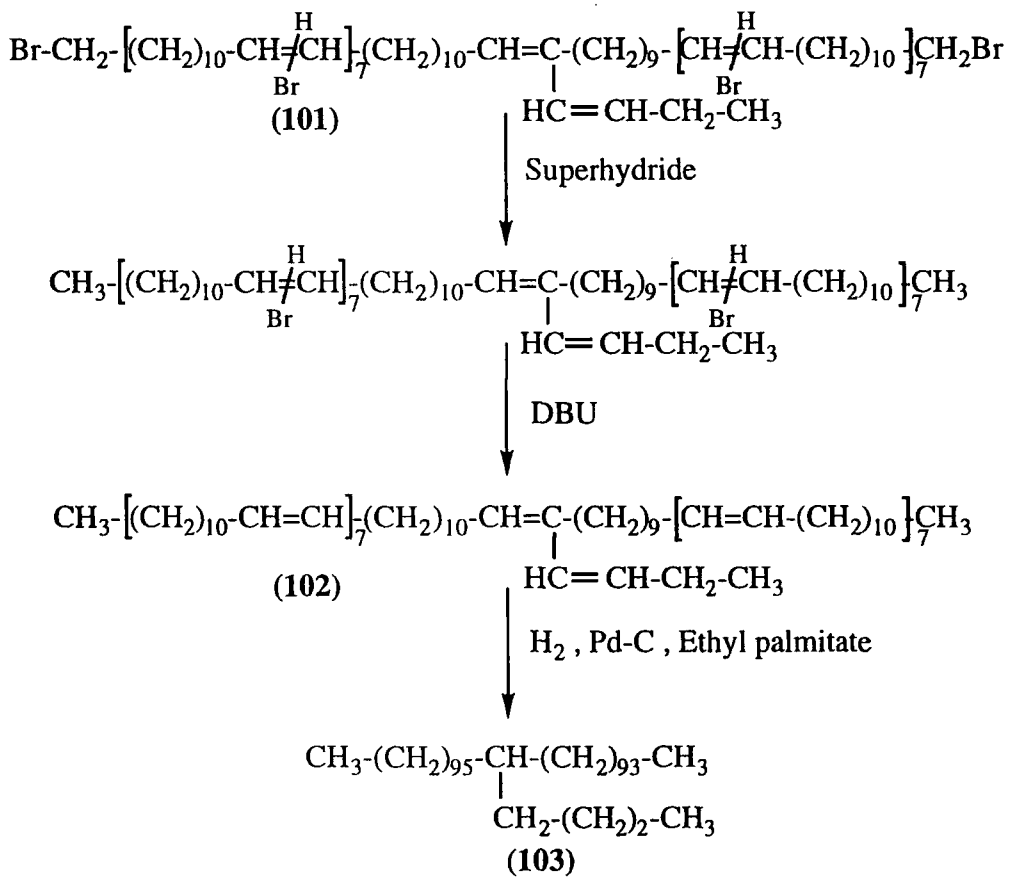
Two further hydrocarbons were produced, using the aldol condensation product (87) which had been salvaged from the disastrous C_{96} halogen exchange reaction described earlier. The presence of the secondary aldehyde opened up the possibility of forming long chain alkanes with a branch at a specific point along the chain. Two such alkanes were prepared:

3.6.1 $C_{191}C_4$ Branched Alkane (103) [16]

The ylide (100) of C_3 triphenylphosphonium bromide, formed by treatment of the salt (99) with LDA in THF was added to the aldol condensation product (87) at room temperature to give the branched hydrocarbon (101) in 55% yield (Scheme 42).



Scheme 42 *Addition of C_3 unit to the aldol product (100) to form a C_4 branch (101).*

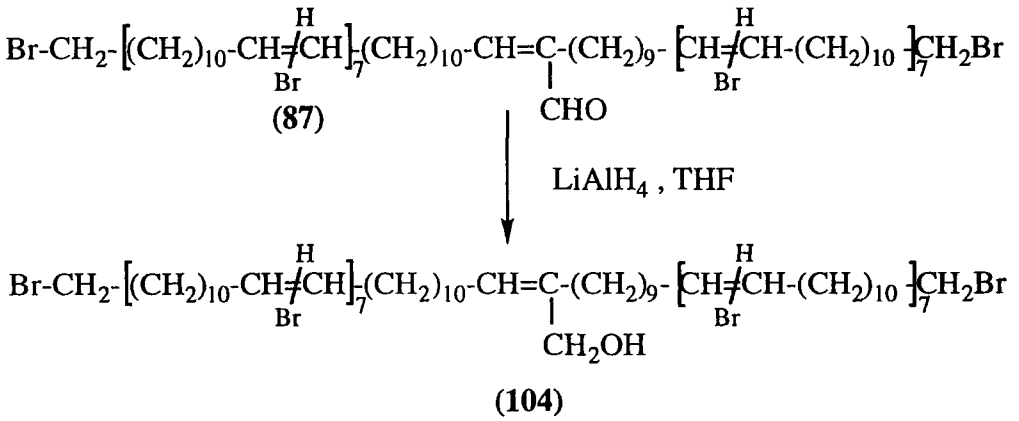


Scheme 43 *Removal of functionality to form $C_{191}C_4$ branched alkane (103).*

The terminal bromine atoms were removed by reduction with "Superhydride", and the secondary bromide, which had also formed in the halogen exchange reaction was removed by treatment with DBU as described earlier, leaving $C_{191}C_4$ polyene (102) (Scheme 43). Hydrogenation of the carbon to carbon double bonds was achieved by heating with 5% Pd / C catalyst in ethyl palmitate under an atmosphere of hydrogen, giving the branched alkane (103).

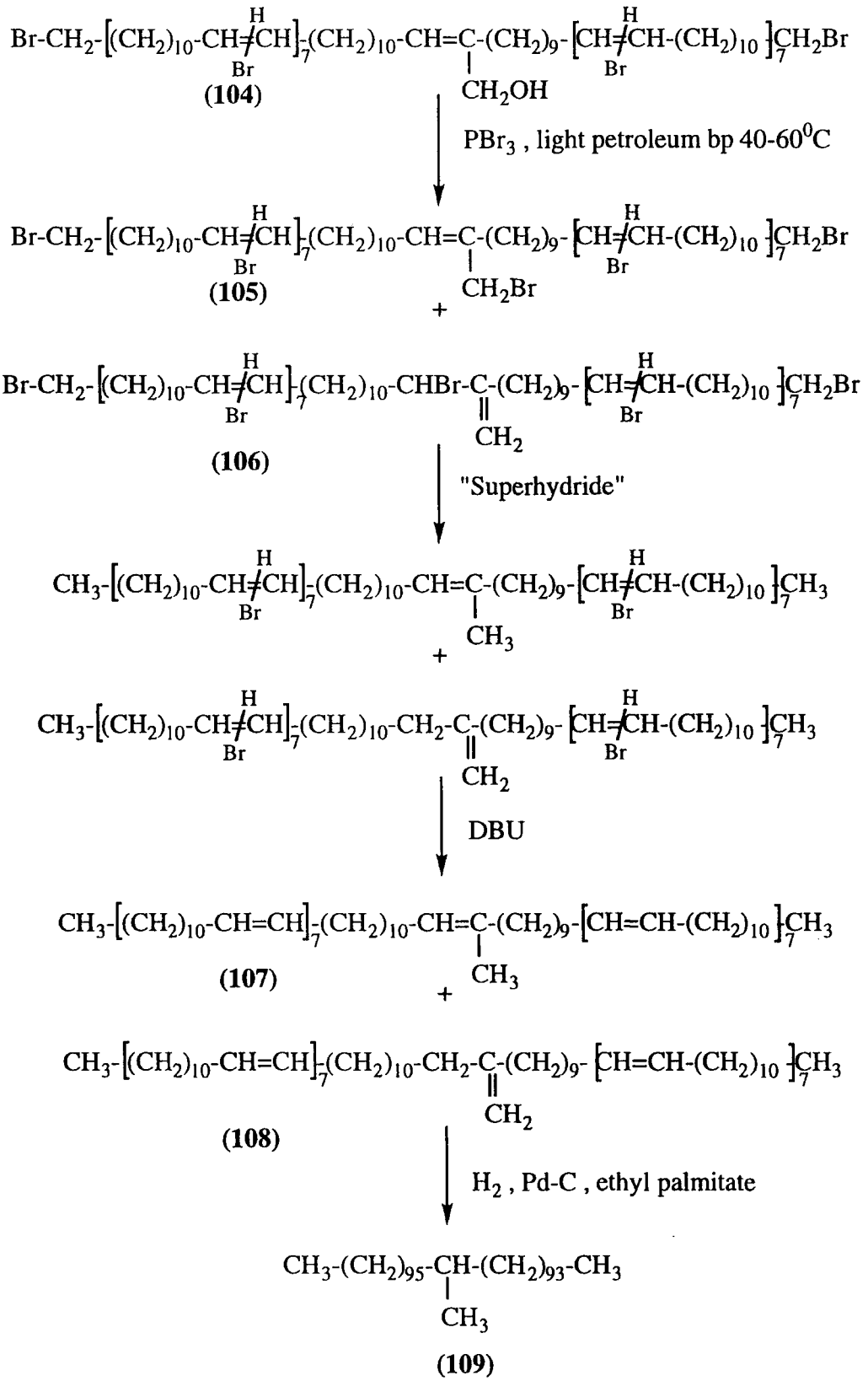
3.6.2 $C_{191}C_1$ Branched Alkane (109)[16]

The $C_{191}CHO$ aldol product (87) was treated with $LiAlH_4$ to give the alcohol (104) in 90% yield (Scheme 44).



Scheme 44 *Reduction of $C_{191}CHO$ (87) to $C_{191}CH_2OH$ (104).*

The alcohol (104) and PBr_3 gave (105) and the isomer (106) which was identified by ^1H nmr (Scheme 45).Treatment of this mixture with "Superhydride", followed by DBU gave the C_{191} polyenes (107) and (108). Finally the carbon to carbon double bonds were hydrogenated by heating with 5% Pd / C in ethyl palmitate under an atmosphere of hydrogen, to give the desired branched alkane (109).



Scheme 45 *Removal of functionality to form the $C_{191}C_1$ branched alkane (109).*

Chapter 4

Synthesis of Further Materials Using New Methodology

Chapter 4

Synthesis of Further Materials Using New Methodology

In order to continue the work carried out by Dr GM Brooke and Dr DG Proctor, described in Chapter 3, a further 3kg of 12-chlorododecanol was purchased[15]. The work on this material was carried out by Dr S Mohammed and the author of this thesis. In addition to producing further quantities of materials with chain lengths similar to those produced in Chapter 3, we aimed to synthesise alkanes with chain lengths of C_{390} and beyond.

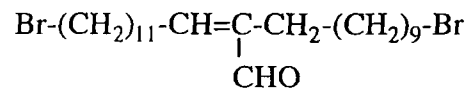
4.1 New Methodology For Previously Made Compounds

The following work, carried out by the author of this thesis, made use of the new methodology developed by Dr GM Brooke and Dr DG Proctor, described in detail in Chapter 3, to synthesise the intermediate compounds used to produce long chain alkanes.

1. Oxidation of 12-chlorododecanol (56) to 12-chlorododecanal (57) using the Swern technique, followed by immediate protection of the aldehyde group as the ethylene acetal (59). In total 3,025g of 12-chlorododecanol were used giving 3,401g of 12-chlorododecanal ethylene acetal in 94% yield.

2. Conversion of C_{12} chloro acetal (59) to C_{12} bromo acetal (50). After refluxing the C_{12} chloro acetal with tetrabutylammonium bromide in 1-bromopropane for 42 hours, the ^1H nmr revealed 9% of the starting material remained and 15% of the ethylene acetal protecting group had been removed; reprotection was carried out by heating with ethylene glycol and p-toluenesulphonic acid in ethyl bromide. A second halogen exchange was carried out to transform the remaining 9% of chloro compound, but this again led to slight (< 5%) deprotection of the aldehyde group. This was reprotected as before, giving a 95% yield of C_{12} bromo acetal.

(A similar halogen exchange reaction was carried out by Dr S. Mohammed. After 4 days ^1H nmr revealed 10% unreacted chloro compound and 40 % deprotection of the aldehyde functionality. The experiment was continued for a further two days when ^1H nmr revealed 13% of the product consisted of the aldol condensation product (110).

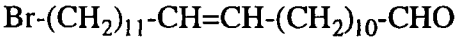


(110)

3 a. Preparation of C_{12} Triphenylphosphonium Bromide Acetal (51). This was formed by refluxing C_{12} bromo acetal (50) with triphenylphosphine in acetonitrile. In total, 1,238g of the salt was formed from 730g of C_{12} bromo acetal (91% yield).

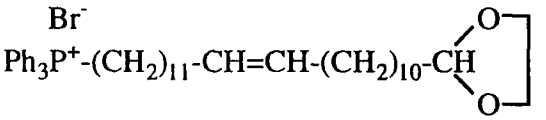
3 b. C_{12} + C_{12} Wittig Reaction → C_{24} Bromo Acetal (53). This and all further Wittig reactions were carried out using LDA to form the ylide of the triphenylphosphonium bromide, which was coupled with the aldehyde as described in Chapter 3. In total 603g of C_{24} bromo acetal (53) was formed, in 56% yield.

4. C_{24} + C_{12} Wittig Reaction → C_{36} Bromo Acetal (54, n=2). Using C_{24} bromo aldehyde (111) and the ylide (52) formed from C_{12} triphenylphosphonium bromide acetal, 0.75g of C_{36} bromo acetal (54, n=2) was formed in 54% yield. The 2,4-DNP derivative of C_{36} bromo aldehyde was prepared and used as a standard for HPLC analysis.



(111)

5 a. Preparation of C_{24} Triphenylphosphonium Bromide Acetal (112). The salt (112) (174g) was formed from 118g of C_{24} bromo acetal in 94% yield.



(112)

5 b. C_{24} + C_{24} Wittig Reaction → C_{48} Bromo Acetal (80). In total 108g of C_{48} bromo acetal (80) was formed in 71% yield. In addition to this a further 308g of crude C_{48} bromo acetal was formed, which has yet to be purified.

6. C_{48} + C_{24} Wittig Reaction → C_{72} Bromo Acetal (54, n=5). Using C_{48} bromo aldehyde (113) and the ylide formed from C_{24} triphenylphosphonium bromide, 0.4g of C_{72} bromo acetal (54, n=5) was formed in 27% yield. This material was used to prepare the C_{72} 2,4-DNP derivative, which was used as a standard for HPLC analysis.

$$Br\text{-}(CH_2)_{11}\text{-}\left[CH{=}CH\text{-}(CH_2)_{10}\right]_3CHO$$

(113)

7 a. Preparation of C_{48} Triphenylphosphonium Bromide Acetal (81). The salt (81) (22g) was formed from 22g of C_{48} bromo acetal (80) in 75% yield.

7 b. C_{48} + C_{48} Wittig Reaction → C_{96} Bromo Acetal (83). In total 57g of C_{96} bromo acetal (83) was formed in 81% yield.

8 a. Preparation of C_{96} Triphenylphosphonium Bromide Acetal (89) In total 28.4g of the salt (89) was formed from 25g of C_{96} bromo acetal (97% yield).

8 b. C_{96} + C_{96} Wittig Reaction → C_{192} Bromo Acetal (91). In total 14.6g of C_{192} bromo acetal (91) was formed in 60% yield.

4.2 New Methodology For New Materials

A major advantage of the method of synthesis developed by Whiting is that alkanes of any required chain length can be produced, whereas a scheme such as that carried out by Schill et al., using the strategy of polymerisation can only produce a series of alkanes whose chain lengths are predetermined by the monomer used. This flexibility allowed the physicists to identify which alkanes would be of particular interest, thereby guiding our work. In response to such a request by Dr G. Ungar, at the University of Sheffield, the following list of target molecules was drawn up, and potential synthetic routes defined, bearing in mind the availability of shorter chain materials.

$$C_{98} \Longrightarrow C_{96} + C_2$$

$$C_{122} \Longrightarrow C_{96} + C_{24} + C_2$$

$$C_{162} \Longrightarrow C_{96} + C_{48} + C_{12} + C_6$$

$$C_{194} \Longrightarrow C_{192} + C_2$$

$$C_{210} \Longrightarrow C_{192} + C_{12} + C_6$$

$$C_{242} \Longrightarrow C_{192} + C_{48} + C_2$$

$$C_{258} \Longrightarrow C_{192} + C_{48} + C_{12} + C_6$$

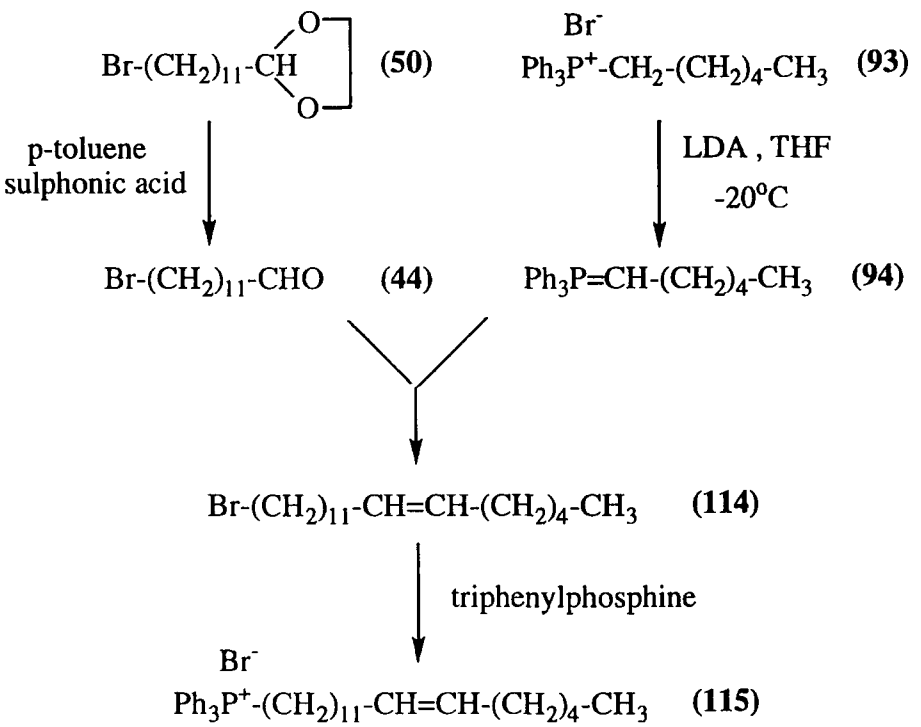
It became apparent that some of these targets required the same sequence of couplings:

$$C_{162} \Longrightarrow C_{96} + \boxed{C_{48} + \boxed{C_{12} + C_6}} \left[\equiv C_{66} \right]$$

$$C_{210} \Longrightarrow C_{192} + \boxed{C_{12} + C_6} \left[\equiv C_{18} \right]$$

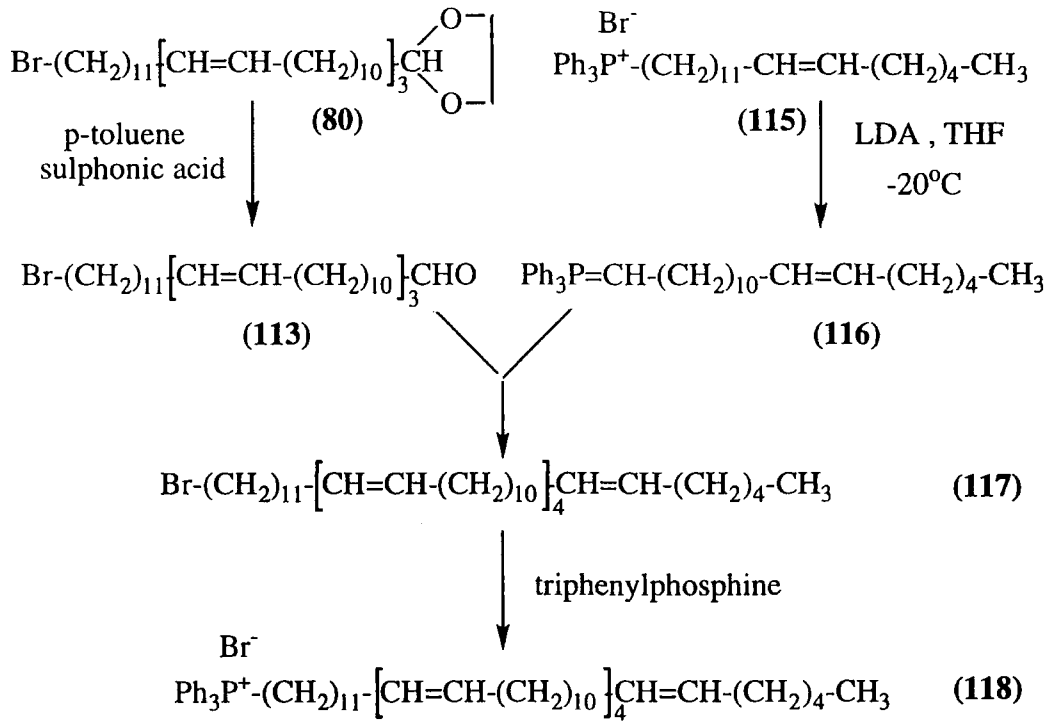
$$C_{258} \Longrightarrow C_{192} + \boxed{C_{48} + \boxed{C_{12} + C_6}} \left[\equiv C_{66} \right]$$

Rather than carry out a series of repetitious Wittig reactions on the precious C_{96} and C_{192} materials, it was decided to form both the C_{18} bromo polyene (114) and the C_{66} bromo polyene (117). Compound (114), formed by coupling C_{12} bromo aldehyde (44) with the ylide (94) from C_6 triphenylphosphonium bromide (Scheme 46), was treated with triphenylphosphine to give the C_{18} triphenylphosphonium bromide (115) for use in reaction with aldehydic material. This work was done by Dr S Mohammed.



Scheme 46 *Preparation of C_{18} triphenylphosphonium bromide (115).*

The C_{66} bromo polyene (117)[17], obtained in 84% yield by coupling the C_{48} bromo aldehyde (113) with the ylide (116) formed from C_{18} triphenylphosphonium bromide (115)[18] gave the triphenylphosphonium bromide (118) on treatment with triphenylphosphine (Scheme 47).



Scheme 47 *Preparation of C_{66} triphenylphosphonium bromide (118).*

4.2.1 Preparation of Target Alkanes

The following alkanes were prepared using the method described in Chapter 3:

1. $C_{98}H_{198}$ (121)[17]: A Wittig reaction between C_{96} bromo aldehyde (84) and the ylide formed from ethyltriphenylphosphonium bromide gave C_{98} bromo polyene (119) in 72% yield. Treatment with "Superhydride" gave the C_{98} polyene (120) (94% yield) and finally hydrogenation of the double bonds produced 1.84g of the desired hydrocarbon (121) (90% yield).

$$Br\text{-}CH_2[(CH_2)_{10}\text{-}CH=CH]_7(CH_2)_{10}\text{-}CH=CH\text{-}CH_3$$

(119)

$$CH_3[(CH_2)_{10}\text{-}CH=CH]_7(CH_2)_{10}\text{-}CH=CH\text{-}CH_3$$

(120)

$$CH_3\text{-}(CH_2)_{96}\text{-}CH_3$$

(121)

2. $C_{210}H_{422}$ (124)[17]: A Wittig reaction between C_{192} bromo aldehyde (92) and the ylide (116) formed from C_{18} triphenylphosphonium bromide[18] gave C_{210} bromo

polyene (122) in 60% yield. Treatment with "Superhydride" gave the C_{210} polyene (123) (81% yield) and hydrogenation of the double bonds produced 1.32g of the hydrocarbon (124) (79% yield).

$$Br\text{-}CH_2[(CH_2)_{10}\text{-}CH{=}CH]_{16}(CH_2)_{10}\text{-}CH{=}CH\text{-}(CH_2)_4\text{-}CH_3$$

(122)

$$CH_3[(CH_2)_{10}\text{-}CH{=}CH]_{16}(CH_2)_{10}\text{-}CH{=}CH\text{-}(CH_2)_4\text{-}CH_3$$

(123)

$$CH_3\text{-}(CH_2)_{208}\text{-}CH_3$$

(124)

4.3 Co-operative Work

The work involved in producing the remaining targets was shared between Dr S Mohammed and the author of this thesis. The debromination step on the C_{258} bromo polyene (125, n=20) and the hydrogenation of the double bonds of the C_{122} (126, n=9), C_{162} (127, n=12), C_{194} (126, n=15) and C_{258} (127, n=20) polyenes, to give the final hydrocarbons, were carried out by the author. The $C_{242}H_{486}$ alkane (128, n=240) was prepared by Dr Mohammed.

$$Br\text{-}CH_2[(CH_2)_{10}\text{-}CH{=}CH]_n(CH_2)_{10}\text{-}CH{=}CH\text{-}(CH_2)_4\text{-}CH_3$$

(125)

$$Br\text{-}CH_2[(CH_2)_{10}\text{-}CH{=}CH]_n(CH_2)_{10}\text{-}CH{=}CH\text{-}CH_3$$

(126)

$$CH_3[(CH_2)_{10}\text{-}CH{=}CH]_n(CH_2)_{10}\text{-}CH{=}CH\text{-}(CH_2)_4\text{-}CH_3$$

(127)

$$CH_3\text{-}(CH_2)_n\text{-}CH_3$$

(128)

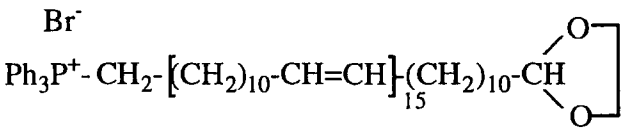
In addition to the materials requested by Dr Ungar, it is hoped that the following hydrocarbons will be produced:

$$C_{390}H_{782} \Longrightarrow C_{192} + C_{192} + C_6$$

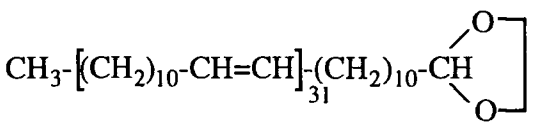
$$C_{582}H_{1166} \Longrightarrow C_{384} + C_{192} + C_6$$

$$C_{774}H_{1550} \Longrightarrow C_{384} + C_{384} + C_6$$

At present 0.93g of C_{384} bromo acetal has been produced by Dr S. Mohammed, from a Wittig reaction between C_{192} bromo aldehyde (92) and the ylide from C_{192} triphenylphosphonium bromide (129). It was decided to remove the terminal bromine before coupling this material with the ylide (94) formed from C_6 triphenylphosphonium bromide. This was achieved by treatment with "Superhydride" in THF, giving 0.82g of C_{384} bromo polyene (130) which was purified by chromatography on silica using light petroleum, bp 40-60°C.



(129)



(130)

Chapter 5

Experimental

Chapter 5

Experimental

5.1 Instrumentation

NMR spectra were recorded on the following instruments at the frequencies listed: Varian Gemini 200 ^1H (200MHz), Varian XL 200 ^1H (200MHz), Varian VXR 400S ^1H (399.952MHz), ^{13}C (100.582MHz). Absorption multiplicities have been abreviated as follows: s (singlet), d (doublet), t (triplet), m (multiplet). All chemical shifts are given in ppm with respect to TMS, present in $CDCl_3$ used as solvent. Silica refers to Merck silica gel F60 (230-400 mesh).

Analytical HPLC was performed on a Star 5065 instrument fitted with Hypersil 5 SAS 25cm x 4.6mm C_1 reverse phase column.

Elemental analyses were performed on an Exeter Analyical Inc CE440 elemental analyser. Melting points were determined on a Gallenkamp melting point apparatus.

Purification of C_{12} and C_{24} materials was carried out by short path distillation as described, using a short path distillation unit (KDL-1), manufactured by U.I.C. GmbH Alzenau, Germany.

5.2 Solvents

All reaction solvents were dried in the appropriate manner : acetonitrile and dichloromethane were freshly distilled from P_2O_5; THF was distilled from $LiAlH_4$ and NaH immediately prior to use. All light petroleum solvents were distilled on a rotary evaporator.

5.3 NMR Analysis

^1H nmr was used in the identification of all compounds. After each chain doubling, the -C<u>H</u>=C<u>H</u>- to -C<u>H</u>-O_2-(C<u>H_2</u>)$_2$ (the ethylene acetal group) ratio increases. This ratio was used to identify a material's chain length, although accurate measurement became more difficult as the number of carbon to carbon double bonds increased. Due to the difficulty in removing the last traces of light petroleum solvents from some products, measurement of the intensity of the -CH_2- signal proved inaccurate. Integral measurements for the final alkanes also proved to be inaccurate, due to difficulties in

shimming the spectrometer at 120°C on a one day basis, so no reliable ratio was achieved between the $-CH_3$ end groups and the internal $-CH_2-$ groups and the ^1H nmr could only be used to demonstrate the absence of carbon to carbon double bonds.

5.4 HPLC Analysis of 2,4-Dinitrophenylhydrazone Derivatives

After each chain doubling reaction it was vital that the product was free from other homologues. ^1H nmr analysis is not sensitive to traces of homologous compounds, so the 2,4-dinitrophenylhydrazone (2,4-DNP) derivative of the product was prepared and analysed by HPLC to determine the purity.

The following method was used to prepare all 2,4-DNP derivatives. The bromo acetal (0.1g) was stirred with 2,4-dinitrophenylhydrazine (0.2g) and concentrated sulphuric acid (0.5ml) in n-butanol (10ml) for 16 hours at 45°C, forming an orange precipitate, the 2,4-DNP derivative, which was filtered, washed with methanol and dried.

5.5 Experimental

12-Chlorododecanal [C_{12} Chloro Aldehyde (57)].[11]

Oxalyl dichloride (132ml, freshly distilled) and anhydrous dichloromethane (1027ml) were stirred and cooled to -70°C under nitrogen. Dimethyl sulphoxide (230ml, distilled from CaH_2 under vacuum) in anhydrous dichloromethane (340ml) was added over 1.5 hours and the mixture was stirred for a further hour. 12-Chlorododecanol (56) (200g) in anhydrous dichloromethane (600ml) was then added over 1.5 hours, causing a white precipitate to form, which was stirred for a further hour. Triethylamine (774ml, freshly distilled) was added over 20 minutes to the reaction mixture, maintained at -77°C. The cold bath was then removed and the resulting mixture was allowed to reach room temperature whilst stirring overnight. Water (400ml) was added rapidly and the mixture was stirred for 15 minutes causing the precipitate to dissolve. The solution was then washed with hydrochloric acid (5M; 2x200ml) followed by aqueous potassium carbonate (10% solution, 1x200ml), the aqueous phase in each case extracted with dichloromethane (3x100ml). The combined organic layers were dried over sodium sulphate and the solvent was removed under vacuum leaving an orange oil (57) (194g). This was analysed by ^1H nmr and shown to be identical to an authentic sample; δ_H ($CDCl_3$) 9.78 [t, -CHO], 3.55 [t, $-CH_2Cl$], 2.45 [td, $-C\underline{H_2}$-CHO] were observed in the

ratio 1 : 2.11 : 1.94 respectively (correct ratio 1:2:2); 1.85 [m, -C$\underline{H}_2$-CH_2Cl] 1.65 [m, -C$\underline{H}_2$-CH_2-CHO], 1.28 [m, -$(CH_2)_8$-].

12-Chlorododecanal Ethylene Acetal [C_{12} Chloro Acetal (59)].[11]

The 12-chlorododecanal (57) formed above was stirred with ethylene glycol (500ml) and p-toluenesulphonic acid (4g) at 80°C overnight. Light petroleum bp 40-60°C (100ml, freshly distilled) was added and the solution was washed with aqueous potassium carbonate (10% solution, 3x200ml), the aqueous phase in each case being extracted with light petroleum bp 40-60°C (3x100ml). The combined organic layers were dried over sodium sulphate and the solvent was removed under vacuum leaving a red / orange oil (233g), which was purified using the short path distillation unit (KDL-1) (85°C, $4x10^{-2}$mbar) giving a pale yellow oil (59) (199g, 84%) which crystallised overnight at room temperature. Analysis by ^1H nmr showed the product to be identical to an authentic sample; δ_H ($CDCl_3$) 4.85 [t, -C$\underline{H}O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.55 [t, -CH_2Cl] were observed in the ratio 1 : 3.91 : 2.09 respectively (correct ratio 1:4:2); 1.85 [m, -C$\underline{H}_2$-CH_2Cl], 1.65 [m, -C$\underline{H}_2$-CH-$O_2(CH_2)_2$], 1.28 [m, -$(CH_2)_8$-].

12-Bromododecanal Ethylene Acetal [C_{12} Bromo Acetal (50)].[13]

1-Bromopropane (2.2L) and tetrabutylammonium bromide (442g) were heated under reflux for 4 hours with a Soxhlet condenser containing molecular sieves (4Å). The C_{12} chloro acetal (59) (332g) was added and the solution was refluxed for a further 42 hours. The product was washed with water (3x500ml) and the aqueous phase extracted with 1-bromopropane (3x100ml). The combined organic layers were dried over sodium sulphate and the solvent removed under vacuum. The ^1H nmr spectrum of the resulting oil showed 9% of unchanged chloro compound (δ_H ($CDCl_3$); 3.5ppm) and 15% of the ethylene acetal protecting group had been removed. Reprotection was achieved by stirring the oil with ethylene glycol (100ml) and p-toluenesulphonic acid (1.5g) in bromoethane (100ml) at 45°C for 16 hours . The solvent was then removed under vacuum, light petroleum bp 40-60°C was added (250ml) and the organic layer was washed with water (3x250ml). In each case the aqueous layer was extracted with light petroleum bp 40-60°C (3x100ml). The combined organic layers were dried over

sodium sulphate and the solvent removed under vacuum, leaving an orange oil which was added to a solution of tetrabutylammonium bromide (170g) in 1-bromopropane (800ml, dried with molecular sieves as described above) and heated under reflux for 42 hours, to remove the remaining chloro material. The product was worked up in the same way as the first halogen exchange reaction. ^{1}H nmr of the resulting oil showed complete absence of any -CH_2Cl absorption, but a small amount (< 5%) of the ethylene acetal protecting group had been removed. Reprotection was again carried out by stirring with ethylene glycol (100ml) and p-toluenesulphonic acid (1.5g) in bromoethane (100ml). The product was worked up by the method used for the first reprotection. The resulting oil was purified using the KDL-1 (80°C, $6x10^{-3}$mbar), giving 12-bromododecanal ethylene acetal (50) as a pale yellow oil (369g, 95%) which formed a crystalline solid at room temperature. Analysis by ^{1}H nmr showed the product to be identical to an authentic sample; δ_H ($CDCl_3$) 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.4 [t, -CH_2Br] were found in the ratio 1 : 4.00 : 2.04 respectively (correct ratio 1:4:2) ; 1.85 [m, -C<u>H</u>$_2$-CH_2Br], 1.65 [m, -C<u>H</u>$_2$-CH-$O_2(CH_2)_2$], 1.28 [m, -$(CH_2)_8$-]. The 2,4-DNP derivative was prepared (as described below) and used as a standard in HPLC analysis (70% THF, 30% water; the desired compound eluting after 3.75minutes).

<u>11-(Dioxolan-2-yl)undecyltriphenylphosphonium Bromide [C_{12} Triphenyl phosphonium Bromide Acetal (51)].</u>[10]

12-Bromododecanal ethylene acetal (50) (334g, 1.09mol, 1 equiv.), triphenylphosphine (313g, 1.19mol, 1.1 equiv.), 2,2-dimethyl-1,3-dioxolane (10ml), and acetonitrile (500ml) were boiled for 72 hours under nitrogen. The acetonitrile was removed under vacuum leaving a thick, pale yellow oil. Light petroleum bp 40-60°C (500ml) was added and the oil was stirred using a metal spatula until it formed a white solid. The white crystalline salt was filtered and washed with light petroleum bp 40-60°C (1.5L) to remove any remaining triphenylphosphine. All solvent was removed under vacuum and the product (51) (535g, 86%) was analysed by ^{1}H nmr and shown to be identical to an authentic sample; δ_H ($CDCl_3$) 7.65 [m, 3xC_6H_5], 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.8 [m, -O-$(CH_2)_2$-O- and -C<u>H</u>$_2P^+Ph_3$] were observed in the ratio

15.72 : 1 : 6.09 respectively (correct ratio 15:1:6); 1.6 [m, -C$\underline{H}_2$-$CHO_2(CH_2)_2$ and -C$\underline{H}_2$-CH_2-P^+Ph_3], 1.28 [m, -$(CH_2)_8$-].

12-Bromododecanal [C_{12} Bromo Aldehyde(44)].[10]

A slurry of silica (1Kg) in 75% light petroleum bp 40-60°C / 25% dichloromethane was stirred with an aqueous solution of p-toluenesulphonic acid (100g in 150ml of water) and the C_{12} bromo acetal (50) (148g, 0.484mol) was passed through a column of the impregnated silica using the same solvent. The product was eluted over 4 hours and the solvent removed under vacuum, at 25°C (heating the aldehyde led to the production of trimer (chloro analogue; 58)), giving a colourless oil (127g, 99%). The product was identified as the aldehyde (44) by ^1H nmr ; δ_H ($CDCl_3$): 9.76 [1H, t, -CHO], 3.4 [2H, t, -CH_2Br], 2.4 [2H, td, -C$\underline{H}_2$CHO], were observed in the ratio 1 : 2.16 : 1.89 respectively (correct ratio 1:2:2) ; 1.85 [m, -C$\underline{H}_2$-CH_2Br], 1.65 [m, -C$\underline{H}_2$-CHO], 1.3 [m, -$(CH_2)_8$-].

24-Bromotetracos-12-enal Ethylene Acetal [C_{24} Bromo Acetal (53)].[10]

The C_{12} triphenylphosphonium bromide acetal (51) (302g, 0.530mol, 1.1equiv.) and THF (700ml, freshly distilled from $LiAlH_4$ and NaH) were cooled to -10°C whilst stirring under nitrogen. Lithium diisopropylamide (LDA) (1.5M in THF, 337ml, 0.506mol, 1.05 equiv.) was added, giving a deep orange / red colour, characteristic of the ylide (52) and the mixture was stirred for 0.5 hours at -10°C. The temperature was held at -10°C whilst a solution of C_{12} bromo aldehyde (44) (127g, 0.482mol, 1 equiv.) in THF (10ml, freshly distilled from $LiAlH_4$ and NaH) was added,with stirring, causing the colour to fade, leaving a very pale cream / yellow mixture. This was allowed to reach room temperature over 16 hours.

Water (20ml) was added to the reaction mixture and the THF removed under vacuum leaving a slurry which was dissolved in acetonitrile (500ml) and extracted with light petroleum bp 40-60°C (7x250ml). The combined petrol layers were washed with water (3x250ml), the aqueous layer being extracted with further light petroleum bp 40-60°C in each case. The petrol layers were combined, dried over sodium sulphate and the solvent was removed under vacuum, leaving an orange oil. This was passed through a short pad of silica (500g) using 10% diethyl ether / 90% light petroleum bp 40-60°C to

remove any remaining phosphorus compounds and / or lithium salts. The resulting yellow oil (215g) was purified by short path distillation, using the KDL-1 to remove C_{12} impurities (3 distillations at 100°C, $4x10^{-3}$mbar, conditions under which the C_{12} chain lengths distilled, leaving C_{24} and C_{36} material) and C_{36} impurities (1 distillation at 155°C, $4x10^{-3}$mbar, conditions under which C_{24} compounds distilled, leaving C_{36} material in the residue). The resulting colourless oil (53) (138g, 60%) formed a white crystalline solid at room temperature. Analysis by ^{1}H nmr showed the product to be identical to an authentic sample; δ_H ($CDCl_3$): 5.35 [m, -CH=CH-], 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.4 [t, -CH_2Br] were observed in the ratio 2.04 : 0.91 : 4 : 2.01 respectively (correct ratio 2:1:4:2) ; 2.0 [m, 2x-C<u>H</u>$_2$-CH=], 1.85 [m, -C<u>H</u>$_2$-CH_2Br], 1.65 [m, -C<u>H</u>$_2$-CH-$O_2(CH_2)_2$], 1.3 [m, 2x-$(CH_2)_8$-]. Analysis by ^{13}C nmr showed the ratio *cis* -CH=CH- to *trans* -CH=CH- to be 4:1; δ_C ($CDCl_3$): 130 [s, *cis* -CH=CH-], 130.5 [s, *trans* -CH=CH-]. Analysis of the 2,4-DNP derivative by HPLC (70% THF, 30% water; the desired compound eluting after 4.41minutes) showed less than 0.2% of C_{12} impurities to be present.

<u>23-(Dioxolan-2-yl)tricos-12-enyltriphenylphosphonium Bromide [C_{24} Triphenyl phosphonium Bromide (112)].</u>[10]

The C_{24} bromo acetal (53) (118g, 0.249mol, 1 equiv.), triphenylphosphine (72g, 0.275mol, 1.1 equiv.), 2,2-dimethyl-1,3-dioxolane (10ml), and acetonitrile (500ml) were boiled for 66 hours under nitrogen. The acetonitrile was removed under vacuum, leaving a thick yellow oil. Light petroleum bp 40-60°C (500ml) was added and the oil was manipulated using a metal spatula until a white solid formed. The white crystalline salt was filtered, washed with light petroleum bp 40-60°C (1.5L) to remove excess triphenylphosphine and dried under vacuum. The product (112) (174g, 94%) was analysed by ^{1}H nmr and shown to be indentical to an authentic sample; δ_H ($CDCl_3$) 7.65 [m, 3xC_6<u>H</u>$_5$], 5.35 [m, -CH=CH-], 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.7 [m, -C<u>H</u>$_2$$P^+Ph_3$] were observed in the ratio 16.56 : 2.10 : 0.98 : 4: 2.09 respectively (correct ratio 15:2:1:4:2) ; 1.95 [m, 2x-C<u>H</u>$_2$-CH=], 1.6 [m, -C<u>H</u>$_2$-$CHO_2(CH_2)_2$ and -C<u>H</u>$_2$-CH_2-P^+Ph_3], 1.28 [m, 2x-$(CH_2)_8$-].

24-Bromotetracos-12-enal [C_{24} Bromo Aldehyde (111)].[10]

A slurry of silica (100g) in 75% light petroleum bp 40-60°C / 25% dichloromethane was stirred with an aqueous solution of p-toluenesulphonic acid (12g in 25ml of water) and the C_{24} bromo acetal (53) (1.05g, 2.21mmol) was passed through a column of the impregnated silica using the same solvent. The product was collected and the solvent removed under vacuum, at 25°C, giving a colourless oil (0.95g, 99%). The product was identified as the aldehyde (111) by ^{1}H nmr ; δ_H ($CDCl_3$): 9.76 [t, -CHO], 5.35 [m, -CH=CH-], 3.4 [t, -CH_2Br], 2.4 [td, -$\underline{CH_2}$CHO] were observed in the ratio 1 : 2.11 : 2.00 : 1.82 respectively (correct ratio1:2:2:2) ; 2.0 [m, 2x$\underline{CH_2}$-CH=], 1.85 [m, -$\underline{CH_2}$-CH_2Br], 1.65 [m, -$\underline{CH_2}$-CH_2-CHO], 1.3 [m, 2x-$(CH_2)_8$-].

36-Bromohexatriaconta-12,24-dienal Ethylene Acetal [C_{36} Bromo Acetal (54, n=2)].

The C_{12} triphenylphosphonium bromide (51) (1.27g, 2.23mmol) in THF (50ml) was stirred and cooled to -25°C under nitrogen. LDA (1.5M in THF, 1.5ml, 2.25mmol) was added, causing an orange colour to form, which was stirred at -25°C for 10 minutes. However, the deep red colour, characteristic of C_{12} ylide (52) formed in previous reactions, was not observed, suggesting incomplete reaction, so further LDA was added (0.2ml) until a satisfactory red colour was achieved. This may have been necessary due to the solvent being slightly wet, the water destroying some of the LDA before it could form the ylide. The mixture was stirred for a further 15 minutes at -25°C, when the C_{24} bromo aldehyde (111) (0.95g, 2.21mmol) was added, causing the red colour to fade to a pale yellow suspension. This was stirred at -25°C for a further 0.5 hours, then allowed to reach room temperature and stirred for 16 hours. Water (2ml) was added to the suspension and the THF was removed under vacuum. The slurry was dissolved in acetonitrile (200ml) and the product extracted with light petroleum bp 40-60°C (5x100ml). The combined petrol layers were then washed with water (2x200ml) and the aqueous layer extracted with further light petroleum bp 40-60°C in each case. The combined petrol layers were dried over sodium sulphate and the solvent removed under vacuum leaving an orange oil (1.37g), which solidified at room temperature. This was purified by chromatography on silica using 10% diethyl ether, 90% light petroleum bp 40-60°C, giving a colourless oil (54, n=2) (0.58g, 41%) which crystallised at room

temperature. Analysis by ^1H nmr showed the product to be identical to an authentic sample; δ_H ($CDCl_3$): 5.35 [m, 2x-CH=CH-], 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.4 [t, -CH_2Br] were observed in the ratio 4.19 : 1.02 : 4 : 2.00 respectively (correct ratio 4:1:4:2) ; 2.0 [m, 4xC<u>H</u>$_2$-CH=], 1.85 [m, -C<u>H</u>$_2$-CH_2Br], 1.65 [m, -C<u>H</u>$_2$-CH-$O_2(CH_2)_2$], 1.3 [m, 3x-$(CH_2)_8$-]. The 2,4-DNP derivative was prepared and used as a standard for HPLC analysis (70% THF, 30% water; the desired compound eluting after 5.37 minutes).

<u>48-Bromooctatetraconta-12,24,36-trienal Ethylene Acetal [C_{48} Bromo Acetal (80)].</u>[10]

The C_{24} triphenylphosphonium bromide acetal (53) (122g, 0.165mol,) was dissolved in THF (500ml) under nitrogen and cooled to -10°C whilst stirring. LDA (1.5M in THF, 111ml, 0.166mol) was added dropwise, forming the deep red ylide (75). The mixture was stirred for a further 10 minutes at -10°C when C_{24} bromo aldehyde (111) (71g, 0.165 mol, prepared as described earlier) in THF (100ml) was added, causing the red colouration to fade, leaving a pale cream / yellow colour. This mixture was allowed to reach room temperature and was stirred for 16 hours. The work up procedure was the same as that described earlier for C_{24} bromo acetal. The crude C_{48} bromo acetal was purified by chromatography using silica and 10% diethyl ether / 90% light petroleum bp 40-60°C followed by recrystallisation from light petroleum bp 40-60°C to give a white crystalline solid (80) (78g, 58%). Analysis by ^1H nmr showed the product to be identical to an authentic sample; δ_H ($CDCl_3$): 5.35 [m, 3x-CH=CH-], 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.4 [t, -CH_2Br] were observed in the ratio 6.12 : 0.99 : 4 : 1.91 respectively (correct ratio 6:1:4:2) ; 2.0 [m, 6xC<u>H</u>$_2$-CH=], 1.85 [m, -C<u>H</u>$_2$-CH_2Br], 1.65 [m, -C<u>H</u>$_2$-CH-$O_2(CH_2)_2$], 1.3 [m, 4x-$(CH_2)_8$-]. The 2,4-DNP derivative was prepared and analysed by HPLC (70% THF, 30% water; the desired compound eluting after 6.51 minutes) which showed effective removal of C_{24} materials and no C_{72} material (see page 72).

47-(Dioxolan-2-yl)heptatetraconta-12,24,36-trienaltriphenylphosphonium Bromide [C_{48} Triphenylphosphonium Bromide Acetal (81)].[10]

The C_{48} bromo acetal (80) (22g, 27.3mmol), triphenylphosphine (7.8g, 29.7mmol), 2,2-dimethyl-1,3-dioxolane (5ml), and acetonitrile (120ml) were boiled for 112 hours, under argon. Initially this formed a heterogeneous mixture, which turned homogeneous after 72 hours. The acetonitrile was removed under vacuum leaving a thick yellow oil. Light petroleum bp 40-60°C (500ml) was added, the mixture cooled to -25°C and the oil manipulated using a metal spatula. The petrol layer was carefully decanted and the procedure repeated until a white crystalline solid formed. This was filtered, washed with light petroleum bp 40-60°C (1.5L) to remove excess triphenylphosphine and dried under vacuum. The product (81) (22g, 75%) was analysed by ^{1}H nmr and shown to be identical to an authentic sample; δ_H ($CDCl_3$) 7.75 [m, 3xC_6H_5], 5.35 [m, 3x-CH=CH-], 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.7 [m, -C<u>H</u>$_2P^+Ph_3$]were observed in the ratio 14.70 : 6.27 : 1 : 3.91 : 2.02 respectively (correct ratio 15:6:1:4:2) ; 1.95 [m, 6x-C<u>H</u>$_2$-CH=], 1.6 [m, -C<u>H</u>$_2$-C$HO_2(CH_2)_2$ and -C<u>H</u>$_2$-CH_2-P^+Ph_3] ,1.28 [m, 4x-$(CH_2)_8$-].

48-Bromooctatetraconta-12,24,36-trienal [C_{48} Bromo Aldehyde (113)].[10]

A slurry of silica (400g) in 75% light petroleum bp 40-60°C / 25% dichloromethane was stirred with an aqueous solution of p-toluenesulphonic acid (40g in 40ml of water) and the C_{48} bromo acetal (80) (38.4g, 47.7mmol) was passed through a column of the impregnated silica using the same solvent. The product was collected and the solvent removed under vacuum, at 25°C, giving a colourless oil (35.8g, 99%). The product was identified as the aldehyde (113) by ^{1}H nmr ; δ_H ($CDCl_3$): 9.76 [t, -CHO], 5.35 [m, 3x-CH=CH-], 3.4 [t, -CH_2Br], 2.4 [td, -C<u>H</u>$_2$CHO] were observed in the ratio 1 : 6.31 : 1.88 : 1.89 respectively (correct ratio 1:6:2:2) ; 1.95 [m, 6xCH_2-CH=], 1.85 [m, -C<u>H</u>$_2$-CH_2Br], 1.65 [m, -C<u>H</u>$_2$-CH_2CHO], 1.3 [m, 4x-$(CH_2)_8$-].

72-Bromodoheptaconta-12,24,36,48,60-pentaenal Ethylene Acetal [C_{72} Bromo Acetal (54, n=5)].

The C_{24} triphenylphosphonium bromide (112) (1.07g, 1.46mmol) was dissolved in THF (50ml), and cooled to -25°C, whilst stirring, under nitrogen. LDA (1.5M in THF, 0.973ml, 1.46mmol) was added dropwise, giving an instant colour change, forming a deep orange suspension. This was stirred between -25°C and -20°C for 20 minutes when C_{48} bromo aldehyde (113) (1.11g, 1.46mmol) in THF (10ml,) was added dropwise, forming a cream coloured suspension. This was allowed to reach room temperature and was stirred for 16 hours. The procedure described earlier for C_{36} bromo acetal was used to work up the product. The crude material (1.27g) was chromatographed on silica using 10% diethyl ether / 90% light petroleum bp 40-60°C, giving a colourless oil (54, n=5) (0.443g, 27%) which formed a white solid on standing at room temperature. This was analysed by ^1H nmr and shown to be identical to an authentic sample; δ_H ($CDCl_3$): 5.35 [m, 5x-CH=CH-], 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.4 [t, -CH_2Br] were observed in the ratio 9.05 : 1.05 : 4 : 1.91 respectively (correct ratio 10:1:4:2) ; 1.95 [m, 10xC<u>H</u>$_2$-CH=], 1.85 [m, -C<u>H</u>$_2$-CH_2Br], 1.65 [m, -C<u>H</u>$_2$-CH-$O_2(CH_2)_2$], 1.3 [m, 6x-$(CH_2)_8$-]. The 2,4-DNP derivative was prepared and analysed by HPLC (70% THF, 30% water; the desired compound eluting after 9.75 minutes).

96-Bromohexanonaconta-12,24,36,48,60,72,84-heptaenal Ethylene Acetal [C_{96} Bromo Acetal (88)].[10]

The C_{48} triphenylphosphonium bromide (81) (60.5g, 56.8mmol, 1.2 equiv.) was dissolved in THF (400ml) and cooled to -10°C whilst stirring under argon. LDA (1.5M in THF, 34ml, 52.1mmol, 1.1 equiv.) was added dropwise and the resulting deep orange suspension was stirred at -10°C for 20 minutes. C_{48} Bromo aldehyde (113) (36g, 47.4mmol, 1 equiv.) in THF (75ml) was added, forming a pale cream / yellow suspension, which was allowed to warm up to room temperature. This was stirred for 16 hours, when the solvent was removed under vacuum and the resulting slurry passed through a pad of silica in 7% diethyl ether / 93% light petroleum bp 40-60°C, a new convenient work up procedure. The crude C_{96} bromo acetal was purified by

chromatography on silica using 7% diethyl ether / 93% light petroleum bp 40-60°C and recrystallisation from light petroleum bp 40-60°C, formed a white crystalline solid (83) (57.3g, 73%). Analysis by ^{1}H nmr showed the product to be identical to an authentic sample; δ_H ($CDCl_3$): 5.35 [m, 7x-CH=CH-], 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.4 [t, -CH_2Br] were observed in the ratio 13.95 : 1.09 : 4 : 1.95 respectively (correct ratio 14:1:4:2) ; 1.95 [m, 14xC<u>H</u>$_2$-CH=], 1.85 [m, -C<u>H</u>$_2$-CH_2Br], 1.65 [m, -C<u>H</u>$_2$-CH-$O_2(CH_2)_2$], 1.3 [m, -8x$(CH_2)_8$-]. The 2,4-DNP derivative was prepared and analysed by HPLC (75% THF, 25% water; the desired compound eluting after 4.98 minutes) showing no C_{48} material or C_{144} bromo acetal (54, n=11)[19] to be present.

<u>95-(dioxolan-2-yl)pentanonaconta-12,24,36,48,60,72,84-heptaenyltriphenyl phosphonium Bromide [C_{96} Triphenylphosphonium Bromide Acetal (89)].</u>[11]

The C_{96} bromo acetal (83) (9.98g, 6.79mmol, 1 equiv.), triphenylphosphine (9.0g, 34.3mmol, 5 equiv.), 2,2-dimethyl-1,3-dioxolane (3ml), and acetonitrile (35ml) were boiled for 112 hours, under argon. Initially a heterogeneous mixture was formed, which turned homogeneous after 3 days. The acetonitrile was removed under vacuum leaving a thick yellow oil which was chromatographed on silica, using 2% methanol / 98% dichloromethane to remove the excess triphenylphosphine. The solvent polarity was then increased to 5% methanol / 95% dichloromethane to elute the salt which formed a pale yellow solid (89) (11.4g, 97%). Analysis by ^{1}H nmr showed this to be identical to an authentic sample; δ_H ($CDCl_3$) 7.75 [m, 3xC_6H_5], 5.35 [m, 7x-CH=CH-], 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.7 [m, -C<u>H</u>$_2P^+Ph_3$] were observed in the ratio 15.23 : 14.71 : 0.95 : 4 : 1.75 respectively (correct ratio 15:14:1:4:2) ; 1.95 [m, 14x-C<u>H</u>$_2$-CH=] 1.6 [m, -C<u>H</u>$_2$-$CHO_2(CH_2)_2$ and -C<u>H</u>$_2$-CH_2-P^+Ph_3] 1.28 [m, 8x-$(CH_2)_8$-].

<u>96-Bromohexanonaconta-12,24,36,48,60,72,84,-heptaenal [C_{96} Bromo Aldehyde (84)].</u>[11]

A slurry of silica (200g) in 75% light petroleum bp 40-60°C / 25% dichloromethane was stirred with an aqueous solution of p-toluenesulphonic acid (7g in 10ml of water) and the C_{96} bromo acetal (83) (4.8g, 3.36mmol) was passed through a column of the

impregnated silica using the same solvent. The product was collected and the solvent removed under vacuum, at 25°C, giving a white solid (4.6g, 99%). The product was identified as the aldehyde (84) by ^{1}H nmr ; δ_H ($CDCl_3$): 9.76 [t, -CHO], 5.35 [m, 7x-CH=CH-], 3.4 [t, -CH_2Br], 2.4 [td, C$\underline{H}_2$CHO] were observed in the ratio 1 : 14.63 : 2.17 : 2.27 respectively (correct ratio 1:14:2:2) ; 1.95 [m, 14x-CH_2-CH=], 1.85 [m, -C$\underline{H}_2$-CH_2Br], 1.65 [m, -C$\underline{H}_2$-CH_2CHO], 1.3 [m, 8x-$(CH_2)_8$-].

192-Bromohexaconta-12,24,36,48,60,72,84,96,108, 120,132,144,156,168,180-pentadecaenal Ethylene Acetal [C_{192} Bromo Acetal (91)].[11]

The C_{96} triphenylphosphonium bromide acetal (89) (7.0g, 4.04mmol, 1.2 equiv.) was dissolved in THF (100ml) and cooled to -20°C (at -5°C a white precipitate of the salt formed), under argon, whilst stirring with a magnetic stirrer. LDA (1.5M in THF, 1.2ml, 1.8mmol, 0.5 eqiv.) was added dropwise, until a permanent yellow colour formed, then further LDA (2.45ml, 3.67mmol, 1.1 eqiv.) was added forming an orange mixture. This was stirred for 0.5 hours at -20°C when a solution of C_{96} bromo aldehyde (84) (4.60g, 3.32mmol, 1 eqiv.) in THF (30ml) was added. This caused the colour to fade to yellow and a thick precipitate formed. The cold bath was removed and the mixture was allowed to reach room temperature. At 5°C the precipitate dissolved, leaving a yellow solution. This was stirred for 17 hours, when the whole solution was passed down a short pad of silica (100g) using 5% diethyl ether / 95% light petroleum bp 40-60°C. A pale yellow oil (9.12g) was collected, which was chromatographed (silica, 4% diethyl ether / 96% light petroleum, bp 40-60°C) giving a white solid (91) (7.25g, 80%). Analysis by ^{1}H nmr showed the product to be identical to an authentic sample; δ_H ($CDCl_3$): 5.35 [m, 15x-CH=CH-], 4.85 [t, -C$\underline{H}O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], 3.4 [t, -CH_2Br] were observed in the ratio 33.51 : 0.92 : 4 : 1.93 respectively (correct ratio 30:1:4:2); 1.95 [m, 30x -C$\underline{H}_2$-CH=], 1.85 [m, -C$\underline{H}_2$-CH_2Br], 1.65 [m, -C$\underline{H}_2$-CH-$O_2(CH_2)_2$], 1.3 [m, 16x-$(CH_2)_8$-]. The 2,4-DNP derivative was formed and analysed by HPLC (gradient elution; t=0: 45% THF, 55% methanol to t=10 minutes: 80% THF, 20% methanol, the desired compound eluting after 6.70 minutes) to showing the absence of C_{96} homologues and any material at longer retention times.

98-Bromooctanonaconta-12,24,36,48,60,72,84,96-octaene [C_{98} Bromo Polyene (119)].

A suspension of ethyltriphenylphosphonium bromide (4.41g, 11.8mmol) in THF (43.7ml, freshly distilled from $LiAlH_4$ and NaH) was cooled to -20°C, whilst stirring under argon. LDA (6.3ml, 9.45mmol) was added, forming the characteristic orange / red colour of the ylide and the solution was stirred for 0.5 hours between -25°C and -15°C. The C_{96} bromo aldehyde (84) (3.2g, 2.24mmol, 1 equiv.), dissolved in THF (20ml) was cooled to -20°C, under argon. An aliquot of the C_2 ylide solution (12.5ml, 3.79mmol of C_2 ylide, 1.6 equiv.) was added to the aldehyde, forming a yellow suspension. The mixture was allowed to reach room temperature and was stirred for 16 hours when it was passed through a short silica column (100g) using light petroleum bp 40-60°C. The crude material was chromatographed on silica using light petroleum bp 40-60°C as eluent, to give a colourless oil (2.48g, 76%), which formed a white crystalline solid on standing, the C_{98} bromo polyene (119). m.p. 37.5-38.5°C. (Found: C, 81.66%; H, 12.77%; $C_{98}H_{181}Br$ requires: C, 81.77%; H, 12.67%). The product was analysed by ^1H nmr ; δ_H ($CDCl_3$): 5.35 [m, 8x-CH=CH-], 3.4 [t, -CH_2Br] were observed in the ratio 16.6 : 2 respectively (correct ratio 16:2) ; 1.95 [m, 15x$C\underline{H}_2$-CH=], 1.85 [m, -$C\underline{H}_2$-CH_2Br], 1.6 [dd, =CH-$C\underline{H}_3$], 1.3 [m, 8x-$(CH_2)_8$-].

Octanonaconta-2,14,26,38,50,62,74,86,-octaene [C_{98} Polyene (120)].

The C_{98} bromo polyene (119) (2.41g, 1.67mmol) and "Superhydride" (lithium triethylborohydride) (1.0M solution in THF, 10mls, 0.1mol), a colourless heterogeneous mixture, were stirred together at room temperature under argon for 4 hours. The product was dissolved in light petroleum bp 40-60°C and washed with dilute sulphuric acid (0.5M, 200ml) and water (200ml). In each case the aqueous layers were extracted with light petroleum bp 40-60°C. The organic layers were combined and dried over sodium sulphate. The solvent was removed under vacuum, leaving a colourless oil, which was chromatographed on silica using neat light petroleum bp 40-60°C, giving a white solid (120) (2.14g, 94%), m.p. 37.5-38°C.(Found: C, 86.56%; H, 13.63%; $C_{98}H_{182}$ requires: C, 86.52%; H, 13.48%). Analysis by ^1H nmr showed; δ_H ($CDCl_3$): 5.35 [m, 8x-CH=CH-], 1.95 [m, 15x-$C\underline{H}_2$-CH=], 1.6 [dd, =CH-$C\underline{H}_3$], 1.3 [m, -$(CH_2)_9$- and 7x-$(CH_2)_8$-], 0.87 [t, -CH_2-$C\underline{H}_3$].

Octanonacontane [$C_{98}H_{198}$ Alkane (121)].

The C_{98} polyene (120) (2.01g), platinum on activated carbon (1g, Pt content 5%) and ethyl palmitate (10ml, redistilled) were stirred under an atmosphere of hydrogen and heated to 130°C for 14 hours. Light petroleum bp 100-120°C (10ml) was added and the mixture was allowed to reach room temperature whilst stirring. The suspension was filtered and washed with light petroleum bp 40-60°C to remove the ethyl palmitate. The resulting solid was placed into thimble and using an apparatus which allowed hot vapours to heat the thimble, was subjected to continuous extraction using boiling light petroleum bp 100-120°C (150ml) for 16 hours to separate the hydrocarbon from the catalyst. On cooling the hot extract, the hydrocarbon crystallised out and was filtered and washed with light petroleum bp 40-60°C. The resulting white solid was heated at 110°C under vacuum (0.01mm Hg) for 48 hours which removed dibutyl and dioctyl phthalate, contaminants which are presumed to have originated from the solvents to give the alkane (121) (1.84g, 90%), m.p. 113-114°C.(Found: C, 85.40%; H, 14.54%; $C_{98}H_{198}$ requires C, 85.50%; H, 14.50%). Analysis by ^1H nmr carried out using 1,1,2,2-tetrachloroethane-d_2, run at 120°C, showed the complete absence of -CH=CH- at δ_H 5.35. ; δ_H (1,1,2,2-tetrachloroethane-d_2): 1.35 [m, -$(CH_2)_{96}$-], 0.96 [t, 2x-CH_3].

192-Bromodononacontahecta-12,24,36,48,60,72,84,96,108,120,132,144, 156, 168,180,-pentadecaenal [C_{192} Bromo Aldehyde (92)].[11]

A slurry of silica (200g) in 75% light petroleum bp 40-60°C / 25% dichloromethane was stirred with an aqueous solution of p-toluenesulphonic acid (3g in 5ml of water) and the C_{192} bromo acetal (91) (free from secondary bromide) (2.57g, 0.919mmol) was passed through a column of the impregnated silica using the same solvent. The product was collected and the solvent removed under vacuum, at 25°C, giving a white solid (92) (2.51g, 99%). Analysis by ^1H nmr showed the product to be identical to an authentic sample; δ_H ($CDCl_3$): 9.76 [t, -CHO], 5.35 [m, 15x-CH=CH-], 3.4 [t, -CH_2Br], 2.4 [td, -CH_2CHO] were observed in the ratio 1 : 32.4 : 2.0 : 1.3 respectively (correct ratio 1:30:2:2) ; 1.95 [m, 30x-CH_2-CH=], 1.85 [m, -$C\underline{H}_2$-CH_2Br], 1.65 [m, -$C\underline{H}_2$-CH_2CHO], 1.3 [m, 16x-$(CH_2)_8$-].

1-Bromodecadicta-12,24,36,48,60,72,84,96,108,120,132,144,156,168,180,192, 204-heptadecene [C_{210} Bromo Polyene (122)].

Octadeca-12-enyltriphenylphosphonium bromide[18] (0.654g, 1.1mmol, 1.2equiv.) was dissolved in THF (50ml) under argon. The solution was cooled to -25°C whilst stirring with a magnetic stirrer (at 0°C the salt formed a white precipitate). LDA (1.5M in THF, 0.4ml, 1.1 equiv.) was added until a permanent yellow colour formed, then further LDA (0.67ml, 1mmol) was added, forming the orange coloured ylide. This was stirred between -25°C and -20°C for 0.75 hours when a solution of C_{192} bromo aldehyde (92) (2.51g, 0.909mmol, 1 equiv.) in THF (20ml,) was added at -25°C, forming a thick, pale yellow precipitate. This was allowed to reach room temperature, the precipitate dissolved at 5°C, forming a yellow solution which was stirred for 65 hours. The THF was removed under vacuum and the remaining slurry was passed through a short pad of silica (200g) in light petroleum bp 40-60°C, giving a colourless oil. This was purified by chromatography on silica using light petroleum, bp 40-60°C, giving a colourless oil (1.65g, 60%) which formed a white solid at room temperature, the C_{210} bromo polyene (122), m.p. 31-32°C.(Found: C, 84.05%; H, 12.96%; $C_{210}H_{387}Br$ requires; C, 84.29%; H, 13.03%). Analysis by ^1H nmr showed; δ_H ($CDCl_3$): 5.35 [m, 17x-CH=CH-], 3.4 [t, $-CH_2Br$] were observed in the ratio 35.0 : 2 respectively [correct ratio 34:2] ; 1.95 [m, 34x-$C\underline{H}_2$-CH=], 1.85 [m, -$C\underline{H}_2$-CH_2Br], 1.3 [m, 17x-$(CH_2)_8$- and -$(CH_2)_3$-], 0.88 [t, -CH_2-$C\underline{H}_3$].

Decadicta-6,18,30,42,54,66,78,90,102,114,126,138,150,162,174,186,198-heptadecaene [C_{210} Polyene (123)].

The C_{210} bromo polyene (122) (1.67g, 0.558mmol) in THF (10ml, freshly distilled) and "Superhydride" (1.0M solution in THF, 2.79ml, 2.79mmol), a colourless heterogeneous mixture, were stirred together at room temperature, under argon, for 4 hours. The product was worked up using the procedure described earlier for C_{98} polyene. The crude material was chromatographed on silica using neat light petroleum bp 40-60°C, giving a colourless oil (1.32g, 81%) which formed a white solid at room temperature, (123), m.p. 31-32°C.(Found: C, 86.48%; H, 13.63%; $C_{210}H_{388}$ requires: C, 86.57%; H, 13.42%). The product was analysed by ^1H nmr ; δ_H ($CDCl_3$): 5.35 [m,

17x-CH=CH-], 1.95 [m, 34x$C\underline{H}_2$-CH=], 1.3 [m, -$(CH_2)_9$, 16x-$(CH_2)_8$- and -$(CH_2)_3$-], 0.87 [t, 2x-CH_2-$C\underline{H}_3$].

Decadictane [$C_{210}H_{422}$ Alkane (124)].

Using the hydrogenation procedure described earlier for C_{98} alkane (121), $C_{210}H_{422}$ (124) (1.23g, 92%) was formed from C_{210} polyene (123) (1.32g). m.p. 125.5-126°C. (Found: C, 85.73%; H, 14.35%; $C_{210}H_{422}$ requires C, 85.57%; H, 14.43%. Analysis by ^1H nmr was carried out using 1,1,2,2-tetrachloroethane-d_2, run at 120°C, which showed the complete absence of -CH=CH- at δ_H 5.35 ; δ_H (1,1,2,2-tetrachloroethane-d2): 1.35 [m, -$(CH_2)_{208}$-], 0.96 [t, 2x-CH_3].

Octapentacontadicta-6,18,30,42,54,66,78,90,102,114,126,138,150,162,174,186, 198,210,222,234,246-hencosaene [C_{258} Polyene (127, n=20)].

Using the procedure described earlier for C_{98} polyene (120), C_{258} polyene (127, n=20) (0.50g, 43%) was formed from C_{258} bromo polyene (125, n=20) (1.19g). m.p. 38.5-39.5°C. (Found: C, 86.40%; H, 13.46%; $C_{258}H_{476}$ requires: C, 86.59%; H, 13.41%). The product was analysed by ^1H nmr ; δ_H ($CDCl_3$): 5.35 [m, 21x-CH=CH-], 1.95 [m, 42x$C\underline{H}_2$-CH=], 1.3 [m, 20x-$(CH_2)_8$-, -$(CH_2)_9$- and -$(CH_2)_3$-], 0.87 [t, 2x-CH_2-$C\underline{H}_3$].

Octapentacontadictane [$C_{258}H_{518}$ Alkane (128, n=256)].

Using the procedure described earlier for C_{98} alkane (121), $C_{258}H_{518}$ (128, n=256) (0.30g, 61%) was formed from C_{258} polyene (127, n=20) (0.48g). m.p. 126-128°C. (Found: C, 85.76%; H, 14.31%; $C_{258}H_{518}$ requires C, 85.58%; H, 14.42%). Analysis by ^1H nmr, carried out using 1,1,2,2-tetrachloroethane-d_2, run at 120°C, showed the complete absence of -CH=CH- at δ_H 5.35 ; δ_H (1,1,2,2-tetrachloroethane-d2): 1.35 [m, -$(CH_2)_{256}$-], 0.96 [t, 2x-CH_3].

Docosahectane [$C_{122}H_{246}$ Alkane (128, n=120)].

Using the procedure described earlier for C_{98} alkane (121), $C_{122}H_{246}$ (128, n=120) (1.62g, 96%) was formed from C_{122} polyene (126, n=9) (1.66g). m.p. 111-112°C. (Found: C, 85.69%; H, 13.98%; $C_{122}H_{246}$ requires C, 85.52%; H, 14.47%). Analysis by ^1H nmr, carried out using 1,1,2,2-tetrachloroethane-d_2, run at 120°C, showed the

complete absence of -CH=CH- at δ_H 5.35 ; δ_H (1,1,2,2-tetrachloroethane-d_2): 1.35 [m, -$(CH_2)_{120}$-], 0.96 [t, 2x-CH_3].

Dohexacontahectane [$C_{162}H_{326}$ Alkane (128, n=160)].

Using the procedure described earlier for C_{98} alkane (121), C_{162} alkane (128, n=160) (2.74g, 91%) was formed from C_{162} polyene (127, n=12) (2.95g). m.p. 121-121.5°C. (Found: C, 85.35%; H, 14.55%; $C_{162}H_{326}$ requires C, 85.55%; H, 14.45%). Analysis by ^{1}H nmr, carried out using 1,1,2,2-tetrachloroethane-d_2, run at 120°C, showed the complete absence of -CH=CH- at δ_H 5.35 ; δ_H (1,1,2,2-tetrachloroethane-d_2,): 1.35 [m, -$(CH_2)_{160}$-], 0.96 [t, 3x-CH_3].

Tetranonacontahectane [$C_{194}H_{390}$ Alkane (128, n=192)].

Using the procedure described earlier for C_{98} alkane (121), C_{194} alkane (128, n=192) (1.41g, 90%) was formed from C_{194} polyene (122, n=15) (1.54g). m.p. 123.5-124.5°C. (Found: C, 85.69%; H, 14.09%; $C_{194}H_{390}$ requires C, 85.57%; H, 14.43%). Analysis by ^{1}H nmr, carried out using 1,1,2,2-tetrachloroethane-d_2 run at 120°C, showed the complete absence of -CH=CH- at δ_H 5.35 ; δ_H (1,1,2,2-tetrachloroethane-d2,): 1.35 [m, -$(CH_2)_{192}$-], 0.96 [, 2x-CH_3].

Tetraoctacontatricta-12,24,36,48,60,72,84,96,108,120,132,144,156,168,180,192,204,216,228,240,252,264,276,288,300,312,324,336,348,360,372-hentriacontaenal Ethylene Acetal [C_{384} Polyene Acetal (130)].[11]

The C_{384} bromo acetal (54, n=31) (0.93g, 0.17mmol), dissolved in THF (2.5ml) and "Superhydride" (1.0M solution in THF, 1ml, 1mmol), a colourless heterogeneous mixture, were stirred together at room temperature under argon for 4 hours. The reaction was worked up using the procedure described earlier for C_{98} polyene (120), giving a colourless oil, which was purified by chromatography on silica using light petroleum bp 40-60°C. The product, C_{384} polyene acetal (130) (0.82g, 89%) was analysed by ^{1}H nmr and shown to be identical to an authentic sample; δ_H ($CDCl_3$): 5.35 [m, 31x-CH=CH-], 4.85 [t, -C<u>H</u>$O_2(CH_2)_2$], 3.9 [m, -O-$(CH_2)_2$-O-], were observed in the ratio 61.03 : 0.85 : 4 respectively (correct ratio 62:1:4) ;1.95 [m, 62xC<u>H</u>$_2$-CH=], 1.3 [m, 32x-$(CH_2)_8$-], 0.87 [t, -CH_2-C<u>H</u>$_3$].

1-Bromohexahexaconta-12,24,36,48,60-pentaene [C_{66} Bromo Polyene (117)].

Octadeca-12-enyltriphenylphosphonium bromide (115)[18] (6.2g, 10.4mmol, 1.2 equiv.) was dissolved in THF (85ml) and cooled to -15°C under argon, whilst stirring. LDA (1.5M in THF, 6.4ml, 9.58mmol, 1.1 equiv.) was added dropwise, giving an orange solution, which was stirred at -15°C for 20 minutes. C_{48} Bromo aldehyde (113) (6.62g, 8.70mmol, 1 equiv.) in THF (25ml) was added at -15°C, giving a pale yellow precipitate. This was allowed to reach room temperature and was stirred for 1 hour. The precipitate dissolved at -5°C forming a yellow solution. The excess ylide was destroyed by the addition of glacial acetic acid (1 drop), which decolourised the solution. The solvent was removed and the resulting slurry was passed through a pad of silica (100g) using light petroleum bp 40-60°C, giving a colourless oil (8.9g). This was purified by chromatography on silica using light petroleum bp 40-60°C, giving a colourless oil (117) (7.40g, 85%) which formed a white solid on cooling. m.p. 26-27°C. (Found: C, 80.02%; H, 12.86%; $C_{66}H_{123}Br$ requires: C, 79.54%; H, 12.44%). The product was analysed by ^1H nmr ; δ_H ($CDCl_3$): 5.35 [m, 5x-CH=CH-], 3.4 [t, -CH_2Br] were found in the ratio 10.4 : 2 respectively (correct ratio 10:2) ; 1.95 [m, 10x-C$\underline{H}_2$-CH=], 1.85 [m, -C$\underline{H}_2$-CH_2Br], 1.3 [m, 5x-$(CH_2)_8$- and -$(CH_2)_3$-], 0.85 [t, -CH_2-C$\underline{H}_3$].

Hexahexaconta-12,24,36,48,60-heptaenyltriphenylphosphonium bromide [C_{66} triphenylphosphonium bromide (118)].

The C_{66} bromo polyene (117) (7.17g, 7.20mmol, 1 equiv.), triphenylphosphine (9.44g, 35.9mmol, 5 equiv.) and acetonitrile (65ml) were heated under reflux and stirred for 166 hours, under argon. The acetonitrile was removed under vacuum leaving a thick yellow oil. This was purified by chromatography on silica, using 5% methanol / 95% dichloromethane giving a sticky, pale yellow solid (118) (8.54g, 94%).(Found: C, 79.19%; H, 11.12%; $C_{84}H_{138}PBr$ requires: C, 80.20%; H, 10.98%). The product was analysed by ^1H nmr ; δ_H ($CDCl_3$) 7.75 [m, 3x-C_6H_5], 5.35 [m, 5x-CH=CH-], 3.7 [m, -C$\underline{H}_2P^+Ph_3$] were found in the ratio 15.14 : 11.30 : 2 respectively (correct ratio 15:10:2) ; 1.95 [m, 10x-C$\underline{H}_2$-CH=], 1.6 [m, -C$\underline{H}_2$-$CH_2P^+Ph_3$], 1.28 [86H, m, 5x-$(CH_2)_8$- and -$(CH_2)_3$-], 0.85 [t, -CH_2-C$\underline{H}_3$].

Hexyltriphenylphosphonium bromide [C_6 triphenylphosphonium bromide (93)].[11]

The 1-bromohexane used to form the salt was distilled on the 'Spaltrohr Fractional Distillation Unit' (oil bath 193°C, mantle 120°C, atmospheric pressure). The fraction distilling between 154-154.5°C was collected and shown to be pure by CG chromatography.

1-Bromohexane (73.69g, 0.447mol, 1 equiv.) and triphenylphosphine (128.8g, 0.491mol, 1.1 equiv.) in acetonitrile (300ml) were boiled for 72 hours, under argon. The solvent was then removed under vacuum, leaving a yellow gum. Light petroleum bp 40-60°C (250ml) was added and the gum manipulated until a white crystalline solid formed. This was filtered and washed with light petroleum bp 40-60°C to remove excess triphenylphosphine and the salt (93) (170.7g, 89%) was dried under vacuum. Analysis by ^1H nmr showed the product to be identical to an authentic sample; δ_H ($CDCl_3$) 7.75 [m, 3x-C_6H_5], 3.7 [m, -$C\underline{H}_2P^+Ph_3$] were found in the ratio 15.79 : 2 respectively (correct ratio 15:2) ; 1.6 [m, -$C\underline{H}_2$-$CH_2P^+Ph_3$], 1.28 [m, -$(CH_2)_3$-], 0.85 [t, -CH_2-$C\underline{H}_3$].

References

References

1. Cowie, J.M.G., Polymers: Chemistry and Physics of Modern Materials, 2nd Edition, Blackie (1991).

2. Ungar, G. and Keller, A., Polymer, **1986**, 27, 1835.

3. Ungar, G. and Keller, A., Polymer, **1987**, 28, 1899.

4. Carothers, W.H., Hill, J.W., Kirby, J.E. and Jacobson, R.A., J. Amer. Chem. Soc., **1930**, 52, 5279.

5. Schill, G., Zurcher, C. and Fritz, H., Chem. Ber., **1978**, 111, 2901.

6. Lee, K.S. and Wegner, G., Makromol. Chem., Rapid Commun., **1985**, 6, 203.

7. Doolittle, A.K. and Peterson, R.H., J. Amer. Chem. Soc., **1951**, 2145.

8. Ställberg, G., Ställberg-Stenhagen, S. and Stenhagen, E., Acta Chemica Scandinavica, **1952**, 6, 313.

9. Reinhard, R.R. and Dixon, J.A., J. Org. Chem., **1965**, 30, 1450.

10. Igner, E., Paynter, O.I., Simmonds, D.J. and Whiting, M.C., J. Chem. Soc., Perkin Trans. 1, **1987**, 2447.

11. Bidd, I., Holdup D.W., and Whiting, M.C., J. Chem. Soc., Perkin Trans. 1, **1987**, 2455.

12. Bidd, I., Kelly, D.J., Ottley, P.M., Paynter, O.I., Simmonds, D.J. and Whiting M.C., J. Chem. Soc., Perkin Trans. 1, **1983**, 1369.

13. Bidd, I. and Whiting, M.C., Tetrahedron Lett., **1984**, 25, 5949.

14. Work carried out by D.G. Proctor, unpublished work.

15. Made by High Force Research Ltd., Mountjoy Research Centre, Stockton Road, Durham, DHL 3SW.

16. Work carried out by G.M.Brooke, unpublished work.

17. Work carried out by the author of this Thesis.

18. Prepared by S. Mohammed, unpublished work.

19. C_{144} Br Acetal (54, n=11) prepared by G.M. Brooke via $C_{96} + C_{48}$ Wittig Reaction

Appendices

Appendix 1

First Year Courses

Polymer Synthesis

Practical NMR

Synthetic Methodology in Organometallic and Coordination Chemistry

Research Colloquia, Seminars and Lectures

Organised by the department of chemistry (August 1993-July 1995)

* Author's attendance.

1993

September 13 Prof. Dr. A.D. Schlüter,* Freie Universität Berlin, Germany
Synthesis and Characterisation of Molecular Rods and Ribbons

September 13 Dr. K.J. Wynne, Office of Naval Research, Washington, USA
Polymer Surface Design for Minimal Adhesion

September 14 Prof. J.M. DeSimone, University of North Carolina, Chapel Hill, USA
Homogeneous and Heterogeneous Polymerisations in Environmentally Responsible Carbon Dioxide

September 28 Prof. H. Ila, North Eastern Hill University, India
Synthetic Strategies for Cyclopentanoids via Oxoketene Dithioacetals

October 4 Prof. F.J. Feher,* University of California, Irvine, USA
Bridging the Gap between Surfaces and Solution with Sessilquioxanes

October 14 Dr. P. Hubberstey, University of Nottingham
Alkali Metals: Alchemist's Nightmare, Biochemist's Puzzle and Technologist's Dream

October 20 Dr. P. Quayle,* University of Manchester
Aspects of Aqueous ROMP Chemistry

October 21 Prof. R. Adams,* University of South Carolina, USA
Chemistry of Metal Carbonyl Cluster Complexes : Development of Cluster Based Alkyne Hydrogenation Catalysts

October 27 Dr. R.A.L. Jones Cavendish Laboratory, Cambridge
Perambulating Polymers

November 10 Prof. M.N.R. Ashfold, University of Bristol
High Resolution Photofragment Translational Spectroscopy : A New Way to Watch Photodissociation

November 17 Dr. A. Parker, Rutherford Appleton Laboratory, Didcot
Applications of Time Resolved Resonance Raman Spectroscopy to Chemical and Biochemical Problems

November 24 Dr. P.G. Bruce,* University of St. Andrews
Structure and Properties of Inorganic Solids and Polymers

November 25 Dr. R.P. Wayne,* University of Oxford
The Origin and Evolution of the Atmosphere

December 1 Prof. M.A. McKervey,* Queen's University, Belfast
Synthesis and Applications of Chemically Modified Calixarenes

December 8 Prof. O. Meth-Cohn,* University of Sunderland
Friedel's Folly Revisited - A Super Way to Fused Pyridines

December 16 Prof. R.F. Hudson, University of Kent
Close Encounters of the Second Kind

1994

January 26 Prof. J. Evans,* University of Southampton
Shining Light on Catalysts

February 2 Dr. A. Masters, University of Manchester
Modelling Water Without Using Pair Potentials

February 9 Prof. D. Young*, University of Sussex
Chemical and Biological Studies on the Coenzyme Tetrahydrofolic Acid

February 16 Prof. K.H. Theopold, University of Delaware, USA
Paramagnetic Chromium Alkyls : Synthesis and Reactivity

February 23 Prof. P.M. Maitlis,* University of Sheffield
Across the Border : From Homogeneous to Heterogeneous Catalysis

March 2 Dr. C. Hunter,* University of Sheffield
Noncovalent Interactions between Aromatic Molecules

March 9 Prof. F. Wilkinson, Loughborough University of Technology
Nanosecond and Picosecond Laser Flash Photolysis

March 10 Prof. S.V. Ley,* University of Cambridge
New Methods for Organic Synthesis

March 25 Dr. J. Dilworth, University of Essex
Technetium and Rhenium Compounds with Applications as Imaging Agents

April 28 Prof. R. J. Gillespie, McMaster University, Canada
The Molecular Structure of some Metal Fluorides and Oxofluorides: Apparent Exceptions to the VSEPR Model.

May 12 Prof. D. A. Humphreys, McMaster University, Canada
Bringing Knowledge to Life

October 5 Prof. N. L. Owen, Brigham Young University, Utah, USA
Determining Molecular Structure - the INADEQUATE NMR way

October 19 Prof. N. Bartlett,* University of California
Some Aspects of Ag(II) and Ag(III) Chemistry

November 2 Dr P. G. Edwards,* University of Wales, Cardiff
The Manipulation of Electronic and Structural Diversity in Metal Complexes - New Ligands

November 3 Prof. B. F. G. Johnson,* Edinburgh University
Arene - Metal Clusters

November 9 Dr J. P. S. Badyal, University of Durham
Chemistry at Surfaces, A Demonstration Lecture

November 9 Dr G Hogarth,* University College, London
New Vistas in Metal Imido Chemistry

November 10 Dr M Block,* Zeneca Pharmaceuticals, Macclesfield
Large Scale Manufacture of the Thromboxane Antagonist Synthase Inhibitor ZD 1542

November 16 Prof. M. Page,* University of Huddersfield
Four Membered Rings and β-Lactamase

November 23 Dr J. M. J. Williams,* University of Loughborough
New Approaches to Asymmetric Catalysis

December 7 Prof. D Briggs, ICI and University of Durham
Surface Mass Spectrometry

1995

January 11 Prof. P. Parsons,* University of Reading
Applications of Tandem Reactions in Organic Synthesis

January 18 Dr G. Rumbles, Imperial College, London
Real or Imaginary 3rd Order non-Linear Optical Materials

January 25 Dr D. A. Roberts,* Zeneca Pharmaceuticals
The Design and Synthesis of Inhibitors of the Renin-Angiotensin System

February 1 Dr T Cosgrove, Bristol University
Polymers do it at Interfaces

February 8 Dr D. O'Hare, Oxford University
Synthesis and Solid State Properties of Poly-, Oligo- and Multidecker Metallocenes

February 22 Prof. E Schaumann,* University of Clausthal
Silicon and Sulphur Mediated Ring-opening Reactions of Epoxide

March 1 Dr M. Rosseinsky, Oxford University
Fullerene Intercalation Chemistry

March 22 Dr M. Taylor, University of Auckland, New Zealand
Structural Methods in Main Group Chemistry

April 26 Dr M. Schroder, University of Edinburgh
Redox Active Macrocyclic Complexes : Rings, Stacks and Liquid Crystals

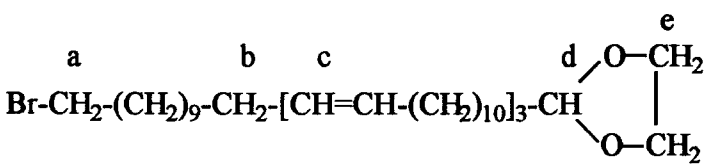
May 3 Prof. E. W. Randall, Queen Mary and Westfield College
New Perspectives in NMR Imaging

May 4 Prof. A. J. Kresge, University of Toronto
The Ingold Lecture Reactive Intermediates : Carboxylic Acid Enols and Other Unstable Species

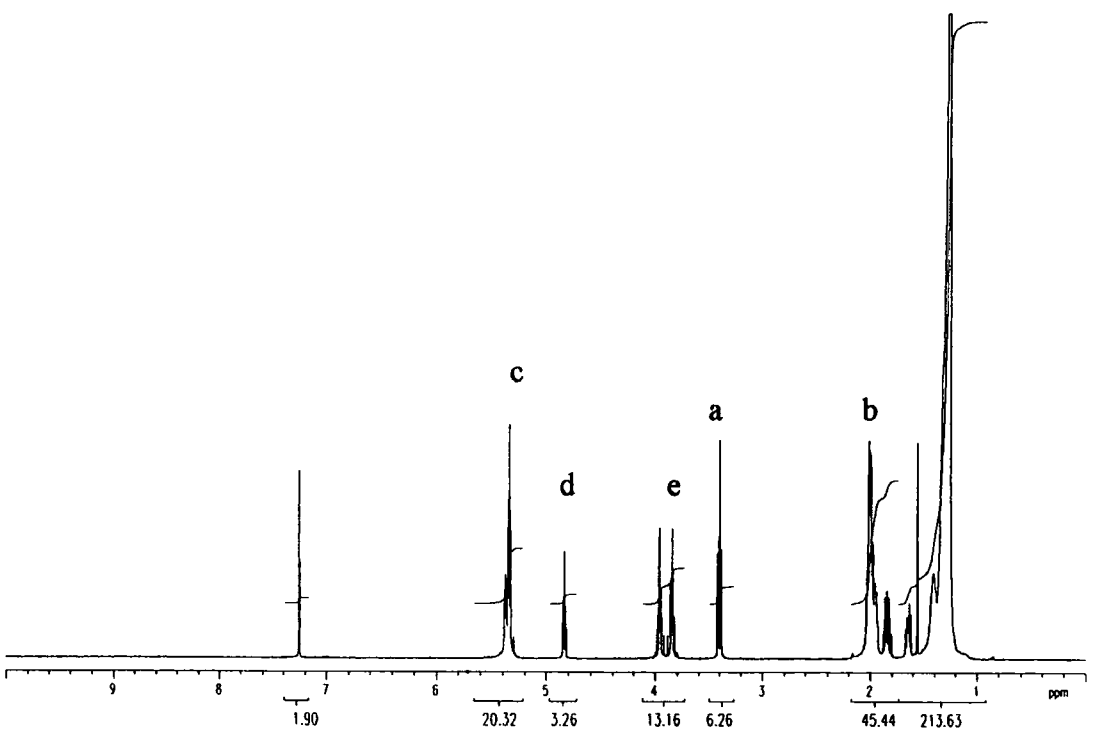
Appendix 2

^{1}H NMR Spectra

C_{48} Bromo Acetal (80)



(80)

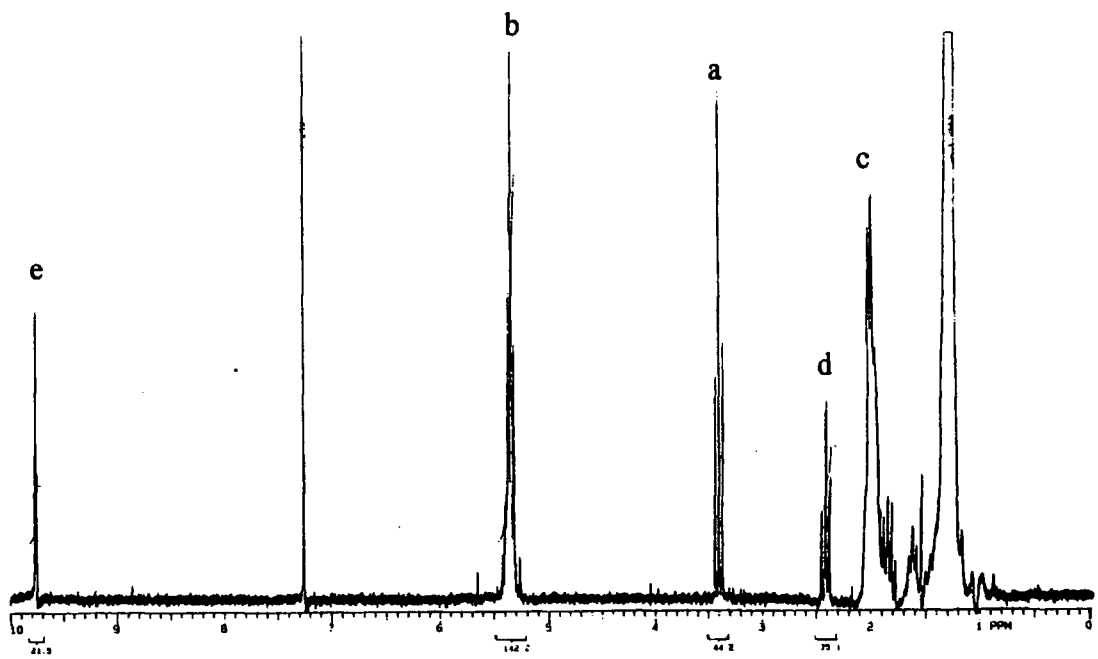


C_{48} Bromo Aldehyde (113)

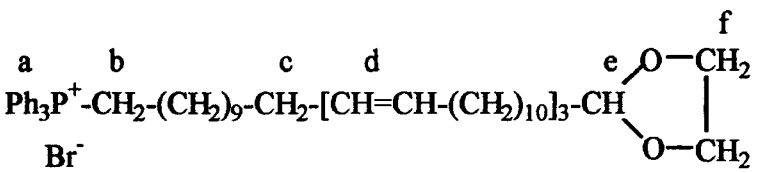
a b c d e

$Br\text{-}CH_2\text{-}[(CH_2)_{10}\text{-}CH{=}CH]_3\text{-}CH_2\text{-}(CH_2)_8\text{-}CH_2\text{-}CHO$

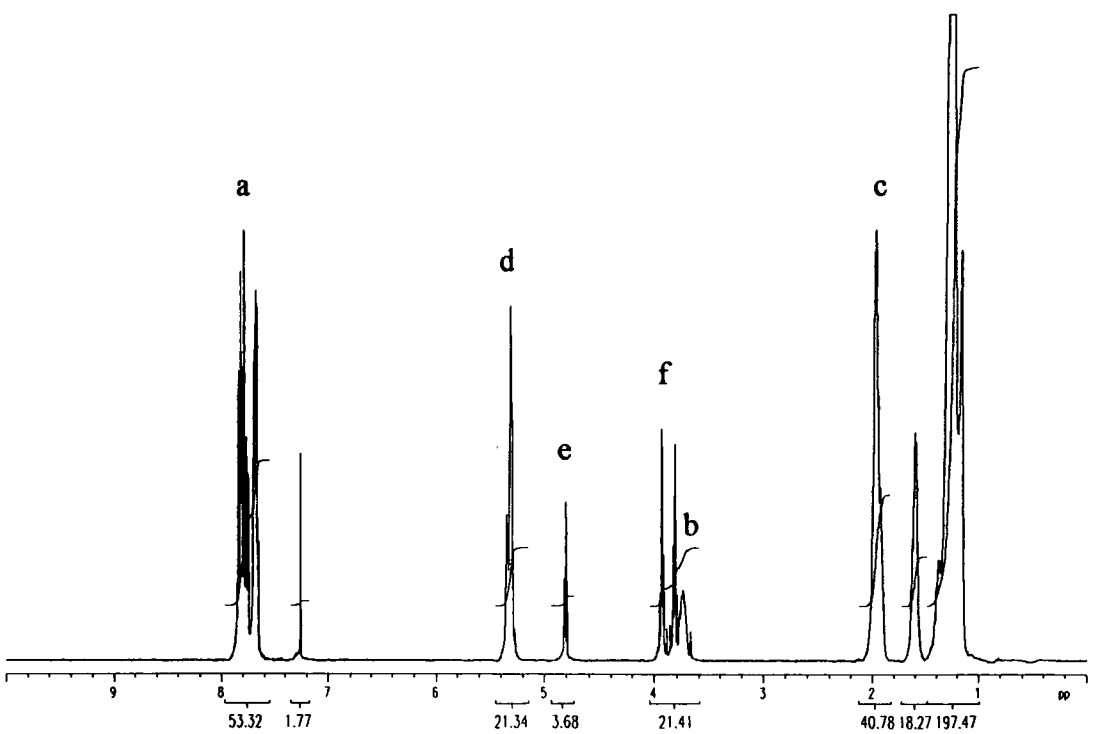
(113)



C_{48} Triphenyphosphonium Bromide Acetal (81)



(81)

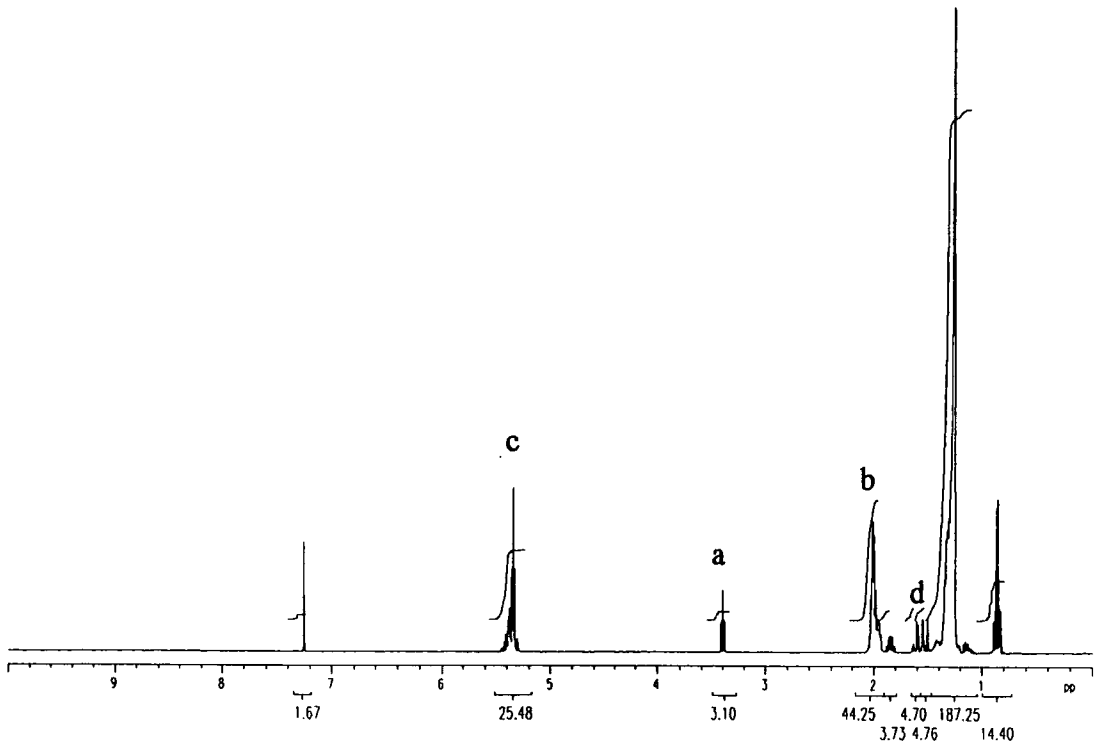


C_{98} Bromo Polyene (119)

a b c d

$Br\text{-}CH_2\text{-}(CH_2)_9\text{-}CH_2\text{-}[CH{=}CH\text{-}(CH_2)_{10}]_7\text{-}CH{=}CH\text{-}CH_3$

(119)



C_{98} Polyene (120)

a b c d

CH_3-$(CH_2)_9$-CH_2-[CH=CH-$(CH_2)_{10}$]$_7$-CH=CH-CH_3

(120)