THE SYNTHESIS AND HOST-GUEST ACTIVITY OF NOVEL CYANOBORATE SALTS

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ABSTRACT

Molecular recognition is a dynamic process based on distinct chemical interactions and not on passive fitting of a lock and key. Complex formation between host and guest molecules is often accompanied by conformational reorganisation, which makes it possible to engineer and fine-tune synthetic receptor analogues for optimal function and selectivity. This thesis primarily describes a supramolecular study of a novel family of air-stable cyanoborate host compounds. The discovery of this clathrand family came about as a result of a study relating to the synthesis of an electrolyte for the Zebra car battery and the thesis begins with this aspect (Chapter 1). Although cyanoborates are well documented as synthetic intermediates in 1,2 migration reactions they have not been studied independently to any degree and this thesis constitutes the first significant study of this class of compound. There are five chapters.

The results relating to this clathrand family begin to take shape in chapter two with the synthesis and evaluation of disodium 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl hexane **15** and its methyltriphenylphosphonium salt **47**. Inclusion studies of the latter are described and conclude that the compound has a low to moderate selectivity towards aromatics. Furthermore, an extremely interesting aspect relating to water-dependent liquid clathrate activity is uncovered in Chapter 3. X-ray structural analyses of the host **47** in its hydrated and anhydrous forms as well as its various inclusion compounds are described. Information gleaned from these analyses sets up a structural model which is used in a structure-activity study described in Chapters four and five. The model views these inclusion compounds as coordinato-clathrates in a coordination assisted lattice. The intermolecular forces operating, centre around hydrogen bonding between a cyano nitrogen and a hydrogen of a phosphonium methyl, as well as C-H···π interactions.

Use of this model in conjunction with synthetic considerations as directives brings about the development of the benzyltriphenylphosphonium analogue of **47** as well as its substituted derivatives as superior clathrands. Following this line of investigation the discovery of arsonium cyanoborates as novel clathrands is made. Finally, the synthesis and inclusion activity of a chiral clathrand, whose structural design is based on the structure-activity study, is described in Chapter five to conclude the thesis.

ABBREVIATIONS

9-BBN	9-borabicyclo[3.3.1]nonane
°C	degrees Celsius
Ar	aryl
b.p.	boiling point
br.s.	broad singlet
Bu	butyl
CHN	elementary analysis
CN	cyano
cm	centimeter(s)
d	doublet
DMF	dimethylformamide
e.e.	enantiomeric excess
emf	electromotive force
eq	equivalents
Et	ethyl
EtOH	ethanol
g	grams
G	guest molecule
H	host molecule
hex	hexyl
hr	hour
Hz	Hertz
IR	infrared
J	coupling constant(s)
m	multiplet
m	meta
M	molar
Me	methyl
MeOH	methanol
mg	milligrams
MHz	Megahertz
min	minute
ml	milliliter(s)
mmHg	millimeter mercury, torr
mmol	millimole(s)
mol	mole(s)

m.p.	melting point
NMR	nuclear magnetic resonance spectroscopy
o	ortho
p	para
pet ether	petroleum ether (boiling point range: 60-79°C)
Ph	phenyl
ppm	parts per million
Pr^i	iso-propyl
q	quartet
RMS	root mean square
RT	room temperature
s	singlet
t	triplet
t-But	t-butyl
THF	tetrahydrofuran
tlc	thin layer chromatography
V	Volt
--->	no reaction

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CHAPTER 1

FROM THE ZEBRA BATTERY TO BORON HOSTS

1.1 THE ZEBRA BATTERY

Man's increasing need for safe, environmentally acceptable energy sources has resulted in a greater investment in energy research in recent times. One such area is that of battery research, aimed at high energy-density applications such as load levelling, electrical vehicles and space. The first rechargeable battery to be formulated was the sodium-sulfur cell developed by Kummer and Weber[1] in the early sixties (1962). Crucial to its development was the discovery that β-alumina could be used as a sodium ion conductor permitting the use of sodium as the anode. By the end of the seventies an alternative cathode, to accompany the sodium anode, had been developed in South Africa. It arose out of the work of J. Coetzer[2] at the Council for Scientific and Industrial Research (CSIR) in Pretoria and was based on using iron(II)chloride as the cathode with sodium tetrachloroaluminate as a liquid electrolyte combined with a sodium anode and a β-alumina solid electrolyte. Since the early 1980's, a joint research effort between Beta Research and Development in the U.K. and Dr.Coetzer's group in South Africa has lead to Zebra batteries with high specific energies. For instance, on a track test in 1986, such batteries were used to power a Suzuki microbus for 130km on one charge at an average speed of 60km/h achieving a maximum speed of 75km/h.

The feature which differentiates the Zebra cell from others[3] is the effective insolubility of the cathode reactants, viz. Fe, $FeCl_2$ and NaCl in sodium tetrachloroaluminate ensuring that they always remain in intimate contact with each other and the current collector, which can be unreacted metal itself or carbon. There would be a potential danger of cation exchange in the beta alumina if soluble metal chlorides were present in the sodium tetrachloroaluminate, which could lead to the poisoning of the beta alumina and an associated resistance rise. Typical cell configurations can be written:
$Na/\beta''\text{-alumina}/NaAlCl_4/FeCl_2(Fe,C)$ or $Na/\beta''\text{-alumina}/NaAlCl_4/NiCl_2(Ni,C)$
and the overall cell reaction can be written as:

$$\underset{\text{charged}}{2\,Na + FeCl_2} \rightleftharpoons \underset{\text{discharged}}{2\,NaCl + Fe}$$

The open circuit voltage of the cell is 2.35V at 250°C, which is constant throughout the charge/discharge cycle.

A variety of different cathodic transition metals have been investigated[4] including Co, Cr, Mo and Cu but only iron and nickel have been chosen for battery development with open cell voltages of 2.35V and 2.59V respectively. The use of $NaAlCl_4$ as electrolyte permits the normal battery operating temperatures to be about 250°C, a good 100°C lower than the sodium-sulfur battery. Furthermore, the cell components have low vapour pressures even well above the cell operating temperature, thus preventing high pressures being generated inside the cell. Safety is reported to be good even in the event of massive β-alumina failure, and both the safety aspect and the lower corrosivety of sodium tetrachloroaluminate[4] compared with sodium polysulfides make the Zebra cell (Figure 1) eminently more attractive than the sodium-sulfur battery.

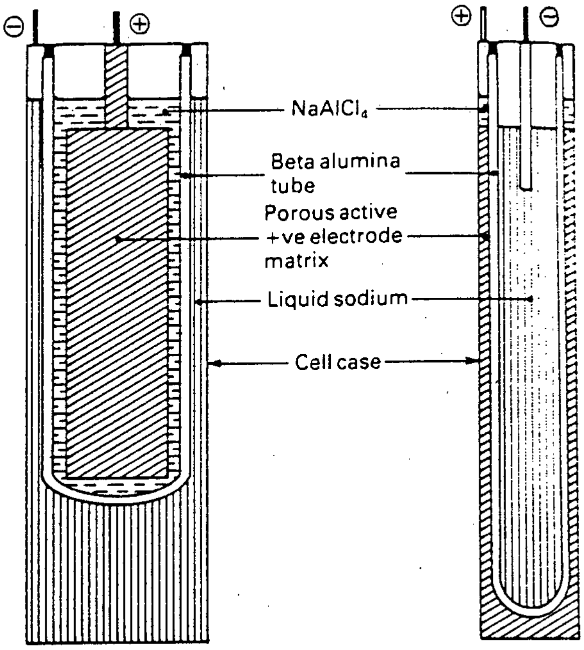


Figure 1

The β-alumina serves as both a sodium ion conductor and to separate the sodium anode from the sodium tetrachloroaluminate with which it reacts resulting in reduction of Al^{3+} to the metal. Scheme 1.

$$NaAlCl_4 + 3\,Na \rightleftharpoons 4\,NaCl + Al \qquad E=1.57V \text{ at } 250°C$$

Scheme 1

Indeed, this reaction occurs electrochemically when the cell is discharged beyond the point at which all the metal chloride has been converted to metal and the change in open circuit voltage provides a useful indication of the end of discharge. However, β-alumina is expensive threatening the viability of the battery. To quote Coetzer[2], "Electrochemical systems are often judged by performance only, but it is frequently high materials cost and adverse safety characteristics that make a system non-viable". The incentive for discovering a novel electrolyte to replace the β-alumina and which would meet certain operational criteria led to the birth of this project and studies towards this objective are described in this thesis. However, although the initial goal of this project was not achieved, its research ultimately led to the discovery of a novel family of cyanoborates with inclusion activity. This deviation from the original goal reflects the importance of the applied/academic research interface, the health of which is vital to the well-being of developing countries.

A formidable set of operational criteria to be met by such an electrolyte were the following:
1)Low melting Na^+ conductor with a melting point below 150°C and preferably 100°C.
2)Chemical stability towards both sodium metal and a Zebra cathode.
3)High conductivity and an electrochemical window of around 3V, i.e. greater than the cell emf.
4)Ease of synthesis and preferential air stability.
5)Cost viability.
Initially, criterion 4 was the dominant one from a practical standpoint.

In 1986, Huggins[5] pointed out that certain alkali organo-aluminium and organo-boron phases exist that are truly stable towards alkali metals. One of these derivatives, sodium tetraethylaluminate has been tested recently at the Max-Planck Institute[6] and is prepared by the reaction of sodium with triethylaluminium. Scheme 2.

$$4\,AlEt_3 + 3Na \rightleftharpoons 3\,NaAlEt_4 + Al$$

Scheme 2

Results showed that $NaAlEt_4$ is stable against sodium and that its melting point and conductivity decreases as the R of $NaAlR_4$ increases in size from methyl to butyl. However, the difficulty associated with its synthesis made it an unattractive proposition, since preparation on a large scale is dangerous. Using aluminium organometallic salts posed a major synthetic problem, since tetraalkylaluminates are highly reactive towards air and water. They are dangerous to synthesise on a large scale since a highly inflammable trialkylaluminium is used as a key intermediate. In view of the difficulties associated with the preparation of sodium tetraethylaluminate, it seemed sensible to shift to sodium organoborates since they are more stable in appropriate cases in view of the lower ionicity of the boron-carbon bond and are well documented in the literature. Furthermore, boron forms strong bonds with a number of elements and gives rise to a vast array of mononuclear as well as network structures[7].

From a literature survey it became apparent that certain borates did meet operational criteria (1) and (4), whereas there was very little if any information on borates with respect to criteria (2) and (3). Organoborates are readily prepared by reacting a nucleophile with a triorganylborane, whereby the nucleophile in this instance would have to consist of a sodium anion because of the relevance of sodium to the Zebra battery. Furthermore, we were aware that two of the operational criteria were in opposition to one another. Heteroatoms, particularly oxygen and nitrogen, stabilise boranes and borate complexes via mesomeric p_π-p_π overlap and are attractive sources of nucleophile. However, the reactivity, the ionicity and hence melting point of borate complexes increases with the number of heteroatoms present. Therefore, borate species with one heteroatom, eg. borinates when the heteroatom is oxygen, were considered as only outside candidates to meet the operational criteria depending on the other three groups, while more than one heteroatom present precluded the borate from consideration in this context.

Three nucleophiles were considered, namely alkyl and alkynyl sodium derivatives and sodium cyanide. R. Köster[8] discovered that sodium trialkyl-1-alkynyl borates are readily available by reacting a sodium trialkylborohydride with a 1-alkyne giving a pure product in a good yield using normal dry techniques. However, on an industrial scale sodium hydride would be required on a large scale which is a major disadvantage. Scheme 3.

$$\mathrm{Na\,(R_3BH) + HC{\equiv}CR'} \longrightarrow \mathrm{Na\,(R_3BC{\equiv}CR') + H_2}$$

Scheme 3

Similarly, an alkylsodium, which is hazardous to prepare especially on a large scale, is required for the synthesis of sodium tetraalkylborates. Even though many documented tetraalkyl and trialkylalkynylborates[7a,8] have low melting points (Table 1) and thus satisfy criterion (1), they are air- and moisture sensitive. Therefore, all things considered cyanoborates based on sodium cyanide as nucleophile became the preferred choice.

TABLE 1
Examples of melting points of sodium tetraalkyl- and sodium trialkylalkynylborates as well as tetraalkylaluminates

salt	m.p.(°C)
$NaBPr_4$	110-112 dec.
$NaAlMe_4$	240
$NaAlEt_4$	125
$NaAlPr_4$	56
$NaAlBu_4$	<20
$Na(Me_3BC{\equiv}CMe)$	163
$Na(Me_3BC{\equiv}CEt)$	166
$Na(Me_3BC{\equiv}CPr)$	146 dec.
$Na(Et_3BC{\equiv}CMe)$	89
$Na(Pr_3BC{\equiv}CMe)$	120

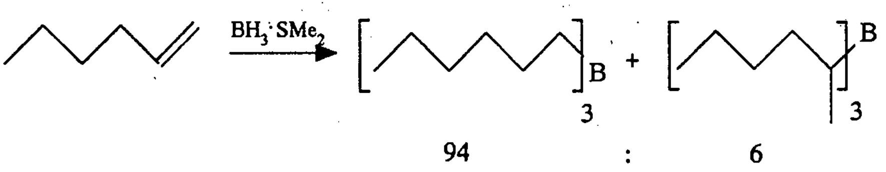
dec. decomposition

Trialkylcyanoborates are well known as synthetic intermediates in the cyanidation reaction, in which solid sodium cyanide is reacted with a trialkylborane in dry THF as solvent[9]. As compounds in their own right, they have not been well investigated with the exception of sodium triphenylcyanoborate and lithium cyanoborohydride[10], and in this regard we were aware of entering new territory.

1.2 SYNTHESIS OF TRIORGANYLBORANES

In this section various synthetic options for the preparation of triorganylboranes as well as their reactivity,are discussed.

Trialkylboranes are readily available via hydroboration of an appropriate alkene using borane as a tetrahydrofuran or dimethyl sulfide complex. Two drawbacks of the reaction in all cases is the use of $BH_3{\cdot}SMe_2$ in large quantities and that the reaction gives a small percentage of the Markovnikov product with 1-alkenes[11]. Scheme 4.



Scheme 4

The mixture of regioisomers would have led to purification problems at a later stage so a transmetallation reaction recently optimised by H.C. Brown[12] was chosen as a cheap, highly regioselective alternative. This involves trisubstitution of boron trifluoride etherate, a commercially available liquid, by three equivalents of Grignard reagent under anhydrous conditions. Scheme 5.

$$RX + Mg \xrightarrow{\text{ether}} RMgX$$

R = alkyl, X = Br

$$3\ RMgX + BF_3\cdot OEt_2 \longrightarrow BR_3 + 3\ MgFX$$

Scheme 5

H. Brown[12] also investigated the effect of ultrasound which seems to dramatically accelerate the formation of triorganylboranes. These workers monitored the progress of the reaction by ^{11}B-NMR spectroscopy and in all cases product formation was complete in 10-30 minutes as compared to 2-3 hours without ultrasound. The preparation of triorganylboranes via transmetallation using ultrasound is direct, exceptionally rapid and highly efficient.

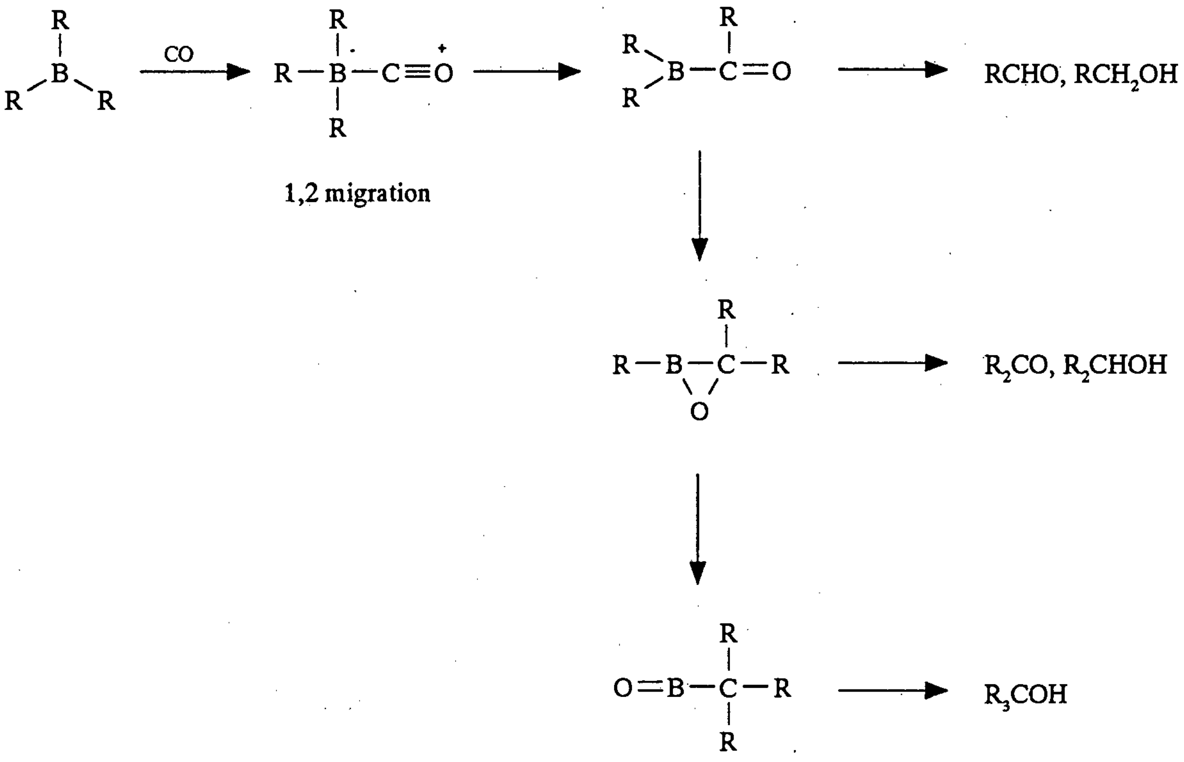
A third method of borane synthesis involves metal-hydrogen exchange. This method, an aromatic electrophilic substitution reaction, only applies to aromatic systems and is therefore very limited. Scheme 6.

$$ArH + BX_3 \longrightarrow ArBX_2 + HX \quad X = \text{halogen}$$

Scheme 6

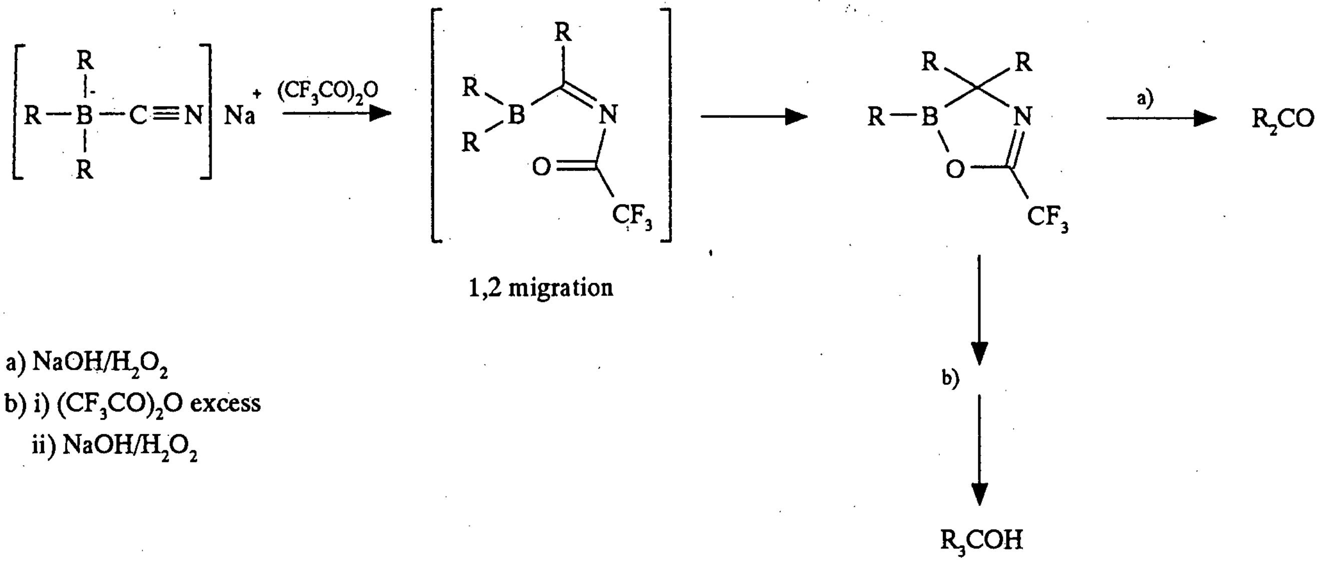
A major drawback is that the boron trihalide reagent is expensive making this a less feasible route.

Borates are well known for their intramolecular 1,2 migration reactions[13], in which a group is transferred from a negatively charged boron to an adjacent atom. Transfer takes place with retention of configuration of the migrating group and inversion of configuration at the migration terminus. Migration reactions may be either spontaneous or non-spontaneous and for the latter type an electrophile or Lewis acid initiator is required. Carbonylation of organoboranes is classified as a spontaneous 1,2 migration reaction, whereby a trialkylborane reacts with carbon monoxide. All three R groups may migrate, but the reaction can be controlled to stop at any one of three intermediates. The products obtainable include aldehydes and ketones as well as primary, secondary and tertiary alcohols. Scheme 7. Carboxylic acids can also be synthesised by a slight variation of the carbonylation reaction, whereby the borane reacts with the dianion of phenoxyacetic acid.



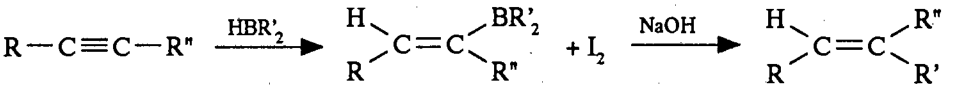
Scheme 7

The cyanidation reaction is a non-spontaneous 1,2 migration reaction and a sodium cyanotriorganylborate is formed as a stable intermediate, but never isolated. The products obtainable after Lewis acid induced migration include ketones and tertiary alcohols in which the mechanism is similar to that of the carbonylation reaction. Scheme 8.



Scheme 8

Other non-spontaneous 1,2 migration reactions of importance in organic synthesis include the conversion of alkynes to alkenes via vinylboranes, i.e. the cis- and trans Zweifel synthesis, and the reaction of trialkylalkynylborates to substituted alkenes. Scheme 9.



Scheme 9

Thus, since these migration reactions are induced by strong electrophiles, such conditions would have to be avoided in the synthesis and subsequent handling of sodium cyanotriorganylborates to prevent unwanted rearrangements from taking place.

1.3 THE SYNTHESIS AND SPECTRAL STUDIES OF SODIUM TRIBUTYLCYANOBORATE

Trialkylcyanoborates are well known synthetic intermediates in the cyanidation reaction and in the presence of electrophiles are converted from stable salts into ylides which then undergo alkyl migrations from boron to carbon[9]. The salts are prepared *in situ* and therefore their properties have not been well investigated. The literature contains more information on tetraalkylborates[14], which are extremely air sensitive and are better characterised by forming stable tetramethylammonium or tetrabutylphosphonium derivatives.

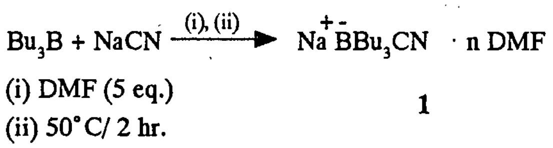
Tributylborane[12] was chosen as the initial target because it is readily isolated as an air sensitive, colourless liquid (b.p. 60°C/0.1mmHg) in a reproducible yield of approx. 80%. The lower homologues are more volatile and hence difficult to isolate, while tributylborane is convenient in view of its boiling point and may be readily prepared in 50g batches. Scheme 10.

$$BF_3 \cdot OEt_2 + BuBr + 3\,Mg \xrightarrow{\text{ether}} Bu_3B + 3\,MgFBr$$

Scheme 10

The literature procedure for cyanoborate formation involves reaction of borane and solid sodium cyanide in dry THF as solvent. In our hands this reaction proved to be sluggish. It could be monitored by observing the dissolution of the sodium cyanide and by the appearance of an upfield signal in the ^{1}H-NMR at approximately δ=0.1ppm due to the α-methylene protons of the 'ate' complex. R. Damico[15] has commented on the transmission of negative charge from a boron atom to the α-methylene carbons of tetraalkylborates. A chemical shift of approximately δ=0 is typical of methylenes adjacent to negative charges and attached to metals[16]. When sodium tributylcyanoborate was isolated and characterised, an interesting feature regarding solvent incorporation was discovered. Removal of the THF *in vacuo* (0.1mmHg) gave an oily residue in which THF was still incorporated. Heating of this oil *in vacuo* failed to remove the THF and prolonged heating led to the decomposition of the compound as evidenced by ^{1}H-NMR. It appears that the sodium cyanoborate forms an inclusion complex involving significant intermolecular forces at low concentrations of the donor solvent, THF. Furthermore, the compound is an ionic liquid, which is of importance for the battery system. G. Wittig and P. Raff[10] observed as long ago as 1951 that lithium cyanoborohydride $LiBH_3CN$ forms a crystalline inclusion complex with 1,4-dioxane, and that the borate is stable to acid.

It was desirable at this stage to use a solvent which could dissolve both reactants so as to accelerate the reaction. Reaction between sodium cyanide and neat tributylborane failed to give the 'ate' complex, because of the borane's weak Lewis acidity and the heterogeneity of the medium. In DMF (approx. 5 equivalents) reaction between sodium cyanide and tributylborane proceeded exothermically and was rapid as expected. The reaction mixture was warmed at 50°C for two hours to ensure complete 'ate' formation. Scheme 11.

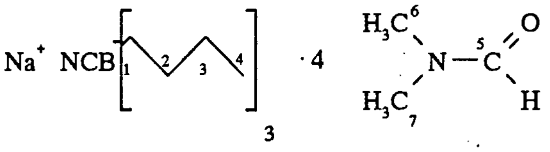


$$Bu_3B + NaCN \xrightarrow{(i),(ii)} \overset{+}{Na}\overset{-}{B}Bu_3CN \cdot n\,DMF$$

(i) DMF (5 eq.)
(ii) 50°C/ 2 hr.

Scheme 11

Once again, removal of excess DMF solvent *in vacuo* became increasingly more difficult at low concentrations of solvent. From the integration in the ^{1}H-NMR spectrum (Figure 2) it was ascertained that when n=4 for **1**, a temperature of 70°C at 0.1mmHg was required for the gradual removal of DMF when neat DMF boils at approximately 40°C at this pressure. Moreover, DMF could never be removed completely which again indicates strong intermolecular forces operating. $NaBBu_3CN \cdot n$ DMF (1<n<4)is an ionic liquid, which is stable to air but hygroscopic, since leaving it in air for 12 hours resulted in appearance of a water peak in the ^{1}H-NMR. The thermal stability of **1** decreases with n. As n decreases the substance becomes more viscous but still remains soluble in non-polar organic solvents such as CCl_4 and hexane. The ^{1}H and ^{13}C spectra of $NaBBu_3CN \cdot 4$ DMF were recorded and they indicated all of the expected signals. Table 2.



2

TABLE 2.

δ($CDCl_3$)	carbons							
(ppm)	1	2	3	4	5	6	7	CN
^{1}H	0.01	0.77	0.94-1.30		7.90	2.81	2.70	-
^{13}C	24.5	30.4	27.3	14.3	163.5	31.5	36.6	151.1

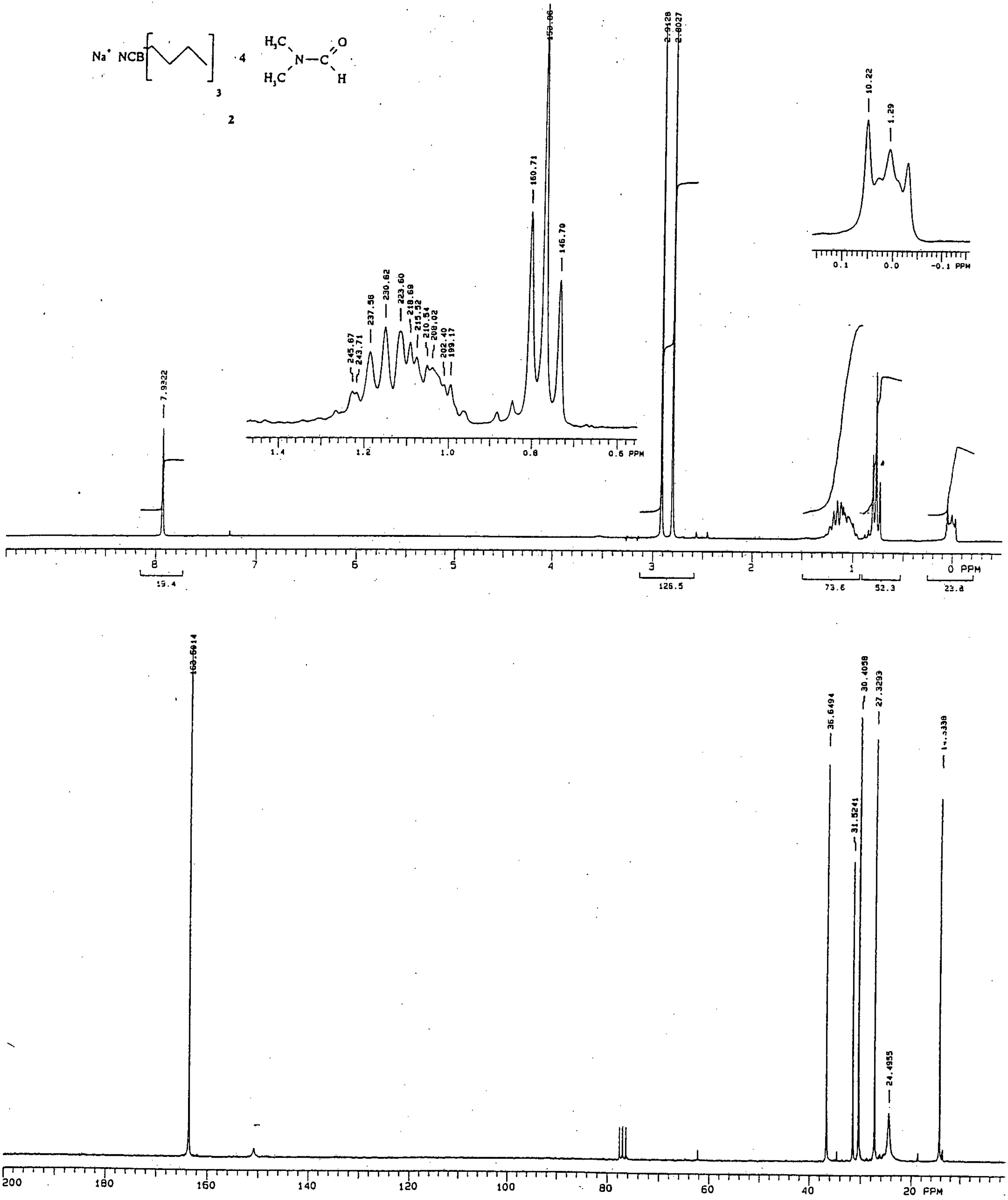
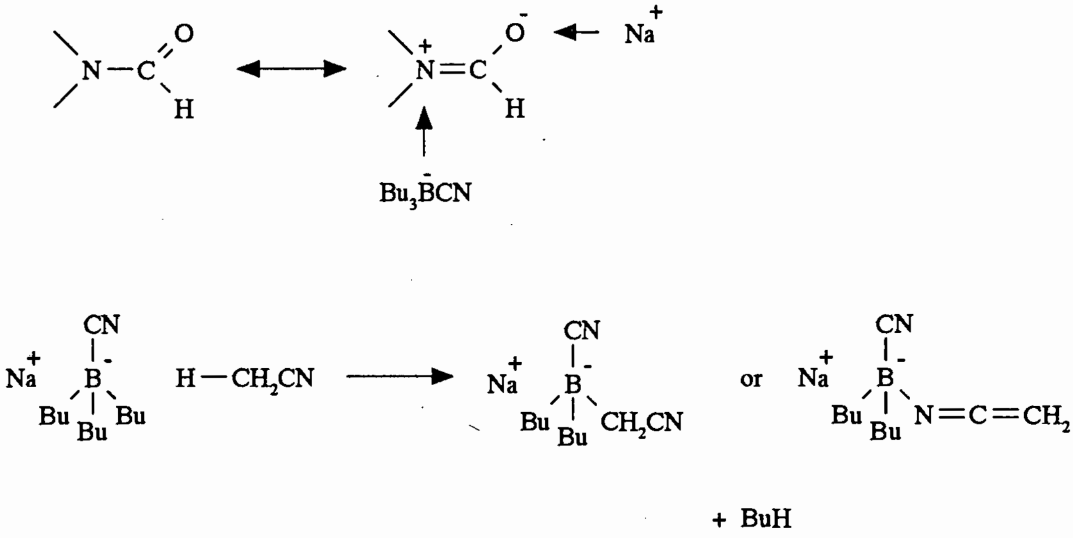

Na⁺ NCB
3
·4
H₃C
N
C
O
H
H₃C
2
7.9322
2.9128
2.8027
150.86
160.71
146.70
245.67
243.71
237.56
230.62
223.60
218.68
215.52
210.54
208.02
202.40
199.17
1.4
1.2
1.0
0.8
0.6 PPM
10.22
1.29
0.1
0.0
-0.1 PPM
8
7
6
5
4
3
2
1
0 PPM
15.4
125.5
73.6
52.3
23.8
163.5914
36.6494
31.5241
30.4058
27.3293
24.4955
14.3339
200
180
160
140
120
100
80
60
40
20 PPM

Figure 2

In particular, in the ^1H spectrum the α-methylene protons appear as a multiplet high field to the methyl triplet region as a result of shielding by the borate formal negative charge. However, this resonance only integrated to 4H and not 6H and diminished in integration with diminishing n. This phenomenon relates to the position of the sodium cation relative to the borate counter-anion. When n=0, there is no upfield shift in the ^1H-NMR of the α-methylene resonance because the sodium cation is close enough to the boron atom to cancel out the effect of the formal negative charge. The ^{13}C spectrum of **2** consisted of the anticipated eight resonances, with the carbons α to boron all equivalent as a broad singlet owing to boron-carbon coupling. $NaBBu_3CN \cdot 4$ DMF, which was an oil, was left to stand at room temperature for approximately one year, when much to our surprise crystalline needles appeared which unfortunately were not of X-ray quality.

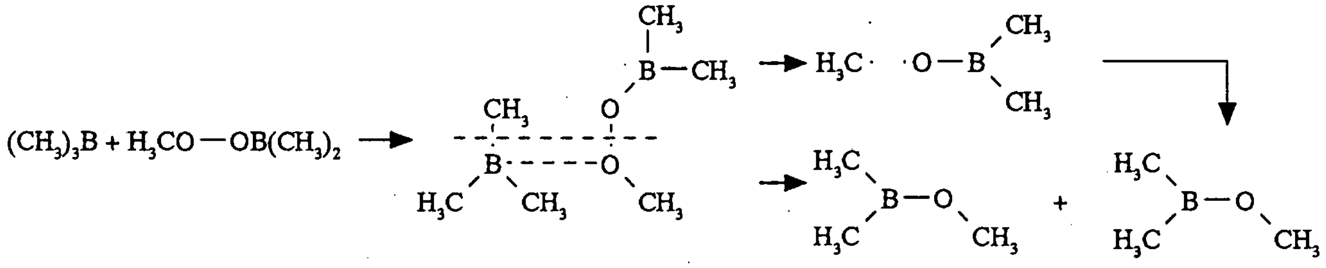
These spectral phenomena indicated that the sodium cation and borate anion are separated at opposite ends of the dipolar DMF solvent molecule. This possibility suggested that other polar solvents might also form inclusion compounds with the cyanoborate. Two classes were identified, the one being polar solvents which react with the borate such as acetonitrile and nitromethane. This was inferred from changes in the ^1H-NMR spectrum. Reaction is believed to proceed by ligand-solvent exchange due to the acidity of the α-methyl hydrogens of these solvents. Scheme 12.



Scheme 12

The second class include very polar, unreactive solvents, such as tetramethylethylene diamine (TMEDA), hexamethylphosphoric triamide (HMPA) and DMF. Dimethylsulfoxide (DMSO) is borderline because of the acidity of its methyl groups. ^1H-NMR data indicated that both HMPA and TMEDA behave similarly to DMF, forming inclusion compounds which are air stable, hygroscopic ionic liquids in which the sodium cation is solvated away from its borate partner. The HMPA complexes, in which dipolar resonance forms may be written as with DMF, appear to be more stable than the TMEDA ones in which nitrogens are present as amines and more susceptible to one electron oxidation by oxygen.

^{1}H-NMR spectroscopic investigation of $NaBu_3BCN \cdot n\,DMF$ indicated that two sets of peaks at δ=3.6ppm and δ=3.8ppm appeared when n decreased. This is due to the compound's increasing air sensitivity as the amount of DMF decreases. Trialkylboranes are known to be extremely air-sensitive, even pyrophoric at times. Their reactivity has been investigated by R. Rensch and H. Friebolin[17], who found that air oxidation of a solution of trimethylborane leads to the peroxide $CH_3OOB(CH_3)_2$ through the insertion of oxygen via a 1,3-migration reaction. Disproportionation via radical species then leads mainly to dimethylmethoxyborane. Scheme 13.



Scheme 13

Dimethyl(methylperoxy)borane resonates at $\delta(OCH_3)$=3.97ppm and dimethylmethoxyborane at $\delta(OCH_3)$=3.68ppm which correspond well to the chemical shifts for neat sodium cyanotributylborate at δ=3.60ppm and δ=3.75ppm when exposed to air and at low concentrations of DMF. (Figure 3) These peaks may be ascribed to the formation of various products such as sodium cyano(butylperoxy)dibutylborate and sodium cyanobutoxy(dibutyl)borate, as well as an OOH fragment being bonded to the carbon α to boron. Also, the reaction of sodium cyanotributylborate with methanol indicates the formation of cyanobutoxy(dibutyl)borate as evidenced by a triplet at δ=3.85ppm via oxygen insertion.

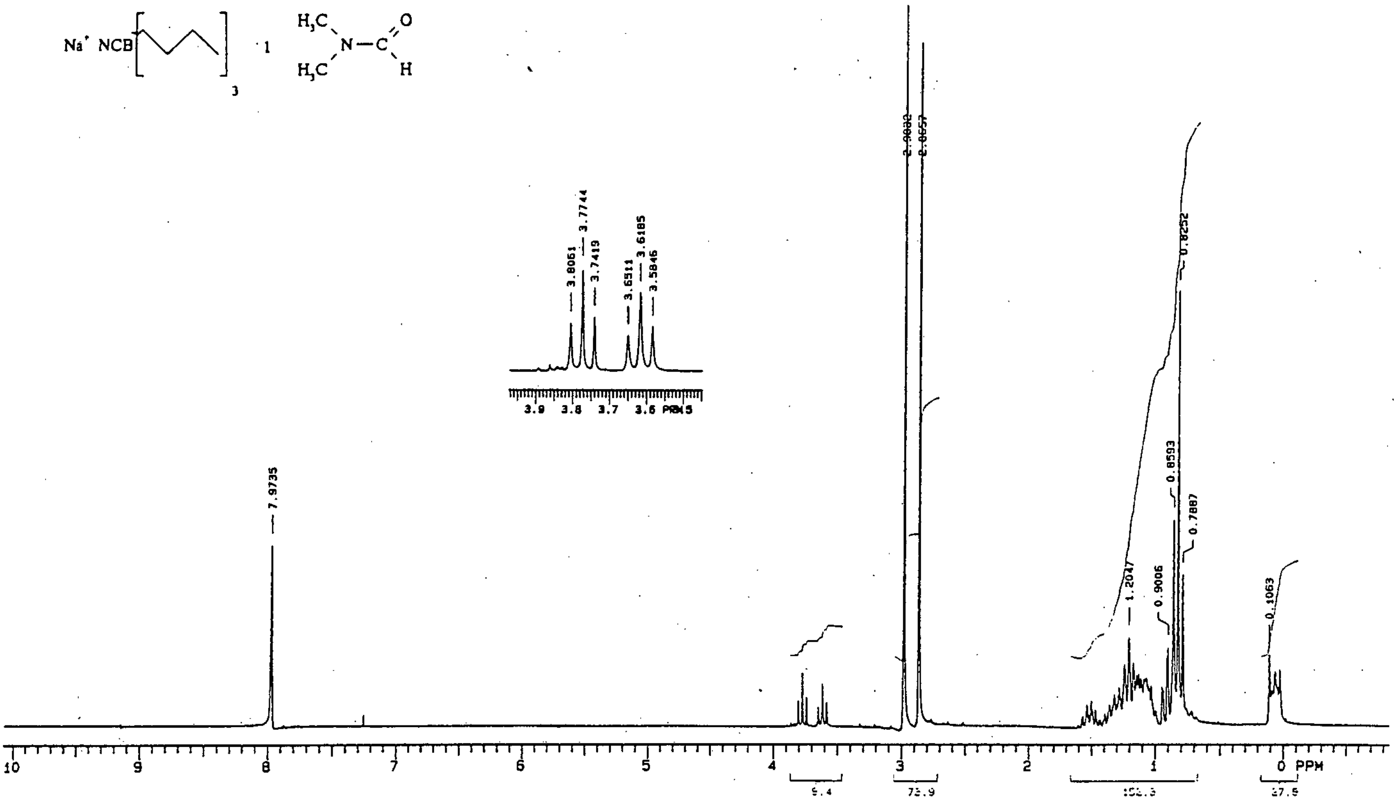


Figure 3

1.3.1 ELECTROCHEMICAL STUDIES OF 2

Cyclic voltammetry of $NaBBu_3CN\cdot4$ DMF was carried out using a microcell. Both platinum and tungsten working electrodes were used with a platinum quasi reference and platinum counter electrodes. The electrochemical windows using platinum and tungsten working electrodes were 1.9 and 3.6 Volts respectively, the difference being attributed to the different catalytic activities of the two surfaces. The voltammogram indicates irreversible REDOX behaviour of the compound. During the cathodic sweep, reduction of the DMF is likely to lead to irreversible chemical change. The conductivity of the sample was also measured as 0.31×10^{-3} ohm^{-1} cm^{-1} at 25°C which is low compared with other low temperature melts. This is probably due to the solvation of the cation and the bulky nature of the anion. Table 4 below gives an indication of the conductivity values that are obtained for some other alkali organoaluminium salts[5,18] and tetrachloroborate melts[19]. Table 4.

TABLE 4.

Salt	M.p.(°C)	Conductivity(ohm^{-1}cm^{-1})	Temp.(°C)
$NaAlEt_4$	125	5.8 x 10^{-2}	130
$NaAlEt_3F$	74	4.0 x 10^{-3}	100
$KAlEt_4$	74	1.3 x 10^{-1}	130
$KAlEt_3F$	56	2.0 x 10^{-2}	-
1:1 BCl_3:BPC	16.5	1.6 x 10^{-2}	100
2:1 BCl_3:BPC	-18	6.1 x 10^{-3}	20
1:1 BCl_3:MEIC	16.5	1.6 x x10^{-2}	20
1:2 BCl_3:MEIC	-12	1.6 x 10^{-2}	20

BPC: *N*-Butylpyridinium chloride MEIC: 1-methyl-3-ethylimidazolium chloride

1.4 THE SYNTHESIS OF SODIUM DIAKLYLPHENYLCYANOBORATES

Since sodium tributylcyanoborate did not fulfill all of the operational criteria set such as the high conductivity and chemical stability across a 3 Volt electrochemical window, attention became directed towards viable synthetic routes for unsymmetrical triorganylboranes of general formula $PhBR_2$, for conversion to the corresponding ionic cyanoborate salt $NaPhR_2BCN$. This target was selected in order to investigate the influence of delocalisation of the borate negative charge on the electrochemical characteristics because it involves a more stable borane as an intermediate. G. Wittig and P. Raff[10] synthesised the stable, crystalline sodium triphenylcyanoborate salt which has a melting point of 290°C in 1951. Thus, the large phenyl groups together with the cyano group lend stability to the borate salt.

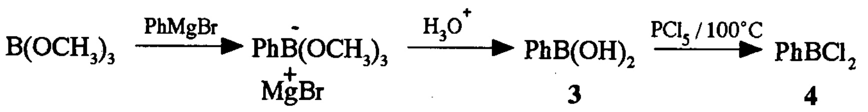
The first synthesis of $PhBR_2$ attempted was based on the monosubstitution of $BF_3{\cdot}OEt_2$ with one equivalent of phenyl Grignard followed by further substitution of the $PhBF_2$ using two equivalents of butyl Grignard. Scheme 14.

$$BF_3{\cdot}OEt_2 \xrightarrow[\text{(ii) 2 BuMgBr}]{\text{(i) PhMgBr}} PhBBu_2 + 3\ MgBrF$$

Scheme 14

This approach appeared attractive in view of the success of Grignard methodology in converting $BF_3{\cdot}OEt_2$ to substituted boranes[20]. However, distillation of the reaction product resulted in isolation of Ph_2BF and Bu_3B indicating that the reaction had produced some disubstitution. Attempts to control the reaction to stop at the monosubstitution stage (eg. low temperature addition of Grignard to the fluoride) failed.

A review article by K. Niedenzu[21] revealed that dichlorophenylborane ($PhBCl_2$) can be prepared from trimethylborate ($B(OMe_3)_3$) via a phenyl substitution, hydrolysis and chlorination sequence. Scheme 15.



$$B(OCH_3)_3 \xrightarrow{PhMgBr} \underset{\overset{+}{Mg}Br}{Ph\overset{-}{B}(OCH_3)_3} \xrightarrow{H_3O^+} \underset{\mathbf{3}}{PhB(OH)_2} \xrightarrow{PCl_5\,/\,100^\circ C} \underset{\mathbf{4}}{PhBCl_2}$$

Scheme 15

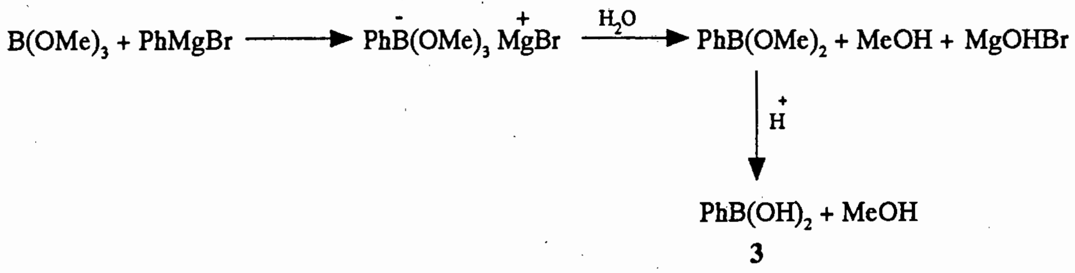
Trimethylborate is commercially available or may be prepared via esterification of boric acid or oxide with methanol under Dean Stark conditions. The latter produces a constant boiling azeotrope which H. Schlesinger and H. Brown[22] have suggested may be separated using lithium or zinc chloride. However, this preparation failed in our hands.

In view of these difficulties it was decided to prepare and use the higher boiling tri-n-propylborate[23], which turned out to be successful. It should be emphasised at this point that the use of high purity ester was essential so as to avoid destruction of the Grignard, present as one equivalent, via metal-hydrogen exchange with free alcohol. Reaction of 3 equivalents of 1-propanol with boric acid under Dean Stark conditions (azeotropic removal of water) furnished tripropylborate[24] in good yield and in high purity as evidenced by high field ^1H- and ^{13}C-NMR. Scheme 16.

$$3\ PrOH + B(OH)_3 \xrightarrow{C_6H_6} \underset{\substack{73\% \\ \mathbf{5}}}{B(OPr)_3} + 3\ H_2O$$

Scheme 16

Reaction with phenylmagnesium bromide at -78°C to 0°C in ether followed by acid hydrolysis gave phenylboronic acid[24,25] consistently in 45% overall yield as colourless needles after recrystallisation from water. A small amount (10%) of diphenylborinic acid (Ph_2BOH) was obtained as a by-product but was easily removed into hexane. Interestingly, when using trimethylborate (now having arrived from Aldrich) instead of tri-n-propylborate, the yield of **3** increased to 65%. Scheme 17.



$$B(OMe)_3 + PhMgBr \longrightarrow Ph\overset{-}{B}(OMe)_3\,\overset{+}{Mg}Br \xrightarrow{H_2O} PhB(OMe)_2 + MeOH + MgOHBr \xrightarrow{\overset{+}{H}} PhB(OH)_2 + MeOH$$

3

Scheme 17

Conversion of the boronic acid to the dichloro compound[26] via the anhydride using PCl_5 proved difficult to follow and required harsh conditions developed in the 1950's. (Scheme 15) Once a mixture of phenylboronic anhydride and phosphorus pentachloride had melted at 160°C, it was refluxed at 120-130°C for 24 hours, before it could be distilled. According to B. Mikhailov[27], using phosphorus pentabromide requires even higher temperatures and the expected bromobutoxyphenylborane product **6** from the reaction of dibutoxyphenylborane with PBr_5 is only recovered in a 31% yield. The reaction is complicated by the dissociation of PBr_5 and subsequent reaction of the ester with bromine to form bromobutoxyborane **7**, which decomposes upon subsequent distillation. Scheme 18.

$$C_6H_5B(OC_4H_9)_2 + PBr_5 \longrightarrow \underset{\mathbf{6}}{C_6H_5BBr(OC_4H_9)} + POBr_3 + C_4H_9Br$$

$$C_6H_5B(OC_4H_9)_2 + Br_2 \longrightarrow C_6H_5Br + \underset{\mathbf{7}}{BrB(OC_4H_9)_2}$$

Scheme 18

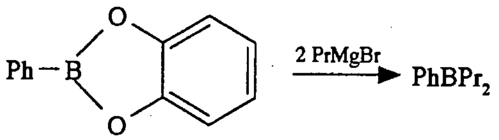
Recently, a method by S. Dandegaonker for preparing organodihaloboranes was modified by T. Cole *et al*[28] in which anhydrides of boronic or borinic acids were reacted with solutions of boron trichloride or boron tribromide in hydrocarbon solvents resulting in clean substitution of oxygen by halogen to form organodihaloboranes in good yields. The solutions of trihaloboranes in hydrocarbon solvents have only recently become commercially available in South Africa (Aldrich), by which time this project had moved away from these target molecules.

An alternative route to $PhBCl_2$ involves aromatic substitution of $PhSi(CH_3)_3$ with boron trichloride. However, there are some problems associated with BCl_3 as it is expensive and a highly reactive gas which has to be liquified using a dry ice/acetone condenser for quantitative reaction procedures. Scheme 19.

$$PhSi(CH_3)_3 + BCl_3 \longrightarrow \underset{\mathbf{4}}{PhBCl_2} + (CH_3)_3SiCl$$

Scheme 19

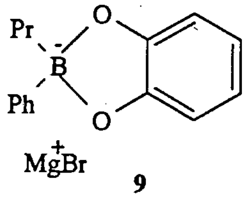
In view of the synthetic difficulties associated with conversion of phenylboronic acid to its dichloride **4**, it was decided to take advantage of the fact that alkoxy groups attached to boron may be substituted by nucleophilic organometallic reagents. Furthermore, boronic esters are air stable and readily prepared by esterification of boronic acids. From the literature[29] it appeared that an attractive leaving group for the much sought after $PhB(OR)_2 \rightarrow PhBR_2$ conversion was catechol. To this end the isolated phenylboronic acid was esterified with catechol under Dean Stark conditions to afford 2-phenyl-1,3,2 benzodioxaborole **8** in 90% yield as colourless, air stable crystals. This was to be reacted with two equivalents of propyl Grignard to yield $PhBPr_2$ according to S. Cabbidu[30]. Scheme 20.



8

Scheme 20

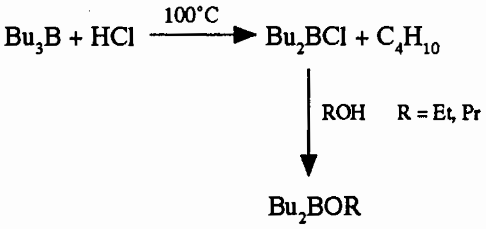
The advantage of this route is that one deals with an air stable starting material and a recrystallisable intermediate. However, in our hands this route failed to yield the desired borane and it was thought that the problem lay in the second substitution and that the catechol derivative formed the 'ate' complex **9**.



9

'ate' complex

An alternative route considered to the elusive $PhBR_2$ compound was introduction of the phenyl group last. To this end, monochlorodibutylborane[31] was prepared by chlorination of tributylborane by anhydrous HCl gas at 100°C. The product, Bu_2BCl was obtained in high yield after distillation and characterised as a borinic acid derivative by reacting Bu_2BCl with ethanol or 1-propanol. Reaction of it with phenyl Grignard failed to yield the desired borane. Scheme 21.



$$Bu_3B + HCl \xrightarrow{100^\circ C} Bu_2BCl + C_4H_{10}$$

$$Bu_2BCl \xrightarrow[R = Et, Pr]{ROH} Bu_2BOR$$

Scheme 21

Recently, H. Brown[32] reported a new hydroborating agent methylborane ($MeBH_2$) which makes mixed methyldialkylboranes MeR^AR^BB attainable. Methylborane in THF hydroborates the first equivalent of alkene quickly, forming a methylalkylborane. The rate of the second hydroboration is much slower than the first and is more dependent on the steric requirements of the alkene. Scheme 22.

$$(MeBH_2)_2 \xrightarrow{\text{2 alkenes}} (MeR^ABH)_2 \xrightarrow{\text{2 alkenes}} 2\ MeR^AR^BB$$

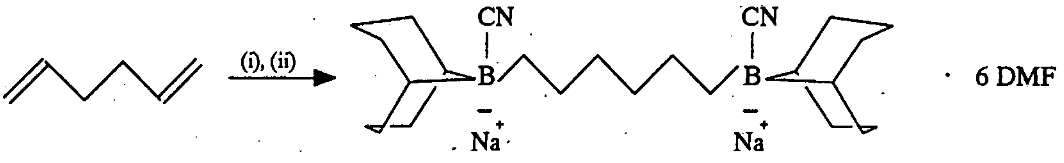
Scheme 22

Another recently introduced hydroborating agent 2,4,6-triisopropylphenylborane[33] ($TripBH_2$) is able to convert monosubstituted alkenes into mixed boranes of the form $TripBR^AR^B$. The tripyl group of $TripBR_2$ can also be selectively removed to give methoxydialkylboranes, which could by Grignard substitution have given the target, $PhBR_2$. However, this methodology only became available after we had moved on from the target. Since $PhBR_2$ was unattainable in our hands, it was decided to focus on another class of compound of interest, particularly with respect to charge and conductivity, namely polyborates. Of interest was the possibility of several centres of interaction being available for the cation resulting in greater mobility of Na^+ ions to increase conductivity.

From the literature it became apparent that the hydroboration of dienes could lead to the desired type of borane intermediate. Reaction of 1,5-hexadiene with dibromoborane-dimethylsulfide complex[34] furnished the tetrabromo derivative as a white solid. The removal of SMe_2, a pre-requisite for success in the Grignard substitution, proved to be difficult even on heating *in vacuo* and thus, the desired product **10** could not be isolated. Scheme 23.

sticky, oily substance, which is probably due to the flexibility of the hexyl chain inhibiting crystallisation.

Since our target was a polyborate, it was decided to prepare a diborane from 1,5-hexadiene and two equivalents of 9-BBN. Cyanidation with NaCN in DMF resulted in an exothermic reaction yielding a clear solution as product. After a period of a week, plate-like crystals slowly appeared, which were filtered and washed with dry diethyl ether to afford an air-stable solid **15** in an isolable yield of 29%. Scheme 29.



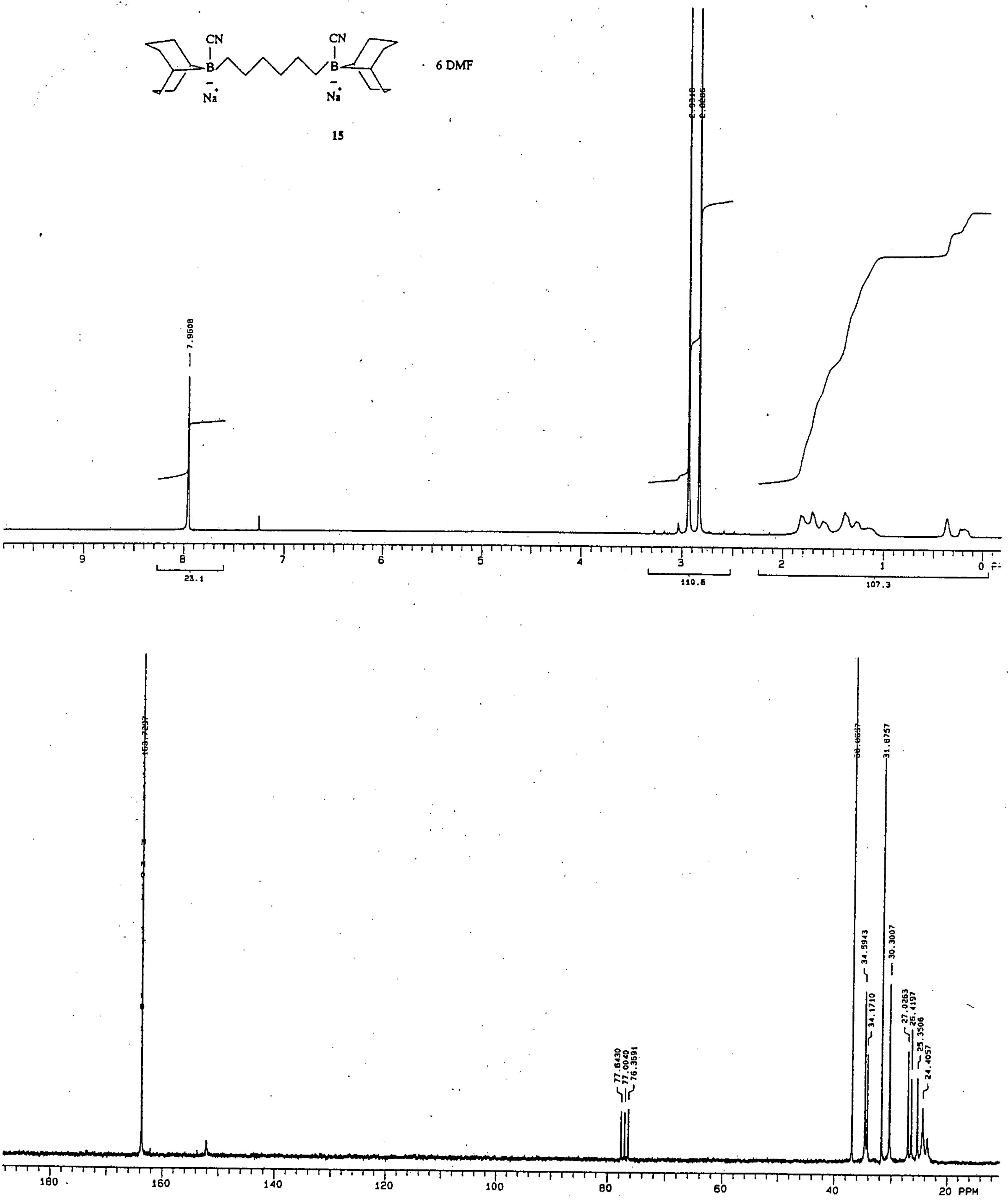
15

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF

Scheme 29

This low yield was attributed to the high viscosity of the oil which seemed to inhibit complete crystallisation. Very little product was lost during filtration with ether, as the bis-9-BBN cyanoborate is only slightly soluble in it.

^{1}H and ^{13}C-NMR spectroscopy revealed **15** to be the desired product as a coordination complex with DMF. Once again in the ^{1}H-NMR, two upfield resonances of the protons adjacent to boron indicated 'ate' formation. (Figure 4) The peak furthest upfield (0.14ppm) was ascribed to the four protons on the hexyl spacer adjacent to boron, whereas the broad singlet at 0.35ppm was assigned to the protons on the bicyclic 9-BBN ring[40b,c]. The slight downfield shift of the latter protons is due to them being bonded to a cyclic system[40b,c]. Regarding the ^{13}C spectrum, resonances of carbon atoms directly bonded to boron are known to be either severely broadened or even undetectable due to ^{11}B - ^{13}C couplings[41] involving the quadrupolar nature of the boron nucleus (^{11}B, 82% natural abundance, I=3/2) causing incomplete relaxation of carbon. The assignment of the ^{13}C resonances was made using R. Köster's table[40a] of ^{13}C peaks for the 9-BBN dimer. The chemical shifts of the ring carbons of **15** are at slightly different positions to those by R. Köster because loss of symmetry at the 'ate' centre results in differentiation between the two sets of β and γ carbons. Also, the cyano group attached to boron resonates at approx. 150ppm compared to the signal of KCN at 165.52ppm.


15

CN
CN
B
B
Na
Na
· 6 DMF
7.9508
2.9318
2.8286
9
8
7
6
5
4
3
2
1
0
23.1
110.8
107.3
163.7297
36.6657
31.8757
34.5943
34.1710
30.3007
27.0263
26.4197
25.3506
24.4057
77.8430
77.0040
76.3691
180
160
140
120
100
80
60
40
20 PPM

Figure 4

The I.R. resonance at approx. 2148cm^{-1} corresponds to the B-CN stretch[42] (Figure 5), whereas NaCN itself resonates at 2049cm^{-1}. The signal at approx. 2830cm^{-1} corresponds to the CH stretch α to boron, which in tetraalkylborates[15,43] appears slightly shifted at 2760-2780cm^{-1}.

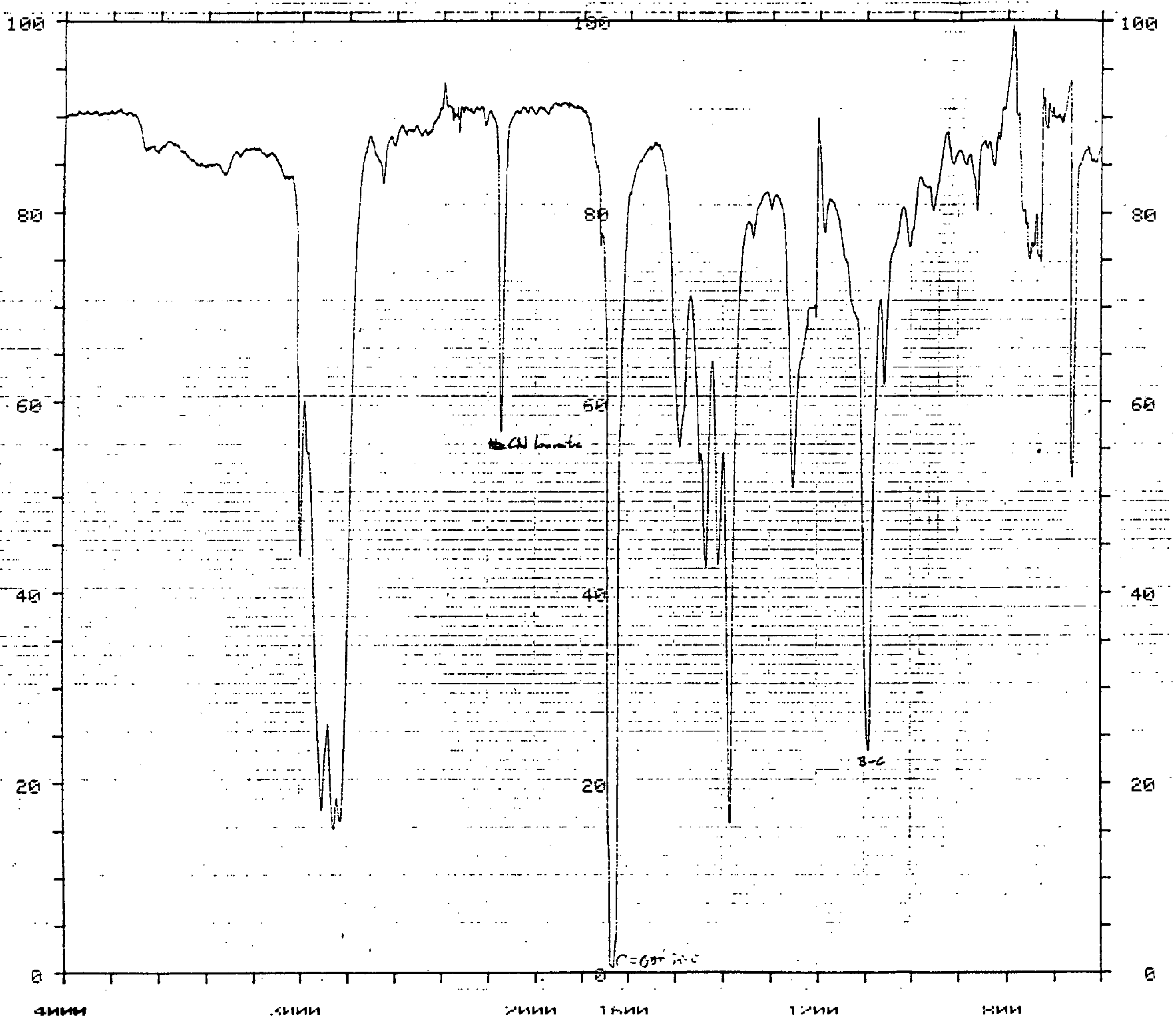


Figure 5

1.5.1 THE X-RAY, TG AND DSC ANALYSES OF DISODIUM 1,6-BIS(B-CYANO-9-BORATABICYCLO[3.3.1]NON-9-YL) HEXANE·DMF CLATHRATE

Since no X-ray analysis had ever been done on a cyanoborate and in view of the compound's relative air stability and complexation with DMF, a single crystal X-ray analysis of **15** mounted in a Lindemann tube with mother liquor but not brought into contact with the latter was carried out which revealed it to be an inclusion compound containing six DMF molecules per molecule of borate. (Figure 6) The borate compound was stable in mother liquor and appreciably stable in the solid state as evidenced by ^{1}H-NMR over a period of weeks. Each sodium atom is coordinated to four DMF oxygens by ion-dipole forces involving the amide carbonyl as well as coordinating to the cyano nitrogens of the anion. Another important structural feature of the complex is the cisoid conformation involving atoms C_2-C_5 of the hexamethylene spacer, which is brought about by syn arrangement of the cyano moieties enabling them to participate in the intermolecular bonding network involving two sodium cations per unit cell. Furthermore, the idea of solvation of the Na^+ ion away from the borate centre as put forward with $NaBBu_3CN{\cdot}4$ DMF is corroborated by this X-ray structure.

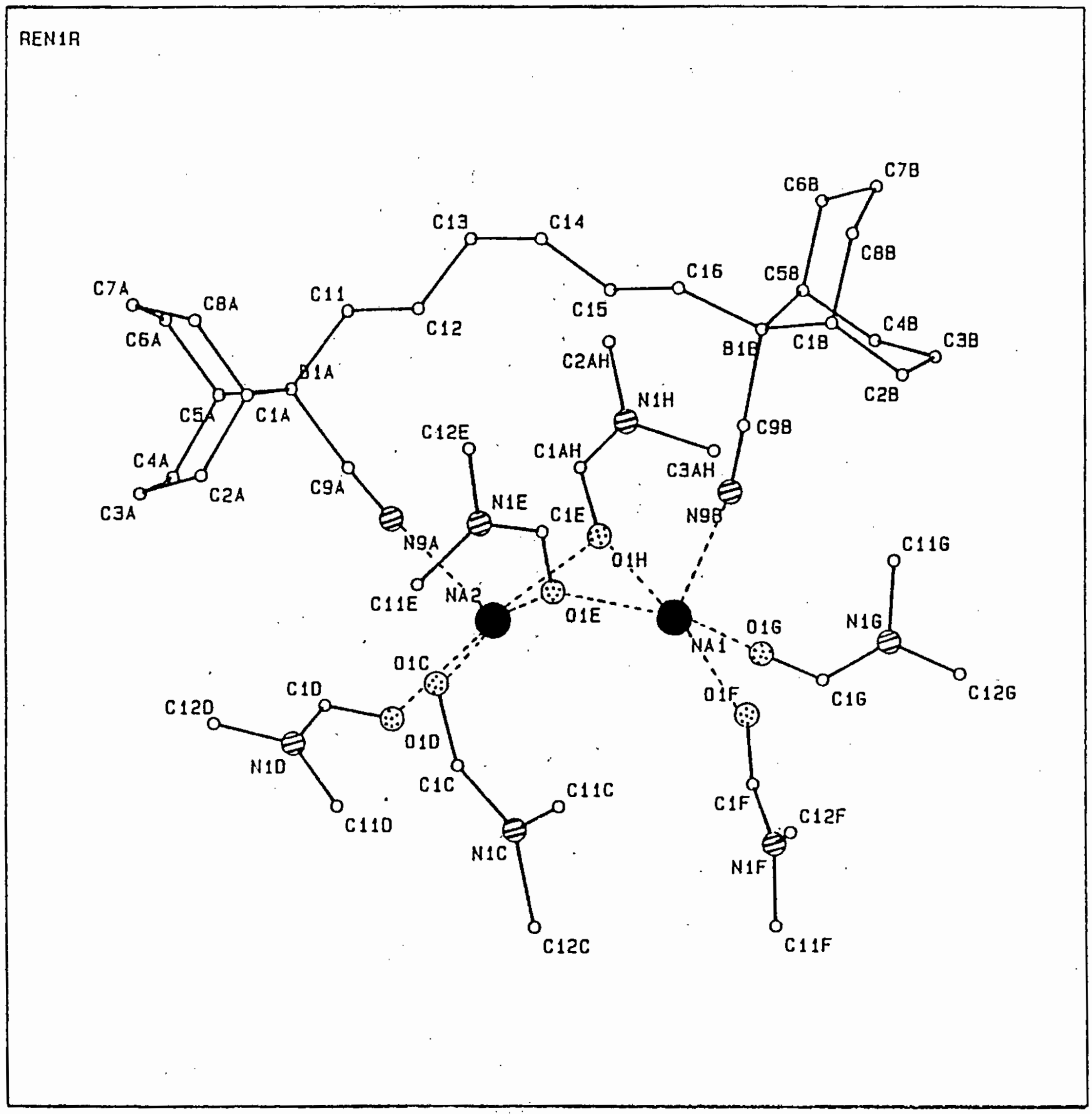


Figure 6

Thermal analysis was carried out on the cyanoborate salt and the TG and DSC traces are shown below in Figure 7. The DSC shows two fairly large endotherms at onset 49°C and 76°C corresponding to a weight loss of 27.8% in the TG trace. This data is consistent with the loss of approximately three DMF molecules with a required percentage weight loss of 25.4%. This is followed by a large diffuse endotherm between 210°C and 270°C associated with a weight loss of 51.2%. This may be ascribed to the decomposition of the entire structure as evidenced by the DSC trace. The precise chemistry occurring here, however, is open to mechanistic speculation and was not actively pursued further.

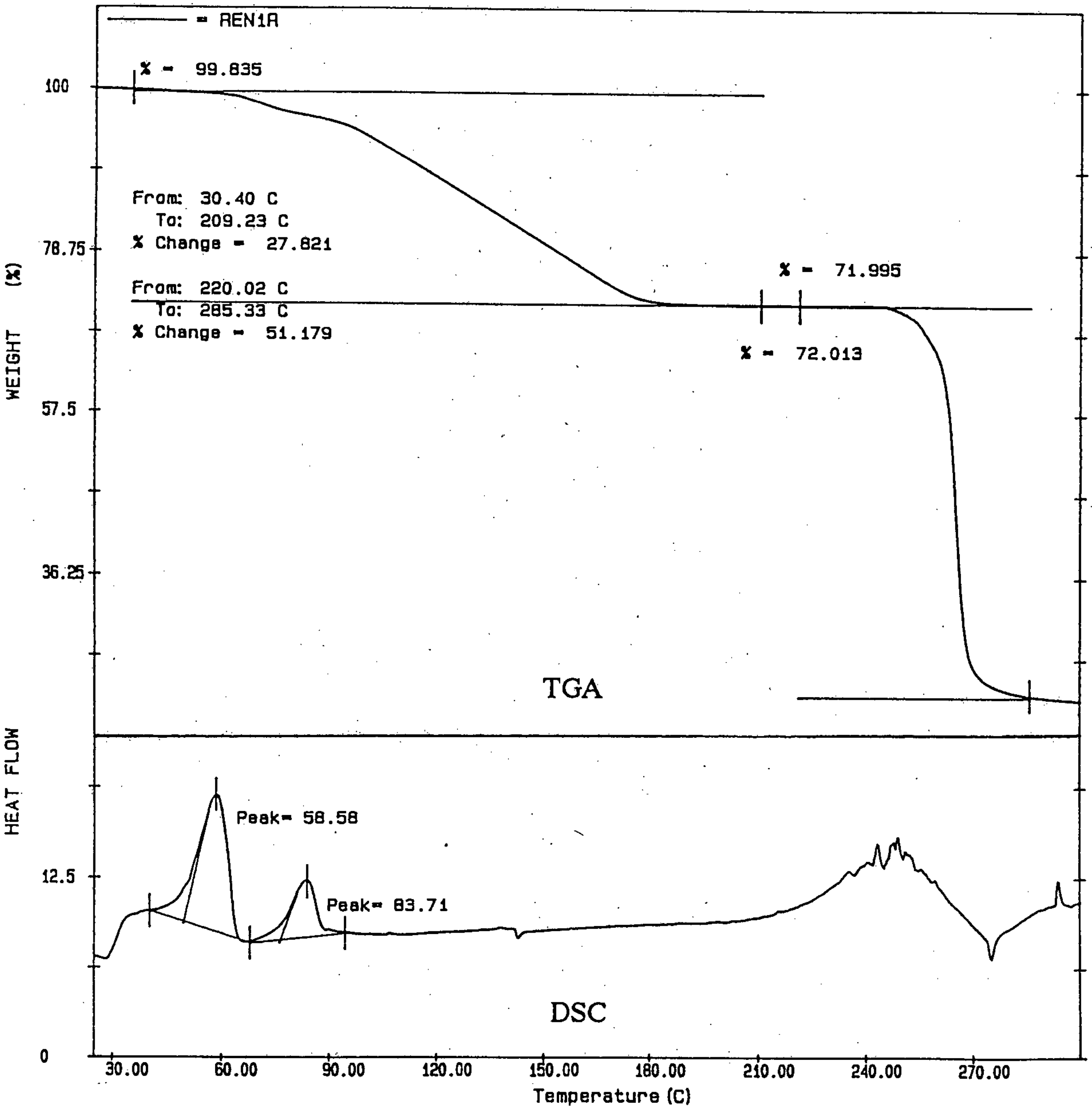


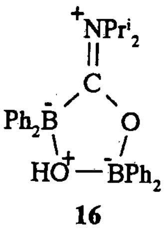
Figure 7

HMPA, TMEDA, DMSO, acetone and ethyl acetate as cyanidation solvents all gave oils, whereas THF produced an amorphous, air-stable solid, which could not be crystallised for X-ray analysis. Cyanidation did not take place in methylene chloride or benzene as evidenced by the absence of an upfield shift in the ^{1}H-NMR of the protons on the α-carbon to boron. MeOH resulted in the decomposition of the cyanoborate salt. Oxidation of the borate seemed to occur with a resonance at δ=3.86ppm as a triplet indicating the presence of B-OR species, where R constitutes the entire hexamethylene spacer or part thereof. This chemical behaviuor was consistent with that of the cyanotributylborate salt **1** mentioned previously.

As with sodium tributylcyanoborate, preparation of the neat cyanoborate with n=0 was pursued, in order to determine its properties. Removal of THF from the THF complex was complete after one hour at 0.8mmHg at 150°C and the resulting solid was highly air sensitive and had to be kept under nitrogen. The ^{1}H-NMR of this unsolvated cyanoborate complex showed no upfield shift of the α-methylene resonance, since the sodium atoms are close enough to the boron atoms to cancel out the effect of the borate negative charge, as was suggested for sodium cyanotributylborate. However, n=0 could not be achieved for the latter compound. An equimolar mixture of DMF and THF was added to the neat cyanoborate host to determine which of the two solvents it would preferentially take up. DMF was taken up to a greater extent and only very little THF was visible in the ^{1}H spectrum. This indicates that there are stronger forces operating with respect to DMF compared with THF and suggested that cyanoborate salts might be capable of forming a variety of inclusion compounds with different guests.

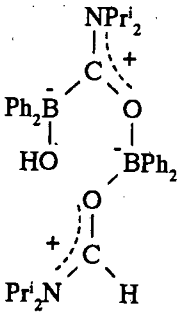
1.6 APPLICATIONS OF SOME STABLE BORANE COMPOUNDS AS HOST STRUCTURES FOR RECOGNITION

Few examples exist of boron host compounds, presumably because of the air sensitivity of many of boron containing functionalities. K. Smith *et al*[44] prepared the heterocyclic boron-containing betaine **16**, which has the ability to form stable, crystalline 1:1 addition complexes with water, amines and simple amides. Adduct formation occurs via opening of the heterocyclic ring of the betaine to give one boron atom in a 3-coordinate state capable of complexation.



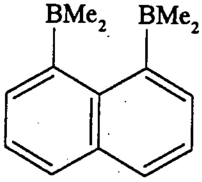
16

Betaine



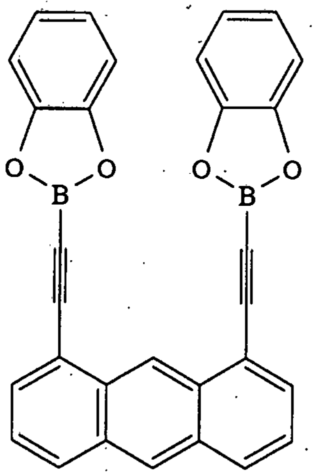
Betaine complexed with di-isopropylformamide

Another investigator in this field is H.E. Katz[45] who has investigated the complexation of anions and Lewis bases by bidentate Lewis acids. He has demonstrated that stereochemically defined 1,8-diborylnaphthalenes, eg. 1,8-naphthalenediylbis(dimethylborane) **17**, display an affinity for small anions and complex with hydride, fluoride and hydroxide.



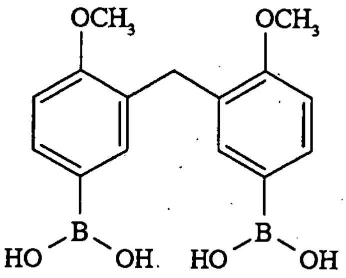
17

Boronic acid derivatives have found favour because of their relative air stability. H. Katz[46] has extended his ideas to using the 1,8-diethynylanthracene group as a rigid framework for attaching a catecholboron grouping as a boronic ester. Molecular modelling determined that guests containing two, basic, sp^2-hybridised atoms in a 1,3 relationship, such as pyrimidine would give a nearly strain-free fit.



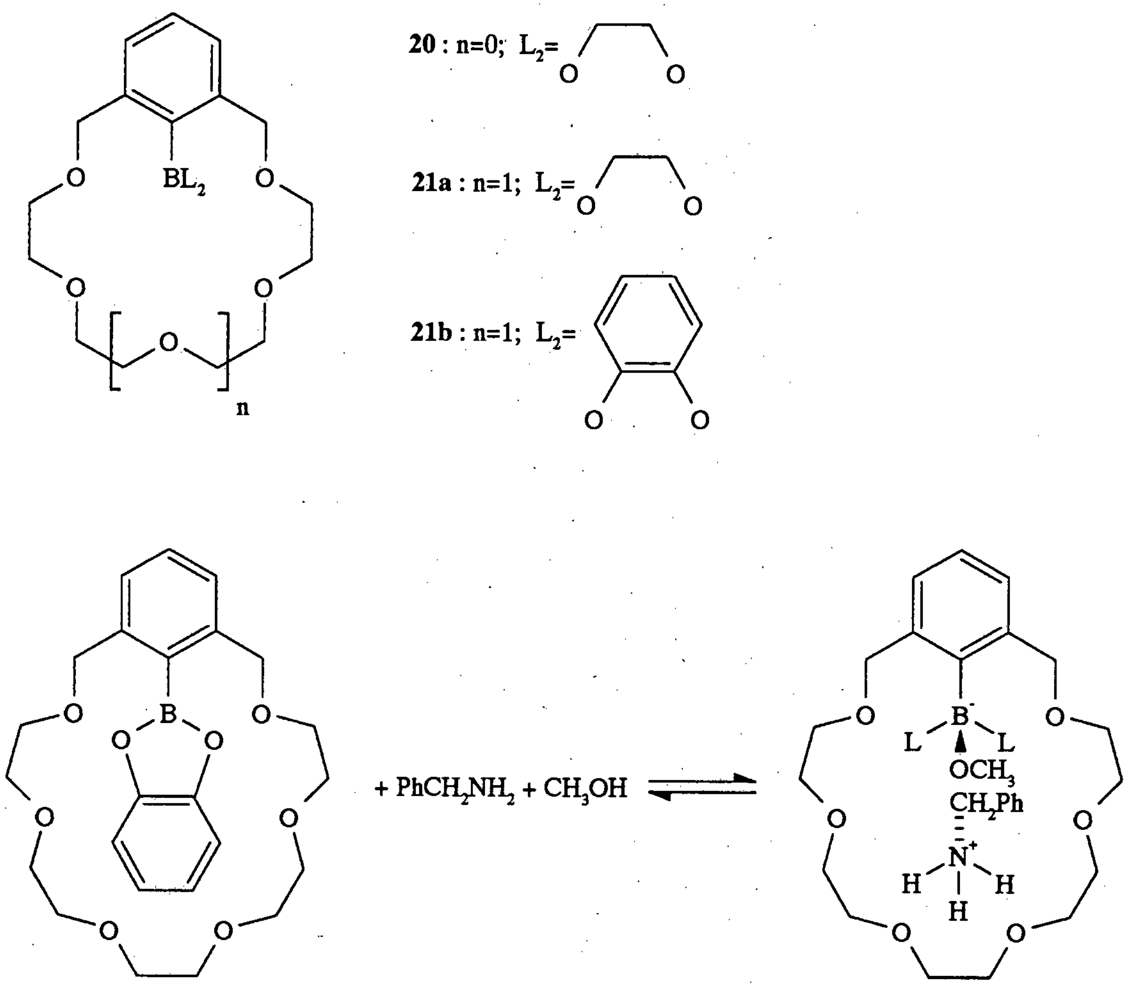
18

Although in practice compound **18** was found to be too labile for anion complexation studies, molecular models showed that the positioning of its receptor groups is appropriate for anions such as acetate and phosphate, in addition to neutral heterocyclic bases. These results open the way for the use of non-boron containing Lewis acid functional sites or else a spacer other than acetylene. Boronic acids have also been investigated as potential receptor molecules. S. Shinkai[47] has reported on the specific complexation of benzeneboronic acid derivatives **19** with mono- and disaccharides using circular dichroism to monitor recognition. Host-guest complexes are formed involving the two hydroxyl groups on each boron, and monosaccharides form stronger complexes than disaccharides which are too flexible because of the central ether linkage.



19

Boronic acid-containing crown ethers have been synthesised recently by M. Reetz *et al*[48] and host amines as well as mixtures of alcohols and amines forming stable host-guest compounds. The alcohols reacted via proton transfer to form a borate species, with the ammonium cation bonding through electrostatic interactions and hydrogen bonds. For the hosting of amines only, ^{11}B and ^{13}C-NMR spectra indicated the existence of a 'dative' B-N bond with synergistic formation of hydrogen bonds between the amine hydrogen atoms and the oxygens of the crown ether. The three-point interaction with benzylamines displays binding constants of varying magnitudes, eg. $795M^{-1}$ and $30M^{-1}$ with two different hosts, **20** and **21a** respectively, depending on the fit of the guest into the crown ether cavity. Scheme 30.

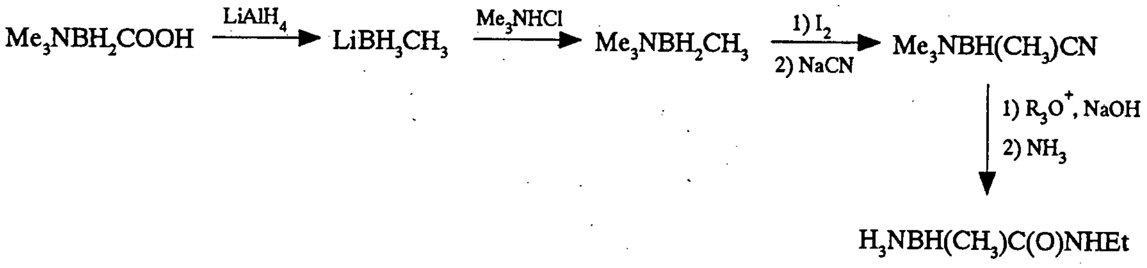


Scheme 30

As mentioned previously, G. Wittig and P. Raff[10] discovered some time ago that lithium cyanoborohydride LiH_3BCN complexes with either one or two molecules of dioxane and that the host-guest complexes are stable even against acids. Another interesting compound in this regard is sodium triethylborohydride[49], which forms a coordination complex with mesitylene. At 190K, it was possible to characterise the host-guest compound in the solid phase, although it is extremely air- and heat sensitive. Two host molecules of $NaHBEt_3$ coordinate to one guest molecule of mesitylene as evidenced by an X-ray analysis. Another similar compound is sodium trimethylborohydride, which forms a solid diethylether tetramer $[Et_2O\text{-}(NaHBMe_3)_4]$.

A borate host displaying liquid clathrate behaviour has been reported by L. Nassimbeni *et al.*[50] They prepared tetraalkylammonium tetraalkylborate salts containing the anion $[(Bu^s)_3B(Bu^n)]^-$ and the cation $[NR_4]^+=[NMe_4]^+$, $[N(Bu^n)_4]^+$, $[N(n\text{-}C_6H_{13})_4]^+$, $[N(n\text{-}C_8H_{17})_4]^+$ and showed that they form liquid clathrates with a number of aromatic and aliphatic hydrocarbons. However, these salts were difficult to purify and no satisfactory crystal structure could be obtained for any one of them.

Compounds containing boron are also being extensively used as new pharmaceuticals and neutron capture agents. B. Spielvogel *et al*[51] have been involved in the synthesis and pharmacological properties of boron analogues of biologically important molecules, such as α-amino acids. These range from simple glycine analogues such as H_3NBH_2COOH and Me_2NHBH_2COOH to more complex amino acids like alanine analogues **22**. Scheme 31.

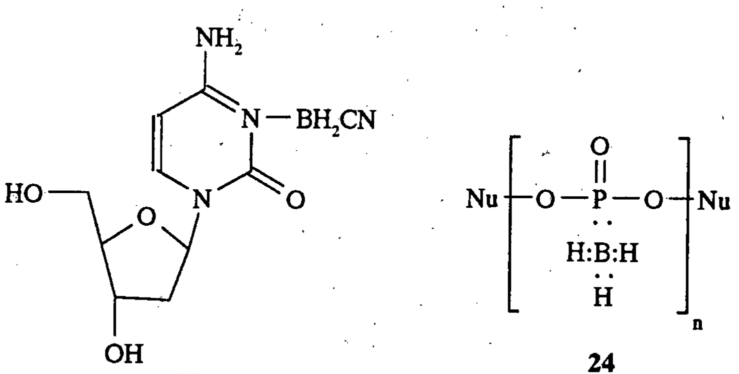


$$\begin{tikzcd}
Me_3NBH_2COOH \arrow[r, "LiAlH_4"] & LiBH_3CH_3 \arrow[r, "Me_3NHCl"] & Me_3NBH_2CH_3 \arrow[r, "1)\ I_2", "2)\ NaCN"'] & Me_3NBH(CH_3)CN \arrow[d, "1)\ R_3O^+,\ NaOH", "2)\ NH_3"'] \\
 & & & H_3NBH(CH_3)C(O)NHEt
\end{tikzcd}$$

22

Scheme 31

These compounds have shown potent activity, including anticancer, antiinflammatory, analgesic and hypolipidemic activity in both animal model studies and *in vitro* cell cultures. Of considerable interest in chemotherapy is the potential for boronated nucleic acids to localise in the nucleus for use in boron neutron capture therapy. Two new classes of boron-containing nucleic acids have been modified to form firstly cyanoborane adducts **23** and secondly boranophosphates **24**. Scheme 32.



23

Cyanoborane

24

Boranophosphate

Nu=nucleic acid

Scheme 32

In addition to having therapeutic potential, these modified nucleosides, mononucleotides and oligonucleotides may be useful as diagnostic agents and for studying fundamental biological processes at the molecular level. Organoboranes are beginning to play a significant role in the synthesis of medically important materials which contain both stable and short-lived isotopes. Boranes[52] have found important applications in modern medical imaging techniques such as positron emission tomography (PET) and magnetic resonance imaging (MRI).

In conclusion, organoboranes are no longer mainly used as reaction intermediates, but have proved themselves as viable materials for ventures in applied chemistry, such as those discussed above.

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CHAPTER 2

CLATHRATES OF BIS(METHYLTRIPHENYLPHOSPHONIUM) 1,6-BIS(B-CYANO-9-BORATABICYCLO[3.3.1]NON-9-YL) HEXANE (47)

2.1. CLATHRATES

The chemistry of inclusion compounds has a long history dating back to the beginning of the nineteenth century, when H. Davy and later M. Faraday[1] reported on a chlorine clathrate hydrate of composition $Cl_2 \cdot 10H_2O$. The most important development, though, emerging from the pioneering X-ray work of H. Powell[2] on inclusion compounds such as the SO_2 clathrate of hydroquinone, was the introduction of the term clathrate compound from the Latin "clathratus", meaning enclosed or protected by cross bars of a grating. Powell defined clathrates as host-guest compounds in which the guest is completely enclosed in a cavity formed in the host lattice. Since the dimensions of the cavity are essentially fixed, the host lattice displays a size selectivity and the complete enclosure of the guest species, in general, confers greater stability on clathrate compounds than on inclusion compounds. The present day usage of the term clathrate refers to any crystalline lattice inclusion compound. Guest molecules in a clathrate are incorporated into existing extramolecular cavities, i.e. in between the layers of host molecules, whereas molecular inclusion compounds consist of guest molecules incorporated into the cavity of a single host molecule.

This phenomenon of inclusion opens the way not only to theoretical study but also to practical applications.

2.1.1 PRACTICAL USES OF CLATHRATES

Clathrates are interesting for industrial purposes because of their ease of preparation and their disintegration upon dissolution. Possible applications[3] of this type of inclusion compound are:

- chemical analysis;
- separation of racemates;
- 'solidification' of gases and liquids;
- stabilisation of sensitive or toxic substances;
- polymerisation inside inclusion channels;
- battery systems and organic conductors.

The applications mentioned, though only outlined by a few examples, are sufficient to illustrate what renders clathrates so attractive.

2.1.2 CLASSIFICATION OF CLATHRATES

In view of the increasing confusion in the literature surrounding the terminology used for the description of inclusion compounds of which clathrates are a part, a system of classification and nomenclature of presently known and possible future types of inclusion complexes has been proposed by E. Weber and H.P. Josel[4]. The main classification is based on the criteria of:
i) the host-guest type and interaction, and
ii) the topology of the host-guest aggregate.
Host-guest aggregates that are derived from coordination between the host and guest units are defined as complexes, whereas the term clathrate is used for host-guest compounds in which the guest is retained by steric barriers formed by the host lattice (crystal lattice forces). Complexes and clathrates can also be distinguished from each other by the fact that complexes retain their identity in solution, compared to clathrates which normally disintegrate on dissolution. In addition, a distinction can be made between inclusion compounds which operate via intramolecular (within a cavity) host-guest aggregation, and extra-molecular (between layers) host-guest aggregates forming clathrates. Host-guest situations in which both complex and clathrate characteristics are present are treated as complex/clathrate hybrids. Coordinatoclathrates demonstrate a dominant clathrate character, whereas the opposite applies to clathratocomplexes. It is also possible to distinguish between a guest-free host molecule, termed clathrand, and clathrate which is its host-guest compound. Clathrates are a type of supramolecular system and thus exhibit the same types of interactional forces.

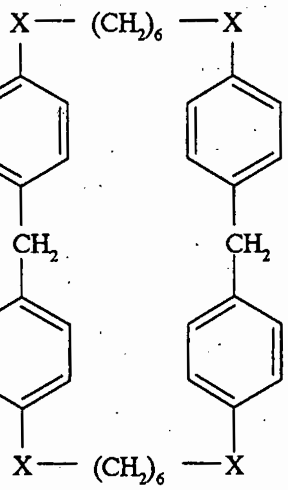
2.1.3 INTERACTIONAL FORCES WITHIN SUPRAMOLECULAR SYSTEMS

In contrast to molecular chemistry, which is predominantly based on the covalent bonding of atoms, supramolecular chemistry is based on intermolecular interactions. The principle aim of synthetic host-guest chemistry is the targeted construction of supramolecular complexes with variable non-covalent interactions arranged in conformationally defined ways. The following forces are dominant in host-guest complexes[5]:
- solvophobic forces (usually with respect to water)
- electrostatic (Coulombic) forces
- van der Waals interactions
- hydrogen bonding.

The nature of such interactions is often complex due to different forces contributing simultaneously to the stabilisation of the lattice[6].

Solvent plays an important role in host-guest complexation. During complexation of an organic guest in aqueous solution, the replacement of surface-solvating water molecules by better matched lipophilic substrates drives the formation of a lower energy complex. An example of this are the water-soluble apolar cyclophane hosts developed by F. Diederich[7], which form inclusion complexes with aromatic substrates in solution. In these inclusion complexes, the most important interaction is that involving lipophilic regions of host and guest. Thus, upon complexation, the less favourable dispersion interactions between solvent molecules of low polarisability and highly polarisable hydrocarbon surfaces are replaced with more favourable dispersion interactions between the surfaces of host and guest. In aqueous medium a hydrophobic host molecule must , however, have a built-in protection against the collapse of internal lipophilic surfaces, which may occur if the host prefers to self-satisfy hydrophobic forces by intramolecular contact rather than forming an intermolecular complex[8]. In general, the binding strength of complexes decreases from water to polar protic to dipolar aprotic and to apolar solvents.

Secondly, electrostatic forces play a major role in molecular association in inorganic as well as in biological systems, such as nucleic acids and proteins. It is the strongest of the four interactions mentioned leading to inclusion complexes with the highest association constants due to the attraction between oppositely charged ions, as for example in the azoniacyclophane complex **25** with naphthalene[5]. In this supramolecular compound the ring ammonium ions are situated with respect to the π systems of the guest in such a way that the former experience electrostatic attraction towards the π system and can at the same time induce dipoles in the arene guests. The azoniacyclophane also binds diiodomethane via Van der Waals interactions (induced dipoles). In host-guest complexes, crystal packing relies on molecular recognition between functionalities on molecular components to direct the self-assembly process into a desirable lattice conformation. However, the role of electrostatic interactions[9] between ionic molecular components during self-assembly and crystallisation has been relatively ignored. This might be due to the fact that electrostatic forces are expected to be long-range compared to hydrogen bonding or Van der Waal's interactions. Although short-range interactions have been assumed to be the most important for crystal packing, long-range forces may govern the initial orientation of the molecules in the aggregate. Thus, electrostatic forces determine the geometry of the lattice arrangement, whereas Van der Waals interactions and solvophobic interactions contribute only to the magnitude of the packing energy.



25: $X=N^+Me_2\ Cl^-$

Host-guest complexes can form between aromatic structures based on π arene-π arene interactions even in nonpolar solvents[10]. These attractive forces between π systems are found, for example, in the packing of aromatic molecules in the crystalline state[11] and in the double-helical structure of DNA, in which there is vertical base-stacking, as well as in the intercalation of drugs and other agents in the DNA strand. Arrangements in which a positively polarised hydrogen atom at the edge of one aromatic ring is directed towards the π-electron cloud of another ring are frequently observed. The so-called T-stacking is a special case of these edge-to-face arrangements in which the interplanar angle is approximately 90°. By comparison, frontal face-to-face stacking is unfavourable on account of the strong repulsion of the π-electron clouds.

Electron-donor-acceptor interactions can play a major role in both biological systems and in the formation of host-guest complexes. F. Diederich and S. Ferguson[12] found that electron-rich host molecules (donors) and electron-poor guest compounds (acceptors) form particularly stable cyclophanes. Other systems based on this type of interaction (and T-stacking effects) are the catenanes synthesised by Stoddart which are constructed from electron-rich aromatic crown ethers and electron deficient cyclic bis(paraquat) units[13], as well as the macro-heterocyclic, viologen-analogue onium host compounds developed by S. Hünig[14]. Electron-donor-acceptor interactions also play a major role in the complex formation of "cyclo-bis-intercalands"[15] and, in addition to hydrogen bonds, in tweezer molecules[16] In general, the distribution of the partial charges[17] within the π-electron systems has a substantial influence on the orientation (edge-to-face) of a guest (additionally bound by hydrogen bonds) relative to the arene surfaces of the host. Thus, π-π or "stacking" complexes may be stabilised by three sources, namely electrostatic, induced dipole and dispersive contributions, in addition to solvophobic effects.

In order to clarify the geometrical requirements for aromatic···aromatic interactions, C. Hunter and J. Sanders[18] have developed a model of charge distribution in a π-system using porphyrin systems. In this model the σ frame and the π electrons are considered separately, with the σ skeleton sandwiched between two negative π-electron clouds. They concluded that attractive π-σ interaction between the electron clouds and the positively polarised hydrogen atoms compensates for unfavourable π-π repulsion resulting in a net favourable π-π interaction between aromatic systems.

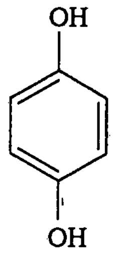
As with electron-donor-acceptor complexes, hydrogen-bonded associations[19] involve the participation of three main interaction mechanisms, namely electrostatic (Coulombic), dispersive and charge-transfer. An important factor for molecular recognition by the formation of hydrogen bonds is the optimum adjustment of the basicity of one component and the acidity of the other[20]. Such interactions dominate not only in proteins but also in the most successful known cases of selective binding in organic host-guest complexes. The groups of J. Rebek[21], A. Hamilton[22], and W. Still[23] have been particularly active in designing systems containing multiple complementary hydrogen donor-acceptor sites, which are also well suited for chiral recognition.

Therefore, an exact knowledge of the energetic and stereochemical characteristics of these non-covalent, multiple intermolecular interactions, such as electrostatic forces, hydrogen bonding, Van der Waals forces, etc., should allow the design of artificial receptor molecules which bind the substrate strongly and selectively by forming 'tailored' supramolecular structures of defined structure and function.

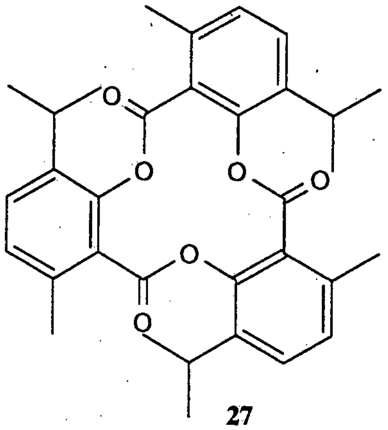
2.1.4 THE HISTORY OF CLATHRATES

Even though X-ray analysis of inclusion compounds was not possible until the middle of the twentieth century, many discoveries of new inclusion compounds and hosts[24] were made prior to this. Among them specified in the literature are those mentioned at the beginning of section 2.1, as well as the graphite intercalates, the hydroquinone **26** and cyclodextrin inclusion compounds, the Hofmann-type and Werner-type clathrates as well as the inclusion compounds of tri-o-thymotide (TOT) **27**, Dianin's compound **29**, choleic acid **28**, triphenylmethane derivatives **30**, various substituted catechols and urea[25]. Figure 8.

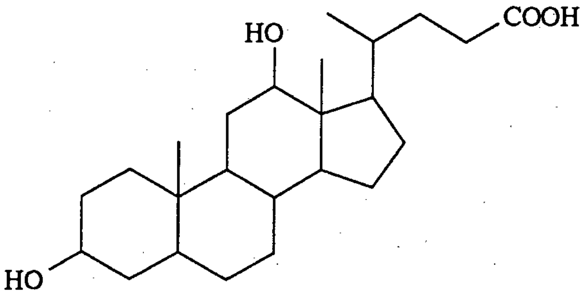
Various guest substances may be included depending on the structure[26] of the host molecule. Hydroquinone molecules form a network structure held together by hydrogen bonding incorporating guest compounds such as SO_2, CH_3OH, HCl, H_2S, HCN, Ar, Kr and Xe. Dianin's compound forms clathrates with a variety of guests including Ar, SO_2, NH_3, benzene, ethanol and chloroform. By comparison, the host lattice of choleic acid contains channel-like cavities in which guest compounds such as fatty acids, alkanes, xylene, naphthalene, benzoic acid, phenol, camphor, cholesterol and others, can be incorporated. TOT has the unusual ability to form channel- and cage-like cavities, depending on the shape and size of the guest molecules. During recrystallisation it may include n-hexane, ethanol, methanol, *m*- and *p*-xylene, benzene, carbon tetrachloride, chloroform and dioxane. It can also be used in the resolution of racemates. In addition, trimesic acid (TMA) **31** is capable, by itself or together with other molecules such as water, to form a host lattice from an extensive network of molecules linked by hydrogen bonding. Typical inclusion compounds formed are $TMA{\cdot}0.7\ H_2O{\cdot}0.09\ HI_5$, $TMA{\cdot}0.7\ H_2O{\cdot}0.167\ HIBr_2$, $TMA{\cdot}H_2O{\cdot}2/9$ PA (PA: Picric acid) and TMA·DMSO. It should be noted that these are non-stoichiometric inclusion compounds, in which the polyhalogen-ions (I_5^- and IBr_2^-) are located in channel-like cavities, while the counterions (H^+) are bound to the water molecules outside the channels and between the TMA networks.



26
Hydroquinone

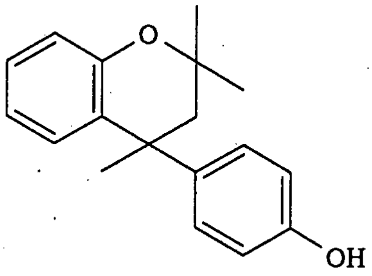


27
TOT



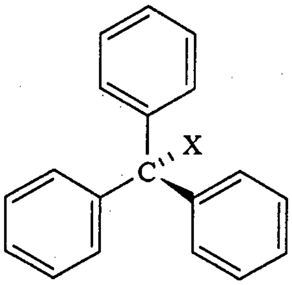
28

Choleic acid

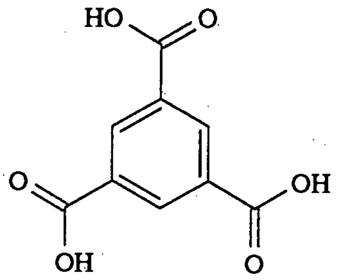


29

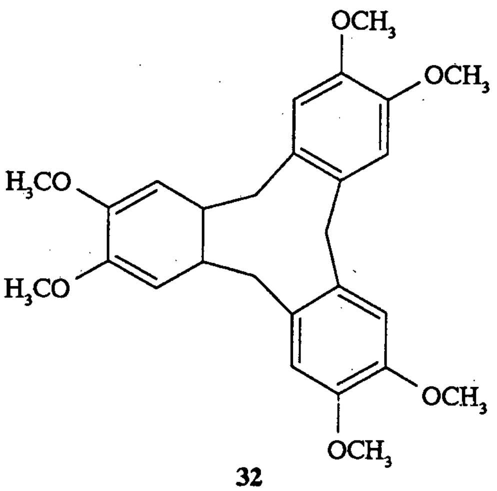
Dianin's Compound



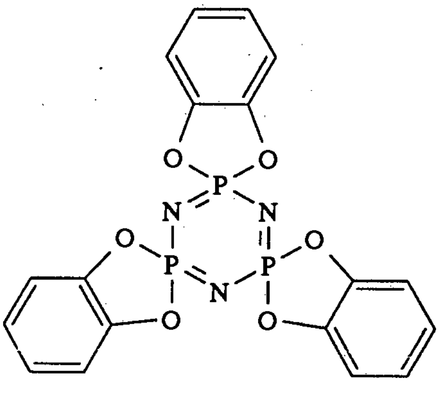
30
X = H, Cl, OH



31
Trimesic acid



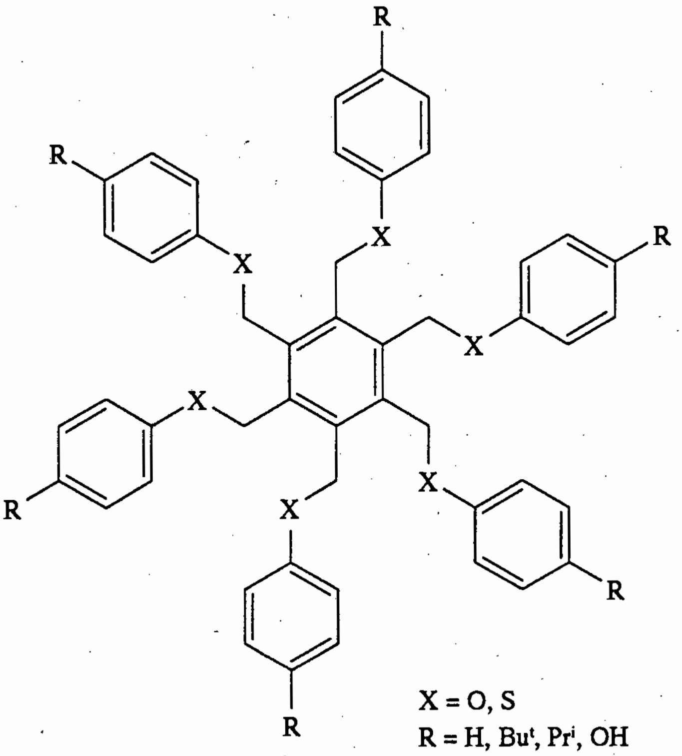
32
Cyclotriveratrylene



33
Cyclophosphazene

Figure 8

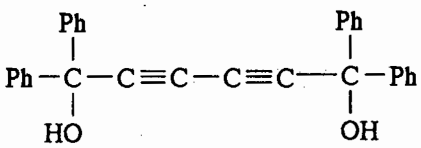
In actual fact, the majority of clathrate compounds known to date have been discovered accidentally and not by directed (rational) synthesis[24e]. However, H. Powell recognised that certain structural units such as the hexagonal unit of hydrogen bonded hydroxyl groups as present in the various quinols or the Dianin's compound could be expected to act as host lattices. D. MacNicol[27] also noted that a feature common to several host lattices was the trigonal symmetry of either the individual host molecule or of the lattice. A new type of host based on these structural features, termed 'hexahosts' **34**, form clathrates with guests such as acetone, dioxane, chloroform, carbon tetrachloride and derivatives of benzene. Different guest selectivities are displayed when recrystallising the host from solvent mixtures such as *o*- and *p*-xylene[28], depending on the structure of the host.



X = O, S
R = H, Bu^t, Pr^i, OH

34
'Hexahost'

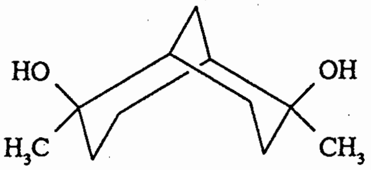
Another strategy that takes the overall molecular shape of a host into account was introduced by F. Toda[29] in 1968. It is based on a diyne-diol **35** and has been coined the "wheel-and-axle" model. Stoichiometric host-guest compounds are formed with alkyl halides, arenes, alkynes, aldehydes, ketones, esters, ethers, amines, nitriles, sulfoxides and sulfides. Subsequently, this host design was expanded upon by Hart[30]. It consists of a linear molecular axis made up of sp carbons with sp^3 carbons at each end bearing large, relatively rigid groups, which prevent the host molecules from forming a close-packed structure in the crystal. Thus, large lattice voids are formed that are able to accommodate aromatic hydrocarbons depending on their chemical nature, size and geometry. In these compounds the intermolecular forces responsible for clathrate inclusion are hydrogen bonding and/or arene π-π interactions and structurally the linear spacer is essential.



$$\mathrm{Ph-\overset{Ph}{\underset{HO}{C}}-C\equiv C-C\equiv C-\overset{Ph}{\underset{OH}{C}}-Ph}$$

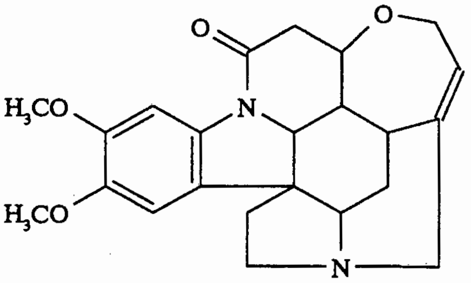
35

In 1979, R. Bishop[31] discovered a new H-bonded channel inclusion network based on a rigid bicyclic aliphatic diol which he extended to a whole series of compounds similar to the prototype **36**. The main structural feature of this particular host is a rigid skeleton with two appropriately syn-positioned hydroxyls which stabilise a hydrogen bonded channel matrix. The channel walls involve a double helical array of hydrogen bonded diol molecules forming a helical tubuland lattice. In a more recent paper[32] by R. Bishop *et al.* different modes of hydrogen bonding in bi- and tricyclic diols were reported on, and a structural rationale presented to open up the possibility of controlled hydrogen bonding.

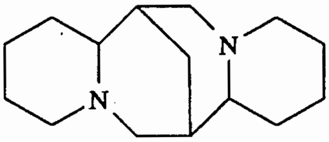


36

Hydrogen bonding is an essential part of the host-guest lattice formation for alkaloids[33] such as brucine **37** and sparteine **38**, which have been shown by F. Toda *et al.* to enantioselectively enclathrate chiral propargylic alcohols.

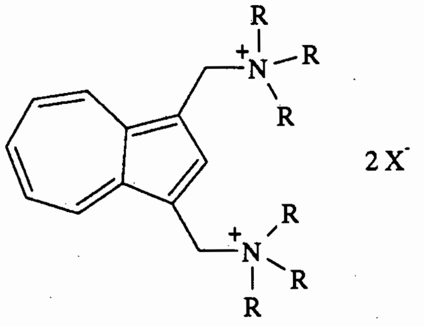


37
Brucine



38
Sparteine

Owing to a chance observation, F. Vögtle[34] discovered that a certain type of organic onium compound such as **39** and **40** with limited molecular flexibility is an exceptional clathrand. The general characteristics that are observed in many clathrate hosts such as bulkiness, limited conformational mobility and the stability of the host's ionic lattice are displayed in these clathrands. This discovery led to the idea of using quaternised alkaloid bases[35] to provide a chiral, non close-packed, ionic crystal lattice, which might display enantioselective, as well as broad based recognition.



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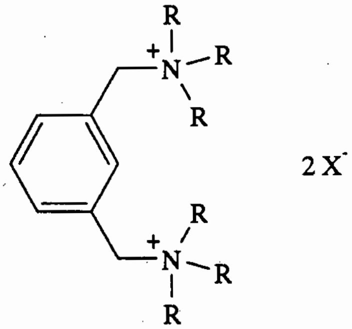
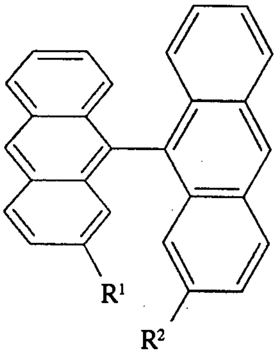


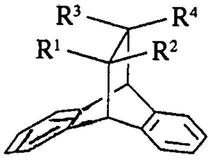
40

At about the same time as F. Vögtle's work just described, the concept of "coordinatoclathrates" as a host-guest type was introduced by E. Weber and H.P. Josel[36]. The design of such a host involves having a bulky basic skeleton for providing the lattice voids, as well as appended functional groups that act as sensors in the coordinative host-guest interaction. It is suggested that coordination-assisted host-guest binding results in the formation of inclusion compounds which are more stable than those that are held together by van der Waals forces alone. In subsequent years, this concept has proved very successful in the design of new host compounds of scissor-like **41** and roof-like **42** appearance. One of the most prolific host clathrands in this category is the trans-dicarboxylic acid **42** shown below, which has a roof-shaped molecular backbone. It forms clathrates with no less than 27 different guests, including n-BuOH and DMF.



41

$R^1 = R^2 = H$
$R^1 = R^2 = Cl$
$R^1 = R^2 = CH_3$
$R^1 = Cl, R^2 = CN$
$R^1 = Cl, R^2 = COOH$
$R^1 = H, R^2 = COOH$



42

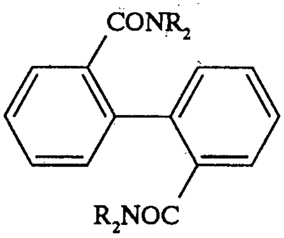
$R^1 = R^4 = COOH$
$R^2 = R^3 = H$

$R^1 = R^3 = COOH$
$R^2 = R^4 = H$

Similarly, symmetry aspects have also been identified by various research groups[27,37] as a criterion of directed clathrate formation, and there are no doubt other physical parameters which will be identified in the future.

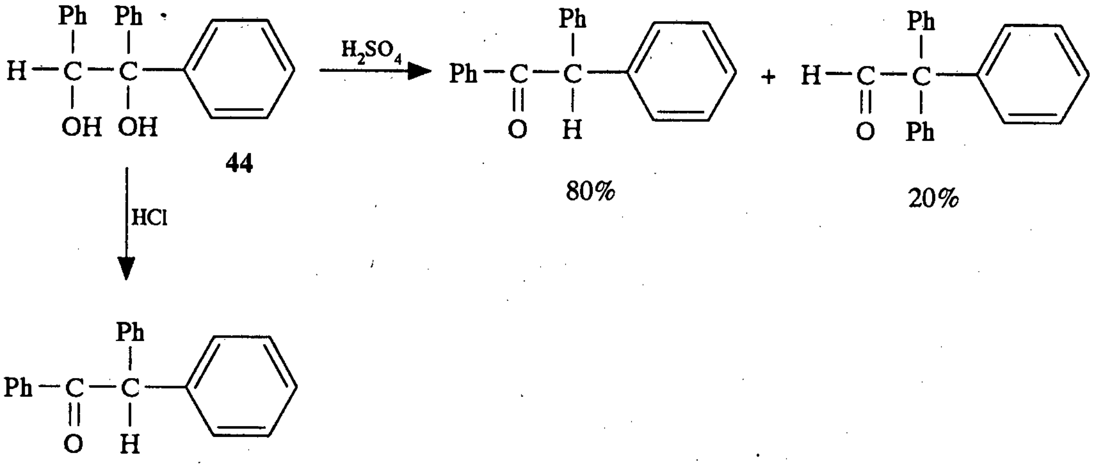
2.1.5 REACTION CONTROL OF GUEST COMPOUNDS WITHIN HOST-GUEST LATTICES

Another interesting feature of host-guest clathrate chemistry is the prospect of controlling the chemical reactivity of the guest by its host environment[38]. For example, the guest may react stereoselectively and efficiently when it is in the channel of a host complex. Thus, an optically active host compound has the potential to control enantioselectivity. For instance, the chiral host **43** has been shown to control the pinacol rearrangement of 1,1,2-triphenylethane-1,2-diol **44** asymmetrically. Host-free rearrangement using the normal reaction conditions of sulfuric acid resulted in a mixture of carbonyl products (80:20) whereas carrying out the reaction using the host with hydrogen chloride gas, not only resulted in controlling the migration reaction but did so to produce one enantiomer in a 90% chemical yield. Scheme 32.



R=cyclohexyl

43



Scheme 32

Other examples of guest reaction control are the preparation of a chiral β-lactam by irradiation of an achiral oxoamide, and the reaction acceleration of the Baeyer-Villiger oxidation of ketones by *m*-chloroperbenzoic acid in the solid state.

It is likely that in future, new, specific host compounds will be able to control specific reaction conversions.

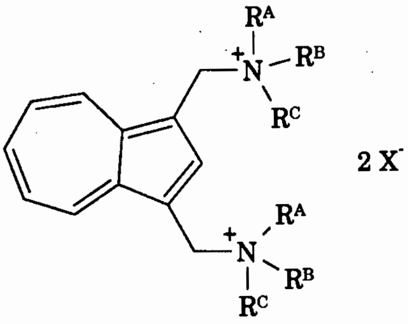
2.2. ORGANIC ONIUM COMPOUNDS AS CLATHRANDS

As already mentioned (Section 2.1.4), F. Vögtle *et al.*[34a] discovered that the bisammonium azulene onium compound **45a** incorporated variable amounts of iodomethane and ethanol on crystallisation. The guests could not be removed even after 'drying' *in vacuo* for several days and a variety of solvent molecules could be incorporated in stoichiometric amounts by recrystallisation. Other organic onium clathrands[34b,34d,39] with modified selectivities were prepared by systematically varying the following structural elements:

- the alkylammonium groups R^A, R^B, R^C;
- the length of the onium side-arms;
- the anchoring group (azulene in the prototype);

- the counter ions.

Table 4 displays the clathrate behaviour of some of these onium compounds.



45

a: $R^A = CH_3$ $R^B = CH_3$ $R^C = CH_3$ $X = I$
b: $R^A = CH_3$ $R^B = CH_3$ $R^C = CH_3$ $X = Br$
c: $R^A = CH_3$ $R^B = CH_3$ $R^C = C_2H_5$ $X = I$

TABLE 4

Clathrates of host compounds **45a-c**

Host[a]	Host:Guest ratio	Guest
45a	1:1	ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, 1-pentanol, 1,2-ethanediol, 1,3-propanediol, 1,4-butanediol, 1,5-pentanediol, ethanethiol, pyridine, DMF, nitromethane, nitroethane, 1-nitropropane, 2-nitropropane, trichloromethane, tetrachloromethane, iodomethane, iodoethane, 1-iodopropane, 1-iodobutane, malononitrile, benzoquinone
	3:2	2-methyl-1-propanol, acetone, acetonitrile
	2:1	1,3-butanediol
	1:3	bromotrichloromethane
	[b]	H_2O, methanol, dichloromethane
45b	1:1	bromomethane, dichloromethane, nitromethane, nitroethane, 1-nitropropane, acetonitrile, acetic acid, acetone, DMF
45c	ca. 1:2	ethanol

[a] H_2O is contained in some of the clathrands and clathrates in stoichiometric amounts.

[b] Non-stoichiometric.

The following conclusions were drawn from the host-guest activity profile of these onium salts:

(i) the presence of similar alkyl groups on the ammonium nitrogens, as well as bulky substituents ($CH_2N^+R_4$) in positions 1 and 3 of the anchoring group (azulene, benzene) enhanced clathrate formation,

(ii) a rigid molecular residue such as benzene, naphthalene, azulene, or other aromatic compound acted as a convenient anchor group,

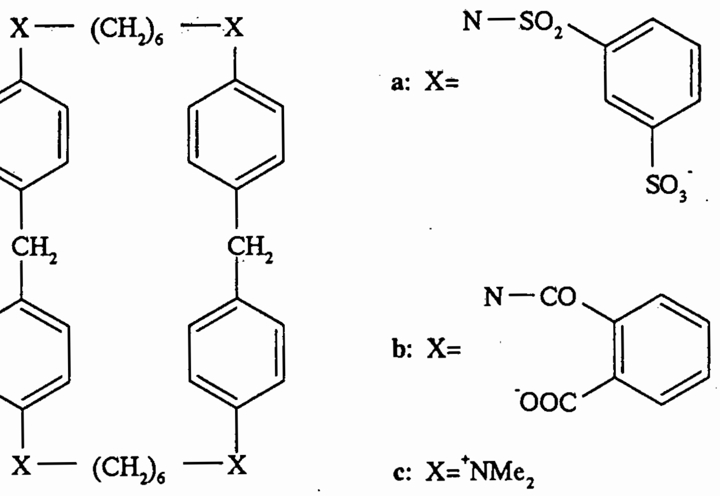
(iii) exchange of iodide for the smaller bromide reduced inclusion activity, as did

(iv) enlargement or removal of the methylene spacer unit between the anchoring group and the ammonium nitrogen.

X-ray structure analyses of the onium salts revealed that the guest molecules were sterically constrained by the ionic lattice of the host without exhibiting strong interactions between individual host and guest molecules, such as specific ion-dipole bonding. Moreover, the inclusion ability of the onium hosts in general was largely determined by its molecular symmetry and flexibility. This in fact is a general feature of hosts. In the formation of host crystal lattices containing cavities, too high a conformational mobility of the atomic groups counteracts the "bulkiness" of the host molecules, whereas a limited flexibility makes the adaptation of the host conformation to the requirements of the guest molecules more difficult. Hence, a balance between flexibility and bulkiness of groups in a host is crucial[34b]. The stability of an ionic host lattice is of great significance and ionic interactions are more important in forcing bulky molecules to crystallise than interactional forces in molecular lattices.

F. Vögtle[40] has extended these onium clathrands into the field of enantioselective recognition. For instance, the (-)-*N*-methylquininium iodide and (-)-*N*-benzylquininium chloride salts form inclusion compounds with one of the enantiomers of 2-butanol in a stoichiometric ratio of 1:1, as well as with short-chain guest compounds. Recrystallisation of the clathrands from racemic 2-butanol and subsequent declathration by heating yielded optically active distillates of (+)-(S)-2-butanol in 16% ee from (-)-*N*-methylquininium iodide and (-)-(R)-butanol in 25% ee from (-)-*N*-benzylquininium chloride.

Another class of onium compound which forms inclusion complexes and not clathrates, and which is based on a tetraaza[8.1.8.1]paracyclophane nucleus, has been extensively studied by H. Schneider *et al.*[41] with respect to the forces operating within the cavity. Cyclophanes **46a, 46b** and **46c** complex aromatic substrates more strongly than aliphatic ones. Complexes of aromatic guests and **46c** are specifically stabilised by Van der Waals (induced dipoles) and electrostatic $N^{+}\cdots\pi$-electron interactions. This stabilisation cannot operate in complexes of hosts **46a** and **46b**, since their nitrogens are neutral and their negatively charged centres would be repulsive to the π-electron cloud of the aromatic guests. These results suggest that ion-dipole interactions are largely responsible for the strong binding of neutral aromatics by protonated or quaternised tetraaza[n.1.n.1]paracyclophane hosts introduced by K. Koga[42] and other cyclophane receptors with positively charged centers in the binding site periphery.



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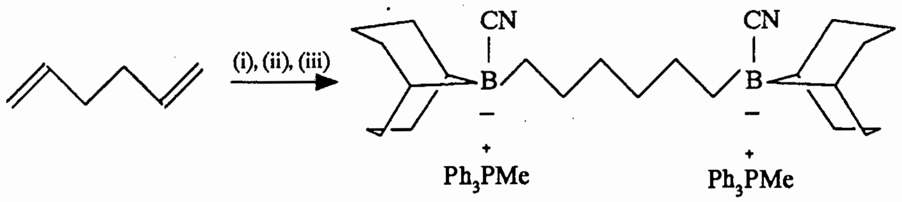
As pointed out by F. Vögtle, onium compounds[34e] fall into a class of clathrate-, cavitate-, and complex-forming molecules with extensive inclusion ability, diverse selectivities, ready availability and wide synthetic variability. Therefore, the broad applicability of the onium clathrate type and the ease of synthesis of suitable host compounds makes this host family an extremely attractive one for both basic and applied research.

2.2.1 SYNTHESIS OF BIS-METHYLTRIPHENYLPHOSPHONIUM 1,6-BIS(B-CYANO-9-BORATABICYCLO[3.3.1]NON-9-YL) HEXANE

As already mentioned in chapter 1.3, sodium tetraalkylborates were first synthesised by R. Damico[43] back in the 1950's. Their analysis proved problematic because of their reactivity in air so Damico converted them to their tetramethylammonium or tetrabutylphosphonium salts to obtain air stable compounds in high yield which could be recrystallised. This indicates that the nature of the cation has a marked effect on the reactivity of these borates with oxygen, and this led us to exchange the sodium in our cyanoborate for a bulky cation. Methyltriphenylphosphonium was chosen in view of its size and the greater likelihood of obtaining a solid borate derivative because of the rigidity of the aromatic groups.

For the preparation of the bis-phosphonium borate salt, the disodium derivative was first synthesised as described previously. Methyltriphenylphosphonium bromide dissolved in methanol was then added to the viscous disodium bis-9-BBN cyanoborate and stirred until a homogeneous mixture was obtained. Methanol was removed *in vacuo* and ether and water then added resulting in the formation of three layers, the bottom and top layer corresponding to the water and ether layer respectively. The middle layer contained the cyanoborate as an oil, which was insoluble in both ether and water and which salted out on addition of a little aqueous NaCl. The extraction mixture was stirred for approx. 5min. to ensure thorough mixing before separation. During the extraction, the middle cyanoborate layer was always kept together with the ether layer. When the combined ether extracts were washed with water, plate-like crystals usually started appearing from the middle layer, until the entire middle section was made up of a solid mass of crystals. However, occasionally the formation of crystals was very sluggish, in which case all the aqueous and organic extracts were combined and left at 0°C to crystallise out. The colourless solid **47** was then filtered, washed and vacuum dried. (Scheme 33)



(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $Ph_3\overset{+}{P}Me\ \overset{-}{Br}$ (2eq)/MeOH

$\cdot n\ H_2O$

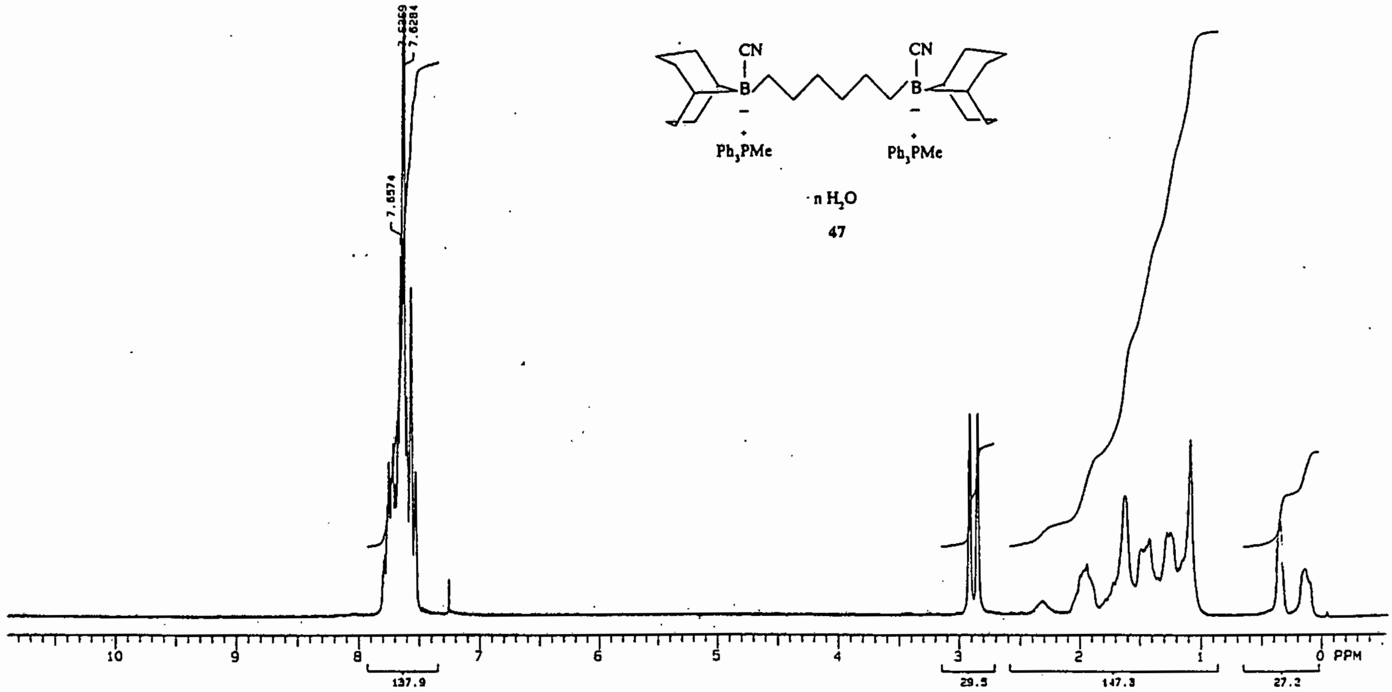
47

Scheme 33

No suitable solvent could be found for the cyanoborate salt's recrystallisation, but the filtered and dried solid was pure as evidenced by its ^1H and ^{13}C-NMR spectra, as well as by its elemental analysis. Figure 9.

As for the sodium cyanoborate DMF complex, the ^1H-NMR spectrum of **47** (shown over the page) displays two sets of peaks below 1ppm corresponding to the protons α to boron. The doublet at δ=2.89ppm for the methyl group on phosphorus is due to phosphorus-hydrogen coupling and the coupling constant of 13.3Hz falls into the known literature range[44] of 10-18Hz for this type of group of phosphonium salt. Often the methyl protons on phosphorus integrated to less than six protons, which was ascribed to the acidity of the methyl group of the phosphonium ion undergoing H-D exchange with $CDCl_3$ in the NMR tube. This was corroborated by an increase in the chloroform signal as the number of methyl protons decreased. The base in such an exchange reaction would have to be the cyanoborate anion reacting via the boron-carbon bond. This is an important indication of the chemical nature of the borate species and has bearing on the host-guest chemistry discussed later on. Indeed it has been reported by S. Alunni[45] that H-D exchange occurs in phosphonium salts with CD_3ONa-CD_3OD and NaOD-D_2O mixtures using kinetic measurements. A broad peak in the ^1H-NMR spectrum of **47** at approx. δ=2.3ppm, but often varying between 2.1 and 3.0ppm was eventually attributed to water from the extraction that was being included by the phosphonium borate salt.

In the ^{13}C-NMR spectrum of **47**, the methyl resonance at 9.9ppm shows a carbon-phosphorus coupling constant of 58Hz. The broad signal, due to boron-carbon coupling, at 24.6ppm corresponds to the two carbons adjacent to boron. The peaks further downfield in the phenyl region of the spectrum appear as doublets due to phosphorus-carbon coupling, the coupling constant decreasing with carbon to phosphorus distance. Another broad, but hardly visible resonance at 150.0ppm corresponds to the cyano carbon. Resonances of carbon atoms directly bonded to boron are known to be either severely broadened or even undetectable due to ^{11}B-^{13}C couplings involving the quarupolar nature of the boron nucleus causing incomplete relaxation of the carbons[44c].



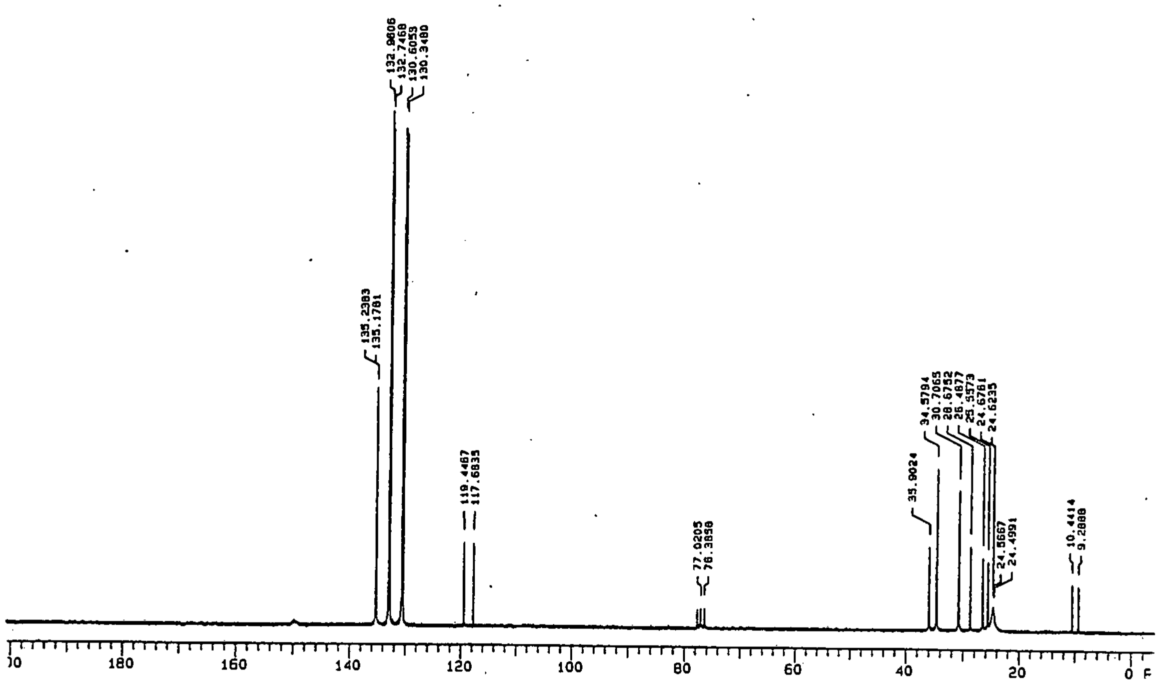


Figure 9

The I.R. spectrum of **47** in solution confirms the presence of water in a qualitative manner. The resonance at 3820cm^{-1} may be attributed to solvent water ('free OH') and the other broader resonance appearing at 3380cm^{-1} may be assigned as 'intermolecularly bonded OH', according to D. Williams and I. Fleming[44b], of water hydrogen bonding to the cyano nitrogens of the host. (Figure 10) The strength of the bond is related to the frequency. The stronger the hydrogen bond, the lower the vibrational frequency and the broader and more intense the absorption band. Both resonances decreased at a similar rate when water was removed from the host at elevated temperatures.

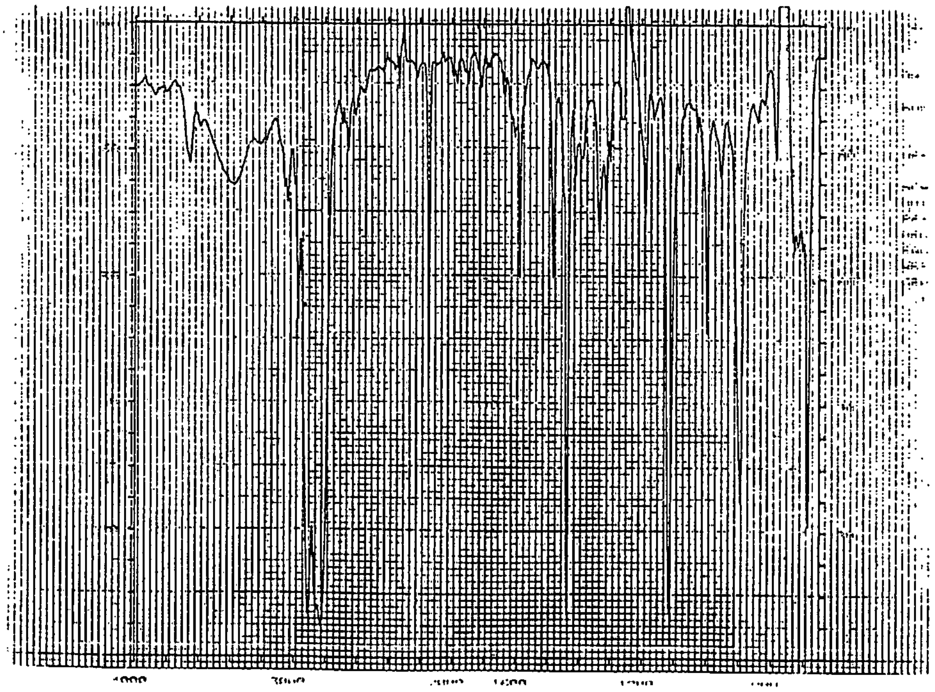


Figure 10

The stability of **47** towards acids was examined by dissolving it in acetic acid and tosic acid. In both instances the borate anion had undergone chemical changes, such as oxidation as evidenced by the spurious peaks in the NMR spectra.

2.2.2 X-RAY ANALYSIS OF BIS-METHYLTRIPHENYLPHOSPHONIUM 1,6-(B-CYANO-9-BORATABICYCLO[3.3.1]NON-9-YL) HEXANE WATER

The X-ray analysis of this air-stable compound as shown in Figure 11 indicates that the two bicyclic rings attached to boron are in a flattened-chair conformation. One water molecule was found equidistant from each cyano group of the anion of the host. The hydrogen atoms of the water molecule could not be located but the proximity of the nitrogen atoms at 2.97Å and 2.86Å indicates the presence of hydrogen bonding between the host cyano nitrogens and the water. In addition, the N···O···N angle is 111°. In this structure the cyano groups on boron are in a syn relationship with respect to the B-B axis. This is a consequence of the hydrogen bonding to the water causing the C_2-C_5 cisoid kink in the hexamethylene spacer which was also observed in the sodium cyanoborate complex with DMF. Thus, the anion once again adopts a higher energy conformation to satisfy intermolecular coordination demands.

X-ray

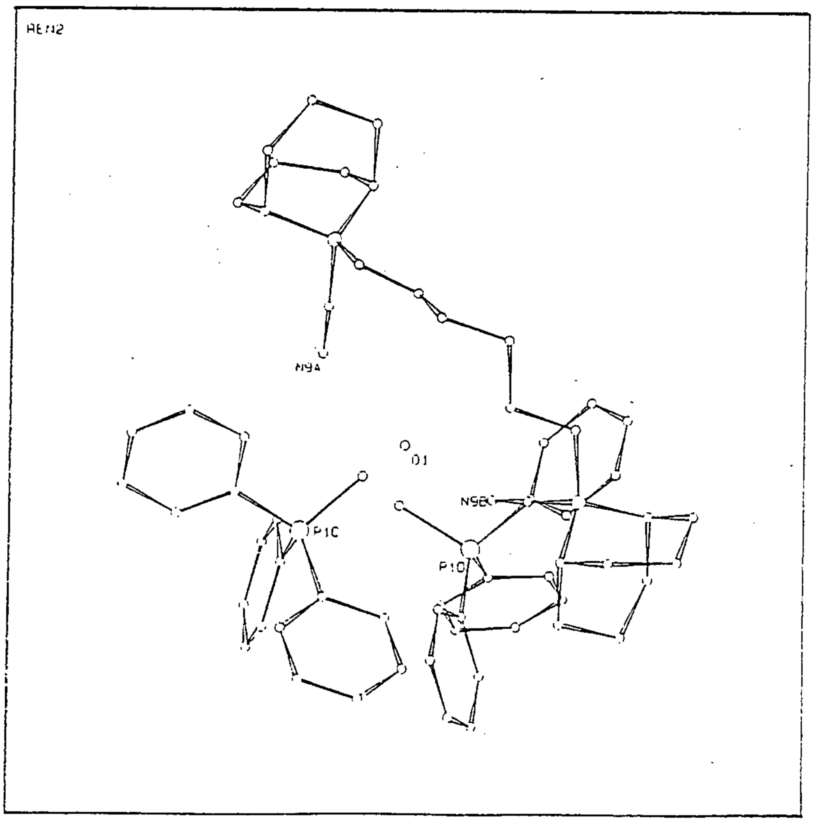


Figure 11

2.2.3 REMOVAL OF WATER FROM THE PHOSPHONIUM BORATE

From TG analyses, it could be determined that the amount of water present in the phosphonium salt **47** differed from batch to batch. The quantity of water (n) in a freshly prepared sample that had been vacuum dried on the laboratory trolley pump (1 hr, RT, 0.1mmHg), ranged from 0.7-1.7. Possible reasons for this large variation were differences in the extraction procedure as well as temperature differences in the laboratory, pressure differences of the vacuum pump and slight variations of pumping time. The gradual removal of residual water to afford an anhydrous sample was investigated by inserting the sample in a vacuum pistol (0.5mmHg) for three hours at a time at varying temperatures. TG analysis of the samples gave an indication of the amount of water still present in the compound. (Table 5) Chemical integrity was monitored by ^{1}H-NMR and it was found that decomposition began around 160°C.

TABLE 5

TG analysis results for $[(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\ 2(Ph_3P^+Me) \cdot n\ H_2O]$

Setting	Temp.(°C)	Δ(%)	n H_2O
1	50	0.75	0.39
2	55	0.43	0.23
3	70	0.41	0.21
4	85	0.24	0.12
5	98	0.17	0.09
6	106	0.04	0.02
7	134	0	0
8	160	0	d

Δ change in gradient of curve
d decomposition

Water can be removed at 134°C *in vacuo* for 3 hours, or else at 70°C *in vacuo* for 16 hours, indicating that it is very tightly hydrogen bonded as observed in the X-ray analysis.

An X-ray structure analysis was carried out on the totally anhydrous form of **47** and proved to be significantly different to that containing water or DMF with **15** as seen in Figure 6. The anion now adopts the thermodynamically more stable zig-zag conformation resulting in the two cyano groups to be anti with respect to the B-B axis. Thus, it appears that it is possible to control the lattice structure and hence the inclusion activity of the host that it is possible to control the lattice structure and hence the inclusion activity of the host by choice of guest. As before, the water-free compound consists of the two 9-BBN rings attached to boron in a half-chair conformation. Furthermore, there appears to be hydrogen bonding between a methyl hydrogen of a phosphonium ion and a cyano nitrogen atom of the host anion as evidenced by H···N distances of 2.45Å and 2.47Å. As shall be seen later on, this intermolecular interaction proved to be extremely important to the clathrate host-guest recognition process. Figure 12.

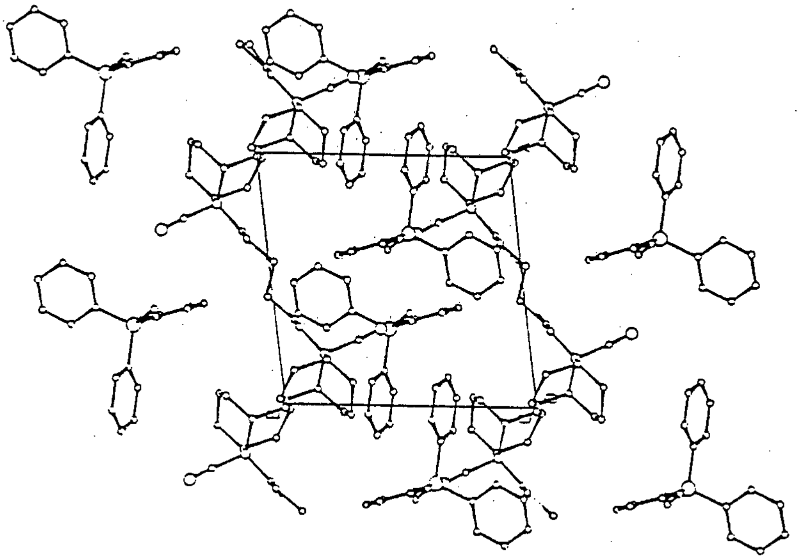


Figure 12

2.2.4 SOME EXAMPLES OF WATER-INCLUDING CLATHRATES

Clathrates are stabilised by both topological as well as functional interactions and selective crystallisation depends significantly on the steric compatibility between the complexing partners[46]. Furthermore, if solvation forces are sufficiently strong in comparison with other intermolecular interactions, the solvating species will be carried out from the solution into the crystal along with the solvated substance. As a result, structural domains that dominate dynamic equilibria in the liquid phase may also persist, to some extent, in the solid inclusion system. Quite often, solvent molecules are enclosed within intermolecular voids of the crystal to fill empty space or to complete a coordination sphere around a functional group, and it is difficult to control such a co-crystallisation process. Solvent inclusion has been revealed in crystallographic analyses of complexes involving water and dichloromethane guests with cyclic urea host binding sites. In these structures the guest species are located on and strongly bound to the surface of the corresponding host containing appropriately sized polar cavities. (Figure 13) Additional molecules of solvent (H_2O, THF or CH_2Cl_2) are located between adjacent units of the complex, supplementing the coordination sphere of the host-bound water.

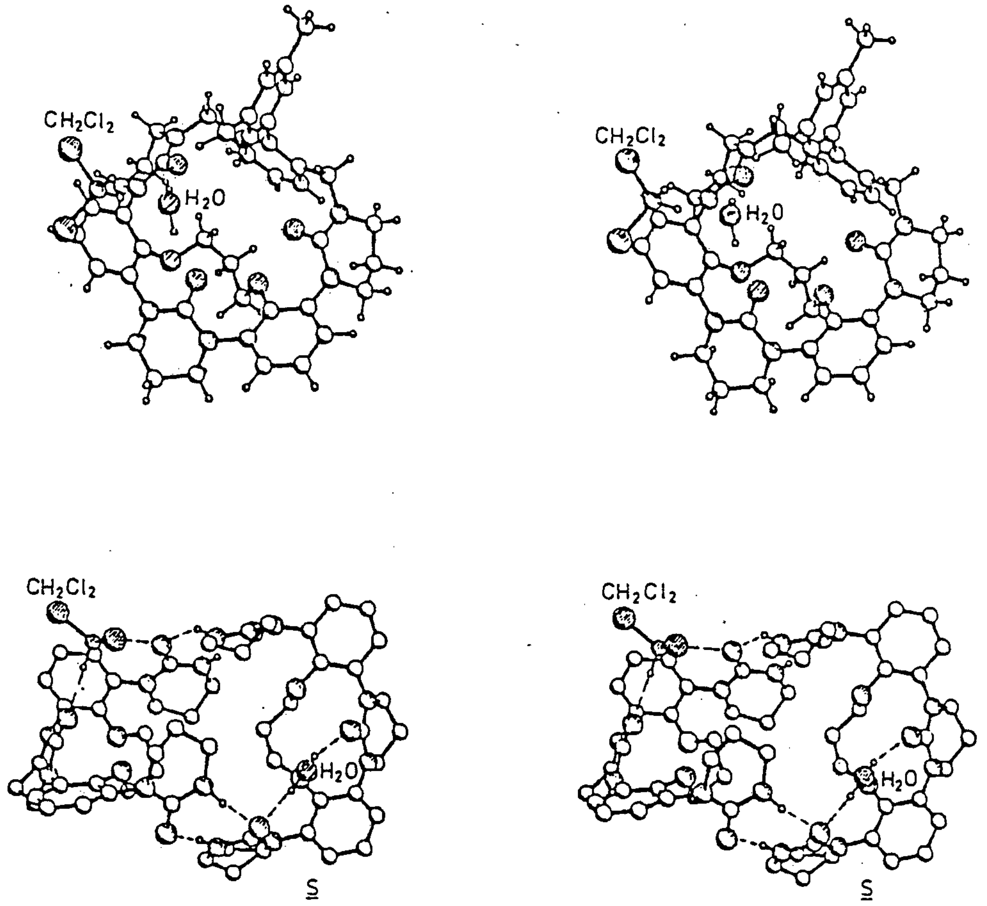
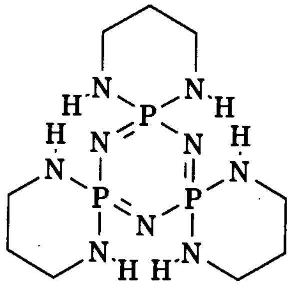


Figure 13

The extent of solvation in the crystalline structure of 2,4,6-tris(1,3-propylenediamine-N,N'-)cyclotriphosphazene dihydrate is very pronounced, owing to strong intermolecular hydrogen bonding between water and suitable couples of N-H groups of the host moiety. The water species also form continuous H-bonded layers



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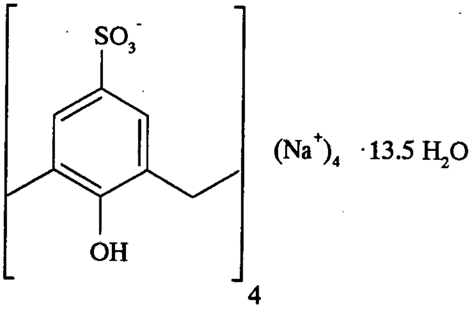
In addition, it is often possible to extract significant information on solvation patterns and their relation to induced structural polymorphism from the structural analysis of solid solvates. This can be illustrated by solvated 2,4-dichloro-5-carboxy-benzenesulfonimide, which contains a large number of polar functions and potential donors and acceptors of hydrogen bonds. It co-crystallises with a variety of solvents in different structural forms, that are found to be primarily dependent on the nature of the solvent environment. In the water solvated compound, continuous layers of water alternate with bilayers of host molecules forming two distinct regions in the solid. Within the bilayers, the structure is stabilised mainly by dipolar interactions between the C-Cl groups turning inward. All the oxygen-containing functions of the host point outward on both sides of the bilayer, and are linked efficiently to the adjacent hydration layers.

Similarly, J. Atwood *et al.*[47], through their interest in water-soluble p-sulfonatocalix[4]arenes have shown that the host compound invariably takes one or more water molecules into the cavity in the absence of an appropriate guest. For instance, Na_4[p-sulfonatocalix[4]arene]·13.5 H_2O **49** has one water molecule deeply imbedded in the cavity and low temperature X-ray structure analysis of this complex displays hydrogen bonding between the water and the aromatic π electrons.



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Interestingly, the structure of $[(H_2O)_4Cu(NC_5H_5)_2](H_3O^+)_3$[calix[4]arene sulfonate]·10 H_2O exhibits second-sphere coordination[48], which has been defined by Stoddart[49] as being the 'non-covalent bonding of chemical entities to the first coordination sphere of a transition metal complex'. In this compound one pyridine ring is imbedded in the calixarene cavity, while the other is intercalated into the bilayer. The primary coordination sphere of the Cu^{2+} contains two pyridine and four water ligands; the calix[4]arene interacts with the ligands on the metal ion in a second sphere manner. The calixarene and the coordination complex are held together by hydrophobic effects or Van der Waals forces. Host-guest compounds based on calix[4]arenes can be further organised into larger dimeric structures by a combination of weak forces, such as ion-dipole, dipole-dipole, dipole-induced dipole, and induced dipole-induced dipole interactions.

H. Nakayama *et al.*[50] has studied the clathrate-type behaviour of tetraisopentylammonium alkanoates, $[(i\text{-}C_5H_{11})_4N]C_nH_{2n+1}COO$ (n=0-9), and bis(tetraisopentylammonium) alkanedioates, $[(i\text{-}C_5H_{11})_4N]_2\text{-}[OOC(CH_2)_nCOO]$ (n=0-10), containing various alkyl chains or methylene chains. Typical hydrates formed by the alkanoates have hydration numbers (number of water molecules per ammonium ion) around 38 and those formed by the alkanedioates around 80. Increasing the alkyl chain length of the alkanoate anion and the methylene chain length of the alkanedioate anion eventually leads to a decrease in the hydration number due to the chain's hydrophobic nature. Table 6

TABLE 6
Melting points and hydration numbers of the clathrate-like hydrates formed by a series of bis(tetraisopentylammonium) alkanedioates, $[(i\text{-}C_5H_{11})_4N^+]_2\,{}^-OOC(CH_2)_nCOO^-$

n	m.p.(°C)	hydration number
0	25.1	80±2
1	22.1	80±2
2	19.8	82±2
3	23.7	79±3
4	27.5	80±3
5	19.8	80±3
6	19.4	75-85
7	18.4	70-85
8	14.5	80-100
	13.9	32±3
10	21.5	30±5

2.2.5 INCLUSION COMPOUND FORMATION WITH BIS-METHYLTRIPHENYLPHOSPHONIUM 1,6-BIS(B-CYANO-9-BORATABICYCLO[3.3.1]NON-9-YL) HEXANE

In view of the clathrate behaviour of other onium salts as previously discussed, as well as the behaviour of the sodium salt **1** towards DMF and the phosphonium salt **47** towards water, the possibility of clathrate activity for **47** was investigated. Inclusion experiments were carried out in the following way. The host compound **47** was dissolved in dichloromethane which was chosen since it readily dissolved the host. Moreover, as it turned out it was not included by it. A small amount of guest liquid, in at least ten times molar excess to the host, was then added and the solution was allowed to evaporate slowly at room temperature until a solid had formed. This was then filtered, washed with diethyl ether and air dried. Ether was chosen since it removed residual non-included guest but not the guest itself. The host could be recycled by using a more polar solvent, e.g. ethyl acetate, to wash the guest out of the clathrate. Guests were chosen on the basis of their polarity and interactional ability in terms of potential intermolecular interactions. The water content of the host caused the host-guest activity to fluctuate greatly, making reproducibility of ratios impossible. Therefore, host-guest experiments were carried out with anhydrous samples, but the uptake of moisture from the atmosphere during evaporation added to the problem as evidenced in Table 7 below. Host-guest ratios were established using TGA and the integration in the ^{1}H-NMR spectrum and it was observed that the host-guest ratios of different crystals varied. Therefore, since, TGA was based on a small sample and ^{1}H-NMR spectra on a larger sample in which there was averaging of inclusion ratios of different crystals, the inclusion ratios from ^{1}H-NMR and TGA were often sightly different.

TABLE 7

Results of Host-Guest ratios of $[(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\cdot 2Ph_3P^+Me\cdot nH_2O]$ in CH_2Cl_2 from ^{1}H-NMR.

Guest	n=0.73		n=0[a]		n=0[b]	
Benzene[e]	1:0.7	1:0.8	1:1.1[c]	1:1.8[c]	1:0.2	1:0.3
Toluene	1:0	1:0	1:Tr	1:0	1:0	1:0
o-Xylene	1:0.3	1:0.3	1:0.2	1:0.3	1:Tr	1:Tr
m-Xylene	1:0.3	1:0.2	1:0.9	1:1.1	1:Tr	1:Tr
p-Xylene	1:0.4	1:0.3	1:Tr	1:Tr	1:Tr	1:Tr
Mesitylene	1:0.2	1:0.3	1:0.2	1:0.2	1:0.2	1:0.2
Anisole	1:0.4	1:0.2	1:0.4	1:0.4	1:0.6	1:0.7
N,N-Dimethylaniline	1:0.8	1:0.7	1:1.0	1:1.1	1:1.2	1:1.3
Furan[e]	1:0	1:0	1:0	1:0	1:0	1:0
2-Methylfuran	1:0	1:0	1:0	1:0	1:0	1:0
Thiophene[e]	1:0	1:0	1:0	1:0	1:0	1:0
DMF	1:0.1	1:0.3	1:0.4	1:0.3	1:0.4	1:0.3
Ethyl acetate	1:0	1:0	1:0	1:0	1:0	1:0
Acetone	1:0	1:0	1:0	1:0	1:0	1:0
MeOH	decomp.		decomp.		decomp.	
t-Butanol	1:0	1:0	1:0	1:0	1:0	1:0
Hexane	1:0	1:0	1:0	1:0	1:0	1:0
Hexene	1:0	1:0	1:0	1:0	1:0	1:0
Benzofuran	d					
Benzothiazole	d					
Pyridine	d					
Pyrrole	d					
Quinoline	d					

[a] and [b] are different batches of host compound.

[c] contains moisture from the atmosphere

d host dissolves in the guest
decomp. decomposition of the host
[e] also displays liquid clathrate behaviour

From Table 7 it is clear that aromatic solvents are included preferentially with toluene being an exception. Slightly higher selectivities were displayed for anisole and N,N-dimethylaniline, which are of a more polar nature and involve electron rich aromatic rings. In contrast, polar guests were not taken up at all. Therefore, it seems reasonable to conclude that the forces operating in the lattice are of π-π origin in conjunction with van der Waals interactions. ^{1}H-NMR spectra revealed water peaks at approx. δ=2.5ppm for clathrates formed from the water-containing host. Interestingly, the crystals of the clathrates of water-containing hosts were of better quality, than those of the water-free compounds.

An interesting feature displayed by the host-guest ratios of **47** is that they are mainly non-integral. H. Powell[25b] noted a similar feature in the 1960's for the composition of hydroquinone clathrates, which exhibited host-guest ratios of 0.85 for HCl, 0.36 for HBr, 0.88 for SO_2 and 0.3-0.85 for Ar. A clathrate was formed by recrystallising hydroquinone from a suitable solvent. However, under these conditions nearly all of the lattice voids in the host became occupied by the solvent. Therefore, most of these host-guest compounds were prepared from a solvent which dissolved both components and thus was not enclosed in the hydroquinone structure. Powell concluded that non-integral inclusion values could be used to distinguish clathrates from other molecular compounds in which a specific interaction of the molecules gives a simple ratio.

Another series of experiments conducted was to stir the host in neat guests (at least ten times molar excess) in which they were insoluble. (Table 8) Furfuraldehyde and DMF proved no good in this respect because they dissolve the host. After overnight stirring the solids were filtered, washed with ether and air dried as before. The inclusion of a small number of guests including *m*- and *p*-xylene, mesitylene and N,N-dimethylaniline indicate that some permeation of the guest into the crystal lattice must have taken place for these guests to have been taken up. However, the degree of guest inclusion is clearly poorer compared to the solvent inclusion experiment. Maybe inclusion via a zeolitic solid-state type character is operating. In this instance, the host displays a good selectivity for *p*-xylene and N,N-dimethylaniline.

TABLE 8

Host-Guest ratios determined by ^{1}H-NMR and TGA for **47** in a solvent compared to Host-Guest experiments performed without solvent(neat) determined by ^{1}H-NMR; n=0 for all cases.

Guest	from CH_2Cl_2 ^{1}H-NMR[a]	TGA[a]	neat ^{1}H-NMR[b]
Benzene	1:0.2	1:0.16	1:0
Toluene	1:0	1:0	1:0
o-Xylene	1:Tr	1:0	1:0
m-Xylene	1:Tr	1:0.08	1:0.2
p-Xylene	1:Tr	1:0.06	1:1
Mesitylene	1:0.2	1:0.17	1:0.1
Anisole	1:0.4	1:0.3	1:0
N,N-Dimethylaniline	1:1.3	1:1.25	1:2
Furfuraldehyde	1:0.5	1:0.44	liq.
DMF	1:0.4	1:0.31	liq.

[a] same batch of sample

[b] different sample

Moreover, methyltriphenylphosphonium bromide itself showed no host-guest activity as compared to the onium bromide salts examined by F. Vögtle mentioned previously in chapter 2.2. Therefore, one may conclude that both the cation and anion of **47** are involved in the inclusion process and this was borne out by subsequent X-ray analysis.

2.2.6 X-RAY STRUCTURE OF METHYLTRIPHENYLPHOSPHONIUM CYANOBORATE WITH P-XYLENE

The affinity of complex **47** for aromatics led to examining the interactional forces operating within the host-guest lattice by X-ray analysis. The quality of crystal for X-ray analysis is of paramount importance and, after some experimentation it was possible to grow fairly good quality crystals of **47** with *p*-xylene as guest. Guest content was monitored by TGA prior to X-ray analysis. The crystals for the X-ray analysis were grown by dissolving methyltriphenylphosphonium cyanoborate (0.4g) in CH_2Cl_2 (4ml) which contained approximately one mole equivalent of water and then adding *p*-xylene (2.6g). After the mixture had been left to evaporate slowly at room temperature for two days, crystals started forming. X-ray analysis was then carried out on a crystal mounted in its mother liquor in a Lindemann tube. The X-ray structure shows that two molecules of *p*-xylenes are included for each host molecule, which is a larger ratio than observed in the tables. As was mentioned previously, the host-guest ratios of different crystals varied, which may have been due to the sensitive nature of the host-guest interactions. Another reason may have been the presence of water in the host lattice, due to fluctuation in the experimental and subsequent work-up conditions. In this instance a hydrated sample was deliberately chosen which was not rigorously dried due to its better crystal quality compared to the anhydrous sample.

In the X-ray structure, the crystallographically centrosymmetric cyanoborate anion exhibits an extended conformation with the cyano groups anti to one another with respect to the B-B axis as seen before in the structure of the anhydrous host. (Figure 12) The two *p*-xylene guest molecules, at approximately perpendicular orientations to each other, occupy constricted channels in a lattice which is held together by C-N···H-(H_2C-P) hydrogen bonds, C-H···π···H-C , C-H···π interactions and Van der Waals forces. (Figure 14) Thus, the cyanoborate-*p*-xylene clathrate can be classified as a coordinatoclathrate in a coordination assisted lattice. The two *p*-xylene molecules participate in crystallographically symmetric C-H···π(Ar)···H-C interactions in which the two hydrogen atoms approach the phenyl ring from opposite faces. This is analogous to the C-H···π(heteroaromatic)···H-C interactions found for the furan clathrate of the same host, which will be discussed in chapter 3, and to a C-H···π(Ar)···Cl-C interaction reported recently[51]. C-H···π(Ar) interactions have been of much interest recently[52] and would be expected to be encountered in the solid state when there is a deficiency of hydrogen bond acceptors[53].

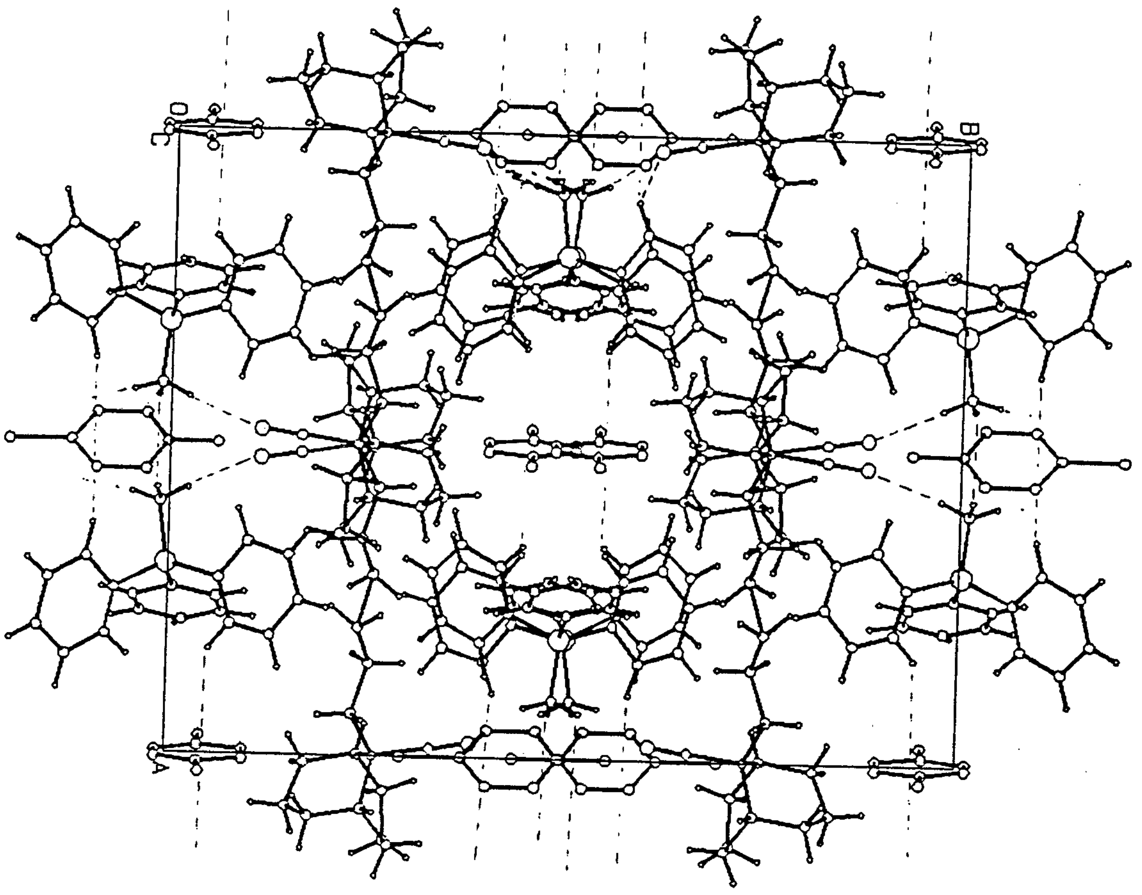

Figure 14

The crystal structure of *p*-xylene[54] itself indicates that the molecules are packed into chains by Van der Waals contacts between the six ring carbon atoms and one methyl hydrogen of a neighbouring molecule. Van der Waals interactions have been the only ones observed in the clathrates based on tetraarylporphyrins[55] with xylenes. Interestingly, the clathrate with *m*-xylene contains a water molecule ligated to the zinc atom of the porphyrin, which assists in maintaining the lattice structure. Therefore, *p*-xylene inclusion compounds are generally held together by Van der Waals forces only, whereas in our cyanoborate host additional C-H$\cdots\pi$ interactions play a major role in the lattice structure.

2.2.7 SELECTIVITY INCLUSION EXPERIMENTS WITH METHYLTRIPHENYLPHOSPHONIUM BORATE SALT

Host-guest chemistry has great potential in separation technology, in which compounds with similar boiling points or of similar polarity are selectively extracted. These criteria were used to choose pairs of guests as evidenced in Table 9 below. Host-guest experiments were conducted with an anhydrous sample of **47** and host-guest inclusion ratios calculated by ^{1}H-NMR integration.

TABLE 9
Host-Guest ratios of two different Guests
in CH_2Cl_2

Guests	H:G:G	H:G:G
Ether/Furan	1:0:0	1:0:0
p-Xylene/*m*-Xylene	1:Tr:Tr	1:Tr:Tr
p-Xylene/*o*-Xylene	1:0.2:0.3	1:Tr:Tr
DMF/Mesitylene	1:0.3:0	1:Tr:0
DMF/Anisole	1:0.5:0	1:0.3:0
N,N-Dimethylaniline/Anisole	1:0.5:Tr	1:0.4:Tr
N,N-Dimethylaniline/DMSO	1:0:0.2	1:0:0.2
Thiophene/Benzene	1:0:0	1:0:0
Mesitylene/Thiophene	wax	

Guests that did not normally include, such as furan (only when n=0) and ether, did not display any host-guest activity, as expected. The figures also indicate that the host is unresponsive to the steric differences between the xylene isomers. N,N,-Dimethylaniline which exhibits a relatively high inclusion activity by itself did not show any inclusion when mixed with DMSO implying that the interactional forces between the host and DMSO are slightly stronger than those of N,N-dimethylaniline. The same holds true for mesitylene and DMF, with DMF being preferentially included. Therefore, selective inclusion is viable in the case of high boiling liquids such as DMF and DMSO. In general, the host-guest ratios of the anhydrous host gave a much better reproducibility of results than the water-containing host compound. A phenomenal feature of the latter, however, is that it displays both solid- and liquid clathrate behaviour with furan, benzene and thiophene depending on water content and this will be discussed in the next chapter. Although, the inclusion activity of the methyltriphenylphosphonium cyanoborate **47** turned out to be fairly modest, these initial results together with the water-dependent liquid clathrate behaviour encouraged us to carry out a comprehensive structure-activity study to ascertain whether **47** was a "one-off" or a member of a class of novel clathrands. As will be discussed in chapters 3 and 4, both the liquid clathrate aspect and the structurally modified clathrands led to some very fruitful inclusion results.

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CHAPTER 3

LIQUID CLATHRATE BEHAVIOUR OF BIS(METHYLTRIPHENYLPHOSPHONIUM) 1,6-BIS(B-CYANO-9-BORATABICYCLO[3.3.1]NON-9-YL) HEXANE (47)

3.1 THE DISCOVERY AND DEVELOPMENT OF LIQUID CLATHRATES

Although clathrates are by definition solid substances, it is possible to apply the same basic concept to liquids as well. The top layer of a liquid clathrate consists of pure guest while its bottom layer constitutes the true liquid clathrate layer of host and guest in a fixed ratio. The latter depends on the nature of host and guest as well as temperature.

The first liquid clathrates discovered were a series of organometallic aluminates by J. Atwood[1], which formed 1:2 liquid clathrates with aromatic solvents. The precursor of these compounds, a trialkylaluminium, is extremely air and water sensitive and therefore, the reactions had to be carried out under an inert atmosphere. Scheme 34.

$$MX + 2AlR_3 \longrightarrow M(Al_2R_6X)$$

M=alkali metal or tetraalkylammonium ion
R=alkyl group
X=halide

Scheme 34

A detailed study by J. Atwood's group revealed that liquid clathrates possess properties in common with solid state clathrates. The host to guest ratio (H:G) depends on the cation, the anion and the guest molecule, an aromatic in this instance, in the following way:

- for a given anion and aromatic, the larger the cation, the larger the G:H ratio,
- for a given cation and aromatic, the larger the anion, the larger the G:H ratio,
- for a given cation and anion, the larger the aromatic, the smaller the G:H ratio.

These conclusions were drawn from the results of Table 10.

TABLE 10

Liquid clathrate host-guest ratios of aluminates

Compound	Guest	Max. G:H ratio
$K[Al_2(CH_3)_6N_3]$	benzene	5.8:1
$Cs[Al_2(CH_3)_6NO_3]$	benzene	12.0:1
$[N(C_4H_9)_4][Al_2(CH_3)_6I]$	benzene	9.4:1
$[N(CH_3)_4][Al_2(CH_3)_6CH_3COO]$	benzene	6.3:1
$Rb[Al_2(CH_3)_6N_3]$	toluene	5.7:1
$[N(C_6H_5)(CH_3)_3][Al_2(CH_3)_6I]$	toluene	12.0:1
$[N(C_6H_{13})_4][Al_2(C_2H_5)_6I]$	toluene	30.2:1
$[N(CH_3)_4][Al_2(CH_3)_6F]$	ethylbenzene	2.4:1
$[N(C_3H_7)_4][Al_2(C_3H_7)_6I]$	ethylbenzene	17.3:1
$[N(CH_3)_4][Al_2(C_2H_5)_6I]$	propylbenzene	8.0:1
$[N(C_6H_{13})_4][Al_2(C_2H_5)_6I]$	o-xylene	39.6:1
$[N(C_5H_{11})_4][Al_2(C_2H_5)_6I]$	m-xylene	9.2:1
$[N(CH_3)_4][Al_2(C_2H_5)_6]$	p-xylene	9.2:1
$[N(C_5H_{11})_4][Al_2(C_3H_7)_6I]$	mesitylene	10.3:1
$[N(CH_3)_4][Al_2(CH_3)_6F]$	1,2,3,5-tetra-methylbenzene	1.3:1

Liquid clathrates can also be prepared from other non-aluminium alkyl bearing complexes, such as $Li[N(SiMe_3)_2]$ and $Na[N(SiMe_3)_2]$ by the addition of an appropriate crown ether[2]. One such example is the formation of a liquid clathrate of composition $[Li{\cdot}CE][N(SiMe_3)_2]{\cdot}16.8\ C_6H_6$, where CE=15-crown-5. This discovery was a significant breakthrough, as silicon-based compounds are much easier to work with than those of aluminium.

The same applies to tetraalkylammonium tetrahaloindates[3], $[R_4N][InX_4]$, which are capable of forming air-stable liquid clathrates with aromatic solvents. The guest:host ratio is generally lower relative to an Al clathrate, e.g. $[Bu_4N][Al_2Me_6I]$, 9.4:1 vs. $[Bu_4N][InCl_4]$, 1.8:1, and the highest ratios are found for benzene, as with the aluminium systems. Table 11.

TABLE 11

Host-guest ratios of tetraalkylammonium tetrahaloindates

guest	G:H[a]	G:H[b]	G:H[c]
benzene	1.8:1	1.7:1	2.6:1
toluene	1.0:1	2.1:1	1.0:1
ethylbenzene	0.5:1	1.0:1	1.6:1
o-xylene	1.0:1	1.1:1	1.4:1
m-xylene	0.6:1	1.4:1	1.1:1
p-xylene	0.4:1	0.5:1	1.3:1

[a] $[Bu_4N][InCl_4]$

[b] $[Bu_4N][InCl_3I]$

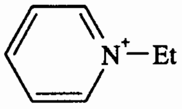
[c] $[Li{\cdot}12\text{-crown-}4][InCl_4]$

In the late eighties, M. Zaworotko *et al.* prepared a new class of air-stable, liquid clathrates[4] by exposing benzene solutions of various simple organic nitrogen containing bases, namely pyridine, 2-ethylpyridine, 2,4,6-collidine, quinoline, N,N,-dimethyltoluidine, 1-methylimidazole, 1-methylpyrrolidine and piperidine, to excess hydrogen halide (chloride or bromide). Table 12

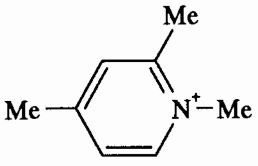
TABLE 12
Data for the liquid clathrate phase of HX/base/benzene ternary systems

base	HX X=	benzene content
pyridine	Cl	1.8
	Br	1.7
2-ethylpyridine	Cl	7.9
	Br	6.2
2,4,6-collidine	Cl	8.3
	Br	5.4
quinoline	Cl	6.4
	Br	2.4
N,N,-dimethyltoluidine	Br	6.7
1-methylimidazole	Cl	1.7
	Br	1.6
1-methyl pyrrolidine	Cl	3.8
	Br	5.8

Furthermore, the same research group showed that a series of air and water stable organic cation triiodide salts[5] form liquid clathrates with benzene and toluene. These low melting salts, eg. 1-ethylpyridinium triiodide, **50**$^+$I$_3^-$, and 1,2,4-trimethylpyridinium triiodide, **51**$^+$I$_3^+$, as well as their derivatives enclathrate benzene and toluene in non-stoichiometric amounts. Colourless liquid clathrates were formed from **50**$^+$[AlCl$_3$I] containing 4.8 moles of benzene and 2.8 moles of toluene per mole of cation and **51**$^+$[AlCl$_3$I] containing 4.3 and 3.8 of benzene and toluene, respectively. This discovery lead to the study of the clathrate behaviour of **50**$^+$[Al$_2$R$_6$I] (R=Me, Et), in which the anions were Atwood's well-known liquid clathrate parent anions. Liquid clathrates of composition **50**$^+$[Al$_2$Me$_6$I]·6.8 benzene, **50**$^+$[Al$_2$Me$_6$I]·5.5 toluene, **50**$^+$[Al$_2$Et$_6$I]·11.1 benzene and **50**$^+$[Al$_2$Et$_6$I]·9.4 toluene were prepared successfully. Therefore, organic cation triiodide salts appear to complement existing liquid clathrate sustaining anions, particularly as the former are more resistant to both air and moisture. X-ray structure analysis of the triiodide salts indicated that interionic interactions in the solid phase appear to be weak and unpredictable. Ordering arises from anion-anion interactions and the absence of any significant cation-anion interactions precludes simple rationalisation of the packing phenomenon.



50$^+$



51$^+$

This new liquid clathrate system is chemically quite different from the other two phase systems but is physically related by its low lattice energy. This is as a result of the steric bulk of the ions involved, suggesting that more classes of logically designed liquid clathrates are attainable with other low melting salts.

Recently, the first report of a stable selenium (selenonium) cation-based liquid clathrate was made by G. Robinson and S. Sangokoya[6]. The compound $[(CH_3)_3Se][ClAl(CH_3)_2(Cl)Al(CH_3)_3]$ is able to accommodate 8.5 guest benzene molecules or 8.3 guest toluene molecules per anionic species. Interestingly, the selenium clathrate will only form when reacted in a 1:3 ratio ($SeCl_4$ to $Al(CH_3)_3$), whereas all previously reported liquid clathrates proceed in a 1:2 ratio (MX to $Al(CH_3)_3$).

From the liquid clathrate systems mentioned, some general chemical prerequisites appear to be that the cation, which by necessity is based on a group V or VI p-block element, must have hydrophobic character by virtue of organic substituents. Similarly, the anion must also have diffuse charge (i.e be soft or borderline) and group IIIA 'ate' complexes provide a rich source of this type.

The current view on liquid clathrates is that this behaviour originates from cation-anion interactions, which are strong enough to prevent complete mixing in organic solvents yet involving species which do not strongly solvate in water. Thus, the all important feature is a blend of hydrophobic character and hydrophilic character to prevent homogeneous mixing with either water or organic solvents respectively and an intrinsically strong enough cation-anion attraction together with a low lattice energy, due to packing considerations. The guest molecules are necessary constituents of the layer-like structure since they are able to provide further stabilisation by virtue of their favourable interaction with the host components.

The conclusions drawn on the origin of liquid clathrate behaviour by workers in this field are based largely on inference from solid state structural studies, since solution structures are difficult to ascertain experimentally. Thus, the solid host-guest compound usually acts as a model for liquid clathrate behaviour. However, the literature suggests that its origin is not well understood at all.

3.1.1 APPLICATION OF LIQUID CLATHRATES

In principle, liquid clathrates have great potential in separation technology, the most obvious separation being aromatics from non-aromatic hydrocarbons. In this regard, results have been obtained by Atwood's group on the extraction of coal with a toluene-based liquid clathrate[7], which turns black instantly upon exposure to coal, whereas toluene by itself will only extract material from coal slowly at room temperature. The experiment, however, was difficult to perform due to the air-sensitivity of the liquid clathrate parent compound. This result inspired L. Nassimbeni *et al.* to investigate this feature further by using tetraalkylammonium tetraalkylborate salts[8a] with the anion $[(s\text{-Bu})_3B(n\text{-Bu})]^-$ and the cations $[NR_4]^+$, $[N(n\text{-Bu})_4]^+$, $[N(n\text{-}C_6H_{13})_4]^+$ and $[N(n\text{-}C_8H_{17})_4]^+$. Although their synthesis involves an air-sensitive borane as intermediate and the host compounds themselves are difficult to work with, these form liquid clathrates with a number of aromatic and aliphatic guest molecules, and can be used directly for coal extraction. The host compounds showed greater affinity for aromatic over aliphatic hydrocarbons. Table 13.

TABLE 13

Composition of liquid clathrate system H·nG.

$H=[N(n\text{-}C_6H_{13})_4]^+[s\text{-Bu})_3B(n\text{-Bu})]^-$ at 25°C.

guest(G)	n
benzene	17
toluene	16
p-xylene	14
p-cymene	4
cyclohexane	3
cyclohexene	6
n-hexane	4
1,4-dioxane	15

Additionally, the toluene-based liquid clathrate of $[N(n\text{-}C_6H_{13})_4]^+[(s\text{-Bu})_3B(n\text{-Bu})]^-$ was tested successfully for its extraction capability of a high grade bituminous South African coal. Hence, these results indicate that the future of clathrates in separation science appears to lie in the development of stable and versatile liquid clathrates. Furthermore, chiral[8b] liquid clathrates to separate chiral substrates are also another desirable research area.

3.2 LIQUID CLATHRATE FORMATION WITH BIS-METHYLTRIPHENYLPHOSPHONIUM 1,6-BIS(B-CYANO-9-BORATABICYCLO[3.3.1]NON-9-YL) HEXANE **47**

While studying the influence of water on the inclusion activity of cyanoborate **47**, a phenomenal feature was observed in that both solid and liquid clathrate behaviour was observed with benzene, thiophene and furan as guests depending on water content. Host samples with varying amounts of water were prepared by varying the drying temperatures as described in chapter 2. With anhydrous samples of the host, the host-guest ratio obtained for furan from CH_2Cl_2 was 1:0, which may be explained in terms of guest-solvent intermolecular forces (Van der Waals) being stronger than host-guest interactions as well as the high volatility of the guest. Inclusion activity with furan was not observed using the solvent-free heterogeneous conditions described in chapter 2 either, although the insoluble host did take on an interesting red colour over a period of time. However, it was observed that for hydrated host samples in which $n\sim1$, warming of the heterogeneous mixture resulted in formation of a liquid clathrate.

Similarly, the host-guest ratio obtained for thiophene with anhydrous samples of host **47** was also 1:0, whereas benzene was retained by the solid clathrate in low ratios of 1:0.2-0.8 and the variation in these ratios was probably due to the water content within the atmosphere. The presence of water presumably forces the anionic borate and cationic phosphonium species slightly apart, therefore letting the guest penetrate more easily. In addition, the hydrophobic nature of benzene may then result in the expulsion of water. With benzene, liquid clathrate character was observed when $n\geq1$, whereas for lower n values a white solid in the bottom layer was formed immediately on cooling. This solid included approximately four benzenes per host molecule by ^1H-NMR. The bottom layer in the liquid clathrate contained approx. 13 benzenes per host compound and crystallised out very slowly when n was slightly less than 1. Conversely, with thiophene as guest, liquid clathrates formed for $0<n<1$ with the bottom liquid clathrate layer containing approximately 14 thiophenes per host molecule. Crystalline complexes with a host-guest ratio of 1:2 formed very sluggishly in small amounts when $n\geq1.0$. Table 14.

TABLE 14

Host-guest ratios of **47**·n H_2O with thiophene and benzene

guest	n=0	n≥1	n<1
thiophene	1:0	1:2[a]	1:14[b]
benzene	1:0.2-0.8	1:13[b]	1:4[a]

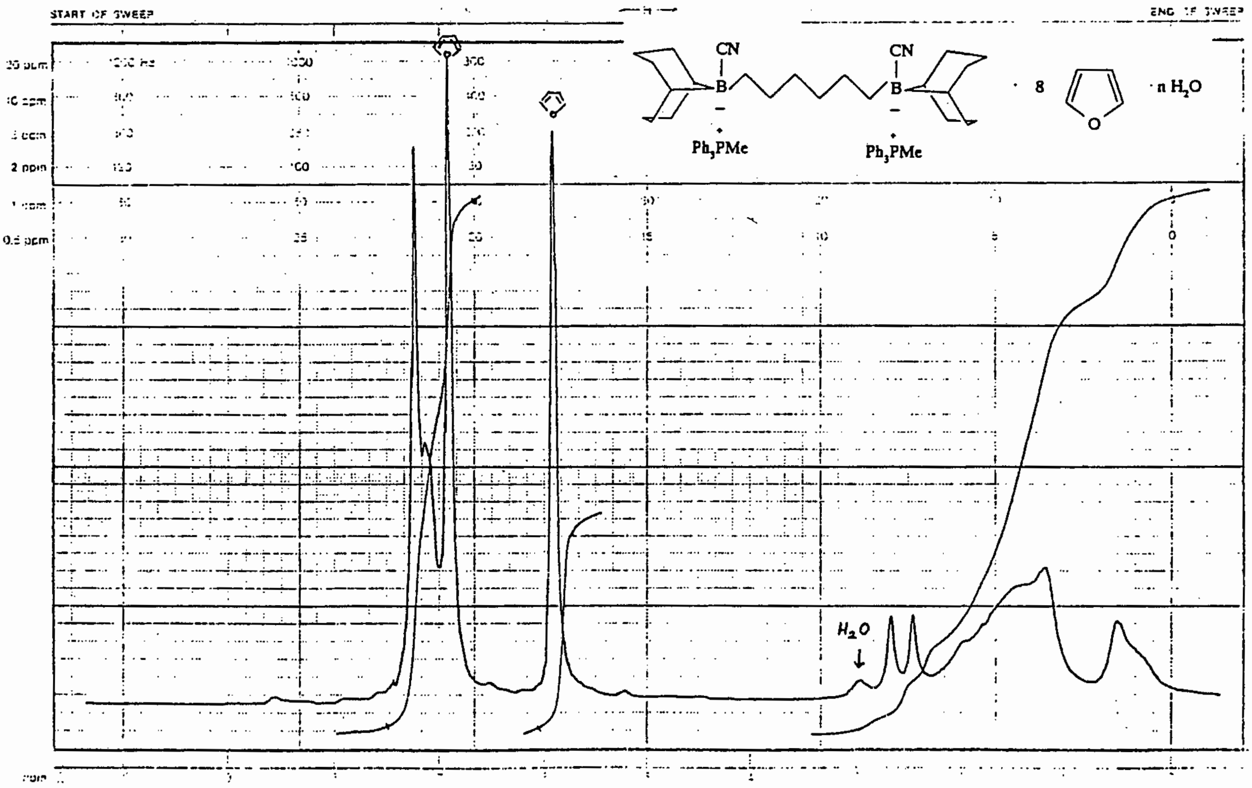
[a] solid clathrate

[b] liquid clathrate

The role of water is open to speculation but it is probably required initially to overcome the lattice energy, allowing the guest to penetrate more easily. Conversely, solid clathrate formation from solution (CH_2Cl_2) is determined by host···guest and CH_2Cl_2···guest interactional forces. These results initiated a detailed study of the furan clathrate described in the next chapter.

3.2.1 THE FURAN CLATHRATE

By ^{1}H-NMR spectroscopy, the furan liquid clathrate layer was estimated to contain about eight furans per borate host (Figure 15), and both an infra-red and ^{1}H-NMR study of the two layers indicated that the water resided in the liquid clathrate layer. The cut-off point for formation of a liquid clathrate was around n=0.8 moles of water, while higher values of n than 1 promoted the formation of three layers, one being water.



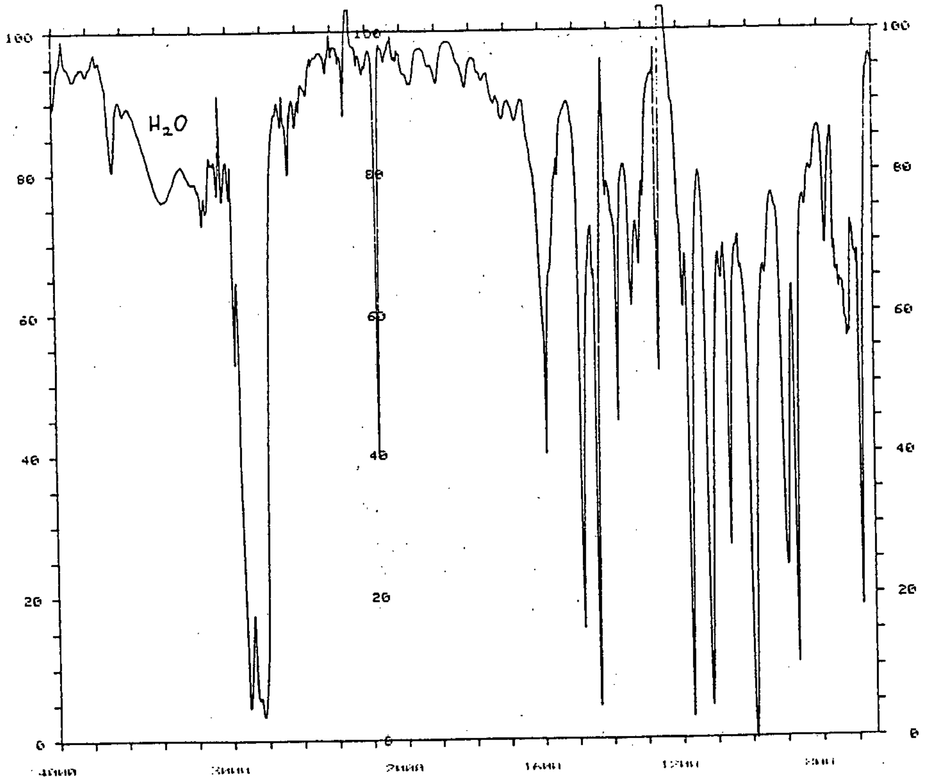
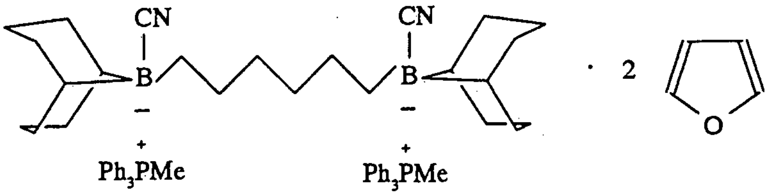


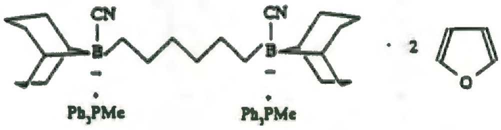
Figure 15

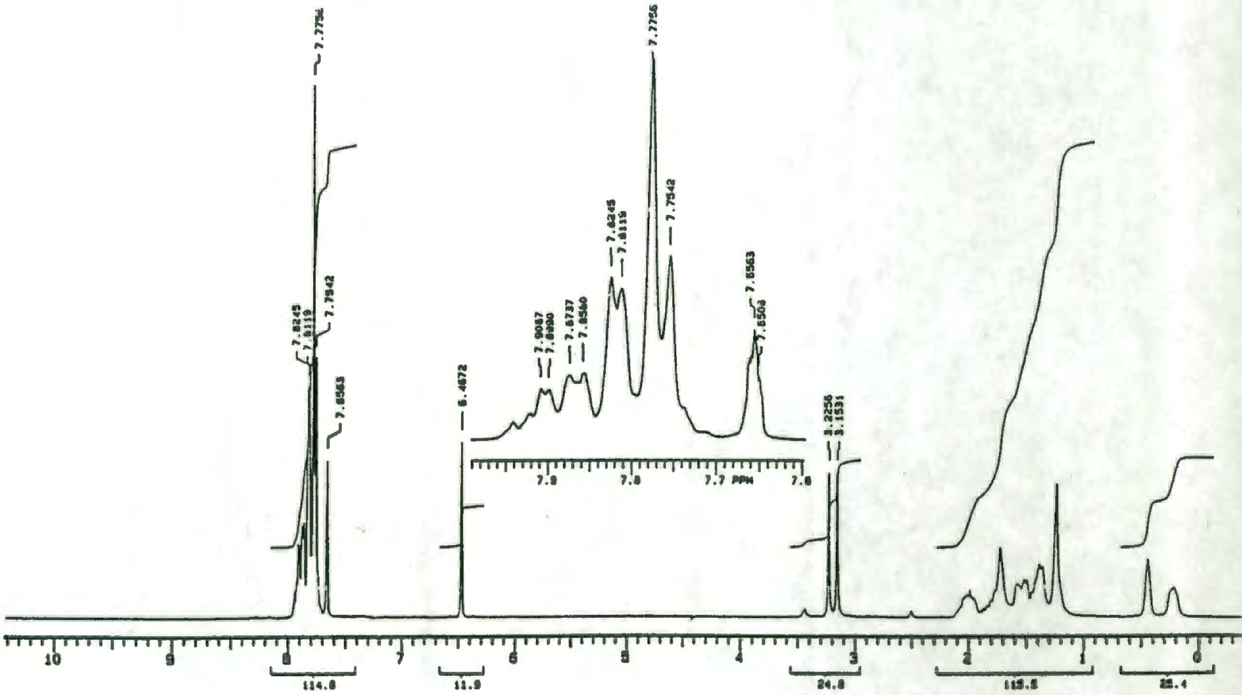
This result is striking since, although a number of groups[9] have discovered liquid clathrate sustaining salts which are considerably more air and water stable than those of Atwood's original alkylaluminates[10], the cyanoborate compound **47** constitutes the first example of a salt forming a water dependent liquid clathrate.

A further interesting aspect was that beautiful transparent crystals of a solid clathrate appeared from the liquid clathrate layer after about two days with the crystallisation time decreasing with diminishing n. (Figure 16) By ^{1}H-NMR and TGA the host-guest stoichiometry in the solid clathrate was established as 1:2. Figure 17.



Solid furan clathrate forming in the bottom liquid clathrate layer.
Figure 16





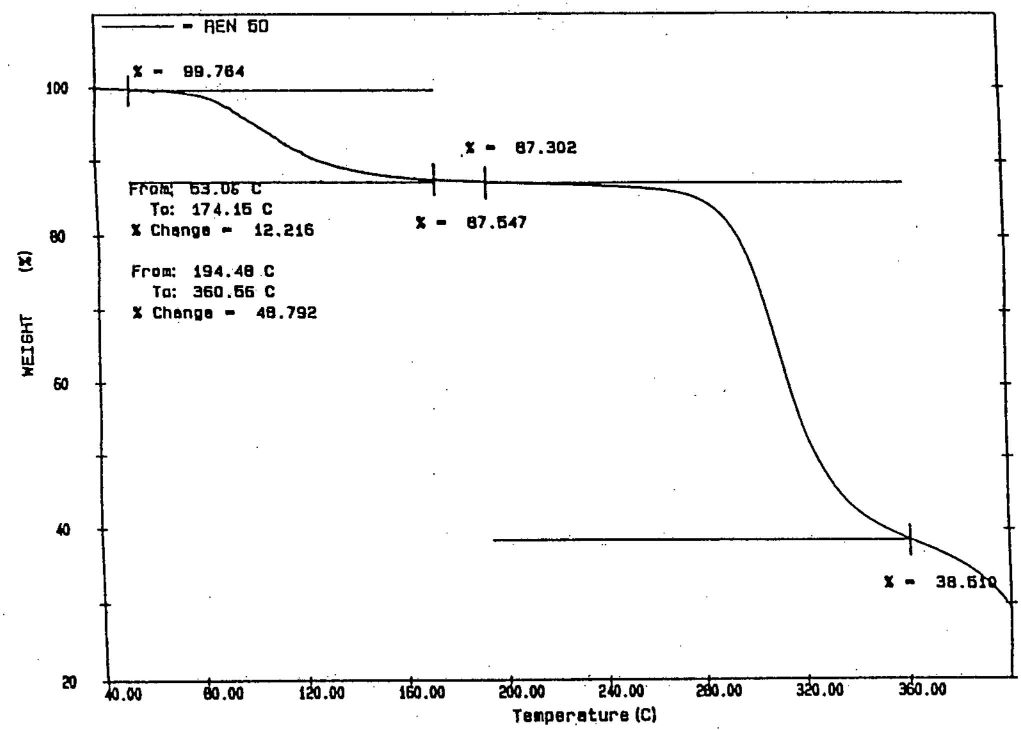


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Figure 17

Furthermore, water was absent in the solid clathrate structure, even though it was necessary for the formation of the liquid clathrate. This seemed to indicate that water contained within the host forces the anionic and cationic species somewhat apart in the lattice, allowing permeation of furan into the lattice voids. Water is then subsequently expelled due to hydrophobic interactions once furan has 'entered' to give a lower energy system.

3.2.2 X-RAY STRUCTURE

The X-ray structure sheds some light on the interactional forces operating within the cavity of the host. (Figure 18) Very few structural analyses have been carried out involving furan as either a π-ligand or as a guest in a solvate, in contrast to aromatic derivatives. An example of the former case[11] is the reaction of furan with $[Cp^*RuCl]_n$ ($Cp^*=\eta^5$-C_5Me_5) in CH_2Cl_2 to afford an unstable π-coordinated complex $[Cp^*Ru(\eta^6$-$C_5H_4O)]Cl$ which could only be observed in solution. Similarly, crystals of decakis(dichloromethyl)biphenyl form a 1:1 solvate with furan by photochlorination of decamethylbiphenyl[12]. An X-ray structure of the complex revealed weak hydrogen bonding between a proton on a dichloromethyl moiety and the furan oxygen, with a distance of ca. 2.6Å.

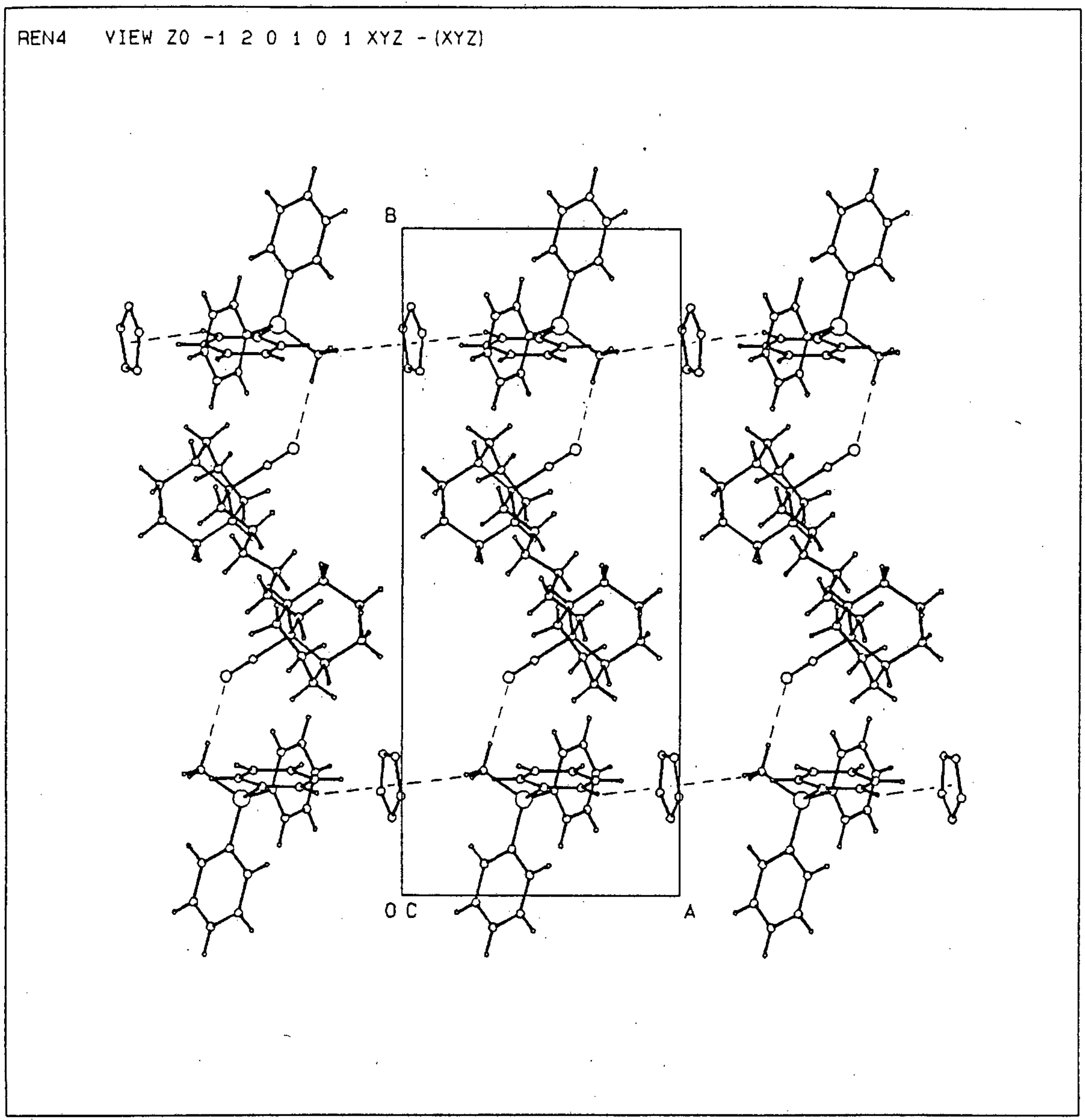
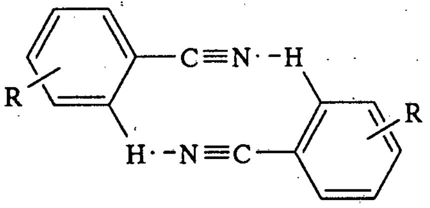


Figure 18

Examination of the X-ray structure of the cyanoborate-furan clathrate reveals it to be a coordinatoclathrate in a coordination assisted lattice[13]. The latter is provided by hydrogen bonding between a nitrogen of a cyano group and a hydrogen of a phosphonium methyl. C-H···N hydrogen bonding between $C\equiv N$ groups and aromatic H atoms is documented in the literature[14], and may result in the formation of network structures[15], such as **52** and **53**. For example, the flat hexagonal array of molecules of 1,3,5-tricyanobenzene **53** are efficiently linked by C-H···N hydrogen bonds of 3.471(4)Å, which are far weaker than O-H···O and N-H···O hydrogen bonds.



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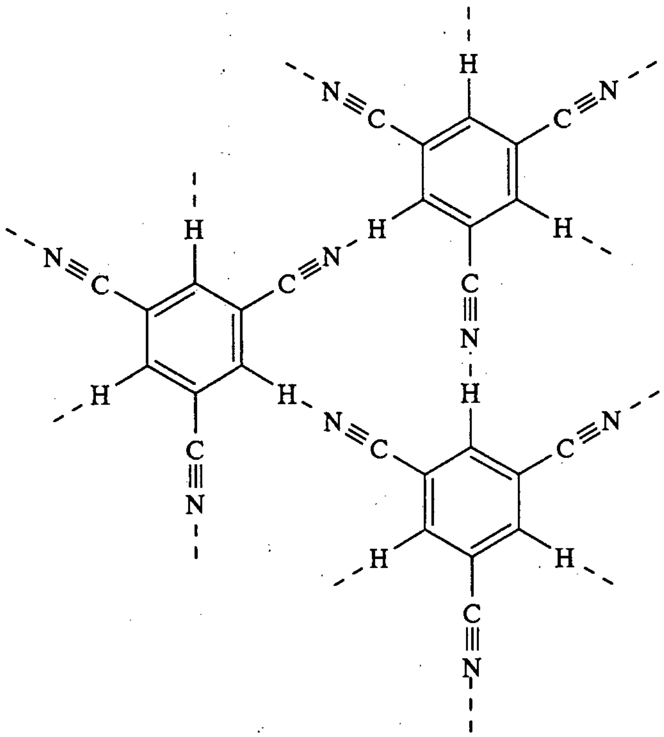

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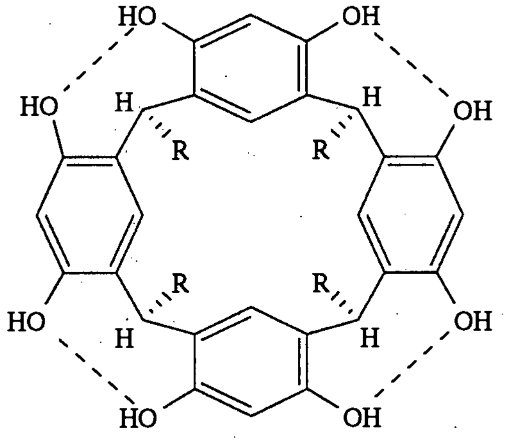
The anion of the furan clathrate is in its preferred zig-zag conformation in which the two cyano groups are trans with respect to the B-B axis. Two hydogen bonds from opposite sides of the plane of the heteroaromatic ring hold the furan in place. The hydrogens involved in this C-H···π(heteroaromatic)···H-C interaction originate from a methyl group and *ortho* position of a phenyl group of two different phosphonium cations. Thus, the phosphonium cation plays a pivotal structural role in this clathrate and became a focal point for subsequent modification. (Chapter 4)

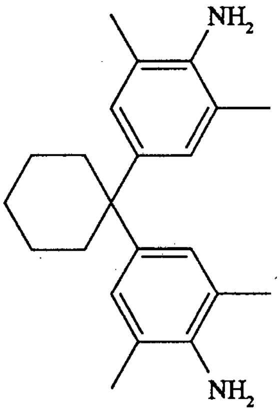
C-H···π(aromatic) interactions have been of much interest recently[16] and are encountered when there is a deficiency of hydrogen bond acceptors (acceptor is not used in the electronic sense here). Van der Waals forces contribute most predominantly to C-H···π interactions, in which electron-rich π-systems are more favoured than electron deficient ones, since hydrogen in C-H is δ^+. A recent topical example of C-H···π interactions playing an important role in host-guest chemistry comes from the calixarene literature[17]. The resorcinol cyclic tetramer **54** shown below, which is made up of four electron-rich benzene rings, is capable of binding guests such as diols, sugars and dicarboxylic acids, via a combination of C-H···π and hydrogen bonding interactions.



$R=(CH_2)_{10}CH_3$

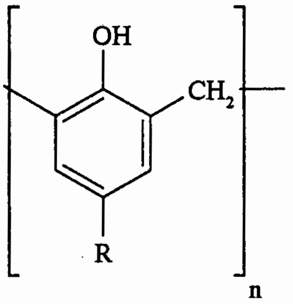
54

It has been argued and indeed demonstrated that in a molecular assembly with a deficiency of H-bond acceptors and an excess of hydrogen bond donors, π-electrons constitute the next best acceptor[18]. In such cases, weak X-H···π hydrogen bonds may be formed or a change in hybridisation may occur, as is the case for the molecular structure **55**.



55

Such interactions have been reported for calixarene cavitates[19] involving π-electron rich phenolic rings, as depicted in structure **56** below.



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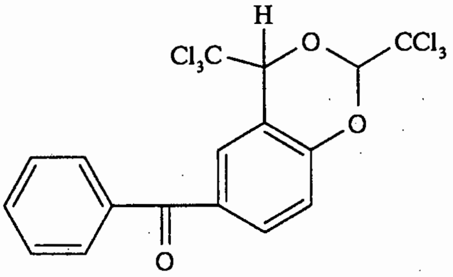
Calixarenes have the ability to include neutral organic molecules in a true clathrate sense. These complexes are stabilised, in the solid state, by weak intermolecular CH_3-π interactions. The cyclic tetramer, p-tert-butylcalix[4]arene, is only able to include guests when in the all cone conformation. Furthermore, inclusion of aromatic guests, such as anisole in a 2:1 host-guest stoichiometry, has been observed only when the para position of the calixarene carries a tert-butyl group[20]. The tert-butyl groups are unable to bend inwards, thus preventing the cavity becoming blocked. This arrangement is believed to provide a favourable CH_3···π interaction between the methyl groups and the π system of the guest molecule. By converting the p-tert-butylcalix[4]arene into a tetracarbonate, a 1:1 clathrate is formed with the non-aromatic acetonitrile[21]. In this case the methyl group of acetonitrile is oriented towards the inside of the cavity of the calix[4]arene. In addition, bridging of two opposite phenolic OH groups of the p-tert-butylcalix[4]arene with a polyethereal chain has been shown to produce a macrobicyclic compound with a hydrophilic and lipophilic cavity suitable for complexing cations and neutral molecules respectively. An inclusion compound of the crowned p-tert-butylcalix[4]arene with pyridine (1:1) has been obtained[22], in which the guest is stabilised by hydrogen bonding between atoms of the tert-butyl groups of the host and the nitrogen of the guest. Furthermore, an attractive CH_3···π interaction between the methyl groups of the host and the aromatic moiety of pyridine plays a major role in the stabilisation of the complex.

Similarly, our cyanoborate clathrate exhibits the first example of an C-H···π(aromatic)···H-C interaction, which may be primarily due to the π-excessive nature of the heteroaromatic guest, as evidenced by an extensive data search. This interaction is spatially analogous, although not electronically so to a C-H···π(aromatic)···Cl-C interaction recently reported by A. Irving[23] in the crystal structure of 6-benzoyl-2,4-bis(trichloromethyl)-1,3-benzdioxin **57**.



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Recently, J. Atwood reported on the first example of two π-Arene···H interactions in an inclusion complex[24] based on an aluminium-fused bis-p-tert-butylcalix[4]arene involving CH_2Cl_2 as the guest.

3.2.3 SELECTIVITY INCLUSION EXPERIMENTS WITH FURAN, THIOPHENE AND BENZENE

Competition experiments were performed on a mixture of benzene and furan and benzene and thiophene with **47** · n H_2O by heating the two host-guest components without any solvent. The heating dissolved the phosphonium cyanoborate to form the liquid clathrate with the top layer consisting of excess guests and the bottom red layer of host and guests. Upon cooling, crystals formed from the liquid clathrate layer containing benzene and furan and benzene and thiophene in ratios of approx. 4:1 and 3:2 respectively. A similar scenario was observed for furan and N,N-dimethylaniline and furan and *p*-xylene. N,N-Dimethylaniline and *p*-xylene were chosen as guests with activated rings (relative to benzene) of different magnitudes. ^1H-NMR was used to establish the ratios of guests in the liquid clathrate layer before crystallisation occurred and the results are given in Table 15.

TABLE 15

Results of host-guest ratios of [$(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\cdot 2Ph_3P^+Me \cdot H_2O$] with two guests without solvent as a solid and as a liquid clathrate.

guest	$H:G_1:G_2$[a]	$H:G_1:G_2$[b]
benzene/furan	1:4:1	1:4:4
benzene/thiophene	1:3:2	-
furan/N,N-dimethylaniline	1:2:1	1:8:8
furan/*p*-xylene	1:0:Tr	-

[a] solid clathrate crystallised out

[b] liquid clathrate from liquid clathrate layer

The results in Table 15 indicate that N,N-dimethylaniline is preferentially included in view of the higher polarity of the amine, suggesting that its interactional forces with the host are stronger than those of furan. Both N,N-dimethylaniline and furan display the same affinity for the host in the liquid clathrate, while in the solid clathrate furan is preferred. In solution the lattice void of the host encapsulating the guests is able to take up a large number of guest molecules, since long range forces are operating. There is, however, presumably still a restriction on the number of guest molecules being included, due to hydrogen bonding of the cyano group on the borate anion to the methyl hydrogen of the phosphonium ion maintaining a long range lattice ordering. No liquid clathrate behaviour was observed for benzofuran with either hydrated or anhydrous samples of **47**, which implies that efficient lattice ordering cannot take place with large guest molecules. The extra hyrophobicity of benzofuran forges favourable interactions with hydrophobic elements of host resulting in complete dissolution. Similarly, benzothiazole dissolves the host inhibiting liquid clathrate behaviour presumably because of its more polar nature.. Other furan derivatives, such as 2-methoxyfuran, methyl 2-furoate, furfural and furfuryl alcohol similarly did not display liquid clathrate behaviour either implying that liquid clathrate behaviour is very sensitive to the polarity and steric nature of the guest as well as water content. However, more work has to be done on the range of guests that may be incorporated into a liquid clathrate layer using furan as partitioning solvent.

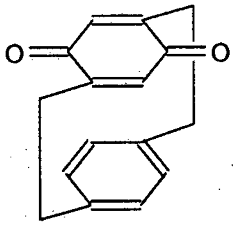
3.3 U.V. EXPERIMENTS

As was mentioned in section 3.2.1. previously, the addition of furan to an anhydrous sample of host compound **47** did not produce a liquid clathrate but resulted in the solid taking on a deep-red colouration over a period of time presumably due to permeation of furan into the host lattice. In solution (CH_2Cl_2), further colour changes were evident and it became apparent that a study of these phenomena was warranted on what is possibly a charge-transfer phenomenum, in order to shed some light on the solution structure of the liquid clathrate.

Charge-transfer complexes have been defined by R. Mulliken[25] as being those formed by the weak interaction of electron donor molecules with electron acceptor molecules. A large number of compounds are known to form these complexes, ranging from simple systems such as the benzene-iodine complex first reported by H. Benesi and J. Hildebrand[26] to the multilayered donor-acceptor cyclophanes studied by H. Staab[27] and S. Misumi[28]. R. Mulliken's theory suggests[29] that in the ground state of the complex normal physical forces such as van der Waals attractions between the complex components are dominant and that a small amount of charge transferred from the donor to the acceptor contributes an additional binding energy to the complex. The ground state complex is then promoted to an excited state on the absorption of light of a suitable wavelength. In the excited state the electron is almost completely transferred to the acceptor, whereas in the ground state it is only slightly shifted towards the acceptor. This electronic transition can be observed by ultraviolet (UV)-visible spectrophotometry, which is the method usually chosen for studying charge-transfer complexation.

A charge-transfer (CT) absorption band is generally broad and intense, with extinction coefficients as high as 50 000 being observed. However, most extinction coefficients for CT absorptions range from 1000 to 5000. Longer wavelenghts for the CT band indicate a greater stability of complex and a more complete transfer of the electron from donor to acceptor[30]. The position of the CT absorption of most complexes has been shown to be solvent-dependent. In a complex possessing a neutral ground state and a polar excited state, a change from a less to a more polar solvent causes a red shift, i.e. to longer wavelenghts, of the CT band[31]. The reason for this is that a polar solvent stabilises a polar excited state more than a non polar solvent does, resulting in a lowering of energy of the excited state. Thus, the smaller the gap between the ground and excited states the greater the red shift.

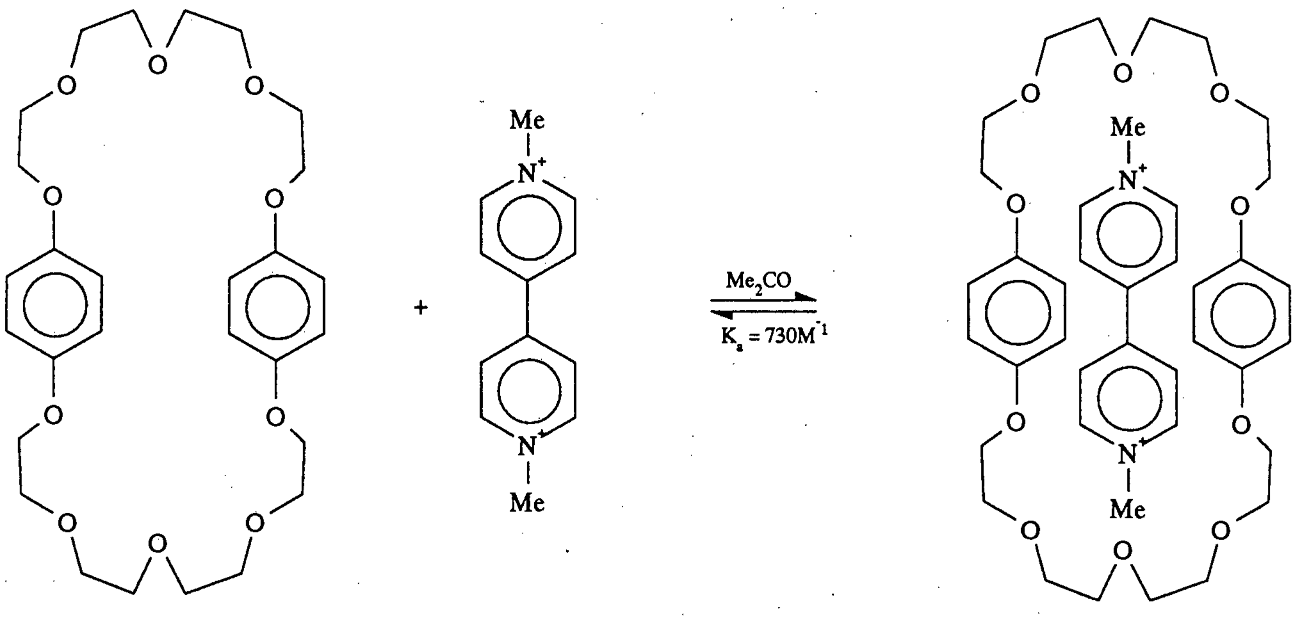
Even though crystal structures have been obtained for a number of CT complexes, the relative orientation of the donor and acceptor moieties of CT complexes in solution has been the subject of considerable discussion, since the solid-phase geometry is not necessarily the same as that in solution. Intermolecular distances between donor and acceptor in the solid state are normally shorter than the sum of the van der Waals distances. The simplest donor-acceptor cyclophane is the [2.2]paracyclophane quinone reported by Cram *et al.*[32] in 1966. It has an ultraviolet absorption spectrum which includes a band at 340nm (ε=597), assigned as an intramolecular CT transition.



58

[2.2] paracyclophane quinone

Similarly, J. Stoddart *et al.*[33] have been interested in the complexing abilities and supramolecular structures of macrocyclic receptors containing π-electron rich aromatic units with π-electron deficient substrates, such as paraquat $[PQT]^{2+}$ **60**. (Scheme 35) A 1:1 complex is formed between the redox-active paraquat and the cyclophane-like receptor, bisparaphenylene-34-crown-10 [BPP34C10] **59**. At room temperature, this complex **61** displays a stability constant of K_a=730M^{-1} in acetone when the counterions are hexafluorophosphate. The reasons for such a good complexation are 1) electrostatic attractions, including C-H···O hydrogen bonding between the positively charged guest and the crown ether oxygens present in the host, and 2) dispersive forces, including CT interactions between the π-electron accepting bipyridinium moiety of the guest and the π-electron donating hydroquinol rings of the host. A deep orange colour is exhibited by the 1:1 complex due to CT interactions. The structure has been fully characterised by X-ray analysis in the solid state, for which the distance between the mean planes of π-donors and π-acceptors is 3.7Å in the complex.



BPP34C10 [PQT]$^{2+}$ [BPP34C10.PQT]$^{2+}$

59 **60** **61**

Scheme 35

In the case of the phosphonium cyanoborate in this thesis, the colour changes with furan could be followed by U.V. spectroscopy. Where appropriate, binding constants of host-guest complexes are invariably calculated from NMR titration experiments, which was not possible in this case, since no chemical shifts were observed in the proton spectra of host with guest. This is not unexpected, since in a coordination assisted clathrate lattice as in this instance, the lattice breaks up on dissolution rendering the host separate to the guest species. In ^{1}H-NMR titration experiments the shift of the host protons is determined at various concentrations of the guest[34] and at the 'coalescence point' the degree of the observed chemical shift of a proton, $\Delta\delta$, is proportional to the percentage of the complexed host relative to the total concentration[35]. The association constant may be determined using the relationship:

$1/\Delta\delta = 1/(K\cdot\Delta\delta_{max})\cdot 1/[\text{guest}] + 1/\Delta\delta_{max}$.

When a ^{1}H-NMR titration experiment cannot be performed, owing to the absence of any observable chemical shifts, the association constant of a CT complex can be calculated by measuring the intensities of UV/vis absorption bands characteristic of the complex and using variations on the Benesi-Hildebrand equation,

$1[A]/A = 1/K\varepsilon[D] + 1/\varepsilon$

where l=path length of cell(cm); [A], [D]=concentration of acceptor, donor respectively (mol l^{-1}); A=absorbance; ε=extinction coefficient($mol^{-1}dm^{3}cm^{-1}$), also molar decadic absorption coefficient.

which is derived from the Beer-Lambert equation

A=εlc

where c=concentration of the absorbing species

The assumption made by the Benesi-Hildebrand analysis is that there is only one equilibrium present in solution, that the absorbance monitored is due only to the complex and that the concentrations of the reactants are very much greater than that of the complex, thus ignoring the concentration of the complex completely.. For $[D]_0>[A]_0$ ($[A]_0$ is the initial concentration of the acceptor), a plot of l[A]/A vs. 1/[D] gives a straight line with a slope of $1/K_\varepsilon$ and a y-intercept of 1/ε. Although this fails for very strong complexes ($[A]_0 \sim [A]_{complexed}$), there are a number of variations on this equation depending on the complexes formed. However, these days association constants and extinction coefficients of CT complexes are increasingly being evaluated by computer-assisted non linear least-squares fitting procedures, that remove the necessity for experimental boundary conditions.

Furan, 2-methoxyfuran and methyl 2-furoate were chosen so as to probe the influence of ring electron density on the host-guest process. While studying the inclusion properties of the host **47** with these guests, it was observed that addition to the host dissolved in THF resulted in a variety of colour changes. This gave an indication that charge-transfer complexes might be forming which could be looked at in more detail using UV spectroscopy. Hence, a 10^{-1}M stock solution of anhydrous host dissolved in THF was prepared to which aliquots of neat guest were added. The solutions were then left at 0°C overnight to equilibrate before recording the spectra. The solutions were kept in an ice-cooled container and only removed from it while recording the spectra at various concentrations of host and guest thereby maintaining a low temperature. Unfortunately the spectrophotometer's chamber was not temperature controlled, which led to reproducibility problems with furan as guest, in view of its volatility.

After the addition of furan to the host, the colour of the solution changed quickly from purple through to red, orange and to yellow. The colour of the solution remained yellow indicating that an equilibrium had been reached. These observable colour changes may be ascribed to the host and guest trying to orient each other to attain the 'best' orientation possible. UV spectra were then run in a region of $335<\lambda<650$nm on the yellow solutions, since furan absorbs at 285nm and the host at approximately 315nm. In the spectrum two broad peaks could be observed; one at approximately 360nm, which increased in absorbance as the concentration of guest was increased and the other at approximately 500nm. (Figure 19) The latter peak increased in absorbance in decreasing increments as the concentration of guest was increased until it reached a maximum, after which it slowly shifted towards lower wavelengths forming a shoulder on the peak at 360nm. The presence of two separate peaks indicates that there are at least two different complexes present in solution. Moreover, it is probable that a variety of complexes are formed due to the interaction of one or more furans with different phenyl rings on a phosphonium cation. The brightly coloured solutions are caused by π-π (face-to-face) interactions of furan, the electron donor, with the aromatic rings of the host acting as electron acceptors, in a charge-transfer complex.

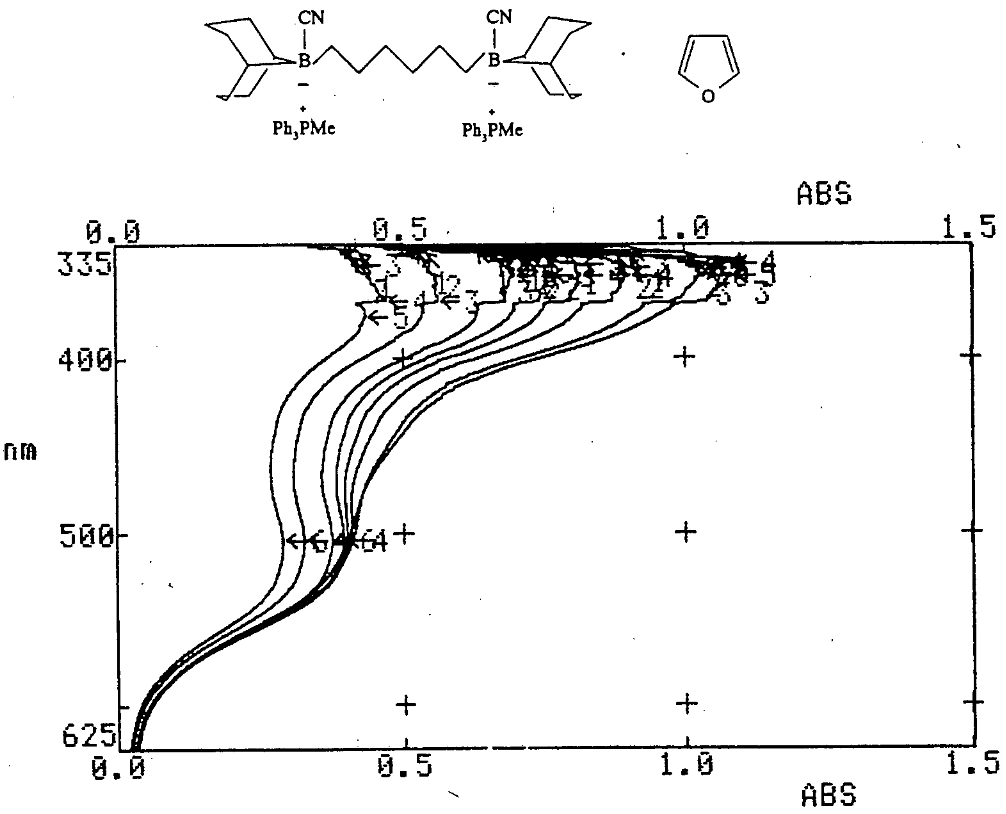


Figure 19

Similarly, colour changes could also be observed for the reaction of 2-methoxyfuran with methyltriphenylphosphonium cyanoborate. This time, the purple colour remained much longer than with furan and subsequently went through the same colour changes, but equilibrating at a more intense yellow. Two peaks were observed in the UV spectrum of the cyanoborate complex with 2-methoxyfuran, one at λ=340nm and the other at λ=462nm, the latter increasing uniformly as the concentration of guest was increased.

Again, the formation of a variety of complexes is likely. The charge-transfer interaction in this instance was envisaged to be stronger than for the furan case due to the more polar nature of the 2-methoxyfuran as well as its more activated ring system.

The host-guest complex of methyl 2-furoate with the phosphonium cyanoborate salt exhibited the same behaviour as with furan and 2-methoxyfuran. The solution containing the host and guest underwent colour changes from purple to red and equilibrated at orange. Interestingly, there was only one peak at 370nm present in the spectrum for this complex, possibly indicating that there were two peaks superimposed into the single one, which slowly shifted to a shorter wavelength as the concentration of guest was increased. A shift of the peak at longer wavelength to a shorter one indicated the formation of a CT complex with a greater energy gap.

It was also possible to follow the colour changes of the THF solution of furan with the host by UV spectroscopy, at room temperature. Absorbances of the complex were measured at 10 minute intervals immediately after the addition of furan to the dissolved host. The absorbance of the peak at approximately 500nm increased steadily with time. After nearly 30 minutes a maximum was reached which then shifted slowly to lower wavelengths forming a shoulder to the peak at 350nm. Therefore, only one broad peak was visible after approximately 80 minutes, which did not undergo any further changes, indicating that an equilibrium had been reached. In the same manner, the colour changes of the host with 2-methoxyfuran in THF were followed. For this solution the colour changes were slower and had not reached equilibrium after 100 minutes. These results show that a dynamic process is occurring, which warrants a thorough kinetic investigation so as to identify chemical processes taking place in solution. However, this was beyond the scope of this thesis.

From a chemical standpoint, the charge-transfer process is complicated by the fact that each methyltriphenylphosphonium ion has three phenyl rings with which to interact with the donor furan derivatives. Exactly how many participate is impossible to say and in this regard the results are somewhat speculative. A high binding constant for the host **47** complexing with the furan derivatives is envisaged due to the intense colours observed in solution, thus disfavouring the use of the Benesi-Hildebrand equation. The association and extinction constants need to be calculated by applying an appropriate least squares algorithm to a multiple equilibrium reaction using a computer-assisted non linear least-squares fitting procedure. Indeed, this will constitute the basis of a detailed study in the future in order to obtain more information on the solution structure of the liquid clathrate.

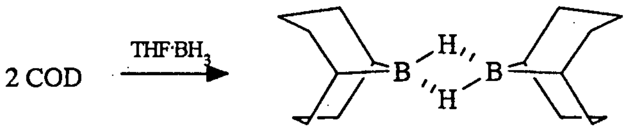
10

Scheme 23

Therefore, it was decided to introduce the boron as a dialkylborane in the form of 9-BBN so that the borane could be obtained in one step. 9-BBN may be reacted with alkenes or dienes yielding boranes or diboranes respectively. It can also be converted to monochloro-9-BBN or methoxy-9-BBN which can be reacted with phenyllithium to afford phenyl-9-BBN[34] which would allow for introduction of delocalisation of the negative charge at the 'ate' level.

1.4.1 THE PROPERTIES OF 9-BBN

The advantage of 9-BBN and its derivatives is that they are often crystalline solids which are invariably easy to isolate. 9-BBN[35] **11** itself is prepared by reacting 1,5-cyclooctadiene (COD) with THF·BH_3 at an elevated temperature to isomerise the two regioisomers that are formed during the reaction. Scheme 24.

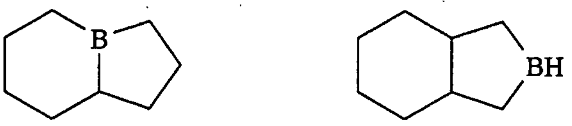


11

Scheme 24

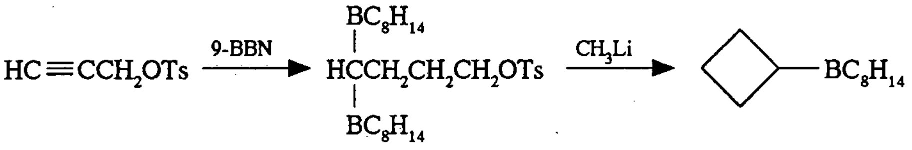
Crystallisation from refluxing heptane gives 9-BBN as long, colourless needles with mp.≥157°C, which are air-stable for several weeks at room temperature. It is dimeric in structure as confirmed by X-ray analysis, with each $C_8H_{14}B$ residue in a chair conformation.

Thermal stability of 9-BBN, which had a bearing on the electrochemistry of the target, is good. DSC analysis shows a relatively rapid thermal degradation of the molecule at only 200°C and at even higher temperatures (eg. 350°C), interesting transformations of 9-BBN[36] including C-skeletal rearrangements can be observed, to give the products depicted below.



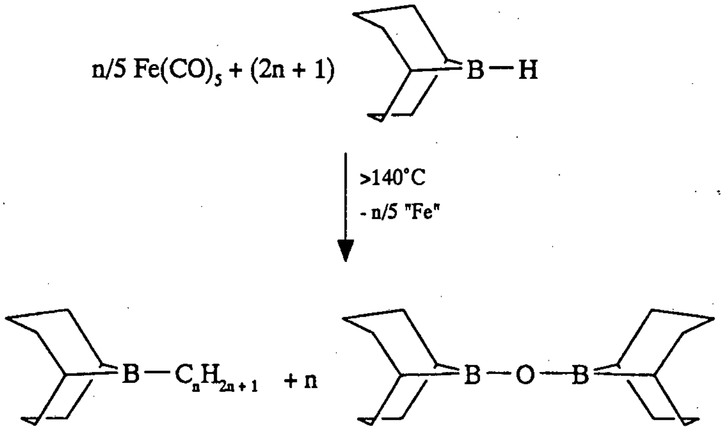
1-Bora- and 8-Borabicyclo[4.3.0]nonanes

The 9-position of the 9-BBN skeleton is often employed as a carrier of organic residues. It can be used for cyclisation[37] and also for chain lengthening[38] with C_1 groups. Scheme 25.



Scheme 25

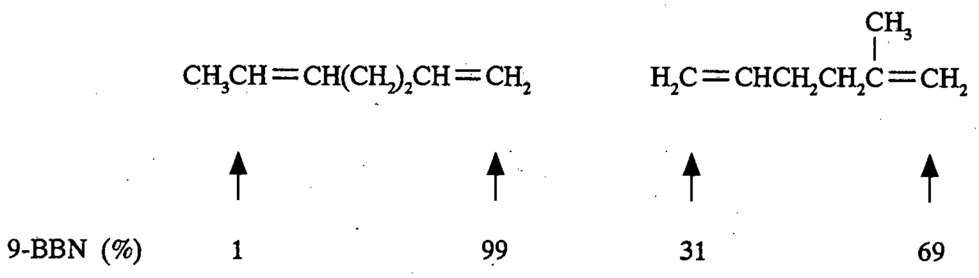
The latter reaction forms the basis of an organoboron model system for Fischer-Tropsch synthesis, in which reductive C_1-polymerisation of CO with 9-BBN to give 9-alkyl-9-BBN products takes place. So far, up to 9-decyl-9-BBN (n=10) has been identified. Scheme 26.



Scheme 26

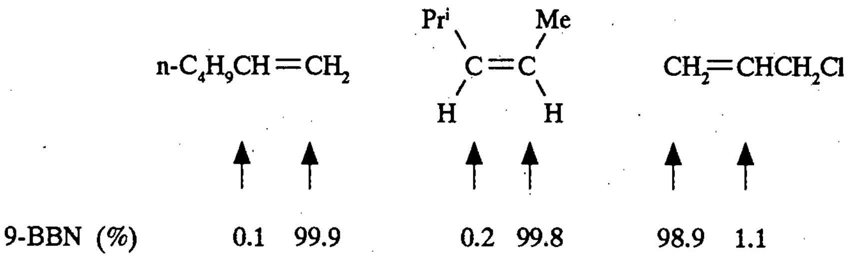
In all these reactions the BBN moiety remains unchanged. In synthetic organic chemistry 9-BBN has found broad application in the hydroboration of multiple bonds[39]. In unsymmetrical non-conjugated dienes, 9-BBN hydroborates the terminal position preferentially to the internal double bond. Dienes containing 2-substituted and

2-unsubstituted 1-alkenes as terminii hydroborate at the 2-substituted alkene with modest chemoselectivity. Schemes 27 and 28.



Scheme 27

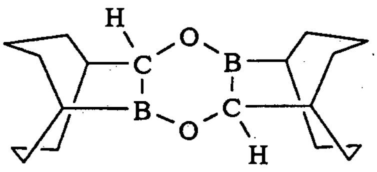
Among dialkylboranes, 9-BBN is the most regioselective reagent of all.



Scheme 28

The stereoselectivity of hydroboration of cyclic alkenes is also impressive. Similarly, 9-BBN hydroborates internal alkynes to form vinylboranes in which selectivity for monohydroboration is governed by steric and electronic effects. 9-BBN's versatility as a synthetic building block is further highlighted by a number of stable, often crystalline oxy-, thio- and amino derivatives[40a], in which the $C_8H_{14}B$ bicyclic ring is left intact.

Another interesting phenomenon investigated by R. Köster[38] only recently is the uncatalysed reaction of 9-BBN with carbon monoxide. A crystalline dimer **12** with two [3.3.2]bicyclic rings is formed at about 100°C when CO is partially reduced and inserted into one of the B-C bonds. At 150°C a boroxin **13** is formed.



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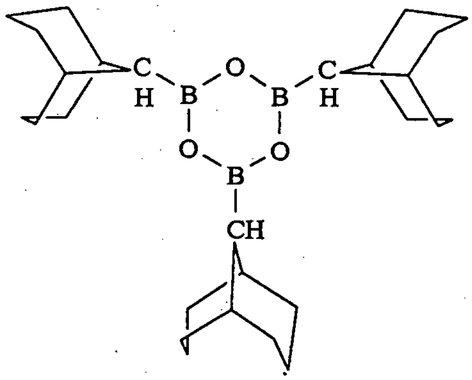
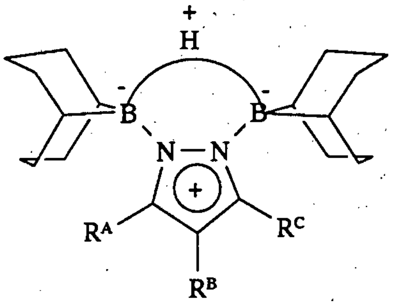


13

Boroxin

A number of interesting 9-BBN adducts called pyrazoboles, e.g **14**, which contain a bridging hydrogen have been prepared by R. Köster *et al*[40a].



14

This short overview on some interesting characteristics of 9-BBN highlights its special features such as sterically rigid structure, Lewis acidity and the restriction it places on substituent exchanges. Also the fact that many of these compounds crystallise readily allows the possibility of X-ray structure analysis.

1.5 THE SYNTHESIS OF DISODIUM 1,6-BIS(B-CYANO-9-BORATABICYCLO[3.3.1]NON-9-YL) HEXANE • DMF CLATHRATE

This section indicates how the synthesis of a novel cyanoborate salt and discovery of its clathrate properties led to a deviation from the initial goal, namely the synthesis of a battery electrolyte. At about this stage in the research, the franchise for the Zebra battery system was bought out by Daimler-Benz in Germany rendering further research unfunded. Once 9-BBN had been chosen as a viable boron source, it was reacted with 1-hexene and then with NaCN in DMF to provide $Na^+HexB^-BBNCN\cdot$ n DMF for comparison with the cyanotributylborate previously described. The resulting borate, however, remained a

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CHAPTER 4

THE SYNTHESIS AND CLATHRATE ACTIVITY OF ONIUM CYANOBORATE SALTS

4.1 INTRODUCTION

The discovery of the solid and liquid clathrate behaviour of the methyltriphenylphosphonium cyanoborate salt **47** pointed the way forward to examining the potential inclusion activity of a range of onium borate salts with a view to establishing whether **47** belonged to a family of materials with selective inclusion profiles.

The various X-ray structural analyses reported in chapters 2 and 3 gave us a comprehensive picture of the intermolecular forces operating in both the host lattice and a number of clathrates of **47**. This information, thus set the scene for an in-depth structure-activity study of its various structural elements. Of particular interest were the following issues regarding clathrate activity:

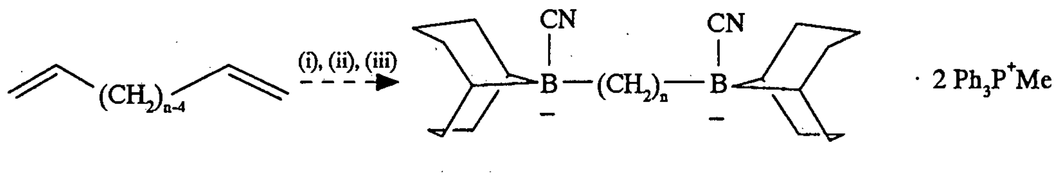
1) The importance of hydrogen bonding involving the cyano nitrogen and the scope of hydrogen bond donors (e.g. hydrogen of a methyl of a phosphorus cation in the furan clathrate).
2) The influence of the ligands groups on phosphorus especially ones modified electronically.
3) The structural influence of the spacer, particularly regarding conformational and electronic aspects.

Synthetically, the same strategy as before was followed, namely; 1) bis-hydroboration of a diene, 2) 'ate' formation and finally 3) cation exchange. Moreover, it was essential that solid host materials were obtained, since recrystallisation of **47** had proved problematic and inclusion experiments with hosts as oils were considered unsatisfactory.

4.2 VARIATIONS IN THE BORATE SPACER

The X-ray structures reported in chapters 2 and 3 revealed that the hexamethylene chain of **47** is conformationally flexible enough to be responsive to guest inclusion. For instance, inclusion of water induced a C_2-C_5 cisoid kink in the chain while with *p*-xylene and furan the lower energy zig-zag conformation was adopted. Therefore, it was decided to begin the structure-activity study by varying the chain length and functional characteristics of the spacer. In each case the counter-ion was retained as methyltriphenylphosphonium.

Decreasing or extending the length of the hexamethylene spacer resulted in oily phosphonium salts which would not crystallise out, even at low temperature. (Scheme 36) The pentamethylene spacer may be too short resulting in disturbance of the anion-cation ordering in such a manner that a crystal lattice cannot be produced. Similarly, chains with n>6 with a greater conformational mobility than that in **47** also rendered oils ineffective for host-guest studies. Thus, as it turned out the hexamethylene spacer was fortuitously the one of choice in the aliphatic series.

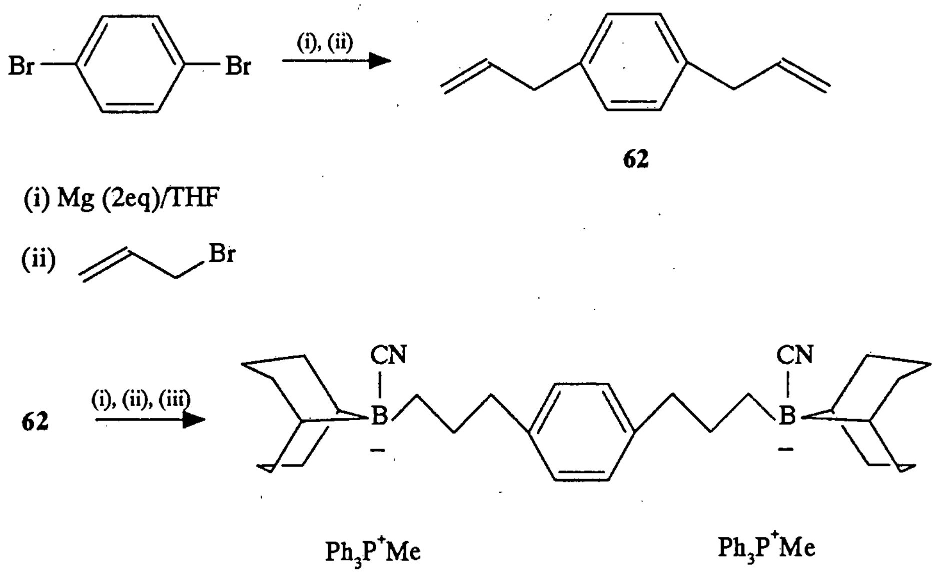


n = 5, 7, 8, 9, 10, 14

(i) 9-BBN (2eq)/THF
(ii) NaCN/DMF
(iii) $Ph_3P^+Me\ Br^-$(2eq)/MeOH

Scheme 36

From both a synthetic and interactional point of view it appeared attractive to incorporate an aromatic ring as "sensor" into the spacer. The precursor, 1,4-bis(allyl)benzene **62**, was prepared by allylating the di-Grignard of 1,4-dibromobenzene in THF with allylbromide[1]. (Scheme 37) After vacuum distillation the diene **62** was hydroborated with 9-BBN and reacted with sodium cyanide. Exchange of the product with methyltriphenylphosphonium bromide as before produced an oily material, which could only be precipitated out with ethyl acetate once it had been left to dry in the atmosphere for approximately 3-4 months. This solid gave a satisfactory elemental analysis as well as ^1H and ^{13}C spectra. In particular, the phenyl protons in the spacer appeared as a singlet at δ=6.80ppm in the ^1H-NMR. This compound **63** was then dissolved in CH_2Cl_2 and host-guest studies carried out by the evaporation method described in chapter 2. The guests examined were benzene, acetonitrile and acetone, of which only benzene was taken up in a host-guest ratio of 1:1. Since, this was a substantial increase in the host-guest ratio for benzene compared to that of the compound **47** with the hexamethylene spacer, it suggests that additional π-π interactions were operating within the cavity. It would have been interesting to synthesise a range of substituted aromatic spacer derivatives but this was not carried out.



62

(i) Mg (2eq)/THF
(ii) allyl bromide

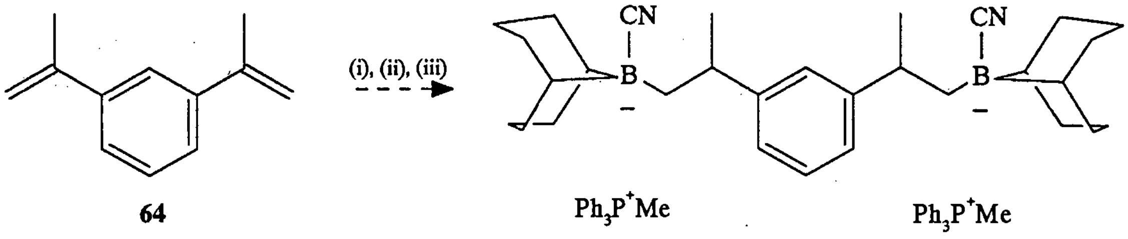
63

(i) 9-BBN (2eq)/THF
(ii) NaCN/DMF
(iii) $Ph_3{}^+Me\ Br^-$ (2eq)/MeOH

Scheme 37

Although the synthesis of 1,4-bis(propynyl)benzene was conducted in the same manner as for 1,4-bis(allyl)benzene, it proved unsuccessful in our hands.

Following on with this line of thought, the next spacer chosen was based on the commercially available 1,3-diisopropenylbenzene **64**. We were aware of the possibility of diastereomer formation but decided to go ahead with the synthesis, since introduction of stereogenicity into the clathrand was of great interest. 1,3-Diisopropenylbenzene readily reacted with 9-BBN but the sodium exchange once again gave an oil from which a few crystals slowly formed. (Scheme 38) Unfortunately, the amount was too small to perform any conclusive host-guest experiments on, and precipitation from ethyl acetate was not possible.

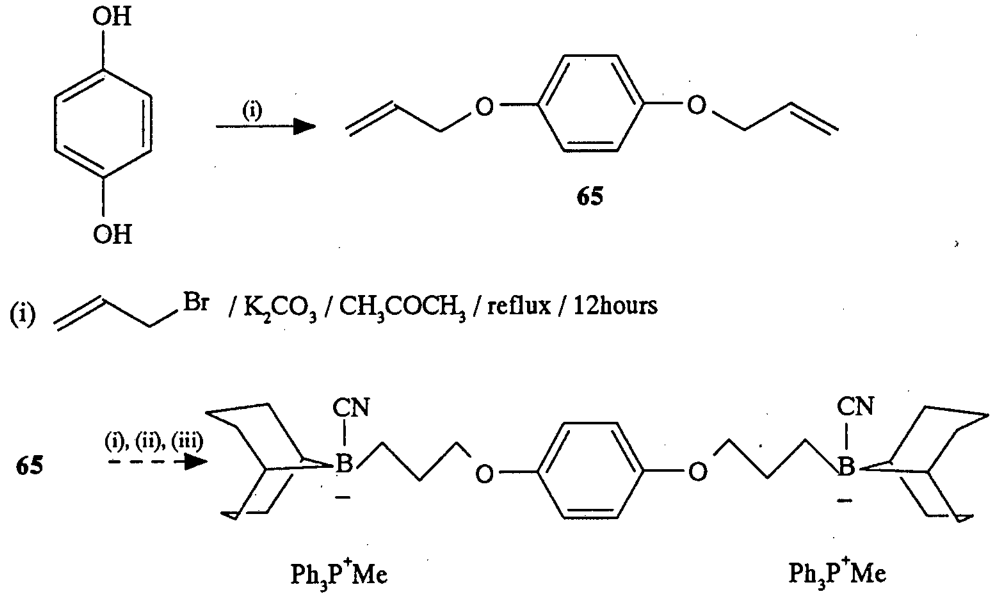


64

(i) 9-BBN (2eq)/THF
(ii) NaCN/DMF
(ii) $Ph_3P^+Me\ Br^-$ (2eq)/MeOH

Scheme 38

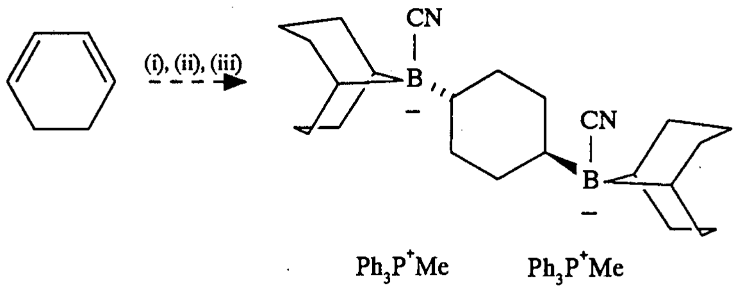
Since some success had been achieved with an aromatic spacer, the product of hydroboration of 1,4-bis(allyloxy)benzene **65** was prepared and subsequently converted to an oily phosphonium salt which was not pursued further. (Scheme 39) However, the intermediate sodium cyanoborate in this synthesis on precipitation with chloroform was found to form an inclusion complex with it in a ratio of H:G=1:0.5. It is likely that chloroform is interacting with the electron-rich aromatic ring in this case. On cyanidation to the borate, a viscous sodium salt was obtained. Precipitation using chloroform (discovered during NMR characterisation) resulted in a host-guest compound with the solvent in a ratio of 1:0.5.



(i) 9-BBN (2eq)/THF
(ii) NaCN/DMF
(iii) $Ph_3P^+Me\ Br^-$ (2eq)/MeOH

Scheme 39

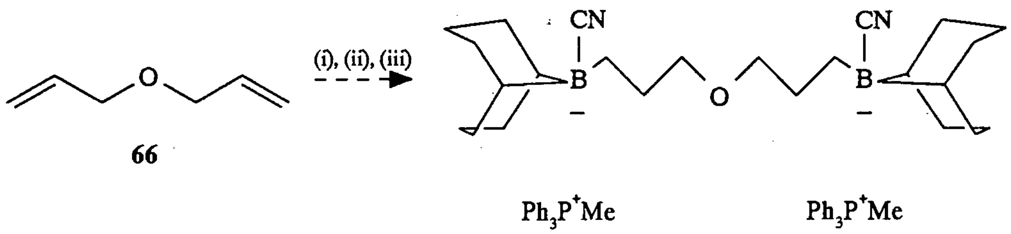
Further variations of the spacer were then considered based on hydroborating different sized rings containing internal double bonds, such as 1,3-cyclohexadiene, 1,3,5-cycloheptatriene and 1,5-cyclooctadiene. The rationale here was to probe the influence of conformational rigidity on inclusion activity. Once again, we were aware that hydroboration with 9-BBN could produce a number of different regio- and stereoisomers, although the major isomer was anticipated as being that with the 9-BBN moieties as far apart from each other as possible on steric grounds. Work-up of the cation exchanged product produced an oil which was impossible to precipitate out. (Scheme 40) In addition, the ^{1}H-NMR spectrum showed the complete disappearance of the borate resonances indicating that either the hydroboration had been unsuccessful or that the borate had been lost into the aqueous layer upon sodium exchange. This occurred in all three cases.



(i) 9-BBN (2eq)/THF
(ii) NaCN/DMF
(iii) $Ph_3P^+Me\ Br^-$ (2eq)/MeOH

Scheme 40

Having a heteroatom in the spacer, which should alter the interactional forces between host and guest substantially, was of further interest. Diallylether **66** was reacted with 9-BBN followed by the normal exchange reaction, but once again an oil formed. If a solid had formed, there might have been the possibility of hydrogen bonding of a guest to the oxygen of the spacer of the host. (Scheme 41)

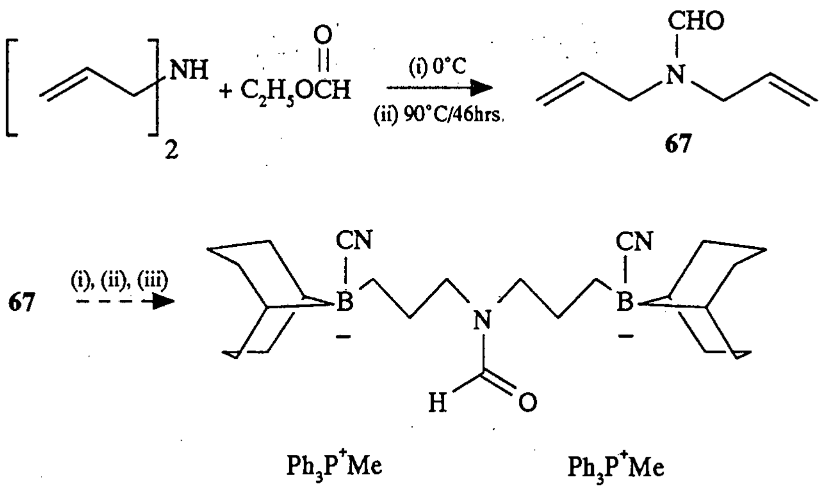


66

(i) 9-BBN (2eq)/THF
(ii) NaCN/DMF
(iii) $Ph_3P^+Me\ Br^-$ (2eq)/MeOH

Scheme 41

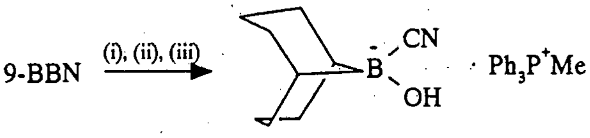
Further possibilities of hydrogen bonding were investigated by synthesising a spacer containing the formamide functionality. Hence, N-formyldiallylamine **67** was prepared by refluxing N,N-diallylamine and ethylformate together. The product was purified by distillation and then reacted with 9-BBN, sodium cyanide and methyltriphenylphosphonium bromide in the usual way to give a colourless solid upon work-up. Scheme 42



(i) 9-BBN (2eq)/THF
(ii) NaCN/DMF
(iii) $Ph_3P^+Me\ Br^-$ (2eq)/MeOH

Scheme 42

However, as evidenced by spectroscopy the product obtained was not the desired host compound, whereas in the spectra of the sodium cyanoborate salt all of the expected resonances were still present in particular that due to the N-formyl group. Thus, a chemical reaction must have occurred during the work-up with methyltriphenylphosphonium bromide suggesting either reaction of the borate anion with methanol or water. This was substantiated by the independent syntheses of B-cyanoborinate **68** and B-cyano-9-methoxyborinate **69** which were both easily accessible via reacting 9-BBN with methanol[2] followed by cyanidation (Scheme 43 and 44). Interestingly in the NMR spectra of the hydroxyl derivative, the hydroxyl proton resonated significantly upfield at δ=-0.18ppm due to shielding while the phosphonium methyl protons had a chemical shift of δ=3.19ppm compared to δ=2.89ppm in the prototype case **47**. (Figure 20) Also, in the ^{13}C-NMR spectrum the methyl carbons on phosphorus resonated further upfield at δ=7.3ppm compared to the same carbon in **47** at δ=9.9ppm. Having fully characterised both the hydroxyl and the methoxyl derivatives, NMR spectra of the product indicated that it consisted mainly of the phosphonium B-methoxyborinate, due to the presence of a resonance at δ=3.12ppm for the methoxyl protons. Therefore, methanol used to dissolve the methyltriphenylphosphonium bromide, must have reacted with the boron-spacer carbon bond displacing the formamide spacer and resulting in the borinate derivative. (Scheme 44(a)) Thus, it would appear that the basicity of the boron-carbon bond, a feature hinted at by the decomposition of the prototype compound **47** with methanol, is enhanced by the presence of the N-formyl group. This chemical feature was considered to be highly relevant to the host-guest chemistry of these clathrands.



68

(i) a) MeOH/THF b) H_2O
(ii) NaCN/DMF
(iii) $Ph_3P^+Me\ Br^-/MeOH$

Scheme 43

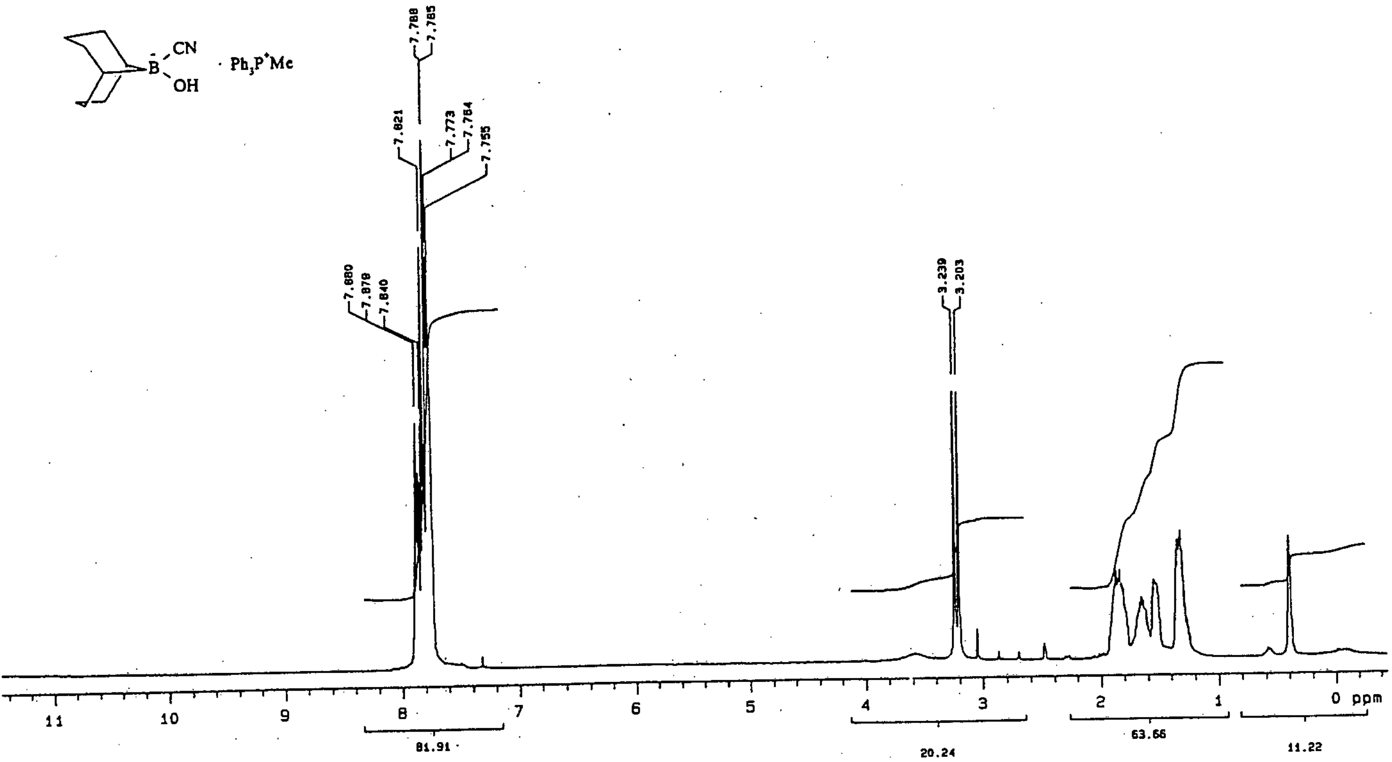
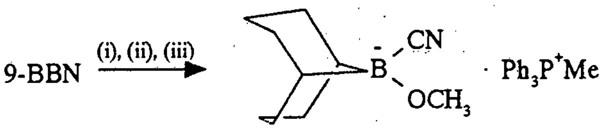


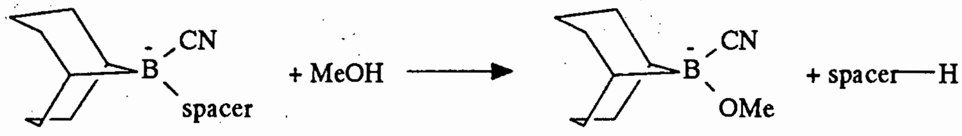
Figure 20



69

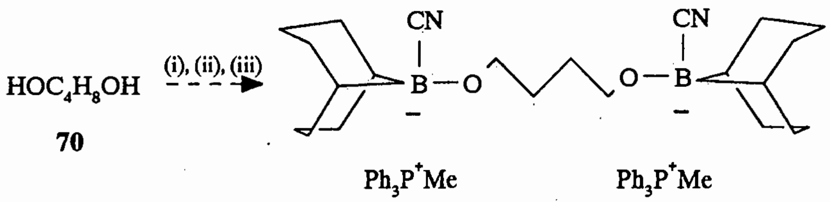
(i) MeOH/THF
(ii) NaCN/DMF
(iii) $Ph_3P^+Me\ Br^-/MeOH$

Scheme 44



Scheme 44(a)

Similar observations were made for the solid product formed from the reaction of 1,4-butanediol **70** with 9-BBN. (Scheme 45) Its phosphonium salt after cyanidation and exchange also displayed resonances corresponding to B-cyano-B-hydroxyborinate **68** as well as B-cyano-B-methoxyborinate **69**, again formed via reaction of the spacer with methanol in an acid-base reaction followed by partial hydrolysis of the methoxyl group in the subsequent aqueous work-up.



(i) 9-BBN (2eq)/THF
(ii) NaCN/DMF
(iii) $Ph_3P^+Me\ Br^-$ (2eq)/MeOH

Scheme 45

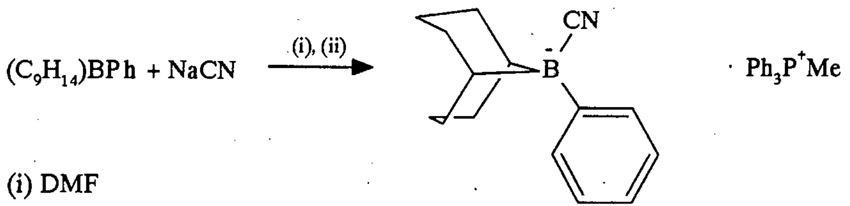
In addition to using the B-cyanoborinate **68** for characterisation purposes, it was decided to investigate its inclusion activity since the hydroxyl group appeared to be an attractive site for hydrogen bonding. However, it turned out to be an unstable waxy solid which only gave undesirable oily substances from host-guest experiments.

In contrast to the polar influence of the hydroxyl and methoxyl group on boron, it was of interest to examine the behaviour of a nonpolar group, such as phenyl. The all important rationale was to explore whether the C_2 symmetry of the anion **47** with the hexamethylene spacer was totally necessary for solid formation and inclusion activity. The synthesis of B-cyano-B-phenylborate involved several steps, involving firstly the preparation of phenyllithium **71** from bromobenzene and butyllithium in a 2M ether medium according to W. Trepka and R. Sonnenfeld[3]. Subsequently, phenyllithium was reacted with B-methoxy-9-BBN **72** to afford B-phenyl-9-BBN **73**[4], which upon cyanidation and sodium exchange resulted in the desired product as depicted in scheme 46. **73A** was satisfactorily characterised by NMR and analysis. No host-guest activity could be observed for benzene, acetonitrile or acetone.

$$PhBr + BuLi \xrightarrow[0°C]{ether} PhLi + BuBr$$

$$(C_9H_{14})BH + MeOH \xrightarrow{THF} (C_9H_{14})BOMe + H_2$$

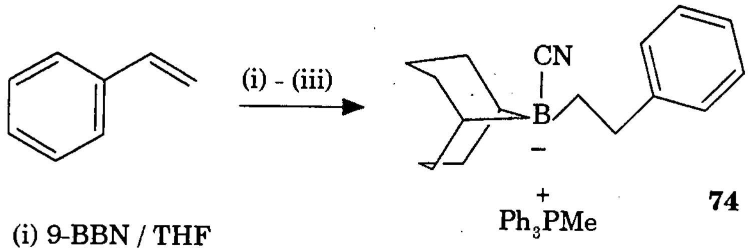
$$(C_9H_{14})BOMe + PhLi \xrightarrow{hexane} (C_9H_{14})BPh + LiOMe$$



(i) DMF
(ii) $Ph_3P^+Me\ Br^-/MeOH$

Scheme 46

In comparison, methyltriphenylphosphonium B-cyano-B-[2-phenethyl]-9-boratabicyclo[3.3.1]nonane **74** was synthesised from freshly distilled styrene and 9-BBN, followed by cyanidation and sodium exchange affording a solid after precipitation of the oil using ethyl acetate. (Scheme 47) The low yield of 29% may be ascribed to the fact that the phenyl group is attached to a flexible ethylene chain, thereby inhibiting crystallisation of the entire product. Indeed, no host-guest activity was displayed with benzene, acetonitrile and acetone for this compound due to its conformational mobility inhibiting crystallisation during the host-guest process.

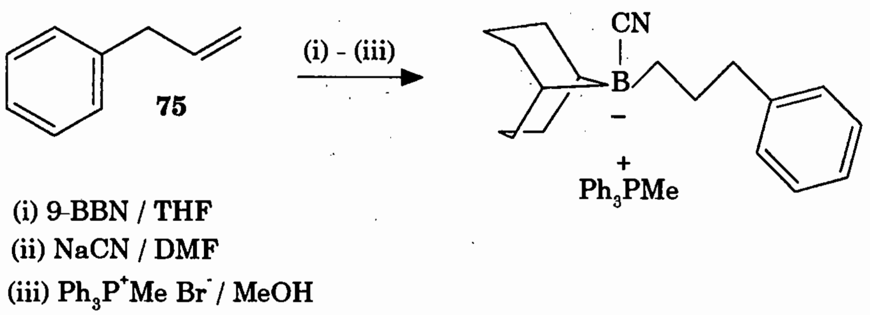


74

(i) 9-BBN / THF
(ii) NaCN / DMF
(iii) $Ph_3P^+Me\ Br^-$ / MeOH

Scheme 47

Furthermore, the reaction of 9-BBN with allylbenzene **75** and subsequent treatment with sodium cyanide and methyltriphenylphosphonium bromide also resulted in an oil, owing to the flexibility of the side chain. (Scheme 48) This corroborates the low yield of the previously described salt **74**.



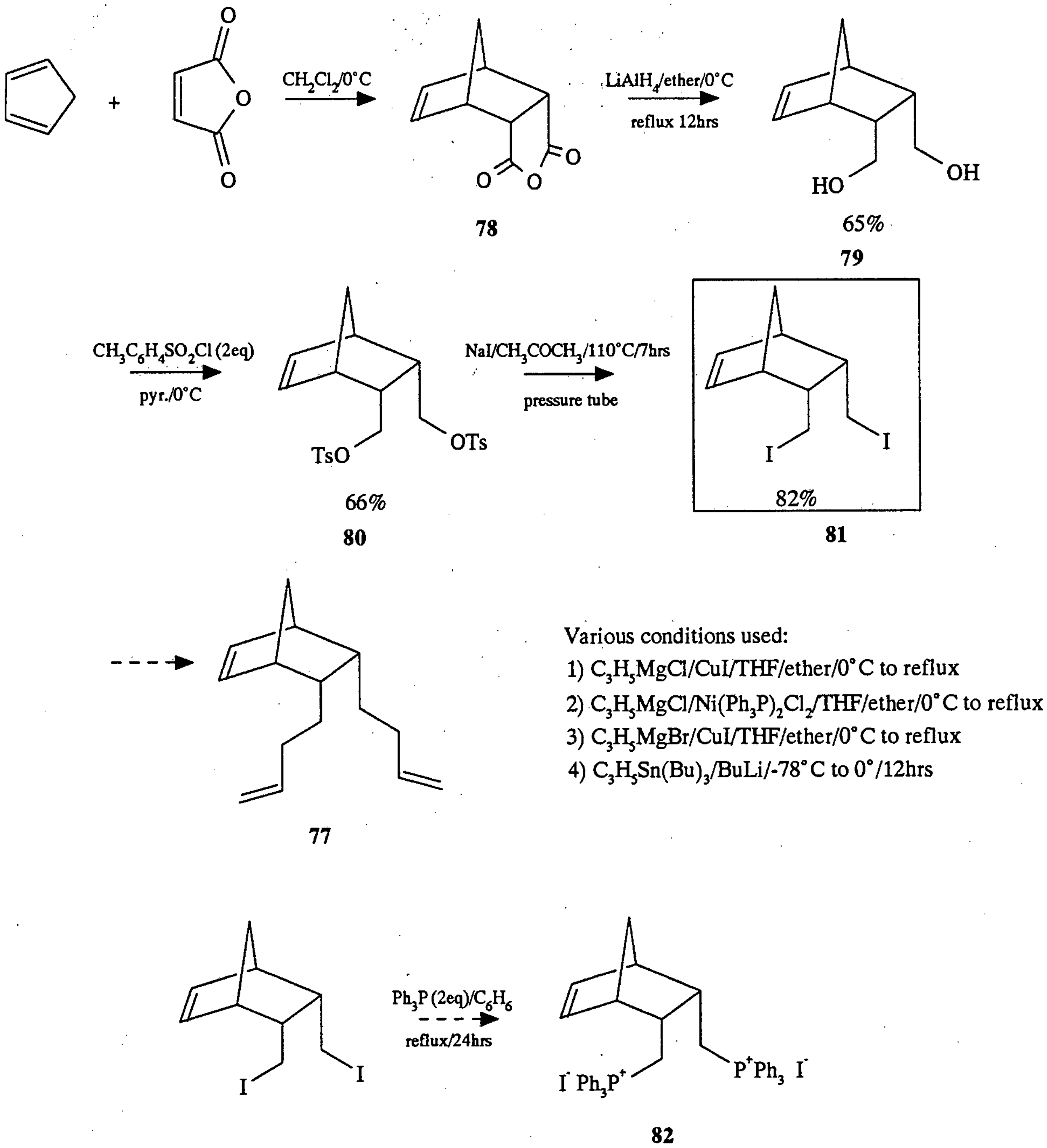
(i) 9-BBN / THF
(ii) NaCN / DMF
(iii) $Ph_3P^+Me\ Br^-$ / MeOH

Scheme 48

Thus, solid monocyanoborate products are only formed when the ligands are rigid enough to promote lattice ordering. In addition, the results of monoborate salts indicate that the C_2 symmetry of the prototype **47** is crucial setting up lattice ordering for efficient guest inclusion.

In view of the problems either at obtaining a solid derivative or with the reactivity of the boron-carbon bond in the spacer, it was decided to opt for an aliphatic spacer of a highly conformationally rigid nature with no activating groups. Since the possibility of including olefins was of interest and with the aforementioned points in mind, a target based on the Diels-Alder adduct **77** of cyclopentadiene as its endo stereoisomer was chosen in which a bulky group with a cis double bond remained in the spacer. The cycloaddition proceeded smoothly producing the endo isomer **78** from a methanol recrystallisation. Use of benzene for the latter gave the exo isomer. The Diels-Alder adduct was then reduced with lithium aluminium hydride to obtain the diol **79**[5]. (Scheme 49) The diol was purified by column chromatography (eluent: ethyl acetate:pet. ether 30:70), and then tosylated with *p*-toluenesulfonyl chloride in pyridine. After column chromatography the ditosylate **80** was obtained in 66% yield. This in turn was reacted with sodium iodide to form the bis-iodide adduct **81** in 82% yield.

Various allylating conditions were employed in order to produce the bis-allyl adduct from the bis-iodide **81**, e.g. activated nucleophilic substitution by either allyl Grignard (2eq.) with either CuI or $Ni(Ph_3P)_2Cl_2$ or allyllithium formed by transmetallation of allyltributyltin with n-BuLi. However, only monoallylation took place as evidenced by ^1H-NMR. Since, hydroboration of the compound would have given an unsymmetrical product, it was decided to convert the bis-iodide adduct **81** to its bis-triphenylphosphonium salt **82** for use as a novel cation later on. This reaction, however, also proved unsuccessful in our hands presumably because of the bulkiness of the two phosphonium groups in close proximity.

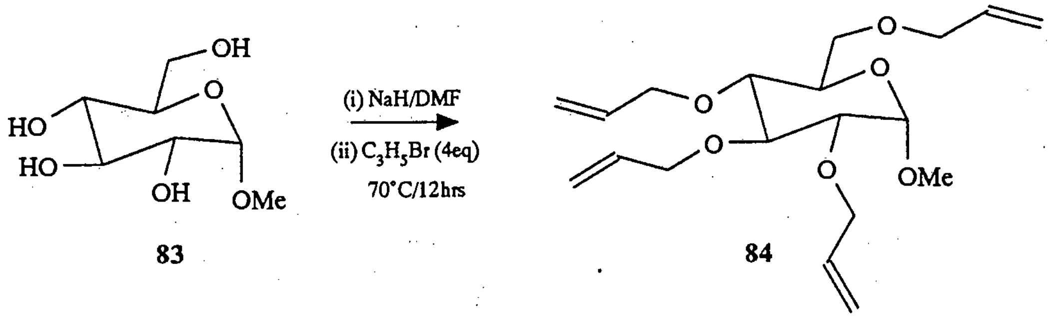


Various conditions used:

1) $C_3H_5MgCl/CuI/THF/ether/0°C$ to reflux
2) $C_3H_5MgCl/Ni(Ph_3P)_2Cl_2/THF/ether/0°C$ to reflux
3) $C_3H_5MgBr/CuI/THF/ether/0°C$ to reflux
4) $C_3H_5Sn(Bu)_3/BuLi/-78°C$ to 0°/12hrs

Scheme 49

Another interesting spacer looked at was based on a carbohydrate backbone. The thinking here was to make use of the oxygen centres for binding as well as the molecule's chirality. Methyl α-D-glucopyranoside **83** was chosen as the starting template and was tetra-allylated with allyl bromide and sodium hydride in DMF to methyl α-2,3,4,6-tetra-O-allyl-D-glucopyranoside **84**[6]. (Scheme 50) In the ^1H and ^{13}C-NMR spectra the allyl protons and the glucopyranoside signals appeared at the expected resonances. (Figure 21) Four equivalents of 9-BBN were then used for hydroboration of the four double bonds, followed by cyanidation, sodium exchange and extraction with ether and water in the normal way. The product formed was an oil, which was presumably too polar to go into the organic layer because of its multiply charged nature.



83 **84**

Scheme 50

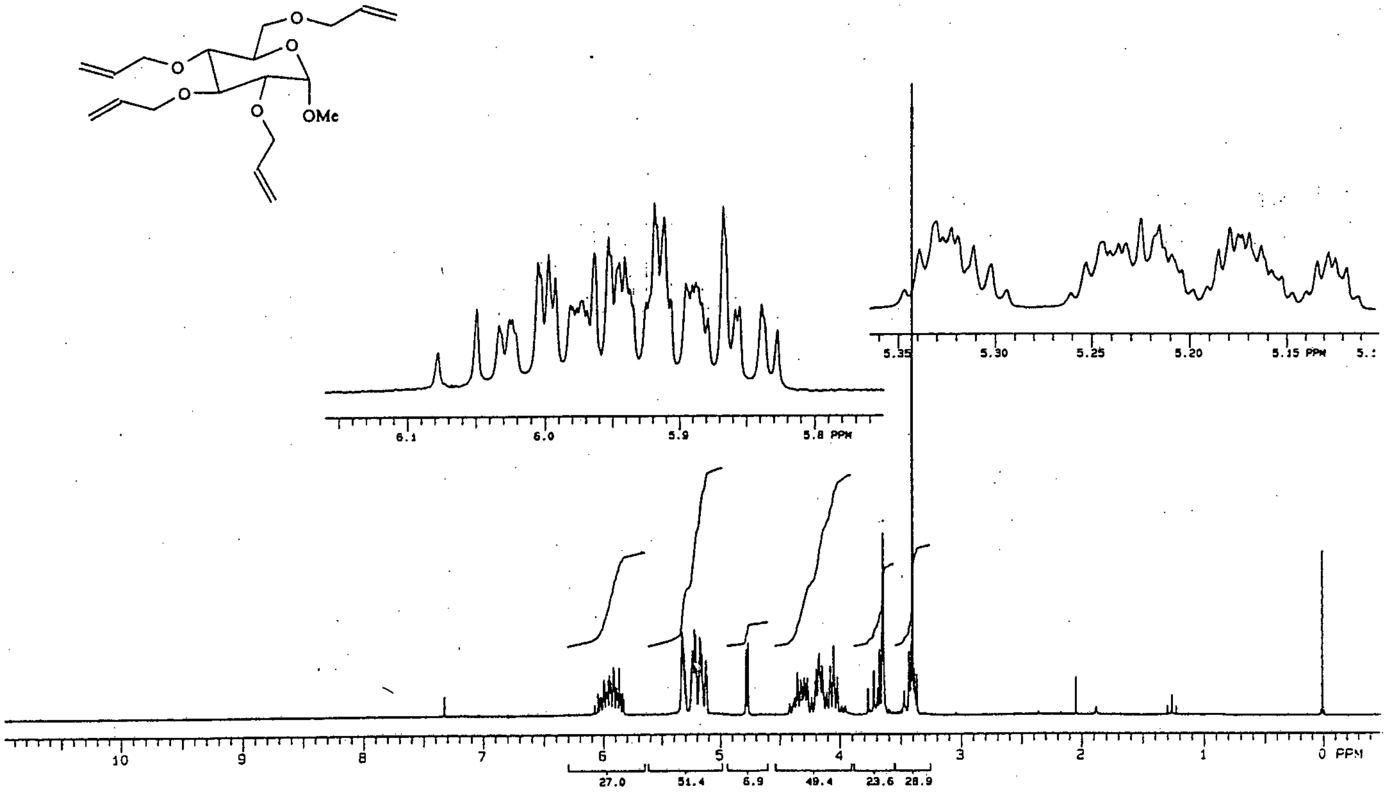
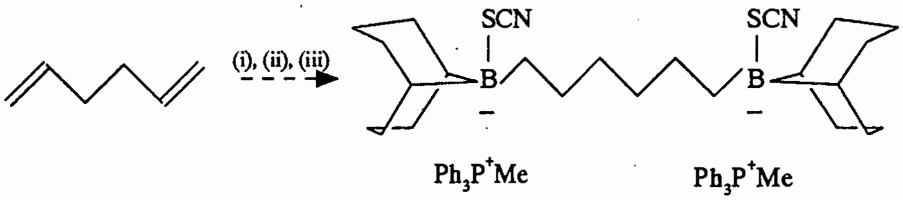


Figure 21

The results obtained in this section indicate that it was quite difficult to come up with a spacer which had both functionality and gave rise to solid borate derivatives. Furthermore, problems arose with the preferential water solubility and/or chemical reactivity of some of the more polar targets.

4.3 VARIATIONS ON THE PRIMER OF THE BORATE ANION

The X-ray structures described in chapters 2 and 3 revealed that a pivotal structural characteristic in the host-guest chemistry was the role of the nitrogen of the cyano group in hydrogen bonding together a coordination assisted lattice. Therefore, it was informative to explore the effect of changing the primer. Once again a major objective was to obtain solid derivatives. Thiocyanate and methoxide were chosen as nucleophilic primers and the corresponding borate phosphonium salts prepared in the usual manner. (Scheme 51) Only a small amount of solid thiocyanate product **85** was obtained, which was insufficient for comprehensive characterisation and host-guest experiments. The reaction of sodium methoxide with 9-BBN and triphenylphosphonium bromide once again formed an oil. This was not unexpected due to the basicity of the boron-carbon bond which readily underwent hydrolysis resulting in a borinate.



85

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaSCN (2eq)/DMF
(iii) $Ph_3P^+Me\ Br^-$ (2eq)/MeOH

Scheme 51

Therefore, to summarise it would be fair to conclude that although changing the spacer/primer element of the anion presented many attractive possibilities on paper, in practice it did not lead to viable, workable materials and it was thus decided to stay with the fortuitous discovery of the hexamethylene spacer and focus on cation variations.

4.4 VARIATIONS ON THE CATION

In view of the disappointment with the handling aspect of spacer modified cyanoborates, the final thrust of the structure-activity study was directed at modifying the cation of the salt. We hoped this to be less problematic regarding the production of solid materials and indeed this proved to be the case. Furthermore, from the outset there was ample scope for changes; specifically the central atom and its coordinated ligands and of particular interest was the influence of such changes on the interactional forces between host and guest according to the X-ray data discussed in chapters 2 and 3.

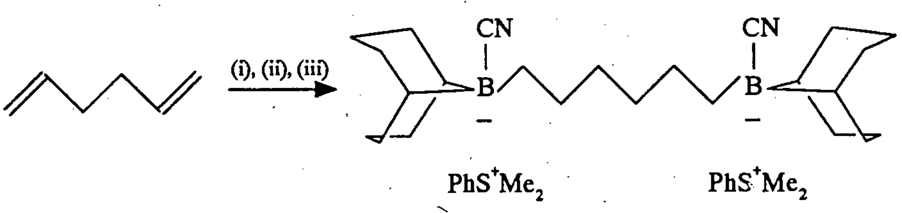
4.4.1 SYNTHESIS AND STRUCTURE ACTIVITY OF A SULFONIUM SALT

Initially, it was decided to vary the central atom of the cation as a group V element and as sulfur. For consistency, it was desirable to keep the substituents the same as the methyltriphenylphosphonium prototype but this proved to be impossible in some cases. Indeed, this was the case with the first cation chosen based on sulfur. In our hands it was only possible to synthesise dimethylphenylsulfonium hexafluorophosphate **86**, via thioanisole methylation with dimethyl sulfate as the key step, and not its methyldiphenylsulfonium counterpart. (Scheme 52) Obviously, in this case the sulfonium ion is pyramidal and not tetrahedral. Sulfonium ion exchange with sodium cyanoborate **15** in the usual manner readily afforded a colourless solid **87** in a high yield of 98%. ^1H and ^{13}C-NMR gave all of the expected signals in the correct ratios with the methyl group on sulfur resonating at 3.27ppm and at 9.9ppm respectively. (Figure 22) The salt showed no host-guest activity with acetonitrile and acetone, and only included benzene in trace amounts. Thus, there was no improvement on the prototype **47**.

$$PhSMe + Me_2SO_4 \longrightarrow PhS^+Me_2\ MeSO_4^-$$

$$PhS^+Me_2\ MeSO_4^- + NH_4^+\ PF_6^- \xrightarrow{H_2O} PhS^+Me_2\ PF_6^-$$

86



87

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $PhS^+Me_2\ PF_6^-$(2eq)/MeOH

Scheme 52

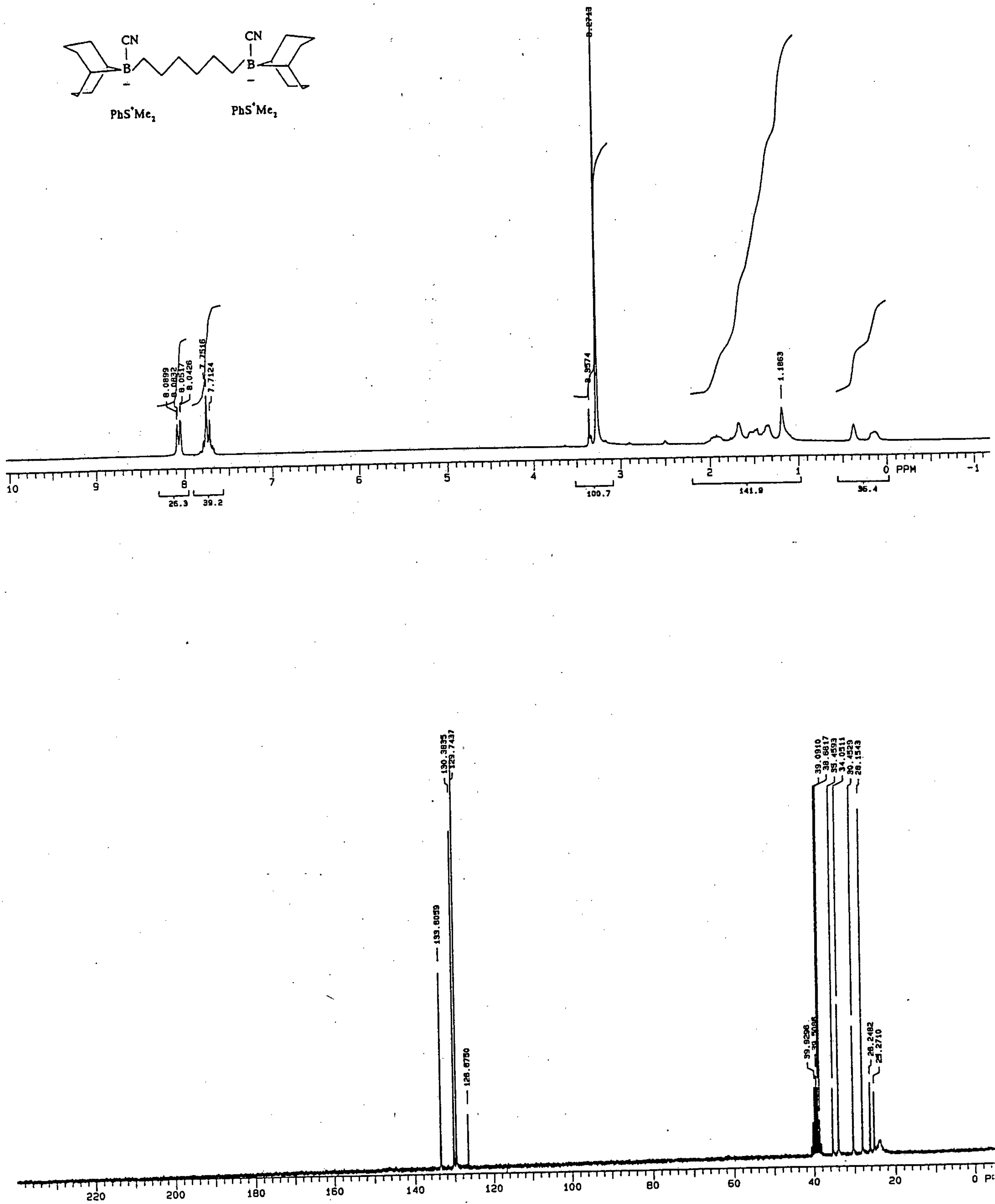
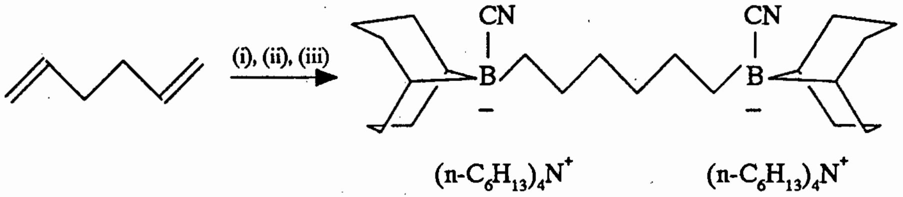

CN
B
CN
B
PhS⁺Me₂
PhS⁺Me₂
8.0899
8.0832
8.0517
8.0426
7.7516
7.7124
3.3574
3.2743
1.1863
10
9
8
7
6
5
4
3
2
1
0 PPM
-1
26.3
39.2
100.7
141.9
36.4
133.6059
130.3835
129.7437
126.6750
39.0910
38.6817
35.4593
34.0511
30.4529
28.1543
39.9296
39.5084
26.2482
25.2710
220
200
180
160
140
120
100
80
60
40
20
0 P

Figure 22

Based on the X-ray structure data in chapters 2 and 3, we can only conclude that the dimethylphenylsulfonium ion does not meet the steric and electronic requirements for establishing a coordination assisted lattice for guest inclusion.

4.4.2 SYNTHESIS AND STRUCTURE ACTIVITY OF AMMONIUM SALTS

Research on the host-guest activity of tetraalkylammonium borates and aluminates by L. Nassimbeni and J. Atwood respectively was described extensively in chapters 2 and 3 and their results suggested that it would be highly informative to synthesise some tetraalkylammonium cyanoborates. Of particular interest was a comparison of L. Nassimbeni's tetraalkylammoniun tetraalkylborate salts[7], in which the anion was $[(s\text{-}Bu)_3B(n\text{-}Bu)]^-$ and the cation $[N(n\text{-}C_6H_{13})_4]^+$ and which formed liquid clathrates with a range of aromatic and aliphatic guest molecules, with our cyanoborate system as a tetrahexylammonium salt **88**. For the synthesis of the latter the sodium cyanoborate **15** was exchanged with tetrahexylammonium bromide in the usual way to give a wax-like product due to the flexibility of the hexyl chains on nitrogen. (Scheme 53) In this regard our compound showed similar physical characteristics to Nassimbeni's. The host **88** displayed inclusion activity towards aromatics, such as benzene and xylene, but the ratios obtained were not reproducible and it did not include any aliphatics.



88

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $(n\text{-}C_6H_{13})_4N^+\,Br^-$ (2eq)/MeOH

Scheme 53

Attention was then turned towards synthesising the methyltriphenylammonium cyanoborate as a comparison with the methyltriphenylphosphonium cyanoborate **47**. However, the preparation of methyltriphenylammonium iodide **89** via methylation of the tertiary amine, proved unsuccessful in our hands. Triphenylamine was reacted with various methylating agents including methyl iodide, dimethyl sulfate and trimethyloxonium tetrafluoroborate under forcing conditions all to no avail[8]. Scheme 54.

$$Ph_3N + MeI \dashrightarrow Ph_3N^+Me\ I^-$$

89

Various conditions:

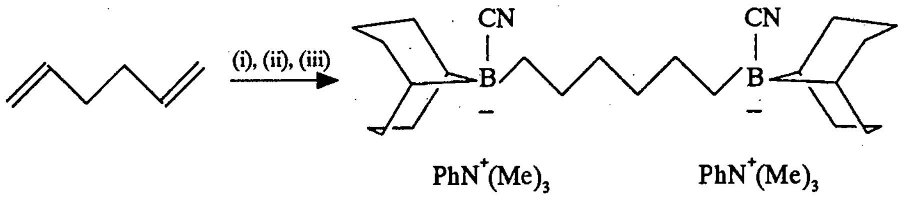
1) C_6H_6/12hrs/RT
2) MeOH/50°C/12hrs
3) DMF/100°C/4hrs

Scheme 54

Therefore, reluctantly we settled for the simpler phenyltrimethylammonium iodide cation **90**, which was readily prepared by reacting N,N-dimethylaniline with methyl iodide followed by recrystallisation from a mixture of ethyl acetate and methanol (3:1). Its reaction with sodium cyanoborate **15** produced a colourless solid **91** in a low yield of 45% after extraction, which was attributed to water solubility of the complex during extraction. (Scheme 55) The ^{1}H-NMR spectrum showed a clear singlet at 3.62ppm for the ammonium methyl group. The downfield shift for this group compared to the methyl of the methylphosphonium ion of **47** is also observed in the ^{13}C-NMR spectrum where it resonated at δ=56.4ppm. Figure 23.

$$PhN(Me)_2 + MeI \xrightarrow{DMF/12hrs} PhN^+(Me)_3\ I^-$$

90



91

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $PhN^+(Me)_3\ I^-$ (2eq)/MeOH

Scheme 55

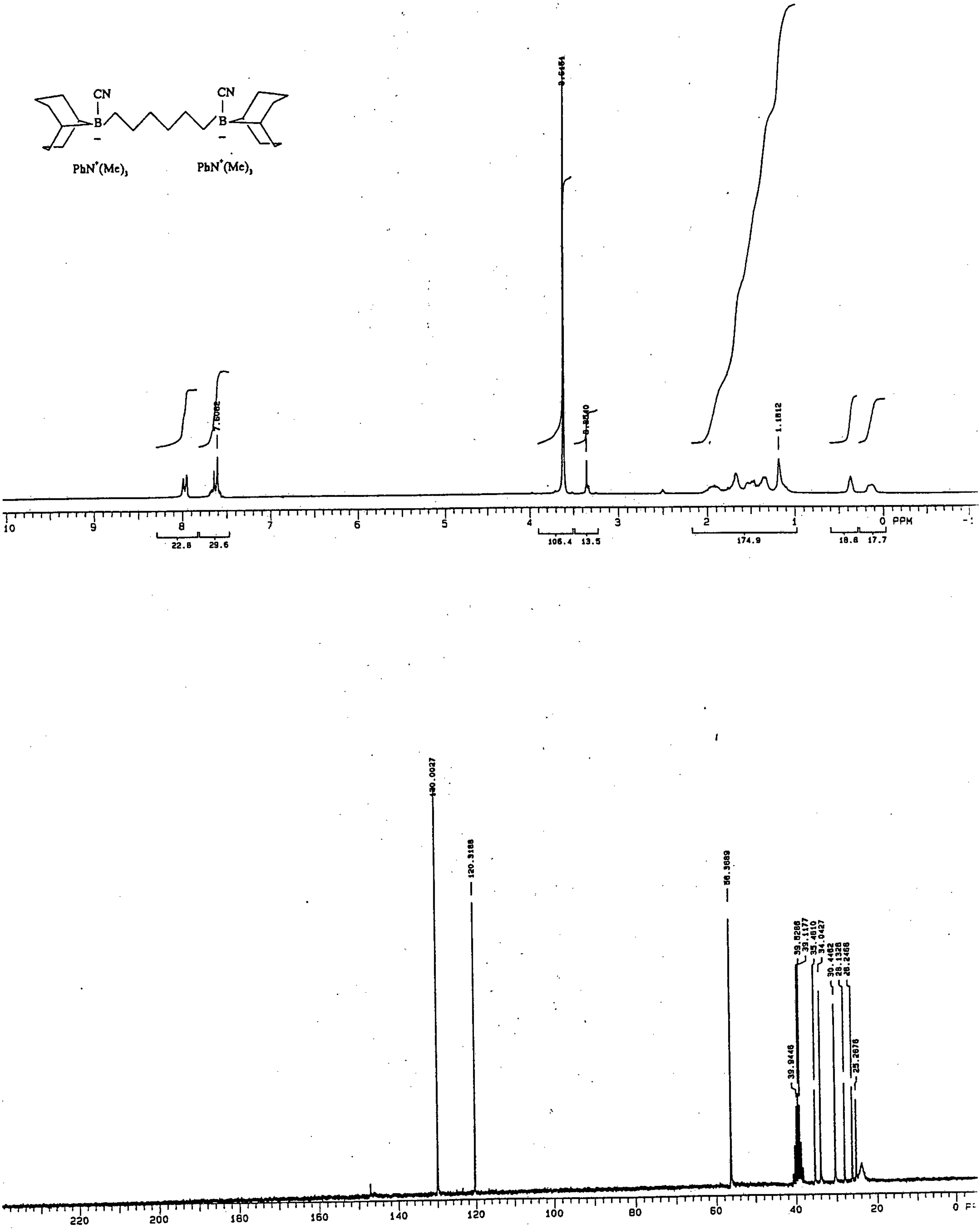

CN
B
CN
B
PhN$^+$(Me)$_3$
PhN$^+$(Me)$_3$
7.5062
3.6461
3.3540
1.1812
10
9
8
7
6
5
4
3
2
1
0 PPM
22.8
29.6
106.4
13.5
174.9
18.8
17.7
130.0027
120.3188
56.9889
39.5286
39.1177
35.4810
34.0427
30.4462
28.1328
26.2466
39.9446
25.2676
220
200
180
160
140
120
100
80
60
40
20
0

Figure 23

A comprehensive inclusion study with **91** was carried out covering a range of guests based on polarity. Absolutely no inclusion was observed which was considered to be a highly significant result. The explanation offered is that the smaller, harder trimethylphenylammonium cation forms a much closer packed lattice compared to the methyltriphenylphosphonium cyanoborate prototype, effectively precluding any clathrate activity because of the absence of lattice voids. This result certainly highlighted the importance of tuning both the steric and electronic characteristics of the cation for successful inclusion activity as we will see in forthcoming aspects of this chapter.

TABLE 16

Results of Host-Guest ratios of
$[(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\cdot 2PhN^+Me_3]$
in CH_2Cl_2/THF by ^1H-NMR.

Guest	H:G[a]	H:G[a]
1-Hexene	1:0	1:0
Benzene	1:0	1:0
p-Xylene	1:0	1:0
Mesitylene	1:0	1:0
Anisole	1:0	1:0
N,N-Dimethylaniline	1:0	1:0
2-Methylfuran	1:0	1:0
Furan	1:0	1:0
Benzothiazole	1:0	1:0
DMF	1:0	1:0
Ethyl Acetate	1:0	1:0

[a] same batch of sample

Since methyltriphenylammonium cyanoborate could not be synthesised, it was decided to try benzylating triphenylamine in the hope that hydrogen bonding between the borate cyano nitrogen and a benzylic methylene hydrogen might be possible to form an ordered lattice structure. Triphenylamine was heated with neat benzyl bromide, but unfortunately only starting material was recovered. Scheme 56.

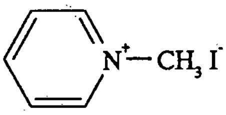
$$Ph_3N + PhCH_2Br \dashrightarrow Ph_3N^+CH_2Ph\ Br^-$$

Scheme 56

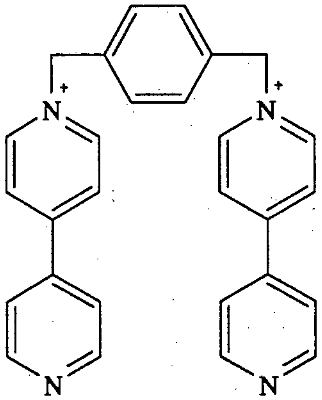
To end off the series of ammonium salts, the exchange of ammonium **92**, methylpyridinium **93** and the Stoddart "horse-shoe" cation **94** with the sodium cyanoborate **15** was carried out. The products in all three instances were oils and could not be crystallised. In the case of methylpyridinium, a highly coloured product indicated the possibility of REDOX activity between cation and anion.

NH_4Cl

92



93



$2\,PF_6^-$

94

Once again, the results obtained were disappointing either from a synthetic or inclusion activity viewpoint. Thus, although more synthetic variations on the ammonium might still have been attempted it was decided to focus on phosphonium and arsonium salts.

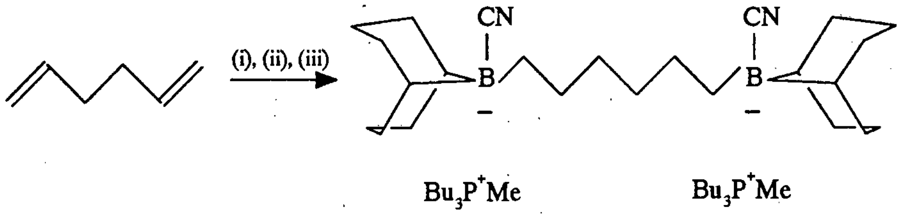
4.4.3 SYNTHESES AND STRUCTURE ACTIVITY OF PHOSPHONIUM SALTS

From the outset in this part of the study, we were aware of being able to take advantage of the greater nucleophilicity of phosphorus compared to nitrogen to prepare a wide variety of phosphonium ions by nucleophilic substitution. Regarding substitution changes, we were particularly interested in the affect of electronically modifying the phenyl groups on phosphorus as well as the hydrogen-bonding centre at the methyl. Firstly, however, the triphenyl group on methyltriphenylphosphonium cation was changed to tributyl, so as to investigate the role of alkyl groups vs. phenyl groups with respect to host-guest activity. Interestingly, Nassimbeni's borates had shown to be inactive with methyltriphenylphosphonium as counterion. Methyltributylphosphonium iodide **95** was prepared by methylation of tributylphosphine[9] and then exchanged with the sodium cyanoborate **15** as depicted in scheme 57 below.

$$Bu_3P + MeI \xrightarrow{C_6H_6} Bu_3P^+Me\,I^-$$

98%

95



(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $Bu_3P^+Me\,I^-$ (2eq)/MeOH

Scheme 57

The reaction conditions and extraction followed the same procedure as for methyltriphenylphosphonium cyanoborate, except an oil was obtained which never crystallised out. Once again, this is presumably due to the flexibility of the butyl moieties on phosphorus compared to the rigidity of the phenyl groups of the prototype **47**, preventing rigid formation of a crystal lattice structure. Owing to this compound being an oil, its host-guest activity was not tested.

In view of problems with the physical characteristics of these compounds, the tetraphenylphosphonium cyanoborate **96** was synthesised via reaction of tetraphenylphosphonium bromide with sodium cyanoborate **15**. This time a solid formed from the extraction procedure, which was isolated in a 72% yield. (Scheme 58) The solid structure can be attributed to the bulky, rigid phenyl rings on phosphorus. In the ^{1}H and ^{13}C-NMR spectra the signals of the borate anion, as well as of the cation resonated at the expected chemical shifts compared to **47**. Figure 24.

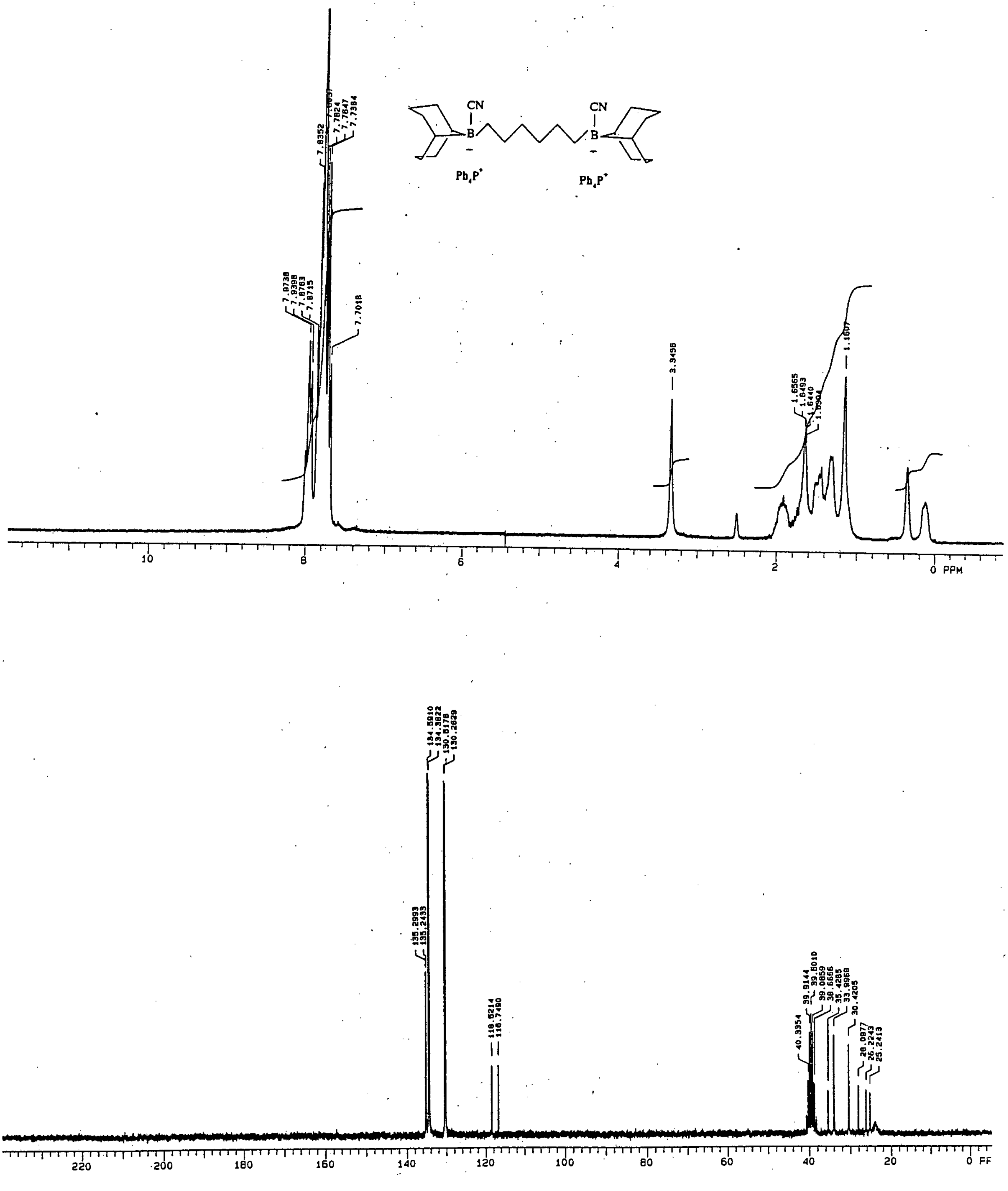
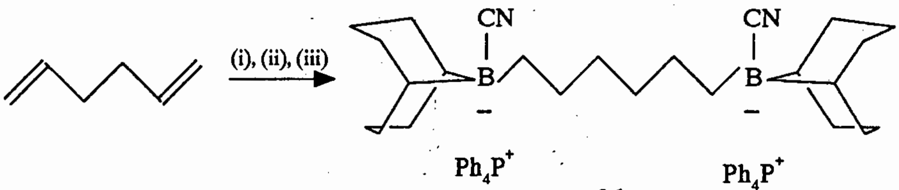

CN
B
Ph$_4$P$^+$
CN
B
Ph$_4$P$^+$
7.8352
7.8037
7.7824
7.7647
7.7384
7.8738
7.9398
7.8763
7.8715
7.7018
3.3456
1.6565
1.6493
1.6440
1.6304
1.1607
10
8
6
4
2
0 PPM
135.2993
135.2433
134.5910
134.3622
130.5178
130.2829
118.5214
116.7490
40.3954
39.9144
39.8010
39.0859
38.6666
35.4285
33.9969
30.4205
28.0877
26.2243
25.2413
220
200
180
160
140
120
100
80
60
40
20
0 PF

Figure 24

Once again, this compound displayed no inclusion activity (Table 17) which was a significant result since it confirmed the importance of having an all important centre involved in hydrogen bonding to the cyano nitrogen for creation of a coordination assisted lattice. In the case of the tetraphenylphosphonium compound, a lack of a suitable hydrogen bonding donor centre[10] as well as possibly the steric bulk of the cation precluded this.



96

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) Ph_4P^+ Br^- (2eq)/MeOH

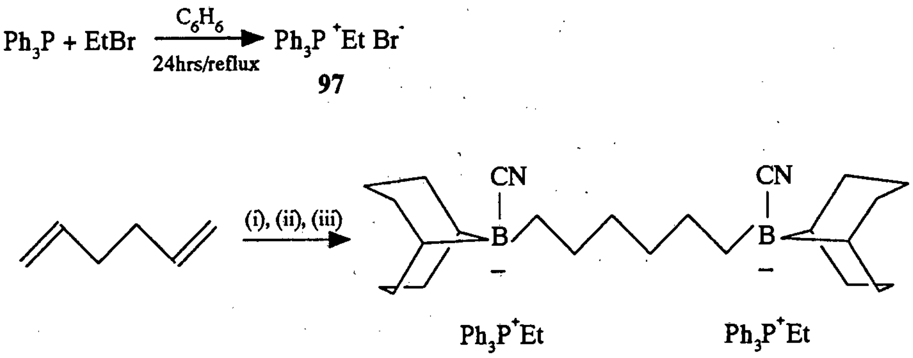
Scheme 58

TABLE 17
Results of Host-Guest ratios of
$[(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\cdot 2Ph_4P^+]$
in CH_2Cl_2 by ^1H-NMR.

Guest	H:G[a]	H:G[a]
1-Hexene	1:0	1:0
Benzene	1:0	1:0
Mesitylene	1:0	1:0
Anisole	1:0	1:0
N,N-Dimethylaniline	1:0	1:0
Furan	1:0	1:0
Ethyl Acetate	1:0	1:0
DMF	1:0	1:0

[a] same batch of sample

The next cation chosen was ethyltriphenylphosphonium **97** since the three phenyl groups on phosphorus seemed to confer some solid character to the phosphonium borate compound. (Scheme 59) Furthermore, it was now important to probe the sensitivity of the said hydrogen bonding donor centre toward functional changes around it. The methyl of the ethyl group is inductively releasing and therefore the methylene hydrogens are less positive compared to those on the methyl group of methyltriphenylphosphonium. Furthermore, the conformational mobility of the extra methyl group was also seen as a complication. Indeed, the only guest to be included was benzene, indicating as perceived, that the steric and electronic characteristics of the methyl hydrogens are of paramount importance in determining inclusion activity.



$$Ph_3P + EtBr \xrightarrow[24hrs/reflux]{C_6H_6} Ph_3P^+Et\ Br^-$$

97

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $Ph_3P^+Et\ Br^-$ (2eq)/MeOH

Scheme 59

TABLE 18
Results of Host-Guest ratios of
$[(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\cdot 2Ph_3P^+CH_2CH_3]$
in CH_2Cl_2 by ^1H-NMR.

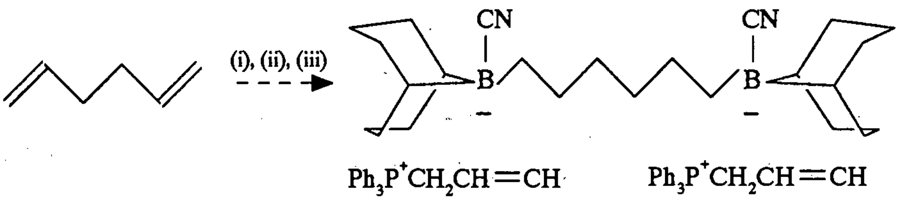
Guest	H:G[a]	H:G[a]
1-Hexene	1:0	1:0
Benzene	1:0.2	1:0.2
Mesitylene	1:0	1:0
Anisole	1:0	1:0
N,N-Dimethylaniline	1:0	1:0
Furan	1:0	1:0
Ethyl Acetate	1:0	1:0
DMF	1:0	1:0
Hexane	1:0	1:0

[a] same batch of sample

From the results in Table 18, it became clear that extending the alkyl chain on phosphorus was unlikely to switch on host-guest activity and so further modifications along these lines were dropped. However, we were still interested on the effect of the presence of a double bond. Thus, it was decided to prepare propenylphosphonium salts, such as 1-propenyltriphenylphosphonium bromide **98** and 2-methyl-1-propenyltriphenylphosphonium chloride **99**[9]. Synthesis of these two phosphonium salts was carried out in a pressure tube without solvent at elevated temperatures. (Scheme 60) Exchange of the phosphonium salts with the sodium cyanoborate **15** resulted in oils, which slowly crystallised out, after washing with ethyl acetate. The cyanoborate of 1-propenyltriphenylphosphonium salt **100** included ether from the work-up and also displayed the ominous triplet at approx. δ=4ppm due to oxidation as discussed in chapter 1. Also in the ^{13}C-NMR spectrum resonances at δ=65.8ppm and 71.5ppm appeared relating to a B-OR species as was discussed in chapters 1 and 2. Conversely, the borate salt of the 2-methyl-1-propenyltriphenylphosphonium ion gave the desired product without any oxidation having taken place.

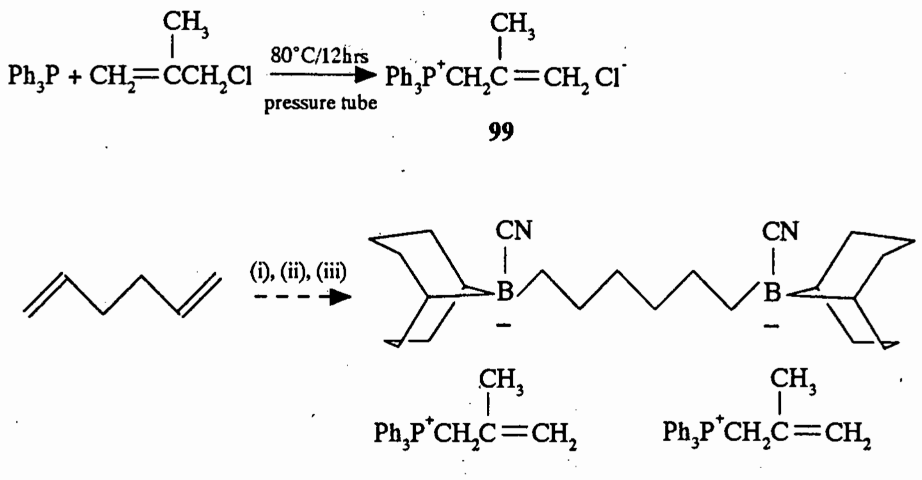
$$Ph_3P + CH_2{=}CHCH_2Br \xrightarrow[\text{pressure tube}]{65^{\circ}C/3hrs/RT} Ph_3P^+CH_2CH{=}CH\,Br^-$$

98



100

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $Ph_3P^+CH_2CHCH\ Br^-$ (2eq)/MeOH



$$Ph_3P + CH_2{=}C(CH_3)CH_2Cl \xrightarrow[\text{pressure tube}]{80^\circ C/12hrs} Ph_3P^+CH_2C(CH_3){=}CH_2\ Cl^-$$

99

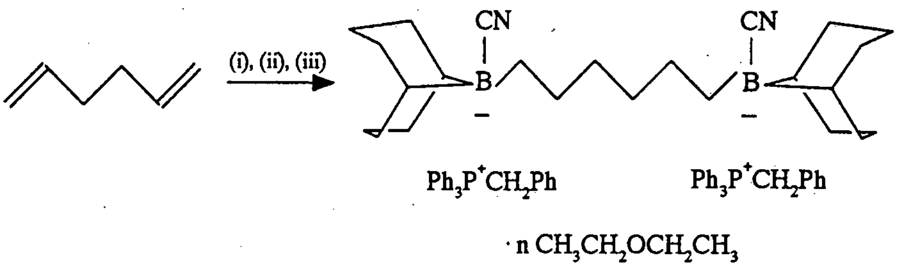
(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $Ph_3P^+CH_2C(CH_3)CH_2\ Cl^-$ (2eq)/MeOH

Scheme 60

At this point we had become aware of the subtle structural requirements of these clathrands. For the next functional group modification we opted for benzyl instead of methyl. We argued that this group would have less conformational flexibility than ethyl and yet still retain enough positive character at the hydrogens of the methylene group or even on the new ring for hydrogen bonding. Moreover, it was synthetically viable. Benzyltriphenylphosphonium bromide **101** was prepared by reacting triphenylphosphine with benzyl bromide[9] and recrystallising from ethyl acetate and methanol. On exchange of the phosphonium salt with the sodium cyanoborate **15**, a solid immediately formed during the extraction. This solid not only gave spectral (Figure 25) data consistent with the bis-benzylphosphonium structure shown in scheme 61, but also included diethyl ether from the extraction in a host-guest ratio of 1:0.4-1.0 after drying *in vacuo*, as determined by TG analyses. (Figure 26) As evidenced by the ^{1}H-NMR spectrum the benzylic methylene protons appeared as a doublet at δ=4.85ppm due to hydrogen-phosphorus coupling, which was a downfield shift as expected compared to the methyl protons of **47**. The benzylic ring protons resonated upfield compared to the aromatic protons of the ring on phosphorus. Similarly, in the ^{13}C-NMR spectrum the benzylic methylene carbon resonated at 30.9ppm compared to 26.0ppm for the methyl group of **47**, with a carbon-phosphorus coupling of 47.6Hz. Carbon-phosphorus coupling can also be observed in all of the benzylic ring carbons, although the *meta* and *para* carbons are relatively far away from the phosphonium centre. Once again, the range of included ether may have been due to pressure changes in the vacuum and/or temperature variations in the laboratory.

$$Ph_3P + PhCH_2Br \xrightarrow[24hrs/reflux]{C_6H_6} Ph_3P^+CH_2Ph\ Br^-$$

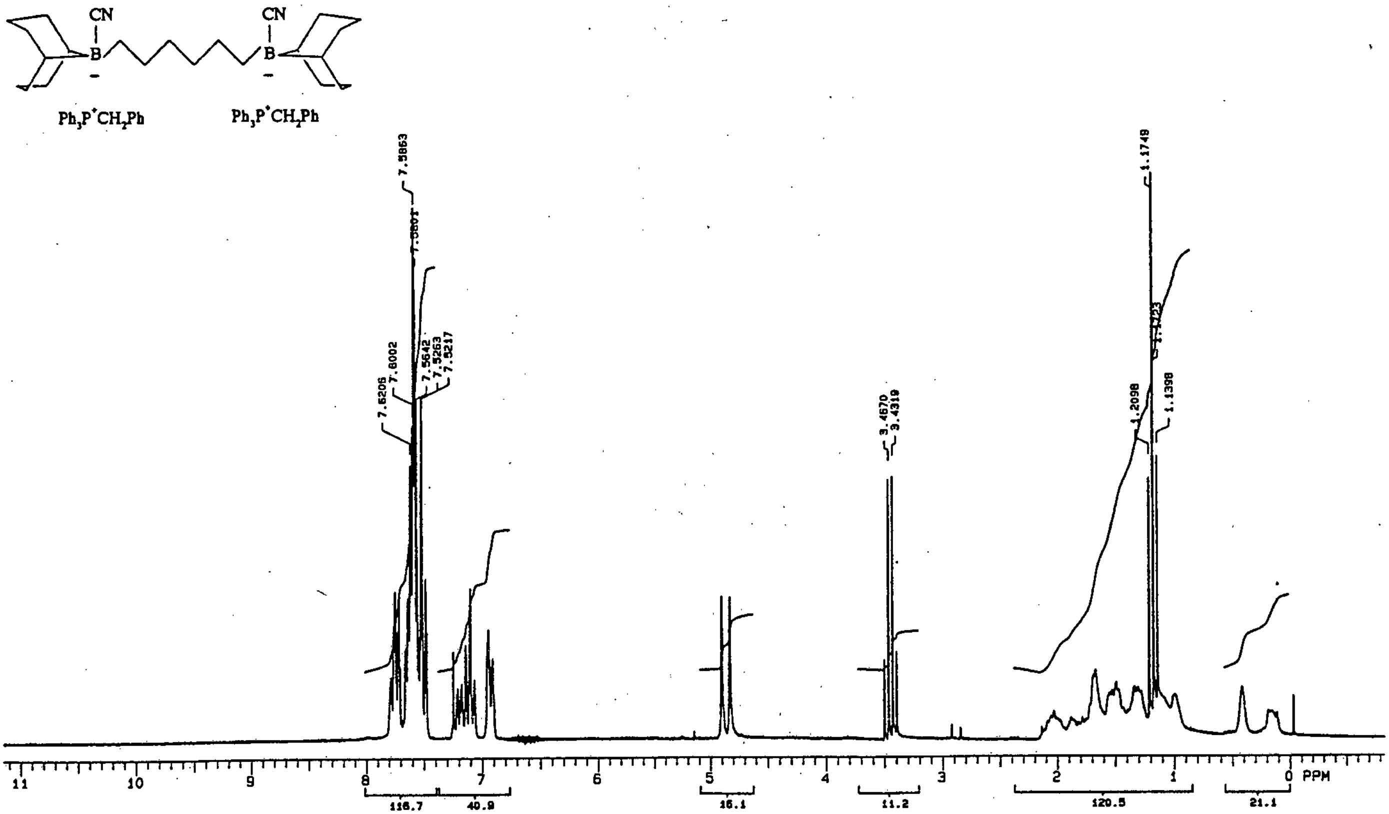
101



102

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $Ph_3P^+CH_2Ph\ Br^-$ (2eq)/MeOH

Scheme 61



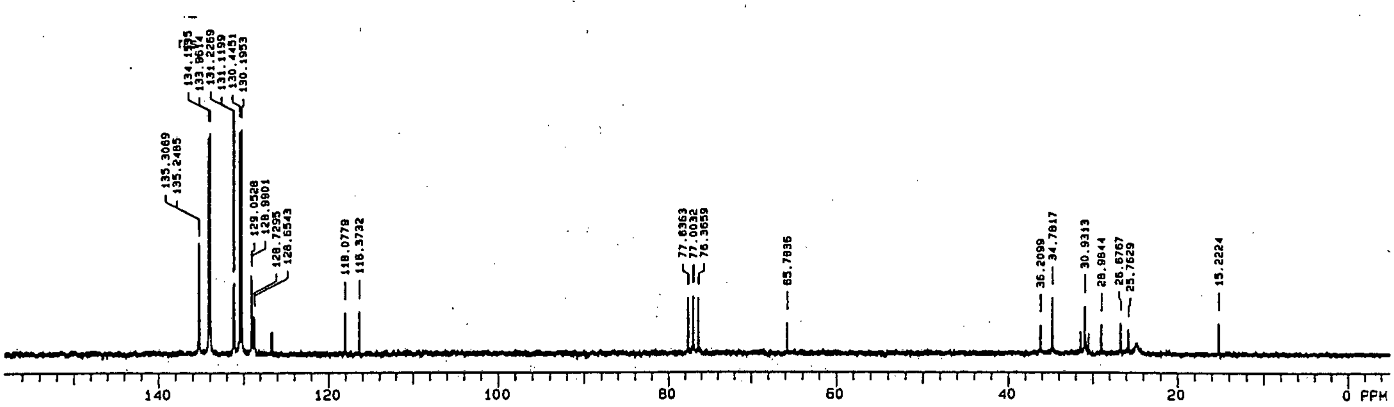


Figure 25

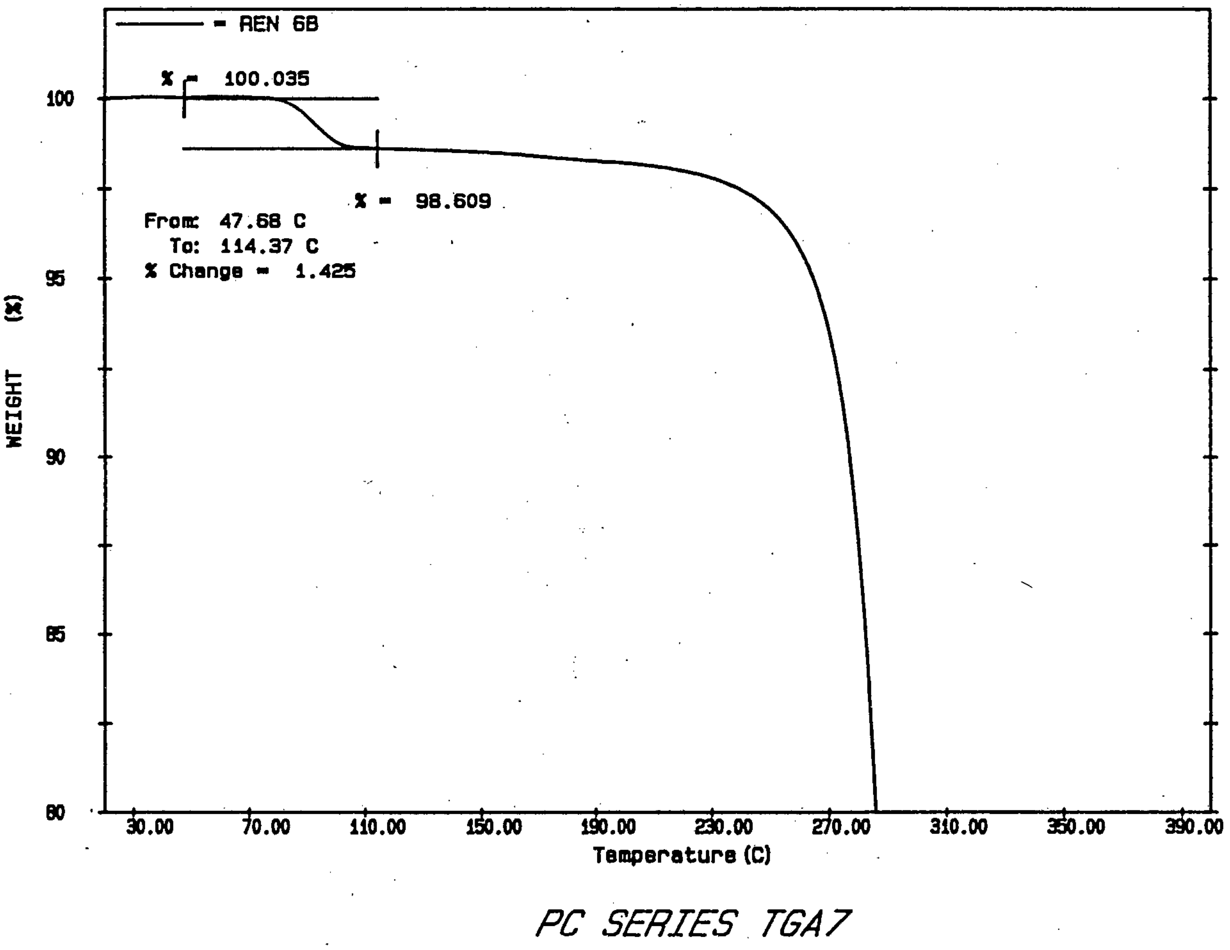


Figure 26

Unfortunately, it was impossible to obtain an X-ray structure of **102 with** included ether, because the solid was amorphous. Hence, diffraction patterns were recorded of the host by itself and the host-guest compound. The patterns were different indicating that the structures were indeed dissimilar and that the host-guest complex was not a mixture of two substances but a unique structural unit. Figure 27.

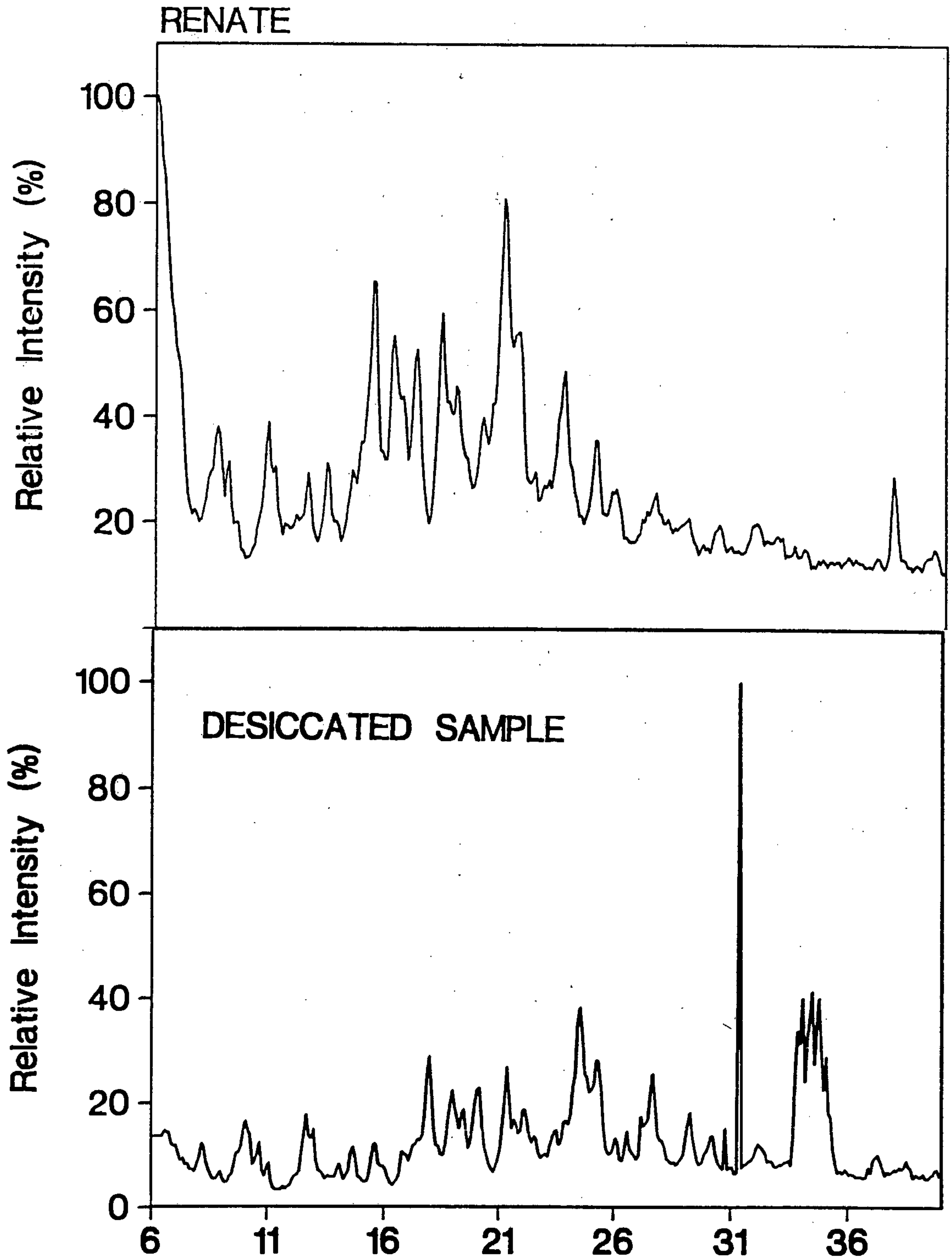


Figure 27

The ether was held very tightly and could only be removed at 70°C *in vacuo* overnight, which was an indication of the strength of the intermolecular forces operating within the lattice. (Figure 26) However, the inclusion characteristics of the benzyltriphenylphosphonium cyanoborate salt **102** was only determined once ether was removed. This was done by vacuum drying (0.5mmHg) the host at 80°C for 16 hours and by ^{1}H-NMR **102** stood up to the drying process.

Host-guest experiments were carried out by dissolving the 'free' host in CH_2Cl_2, which was not included. The mixtures were then left to evaporate until crystals formed which were filtered, washed with hexane and air dried. A range of guests was examined, a particular interest being whether or not the guest spectrum would be shifted towards a more polar range compared to **47**. Table 19 summarises the results. Inclusion experiments were run in duplicate and the H:G ratios gave good reproducible results. Indeed, we were gratified to observe that in general the host:guest ratios were much higher than for the methyltriphenylphosphonium cyanoborate salt **47**. Also, polar solvents were included to a greater extent, such as anisole, N,N-dimethylaniline, benzothiazole and 2-methoxyfuran, which is an indication that the benzyl moiety is capable of shifting the guest range to a more polar spectrum. Furthermore, this host is much more selective than the methyltriphenylphosphonium cyanoborate prototype salt **47**. Thus, the structure-activity study suggests that substituting a benzyl group for a methyl group gives the borate salt enough bulkiness together with limited conformational flexibility, to form a stable ionic host lattice with larger voids and with the methylene protons on benzyl still being able to participate in CH···N hydrogen bonding.

TABLE 19
Results of Host-Guest ratios of
$[(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\cdot 2Ph_3P^+CH_2Ph\cdot 0$ ether]
in CH_2Cl_2 by ^1H-NMR.

Guest	H:G[a]		H:G[a]		TGA[a]
Hexane	1:0	1:0	1:0	1:0	1:0
1-Hexene	1:0	1:0	1:0	1:0	1:0
Benzene	1:1.0	1:1.1	1:1.5	1:1.8	1:0.9
Toluene	1:1.8	1:2.1	1:1.4	1:1.4	1:1.4
o-Xylene	1:1.2	1:1.3	1:1.2	1:1.0	1:0.9
m-Xylene	1:2.5	1:2.0	1:2.3	1:2.7	1:1.8
p-Xylene	1:1:9	1:2.1	1:2.4	1:2.6	1:2.0
Mesitylene	1:2.2	1:2.0	1:1.8	1:1.9	1:1.1.8
Anisole	1:2.1	1:2.2	1:1.9	1:2.2	1:2.0
N,N-Dimethylaniline	1:1.2	1:1.1	1:1.3	1:1.5	1:0.9
Furan	1:0	1:0	1:0	1:0	1:0
2-Methylfuran	1:1.0	1:0.9	1:0.8	1:0.8	1:0.8
2-Methoxyfuran	1:1.6	1:1.8	1:1.5	1:1.6	1:1.4
Thiophene	1:0	1:0	1:0	1:0	1:0
Furfuraldehyde	1:1.1	1:0.9	1:0.8	1:0.9	1:0.7
Benzothiazole	1:2.3	1:2.6	1:2.5	1:2.7	1:2.1
DMF	1:1.3	1:1.5	1:1.2	1:1.1	1:1.0
Acetone	1:0	1:0	1:0	1:0	1:0

[a] same batch of sample

The host-guest activity was also determined without any solvent by mixing the two substances together and leaving the excess guest to evaporate as before (Chapter 2). In this case, the host includes polar guests more readily, than nonpolar ones. Moreover, the host-guest ratios are larger than those obtained by using a solvent. Table 20.

TABLE 20
Host-Guest experiments performed without solvent (neat) and ratios calculated from ^{1}H-NMR spectrum.

Guest	H:G
Hexane	1:0
1-Hexene	1:0
Benzene	1:2
Toluene	1:0
o-Xylene	1:0
Mesitylene	1:Tr
Anisole	1:2.2
N,N-Dimethylaniline	1:2.5
2-Methylfuran	1:0
Thiophene	1:1.2
Thiophenol	wax
THF	1:0
Acetone	1:0
Tetrahydrofuran	1:0
Benzothiazole	1:2.9

The preferential inclusion of one guest over another was also looked at for guests of similar boiling points and polarity. (Table 21) In general, the more polar solvent was taken up preferentially, except in the case of DMF and anisole. In this case, the host-guest ratio was higher for anisole than for DMF indicating that the interactional forces complexing anisole are stronger than those for DMF, which is the other way round for the prototype salt **47**, which includes only DMF and not anisole. Thus, the extra phenyl ring on the phosphonium cation plays an important role in modulating selectivity compared to **47**. The benzylic group is probably capable of undergoing stronger π-π interactions with aromatic guests, and the length of the benzylic group increases the size of the lattice void between anion and cation, thereby increasing the number of guests which may be included compared to the methyltriphenylphosphonium cyanoborate.

TABLE 21
Host-Guest ratios with two different Guests
in CH_2Cl_2 by ^{1}H-NMR.

Guest	H:G:G[a]	H:G:G[a]
Diethylether/Furan	1:0:0	1:0:0
Ethyl Acetate/Hexane	1:0:0	1:0:0
DMF/Mesitylene	1:1.8:1.2	1:1.7:0.9
DMF/Anisole	1:0.5:1.2	1:0.4:1.5
Mesitylene/Thiophenol	wax	
N,N-Dimethylaniline/DMSO	1:2.1:2.5	1:1.8:2.3
Toluene/Pyridine	1:0.5:0.6	1:0.4:0.3
Thiophene/Benzene	1:0:0.6	1:0:0.5
1-Hexene/2-Methylfuran	1:0:0	1:0:0

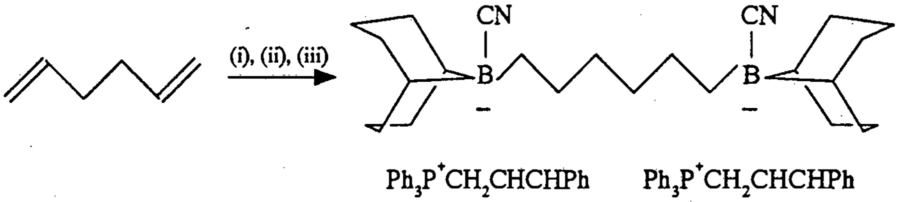
[a] same batch of sample

Interestingly, this host does not exhibit any water-dependent liquid clathrate behaviour, but upon the addition of furan does turn red, presumably due to a weak charge-transfer process. However, it remains an emulsion-like solid upon the addition of furan without ever dissolving totally even when heating.

Having thoroughly investigated the properties of the benzyltriphenylphosphonium cyanoborate salt, it was decided to explore the host-guest subtleties of the benzyl connection by making the synthetically viable cinnamyl derivative **103**. Cinnamyltriphenylphosphonium chloride **104** was prepared by heating triphenylphosphine in neat cinnamyl chloride[9]. Recrystallisation from ethyl acetate and methanol resulted in decomposition as evidenced by spurious peaks in the ^{1}H-NMR spectrum. Hence, the phosphonium salt was copiously washed with ethyl acetate and then further exchanged with sodium cyanoborate in the normal way to afford a pink solid, which turned white on washing with ethyl acetate. (Scheme 62) This time, ether was not included from the extraction as for the benzyl complex. The ^{1}H-NMR spectrum of this compound showed the vinylic protons as a multiplet at δ=6.12ppm and as a doublet of doublets at δ=6.60ppm and the vinylic carbons at δ=115.1ppm and δ=138.6ppm in the ^{13}C-NMR spectrum. Figure 28.

$$\mathrm{Ph_3P + PhCH{=}CHCH_2Cl \xrightarrow{1hr/reflux} Ph_3P^{+}CH_2CH{=}CHPh\ Cl^{-}}$$

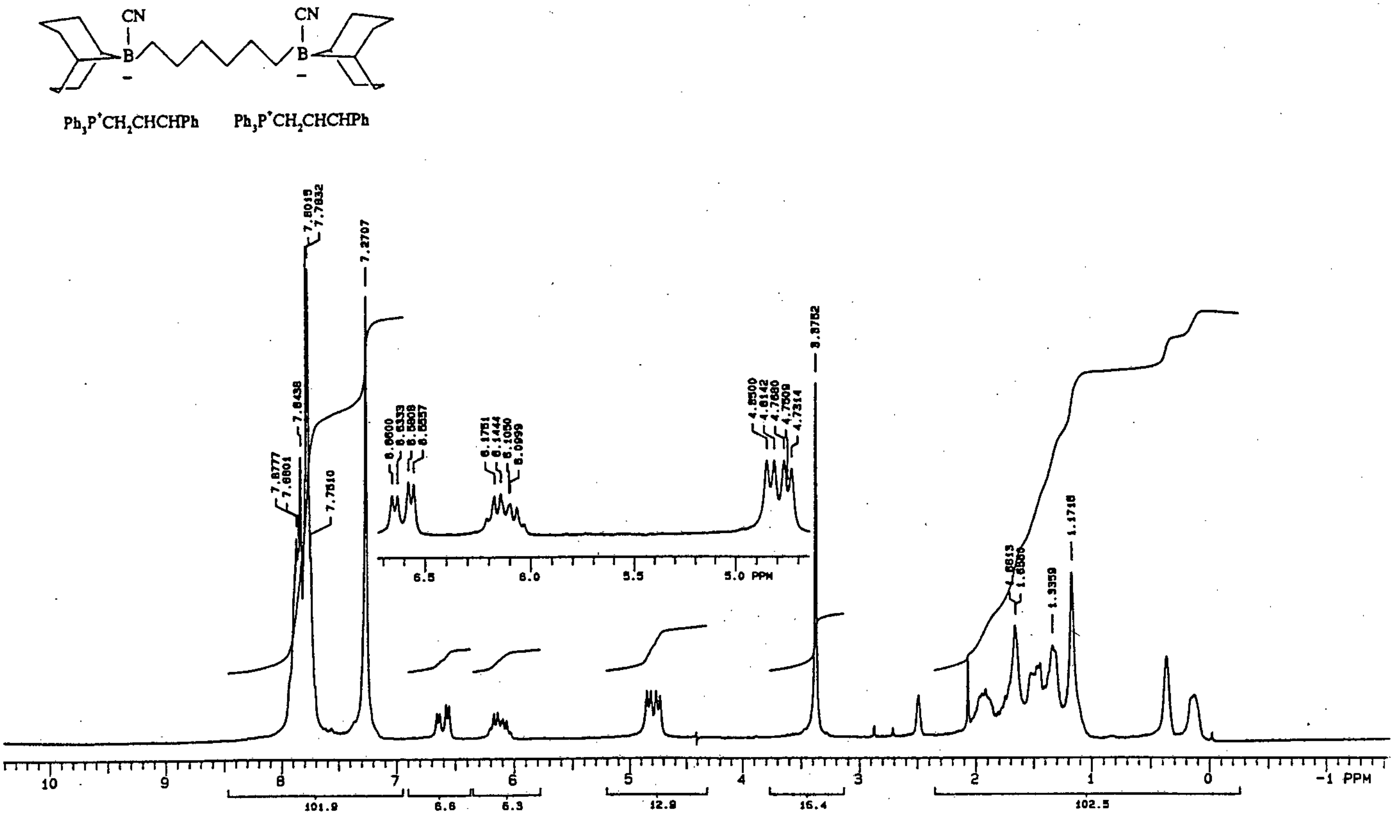
104



103

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $\mathrm{Ph_3P^{+}CH_2CHCHPh\ Cl^{-}}$ (2eq)/MeOH

Scheme 62



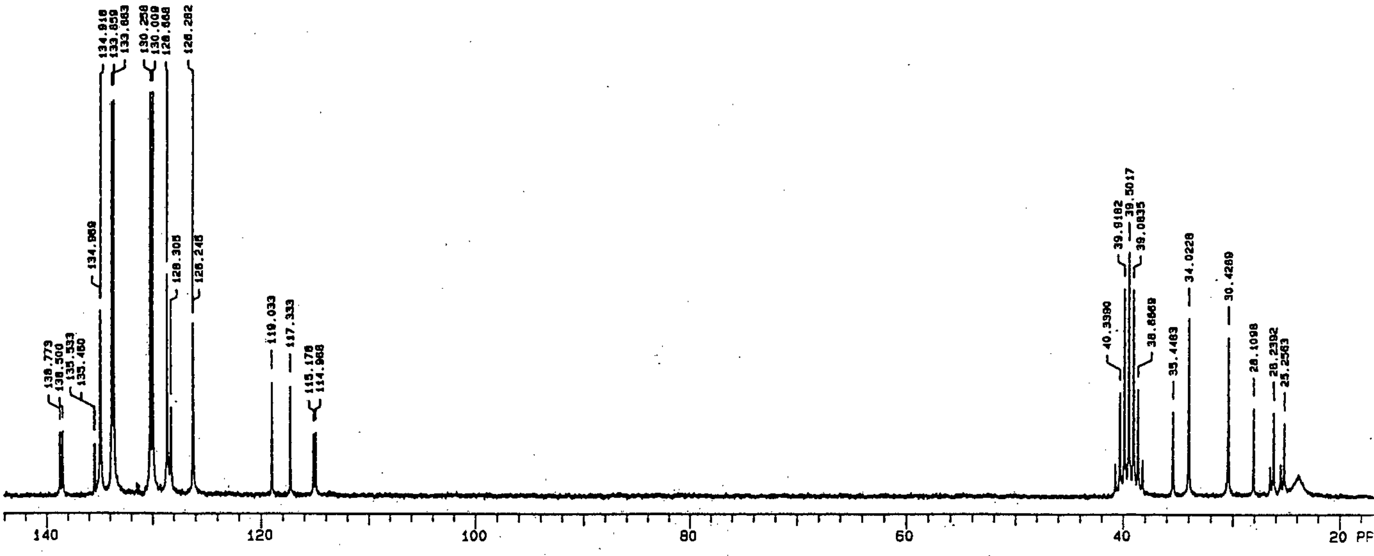


Figure 28

The presence of an (E)-double bond in the phosphonium cation made this compound an interesting target molecule for inclusion studies. Host-guest ratios were found to be severely reduced, however. (Table 22) Possible explanations for this may be that the alkenyl substituent confers a degree of flexibility on the lattice making host-guest ordering more difficult as well as the increased electron density around the allylic methylene hydrogens, destabilising hydrogen bonding interactions with the cyano nitrogen.

TABLE 22

Results of Host-Guest ratios of
$[(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\cdot 2Ph_3P^+CH_2CH{=}CHPh]$
in CH_2Cl_2 by ^1H-NMR.

Guest	H:G[a]	H:G[a]	neat[a]
1-Hexene	1:0	1:0	1:0
Benzene	1:0	1:0	
Toluene	1:Tr	1:Tr	
Mesitylene	1:Tr	1:0.2	
Anisole	1:0.4	1:0.5	
N,N-Dimethylaniline	1:0.6	1:0.7	
Furan	1:0	1:0	1:0
2-Methylfuran	1:0	1:0	1:0
DMF	1:2	1:2.2	
Ethyl Acetate	1:0	1:0	1:0
Diethylether	1:0	1:0	1:0

[a] same batch of sample

4.4.3.1 POLAR MODIFICATIONS TO THE BENZYL GROUP

At this stage of the study, it had become clear that clathrate activity was very sensitive to functional group changes around the methyl group. However, a gratifying improvement had been obtained with the benzyl substituent and so it was a logical thing to now modify the electronic character of the benzyl phenyl ring. (Figure 29) This was considered desirable in order to include more polar guests. Thus, a series of substituted benzyltriphenylphosphonium salts were prepared by nucleophilic substitution of the corresponding benzyl halide, and then converted to the borate salt. Figure 29 summarises the groups selected.

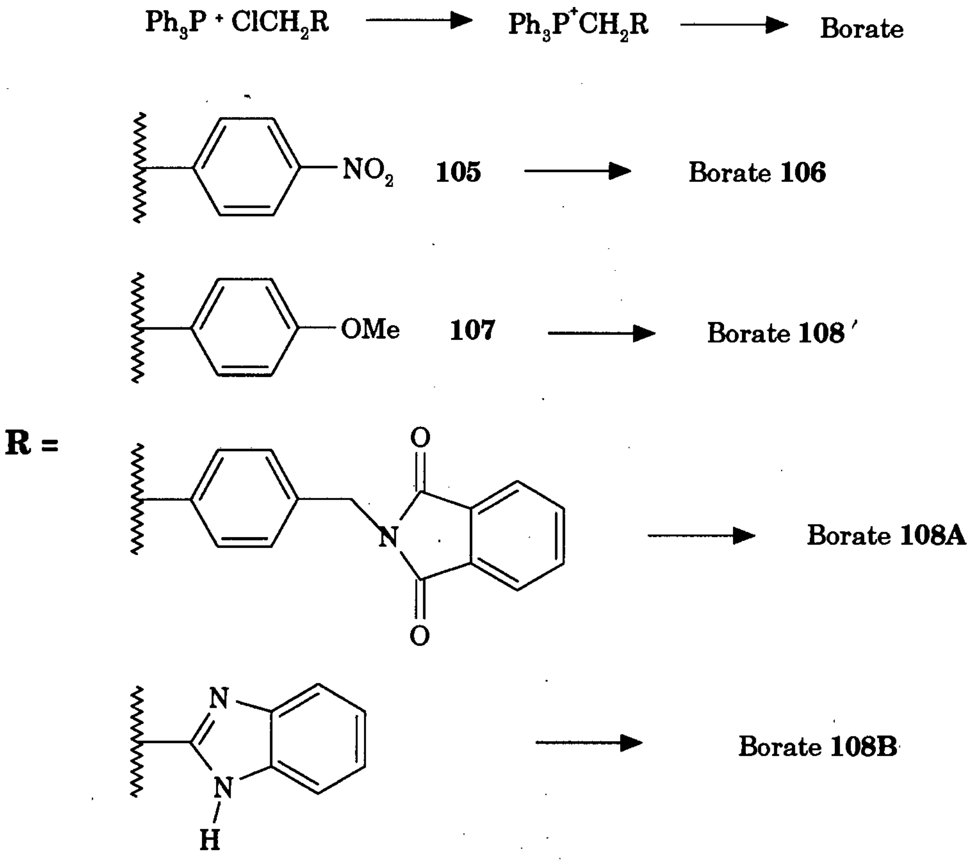


Figure 29

The 4-nitrobenzyl and 4-methoxybenzyl groups were selected as deactivated and activated benzyl groups respectively. Exchange of sodium cyanoborate **15** in the normal way with 4-nitro **105** and 4-methoxybenzyltriphenylphosphonium chloride **107** gave the desired salts in 42% and 83% yield respectively. The electron-withdrawing influence of the nitro group in **106** resulted in the aromatic protons *ortho* to this functionality resonating at 8.11ppm in the ^{1}H-NMR spectrum (Figure 30) compared to the equivalent proton in the methoxy derivative **107** which appeared at 6.76ppm. In the ^{13}C-NMR the methoxy group of **108** resonates at an expected shift of 55.0ppm and the carbon adjacent to it at 159.1ppm, further downfield compared to the equivalent carbon of **106** at 147.3ppm. The nitro derivative exhibited a red colour upon dissolution in solvents such as DMSO and acetone giving an indication of a charge-transfer reaction taking place. However, no inclusion was observed for either of these compounds with benzene, acetonitrile and acetone. Thus, the clathrate activity had been switched off once again reminding us of the subtleties of the intermolecular forces in the lattice.

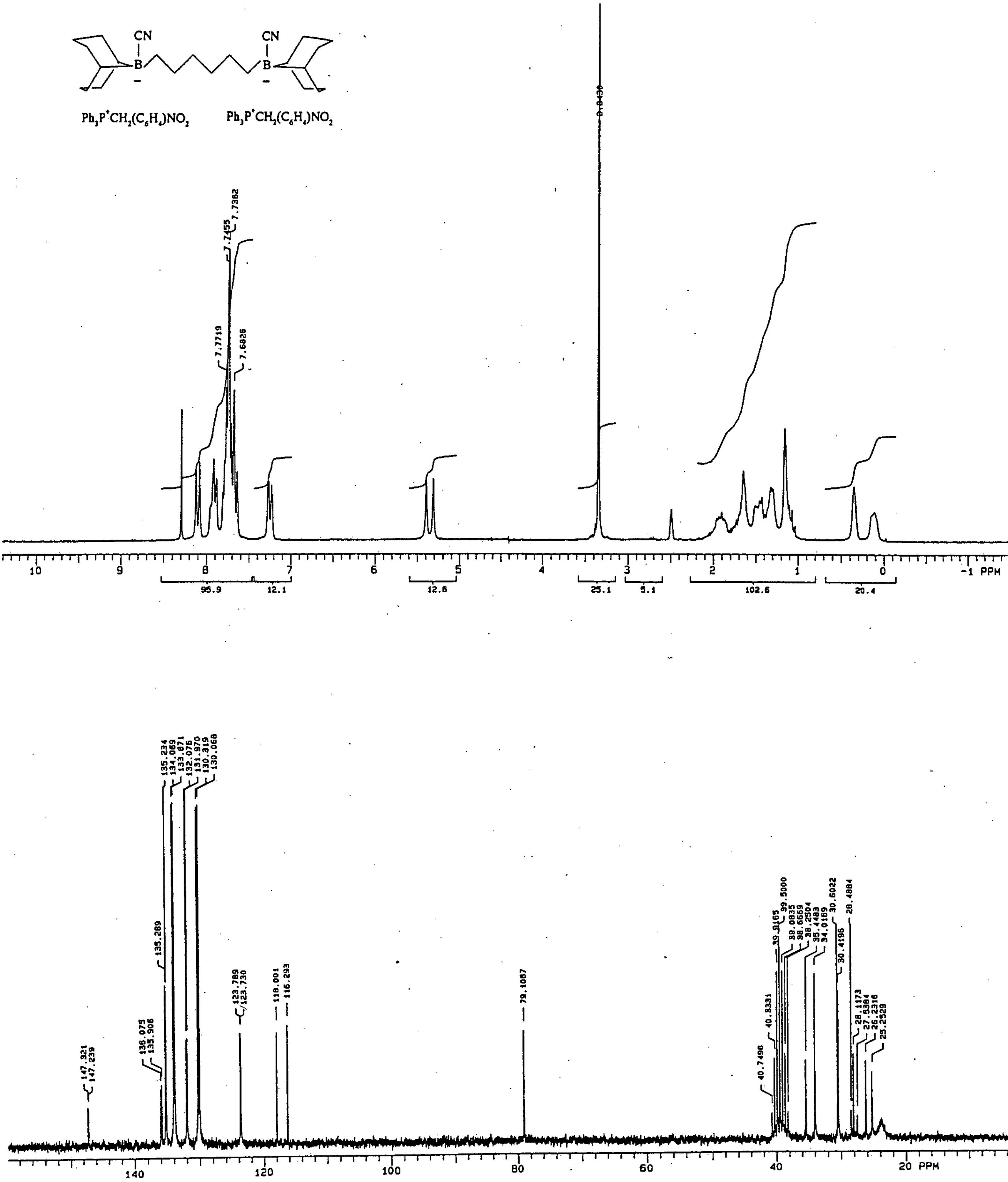
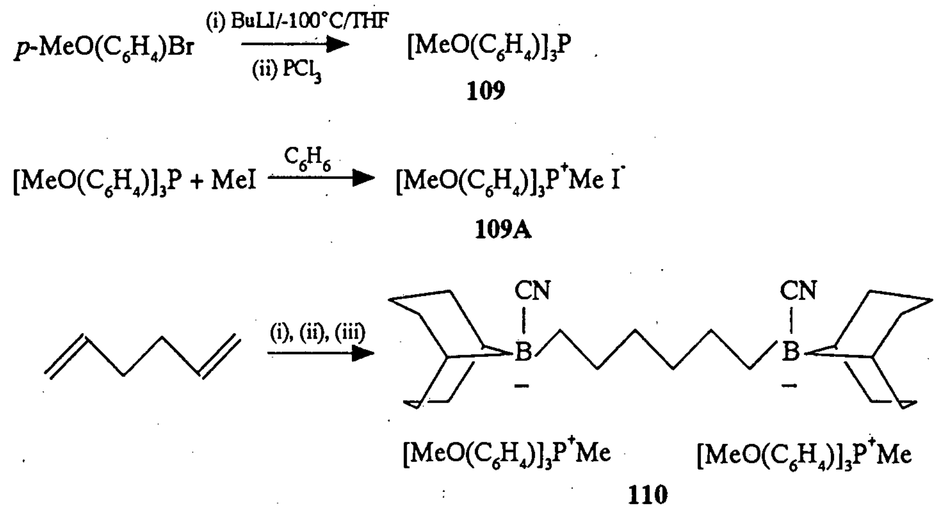

CN
B
CN
B
Ph3P+CH2(C6H4)NO2
Ph3P+CH2(C6H4)NO2
7.7719
7.7455
7.7382
7.6828
3.3430
10
9
8
7
6
5
4
3
2
1
0
-1 PPM
95.9
12.1
12.6
25.1
5.1
102.6
20.4
147.321
147.239
136.075
135.906
135.289
135.234
134.069
133.871
132.075
131.970
130.319
130.068
123.789
123.730
118.001
116.293
79.1087
40.7498
40.3331
39.9165
39.5000
39.0835
38.6669
38.2504
35.4483
34.0169
30.6022
30.4196
28.4884
28.1173
27.5384
26.2316
25.2529
140
120
100
80
60
40
20 PPM

Figure 30

It was then decided to extend the functionality on the phenyl ring of the benzylphosphonium cation via a carbon attached grouping. A phthalimido was selected for its ease of attachment and hydrogen bonding possibilities. The phthalimide derivative **108A** was synthesised by firstly preparing the monotriphenylphosphonium salt of α,α'-dibromo-*p*-xylene, which was then reacted with phthalimide in a Gabriel-type displacement to obtain a solid in a 72% yield. Interestingly, the monophosphonium chloride salt included of ethyl acetate from the washing procedure, which was not observed in any of the other salts. The borate salt was prepared in the normal way but proved to be difficult to purify. Even though it was not pure, it dissolved readily in host-guest experiments but remained a sticky oil upon evaporation.

Finally in this series, another nitrogen containing functionality based on benzimidazole was investigated, since in this case the heteroaromatic ring is deactivated and has hydrogen bonding options. The preparation of the borate proceeded as usual, but only an oily substance could be obtained, which would not solidify, therefore precluding it from host-guest studies.

As a final attempt, we turned our attention towards electronically modifying the phenyl ligands on phosphorus. 4-Bromoanisole was reacted with butyllithium at low temperature in a metal-halogen exchange reaction followed by reaction with phosphorus trichloride to form tris(4-methoxyphenyl)phosphine **109**, which was purified by washing copiously with methanol. Methylation of this phosphine with methyl iodide followed by the normal exchange reaction with sodium cyanoborate **15** furnished the desired product **110** with activated phenyl groups on phosphorus. (Scheme 63) During the extraction both a solid and an oil formed and the latter could be precipitated out using a mixture ethyl acetate : petroleum ether (50:50). The host-guest experiments of **110** were carried out in dichloromethane as usual with benzene, acetonitrile and n-butanol. Interestingly, a beautiful crystalline solid formed from n-butanol after evaporation of solvent, which was washed with pet. ether and as evidenced by ^{1}H and ^{13}C-NMR spectra displayed a peak for dichloromethane. (Figure 31) The TGA results for the amount of included guest was slightly higher than that from ^{1}H-NMR and there was suspicion of traces of butanol being present. However, since the inclusion of dichloromethane did not occur with benzene, an interesting inclusion dependency on n-butanol appears to have been discovered. An approximate host-guest ratio of 1:1.5 could be calculated from the ^{1}H-NMR spectrum and TGA confirmed this result giving an indication of strong binding forces operating within the cavity, since the loss of the guest is only complete at 150°C. Scrutiny of the furan clathrate X-ray structure described in chapter 3 suggests that the dichloromethane guest is coordinating via a chlorine to the methyl hydrogen on phosphorus and via a hydrogen to the oxygen of the methoxy group or the activated benzyl aromatic ring. A coordination assisted lattice with the methoxyl group as a sensor for the guest makes this host a revolutionary finding. An X-ray analysis is required to test out this proposal.



p-$MeO(C_6H_4)Br \xrightarrow[\text{(ii) } PCl_3]{\text{(i) BuLi/-100°C/THF}} [MeO(C_6H_4)]_3P$

109

$[MeO(C_6H_4)]_3P + MeI \xrightarrow{C_6H_6} [MeO(C_6H_4)]_3P^+Me\ I^-$

109A

$[MeO(C_6H_4)]_3P^+Me$ $[MeO(C_6H_4)]_3P^+Me$

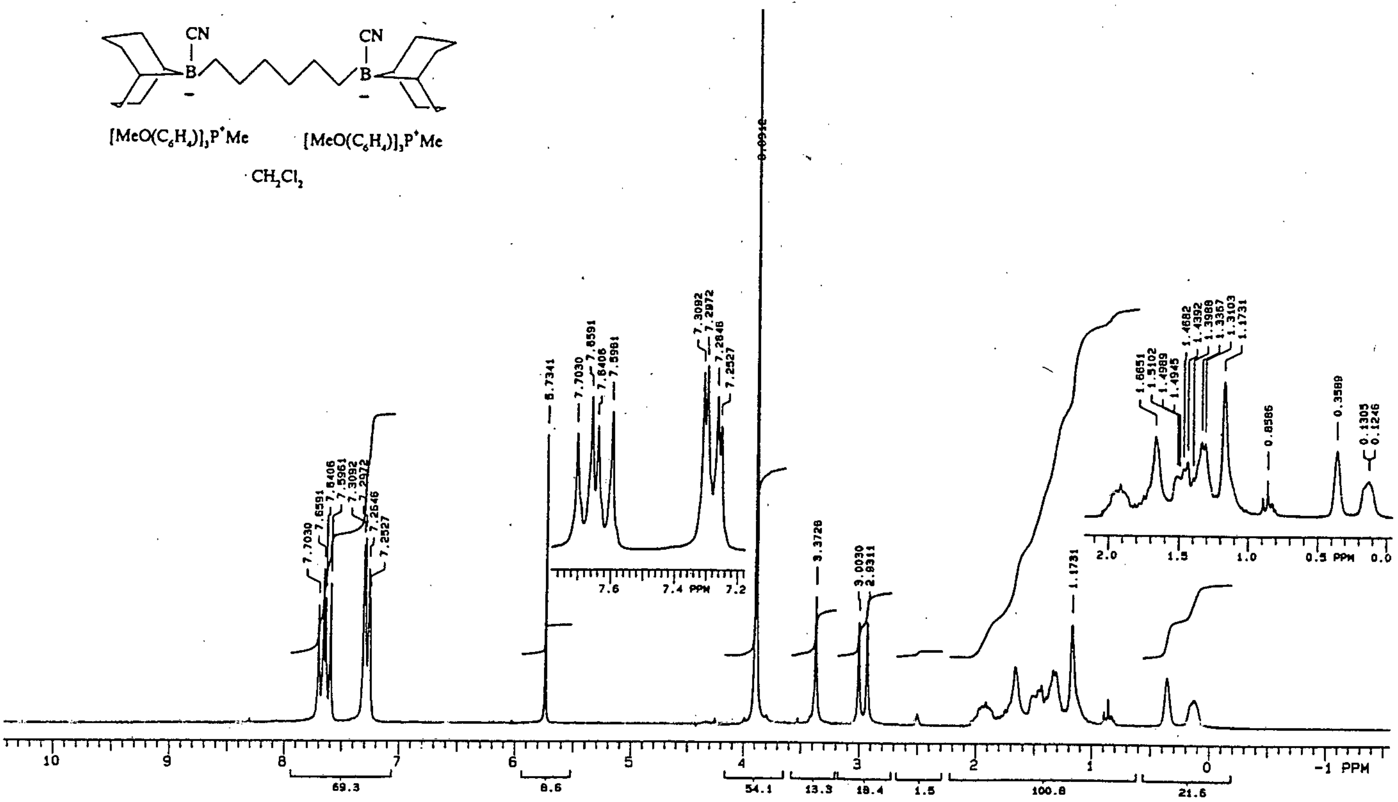
110

(i) 9-BBN (2eq)/THF/0°C to RT

(ii) NaCN (2eq)/DMF

(iii) $[MeO(C_6H_4)]_3P^+Me\ I^-$ (2eq)/MeOH

Scheme 63



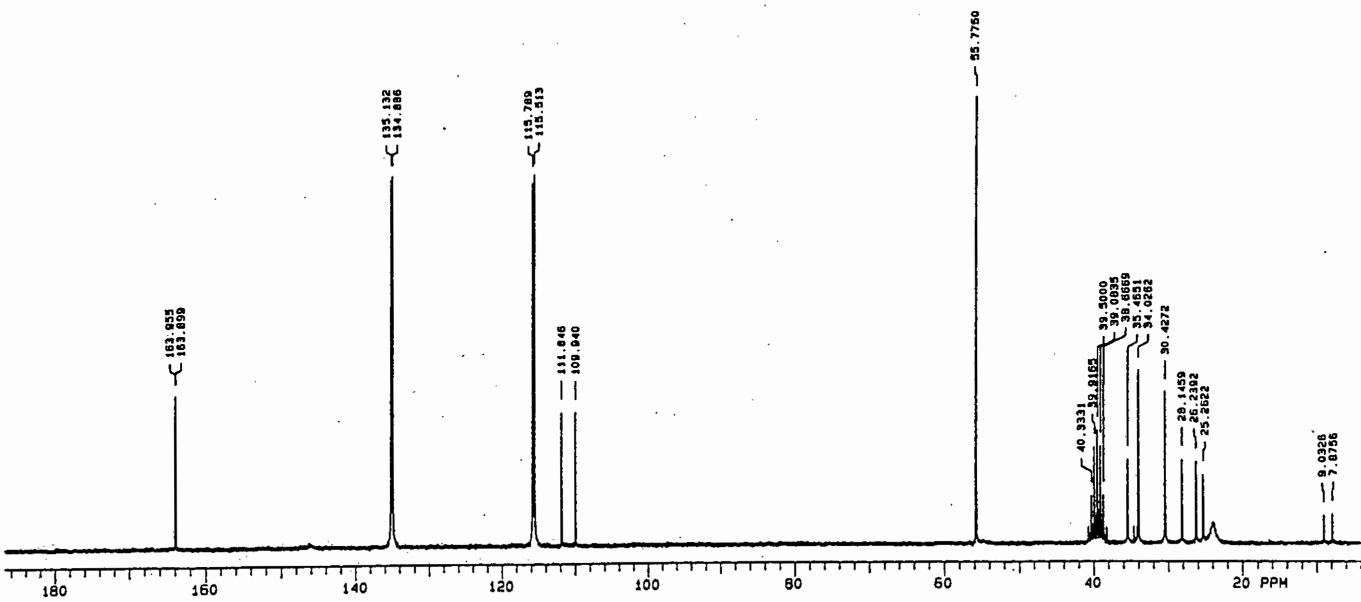
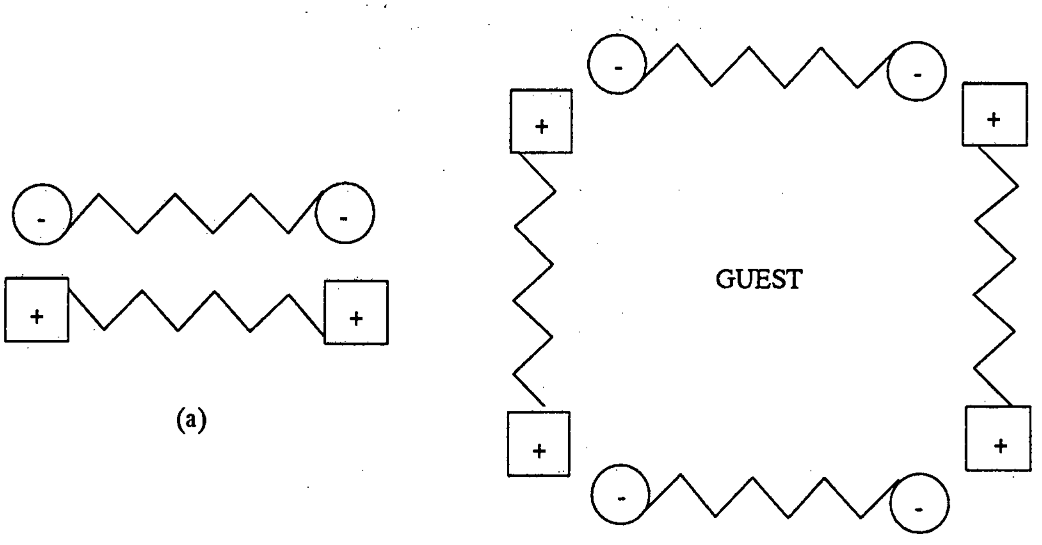


Figure 31

In summary, the modifications on the benzyl group proved disappointing, with the exception of **110**, which forms an inclusion complex with a medium-polar guest indicating a shift in the inclusion profile compared to the prototype **47**. This exciting result could lead to a multitude of synthetic variations on the triphenyl component of the phosphonium salt shifting the host-guest profile into the more useful polar region.

4.4.3.2 MODIFICATIONS TO FORM PHOSPHONIUM DIMERS

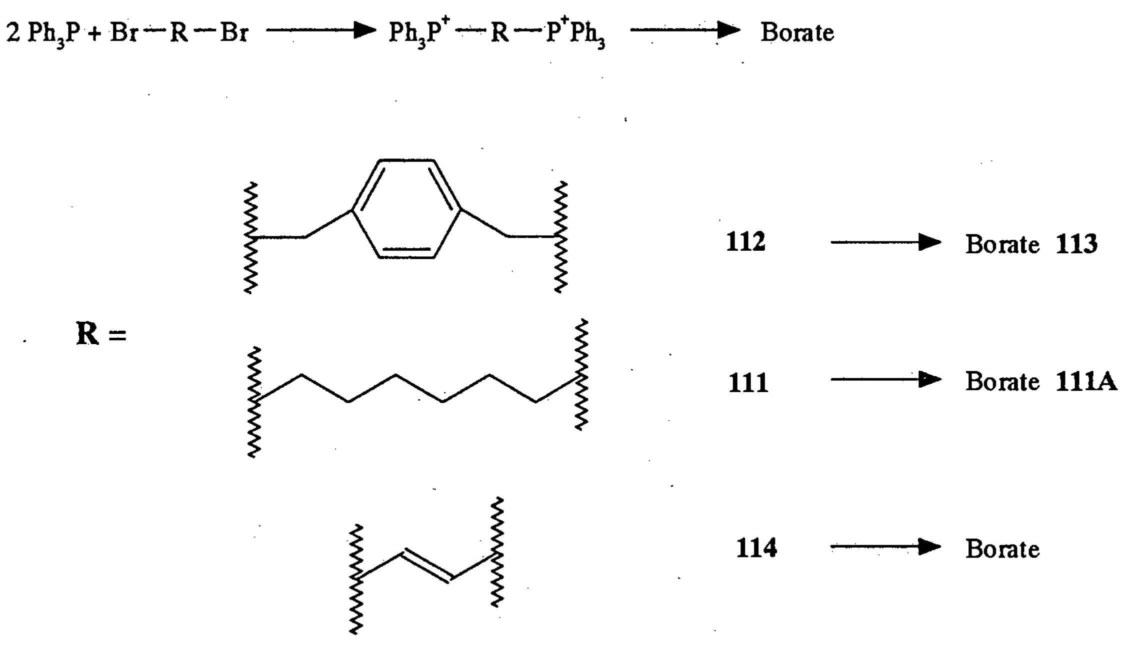
The flexibility aspect of the phosphonium cyanoborate salts plays a pivotal role in the ordering of the lattice structure as has been mentioned already and therefore it was of interest to expand upon this aspect. Of interest conceptually was the influence of connecting the phosphonium centres together via a spacer group rather like in the anion. One could envisage a number of structural motifs, two of which are depicted in Figure 32. The first structural motif (a) would prevent any inclusion of guests due to close packing of the charged units. By comparison, in the second case (b) a large lattice void for inclusion would be formed. The type of structure actually adopted would largely depend on the matching of the two spacer units and so this was taken into account in the synthetic planning.



(a)

(b)

Figure 32



Scheme 65

Three spacers were selected. (Scheme 65) The first cation spacer chosen was hexamethylene so as to have parity between the cation and anion. The dibromide of 1,6-hexanediylbis(triphenylphosphonium) **111** was synthesised by heating 1,6-dibromohexane and triphenylphosphine together in DMF[9], and then recrystallising from ethanol. Exchange of **111** with sodium cyanoborate **15** afforded a solid product **111A**, which had to be washed copiously with warm water to remove any impurities. However, it was impossible to carry out any inclusion experiments with **111A**, since it was insoluble in solvents, such as CH_2Cl_2 and THF, due to its ionicity suggesting a close packed arrangement as in motif (a).

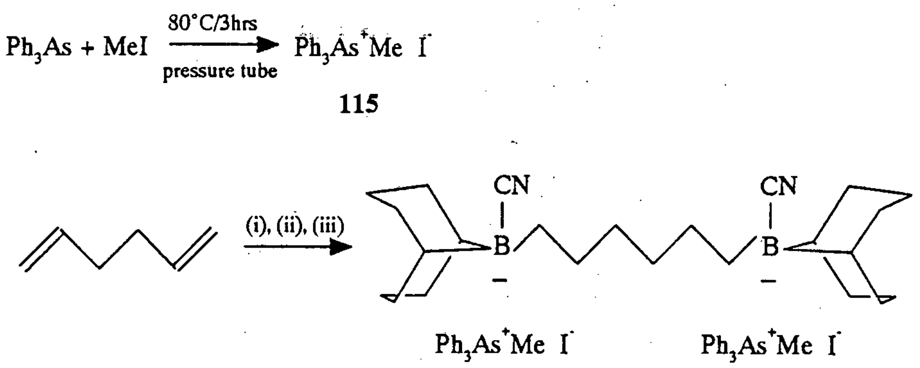
The next tether group between the phosphonium groups chosen was based on the commercially available α,α'-dibromo-*p*-xylene. Here we felt that structural motif (b) might be followed, since cation and anion spacer are of different steric and electronic constitutions. Furthermore, the phenyl group within the spacer might provide π-π interaction sites for the possible inclusion of aromatics. Although the synthesis presented no problems and gave a solid derivative **113**, it also proved to be unattractive for host-guest experiments, since it would not dissolve in solvents such as CH_2Cl_2 and THF due to strong ionic lattice forces.

Finally, the commercially available 1,2-vinylenebis(triphenylphosphonium) dibromide **114**, which contains an internal double bond, was exchanged with sodium cyanoborate **15**. A product crystallised out very slowly at room temperature, which was not the desired salt. From ^1H and ^{13}C-NMR spectra, it was observed that there was too little of the borate species present and that some side reactions must have taken place as evidenced by spurious peaks in both spectra. Hence, once again we found that the physical properties of these targets thwarted our attempts to practically realise a clathrand design concept.

4.4.4 SYNTHESIS AND STRUCTURE ACTIVITY OF TWO ARSONIUM SALTS

With the subtle implications of structural changes made so far in mind, we decided to study one more change, namely that of the central atom. We rationalised that changing from phosphorus to the larger arsenic would create a less closed packed structure with larger lattice voids for inclusion. What was not clear was whether, the α-hydrogens would still participate in a hydrogen bonded assisted lattice.

Therefore, in line with the phosphonium work, the first clathrand synthesised was based on methyltriphenylarsonium as cation. Methyltriphenylarsonium iodide was prepared in a pressure tube at 80°C and then exchanged with **15** in the normal way to give a solid after extraction which included 0.5-1.2 water molecules by TGA and ^1H-NMR.


$Ph_3As + MeI \xrightarrow[\text{pressure tube}]{80°C/3hrs} Ph_3As^+Me\ I^-$

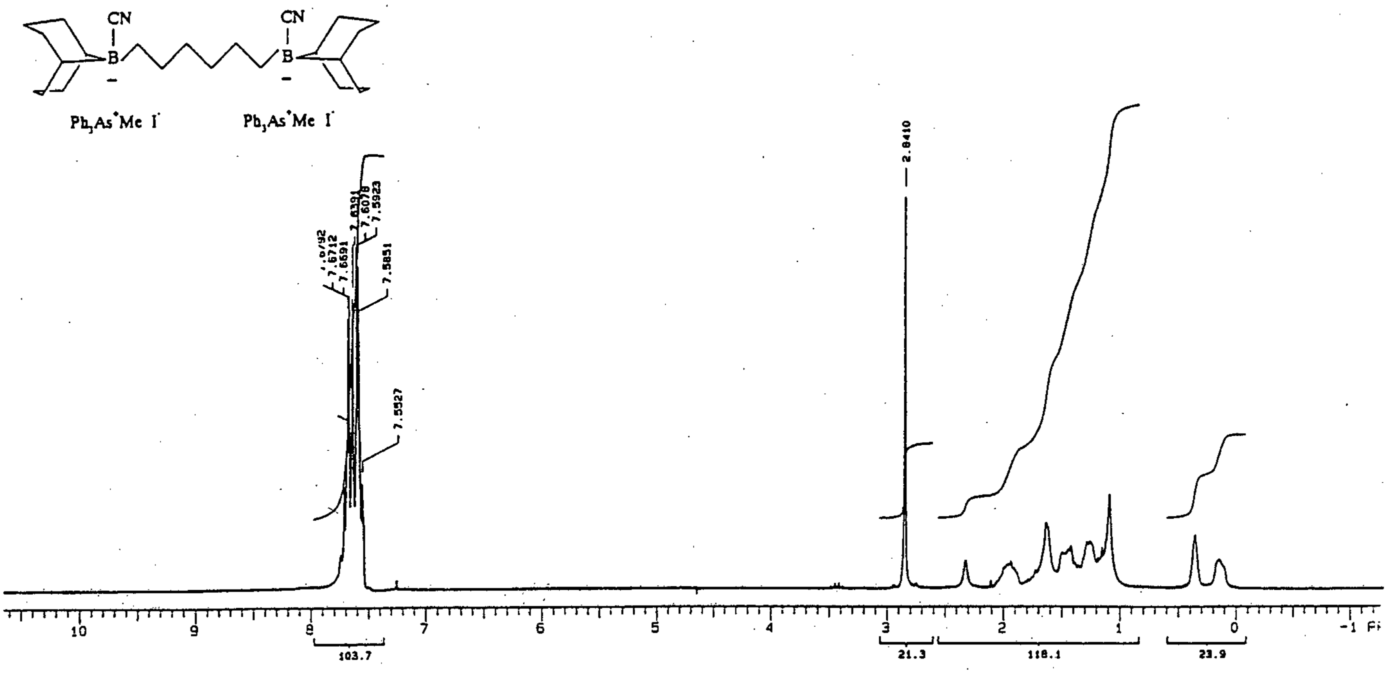
115

116

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $Ph_3As^+Me\ I^-$(2eq)/MeOH

Scheme 66

As evidenced by NMR spectroscopy the chemical shifts of the protons and carbons are comparable to those of the prototype **47**. The methyl group on arsenic appears as a singlet, since I=0 for arsenic. Figure 33.



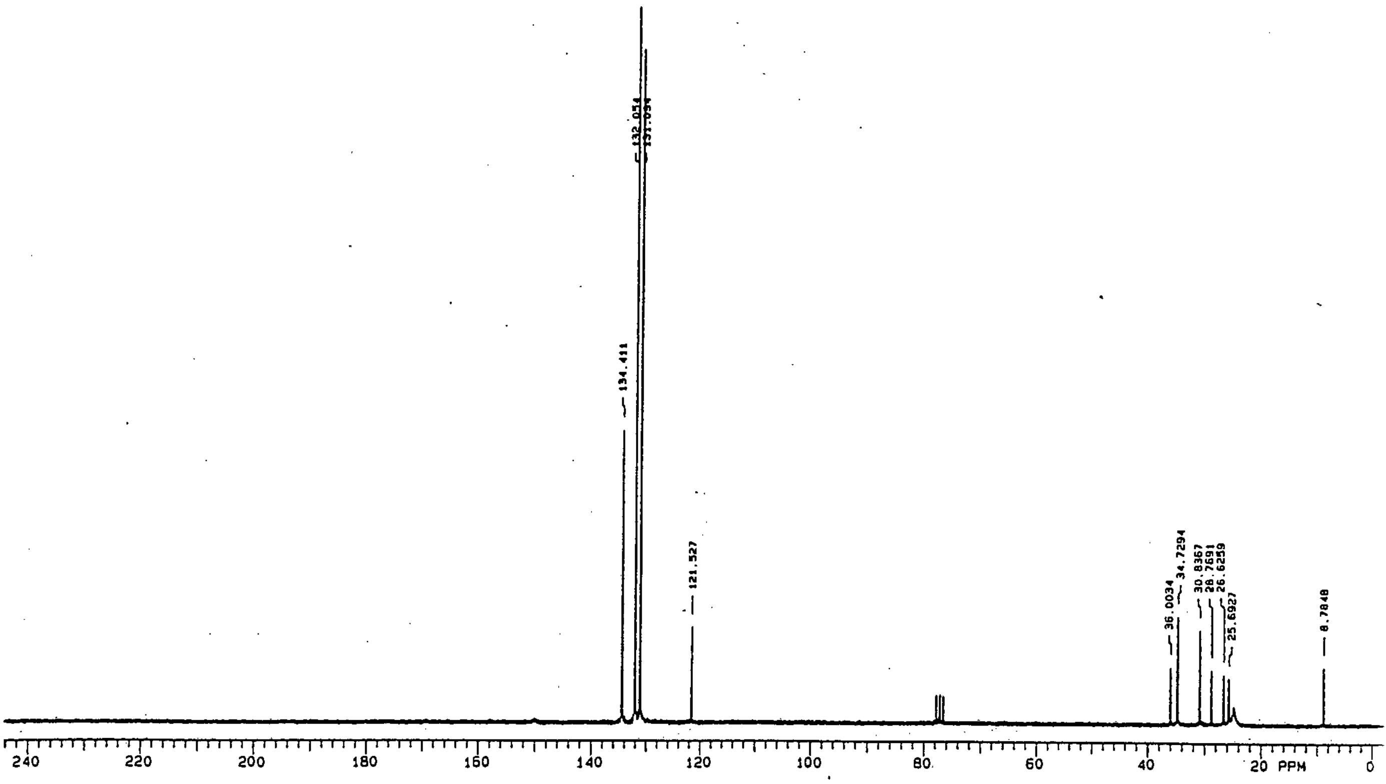


Figure 33

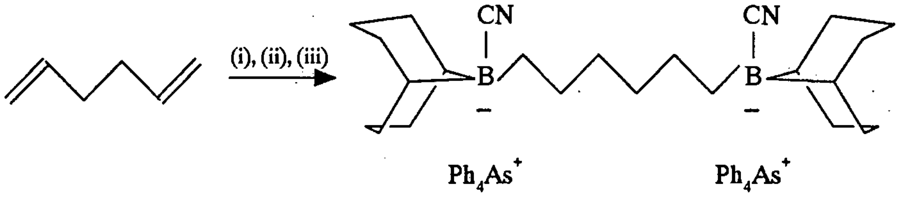
We were pleased to discover that a preliminary study of the inclusion activity of anhydrous **116** revealed a much greater activity generally than the phosphonium prototype. (Table 23) As discussed before we would ascribe this to the larger size of the central arsenic atom. Gratifyingly, it is most likely that hydrogen bonding is still maintained but this needs to be verified by an X-ray structure analysis.

TABLE 23
Results of Host-Guest ratios of
$[(C_8H_{14})(CN)B^{-}(C_6H_{12})B^{-}(CN)(C_8H_{14})\cdot 2Ph_3As^{+}Me \cdot H_2O]$
in CH_2Cl_2 by ^{1}H-NMR.

Guest	H:G[a]	H:G[a]
1-Hexene	1:0	1:0
Benzene	1:2.2	1:2.4
Mesitylene	1:2.2	1:2.1
Anisole	1:Tr	1:Tr
N,N-Dimethylaniline	1:1.9	1:1.8
Furan	1:0	1:0
DMF	1:1.3	1:1.0

[a] same batch of sample

The next arsonium salt synthesised was based on the readily available tetraphenylarsonium chloride hydrate, which was isolated as a yellow solid, which became colourless upon washing with ethyl acetate (Scheme 67). As with the tetraphenylphosphonium cyanoborate **96**, the tetraphenylarsonium salt showed absolutely no inclusion activity which we ascribe to the absence of a suitable C-H donor site for sustaining a coordination assisted lattice. (Table 24) Although the lattice is held together by electrostatic interactions, it would appear that host-guest ordering requires the additional interaction as a pre-requisite of clathrate formation.



117

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $Ph_4As^+\ Cl^- \cdot n\,H_2O$ (2eq)/MeOH

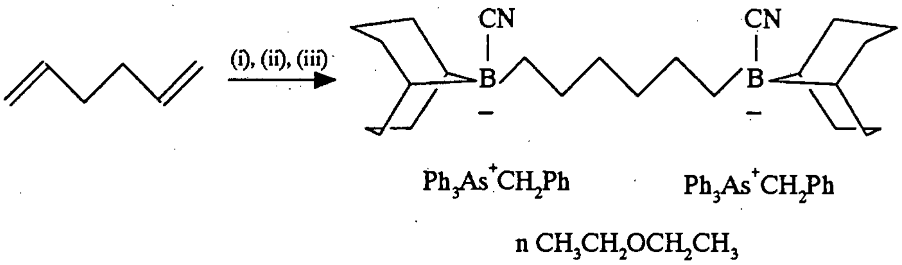
Scheme 67

TABLE 24
Results of Host-Guest ratios of
$[(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\cdot 2Ph_4As^+]$
in CH_2Cl_2 by ^1H-NMR.

Guest	H:G[a]	H:G[a]
Hexane	1:0	1:0
1-Hexene	1:0	1:0
Benzene	1:0	1:0
Mesitylene	1:0	1:0
Anisole	1:0	1:0
N,N-Dimethylaniline	1:0	1:0
Furan	1:0	1:0
DMF	1:0	1:0
Ethyl Acetate	1:0	1:0

[a] same batch of sample

Finally, to complete the series the benzyltriphenylarsonium analogue **118** was prepared. The intermediate benzylarsonium bromide was prepared from triphenylarsine and benzyl bromide in a pressure tube at 90°C for 6 hours resulting in a colourless solid, which was recystallised from acetone. This was then exchanged with the sodium cyanoborate **15** to form a precipitate upon work-up, which as with benzyltriphenylphosphonium cyanoborate **102** included ether in a host-guest ratio of 1:1.6.(Scheme 68) Ether was removed *in vacuo* at 70°C overnight to afford a pure salt and the host-guest activity profile was studied as before by dissolving the host in CH_2Cl_2, adding guest and allowing the clathrate to crystallise out. Ratios, in general, were similar to those of the methyltriphenylarsonium salt. Table 25.



118

(i) 9-BBN (2eq)/THF/0°C to RT
(ii) NaCN (2eq)/DMF
(iii) $Ph_3As^+CH_2Ph\ Br^-$ (2eq)/MeOH

Scheme 68

TABLE 25
Results of host-guest ratios of
$[(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\cdot 2Ph_3As^+CH_2Ph]$
in CH_2Cl_2 by ^1H-NMR.

Guest	H:G[a]	H:G[a]
Benzene	1:2	1:2.2
p-Xylene	1:1	1:0.8
N,N-Dimethylaniline	1:1.2	1:1.1
DMF	1:1.5	1:1.6
CH_3CN	1:0	1:0
Acetone	1:0	1:0

[a] same batch of sample

From these results, it may be concluded that aryl substituted arsonium cyanoborate salts compare well with their phosphonium counterparts, and in certain instances, such as the methyltriphenylarsonium borate, show an even higher selectivity. This also suggests some interesting targets for future studies.

This concluded the structure-activity study of this clathrand family. The results have revealed that clathrate activity is strongly dependent on having CH-N hydrogen bonding involved in the lattice ordering process. While this feature, along with the handling aspects of some of the materials, has resulted in clathrate activity being fairly sensitive to structural changes, it has led to the important conclusion that substituted methyltriphenylphosphonium, benzyltriphenylphosphonium and aryl substituted arsonium cyanoborate salts form the basis of a clathrand family with broad spectrum inclusion activity. In the fifth and final chapter, studies will be discussed on a chiral substituted benzyltriphenylphosphonium cyanoborate salt.

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CHAPTER 5

THE SYNTHESIS OF A CHIRAL PHOSPHONIUM CYANOBORATE

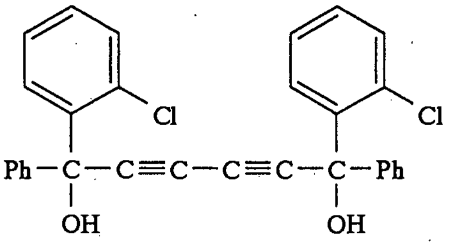
5.1 CHIRAL CLATHRATES

Nowadays, the production of pure enantiomers is a very important aspect of pharmaceutical chemistry and is the focal point of much research. Their industrial production is possible, although often at great cost and involving either asymmetric synthesis or racemate resolution, of which the latter is more suitable for large-scale production. The essential point of departure in racemate resolution is from classical, i.e. that involving covalent diastereomers, to supramolecular non-covalently bonded diastereomers. In the latter, differentiation of enantiomers[1] occurs by virtue of the "chiral environment" in the crystal or the interior of the host molecule. The formation of diastereomeric host-guest compounds involves different activation energies, thus resulting in selective crystallisation of a particular enantiomer.

Achiral compounds as host crystals can also effect discrimination of enantiomers. For instance, urea[2] was being used for the resolution of racemates as early as the 1970's. Although urea is not chiral itself, it forms chiral lattices[3] consisting of wide channel-type cavities. Low ee values (ca. 5-15%ee) are observed for urea because of minimal lattice energy differences between diastereomeric clathrates, which renders the steering of recrystallisation a difficult process. This has resulted in urea being replaced by more efficient chiral host substances.

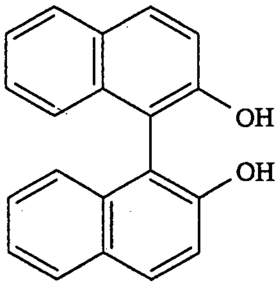
As mentioned in chapter 2, tri-o-thymotide (TOT) is also known as a versatile clathrand. It crystallises in an achiral form consisting of two chiral helical propeller-shaped conformers[4], the (-)- and (+)-configurations, which rapidly interconvert at room temperature. Thus, racemate resolution may be achieved with TOT in which a specific enantiomer crystallises preferentially with either the (+) or (-) TOT forms. In general, the enantiomeric excess per clathration step is higher for the cage-type clathrates of TOT (e.g. 2-bromobutane, 37%ee) than for channel-like inclusions (e.g. 2-bromononane, 5%ee). TOT clathrates also exhibit the ability to crystallise in a variety of space groups and to display different forms of cavities, such as cage, quasi-uniform channels and channels of variable size.

These days, the synthesis of chiral, tailor-made host molecules for racemate resolution is moving at an ever increasing pace. One example is the chiral clathrand, 1,6-bis(o-chlorophenyl)-1,6-diphenylhexa-2,4-diyn-1,6-diol[5] **119**, derived from F. Toda's "wheel-and-axle" 1,6-tetraphenylhexa-2,4-diyn-1,6-diol. This host compound has been successful in separating numerous guest substances into their enantiomers. For instance, 2,3-epoxycyclohexanones were easily resolved by the host in 100%ee.

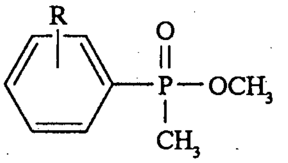


119

Chiral inclusion complexes have also been formed between 2,2'-dihydroxy-1,1'-binaphthyl and phosphinates, phosphine oxides, sulfoxides and selenoxides[6]. The host molecule possesses a particularly useful shape due to the two naphthyl groups being oriented at nearly right angles to each other, and the hydroxyl groups acting as sensors enable efficient guest binding. The host **120** was resolved by complexation with several optically pure guest components in 100%ee. The optically pure compound can easily be recovered from the complex by column chromatography. The simplicity of the method can be illustrated by the reaction between the host **120** and the phosphoric ester **121**. A 1:1 complex of (+)-**121A** with (-)-**120** was formed from the racemic phosphinate **121A** with (-)-**120** in benzene. Two subsequent crystallisations of the complex from benzene gave an optically pure compound. Efficient optical resolution of alkylaryl-substituted phosphine oxides, sulfoxides and selenoxides was only possible with substituents R=H and R=*m*-CH_3 on the guest aromatic ring. Thus, in this case both steric and functional features are of significance in selective crystallisation.



120



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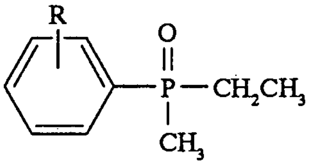


122

a R=H
b R=*o*-CH_3
c R=*m*-CH_3
d R=*p*-CH_3

In the design of receptor molecules, more and more attention is been given to the design and synthesis of chiral hosts which separate racemic mixtures. In cases where a particular model is known to have a large inclusion range, it is fitting to try to design a related compound with the ability to uniquely include one enantiomer of a mixture.

5.2 SYNTHESIS OF THE CHIRAL PHOSPHONIUM SALT

The clathrate behaviour of the various phosphonium cyanoborate salts encouraged us to study a chiral host system which might have both solid and liquid clathrate behaviour like the prototype **47** and so include one enantiomer in a separable layer of liquid or as a solid clathrate. The former type of system could be more efficient than one based on purification by recrystallisation of host-guest crystals[7]. This also raised the possibility of developing a clathrate which would work under the same conditions as those set up by Cram[8]. His resolution machine (Figure 34) gives α-amino-acids as well as some water soluble esters in high enantiomeric purity (86-90%ee), extracted from aqueous solution into the organic phase by the liquid clathrate. In addition, this system has the added advantage of having a fully recyclable host.

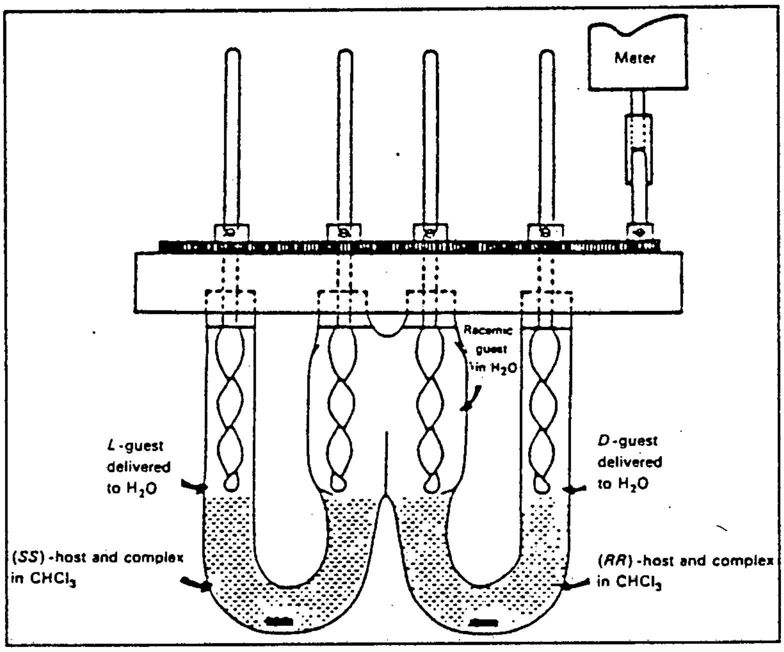


Figure 34

Modification of the basic framework of our prototype system **47** to form a chiral salt could have followed one of three options: 1) alteration of the hexamethylene spacer, 2) attachment of the chiral auxiliary to one of the phenyl rings on triphenylphosphine and 3) modification of the methyl ligand. The first option was ruled out, since the hexamethylene spacer proved to be essential for obtaining solid derivatives. (Chapter 4) The second method was considered but the ease of accomplishment of the third made it the option of choice. Chiral phosphonium salts based on asymmetric phosphorus were considered beyond the scope of this project given the time limitations. Attachment of triphenylphosphine to the chiral auxiliary was accomplished by nucleophilic substitution of a benzyl halide bearing the chiral group. (Scheme 69) Moreover, we were interested in extending our findings on substituted benzyltriphenylphosphonium salts described in chapter 4.

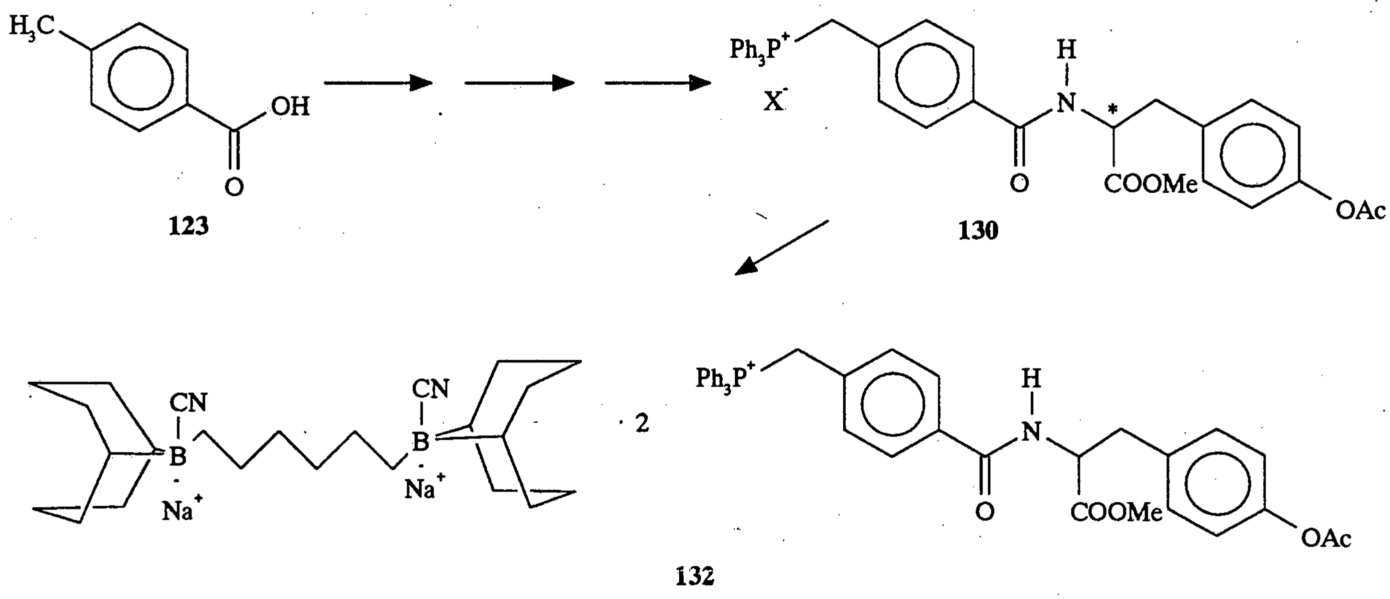
$$\mathrm{Ph_3P + X{-}CH_2R \longrightarrow Ph_3P^+{-}CH_2{-}R\ X^-}$$

R = chiral auxiliary

Scheme 69

p-Bromomethylbenzoic acid **123** was chosen as a bifunctional reagent for the attachment of both auxiliary and phosphine. *l*-Tyrosine **127**, an α-amino acid, was selected as the chiral auxiliary in view of its availability, and that the the amide linkage would provide hydrogen bonding coordination sites for guest inclusion. The aromatic rings were also considered to be desirable centres for other types of interaction, e.g. CH···π as seen with the *p*-xylene inclusion compound **47**. Scheme 70.

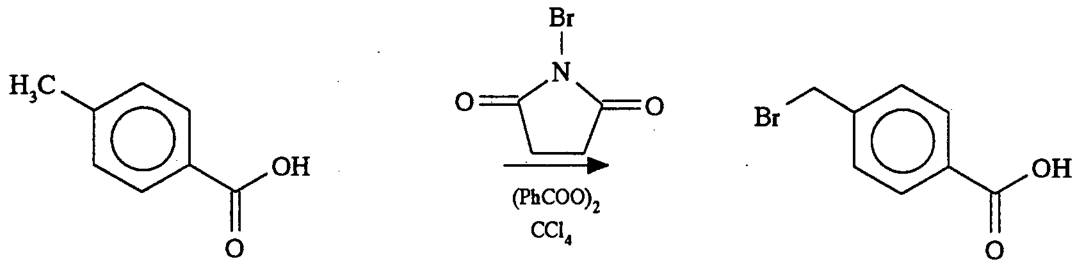
The phenolic hydroxyl group of the tyrosine was protected as a precaution against proton exchange with the basic borate anion. At all stages in the synthetic pathway conditions were chosen to minimise racemisation of the chiral centre by enolisation.



Scheme 70

5.3 SYNTHESIS OF BIS-4[N(1'-(S)-METHOXYCARBONYL-2'-*p*-ACETOXYPHENETHYL)AMIDOBENZYL] TRIPHENYLPHOSPHONIUM 1,6-BIS(B-CYANO-9-BORATABICYCLO[3.3.1]NON-9-YL) HEXANE 131

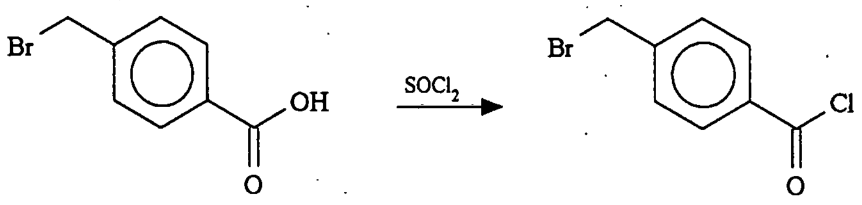
The first step was a straight-forward functional group interconversion involving firstly the conversion of the *p*-methyl group into a bromomethylene group[9] by radical bromination. (Scheme 71) The product has been used as precursor to a phosphonium salt in the Wittig preparation of *p*-carboxystyrene[10], and was used here as a bifunctional molecule for linking the phosphonium and amino acid groups.



Scheme 71

Under the given conditions this reaction was supposed to give a single product. However, in the ^{1}H-NMR spectrum of subsequent products, there seemed to be a residual peak for the product of unbrominated acid. Starting material was not apparent in the tlc experiments carried out on the bromination reaction mixture prior to work up (R_f=0.14(product), R_f=0.36(starting material); ethyl acetate:hexane 4:6), and the residual peak in the ^{1}H-NMR was interpreted as being due to residual acetone. Since we were at this point unaware of the nature of this impurity no recrystallisation was carried out at this step, since distillation was planned for step 2. This impurity hampered the progress of subsequent steps of the synthesis, and in retrospect, this reaction should have been left longer under reflux and the product carefully recrystallised.

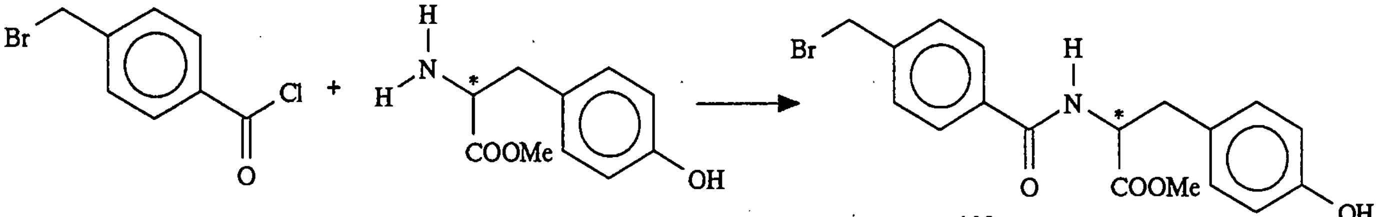
The second step in the synthesis was the formation of the acid chloride **126** (Scheme 72). For this reaction thionyl chloride was used as both solvent and reactant, and the solid p-bromomethylbenzoyl chloride **126** was obtained in a 78% overall yield after vacuum distillation.



124 **126**

Scheme 72

The chiral auxiliary was introduced in the third step via the condensation of the acyl chloride **126** with *l*-tyrosine-methyl ester under Schotten-Bäumann conditions (Scheme 73)[11] to yield only one product on tlc. The crude solid was recrystallised from ethyl acetate/methanol (3:1) and ^{1}H and ^{13}C-NMR showed it to be pure apart from a small amount of unbrominated compound that had been carried through from step 1. It was not possible to fully eliminate this impurity by recrystallisation nor by chromatography.

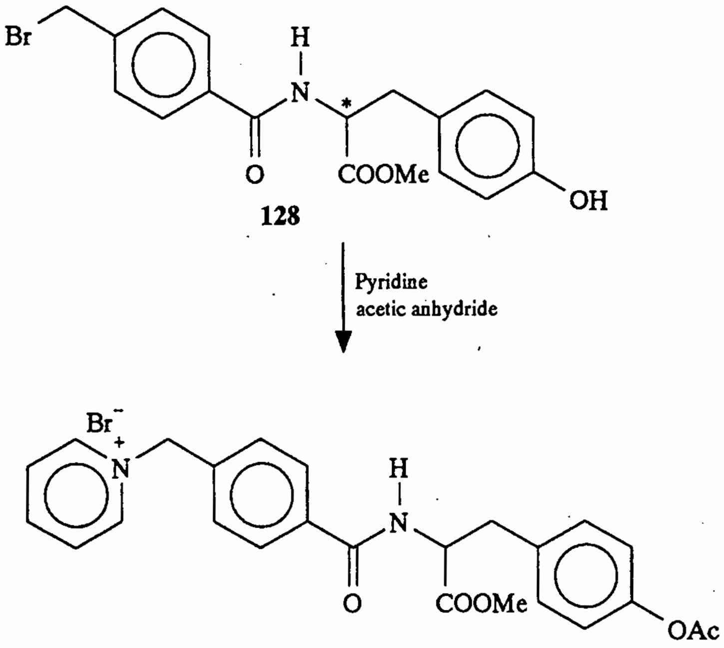


126 **127** **128**

Scheme 73

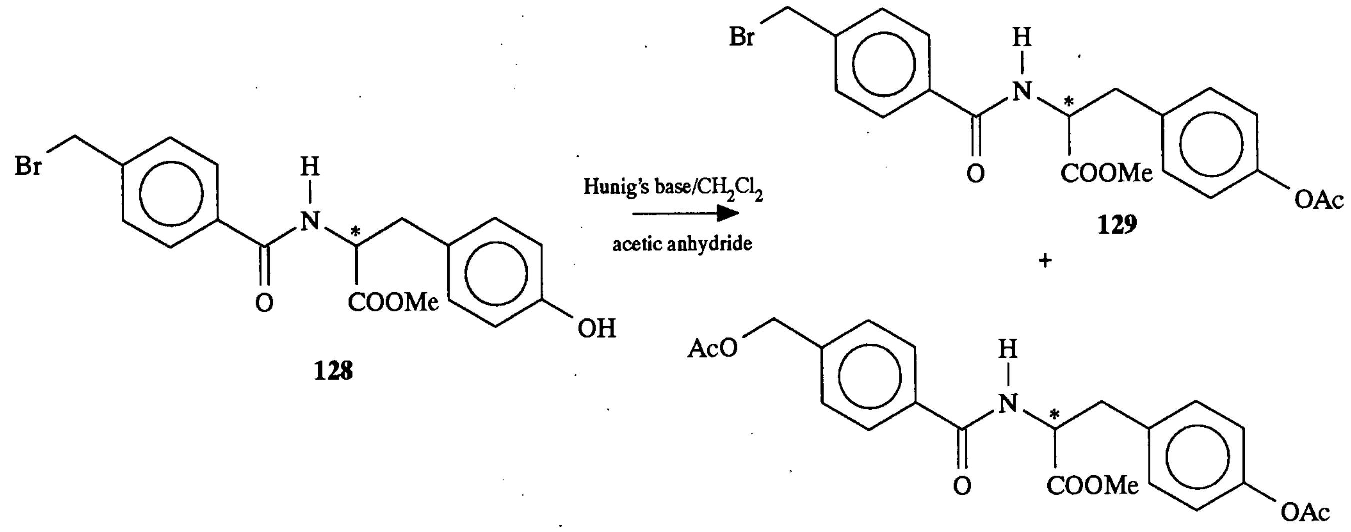
In the ^{1}H-NMR the exchangeable phenolic hydroxyl and amide protons could be observed as two downfield peaks at δ=8.8ppm and δ=9.2ppm respectively, each integrating for one proton in d_6-DMSO. A spectrum run in d_6-acetone indicated exchange occurring. The proton at the chiral centre resonated at 5.00ppm and the two adjacent benzylic protons at δ=3.27ppm formed an AA'B system. Of the four aromatic signals, the one furthest upfield at δ=6.66ppm was assigned as the two protons *ortho* to the hydroxyl group, due to mesomeric shielding. The signal at d=7.08ppm was assigned as the protons *meta* to the hydroxyl group, whereas the most downfield of the aromatic signals was assigned to the protons *ortho* to the bromide group δ=7.79ppm followed by those *meta* to it at δ=7.52ppm. The bromomethylene signal appeared as a singlet at δ=4.73ppm in the ^{1}H-NMR spectrum and, although diastereotopic protons, did not undergo coupling. In the ^{13}C-NMR spectrum the furthest upfield of the aromatic signals was assigned as the carbons at the *ortho* positions of the phenolic ring (δ=115.0ppm).

The next step in the sequence involved protection of the tyrosine phenolic OH so as to prevent exchange with the basic borate anion once cation exchange had taken place to the cyanoborate salt. Acetylation was chosen as the protection step as it involved mild conditions. However, complications arose with the lability of the benzylic halide. Use of the normal acetylation conditions (pyridine/acetic anhydride) resulted in the formation of the N-benzyl pyridinium salt. (Scheme 74(a)) Although this could have been used as the cation of the borate salt, previous work had established that the pyridinium cation is incompatible with the borate anion.

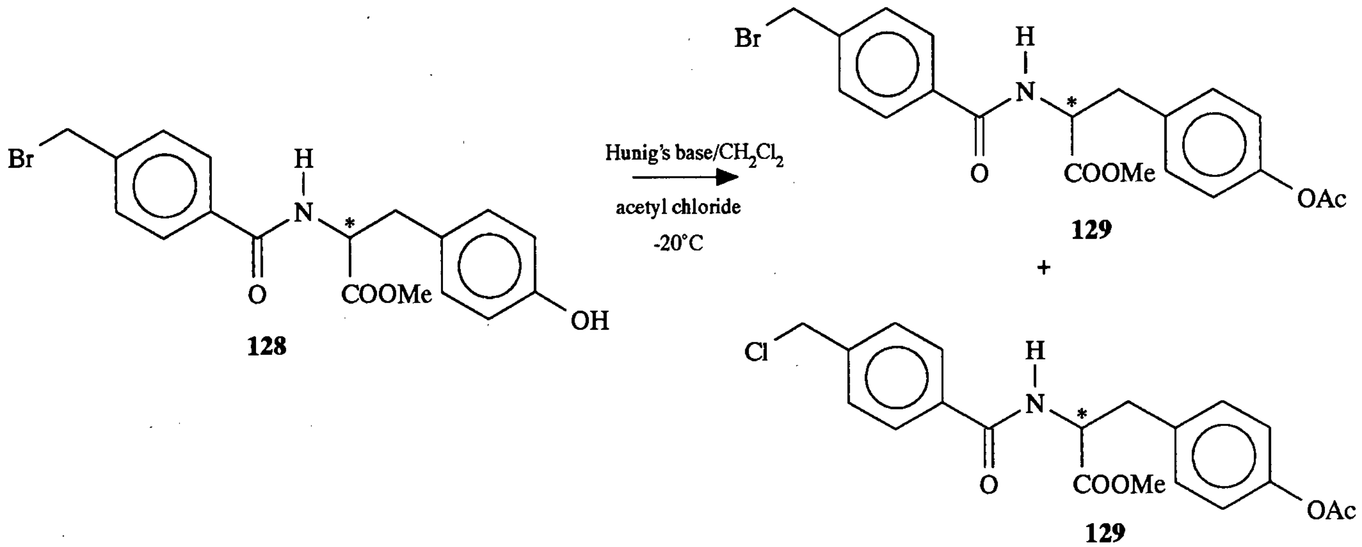


Scheme 74(a)

In view of this complication the base was changed to Hünig's base (N,N-diisopropylethylamine) which is a lot more basic than pyridine, but essentially non-nucleophilic. Owing to the danger of racemization, the reaction was carried out at low temperatures (-78°C warming up to 0°C). However, this time complications arose with nucleophilic substitution of the benzylic halide by acetate. (Scheme 74(b)) This was evidenced by the appearance of a second acetate resonance at δ=2.10ppm in the ^{1}H-NMR, as well as a new signal for a carbonyl group and doubling up of the bromomethylene signal in the ^{13}C-NMR spectrum. The reaction was monitored by tlc and even after two days there was still some bromide, indicating that there was an equilibrium between the two products. From the product ^{1}H-NMR spectrum it was clear that the equilibrium was in favour of the di-acetate, acetate being a better nucleophile. Both products had very similar R_f chromatographic values. Acetate was considered unlikely to be a suitable leaving group for introduction of the phosphonium group, and so the acetylating agent was changed to acetyl chloride.(Scheme 74(c))



Scheme 74(b)



Scheme 74(c)

This reaction went at low temperature according to plan but the reactivity of the benzylic bromomethylene group was further demonstrated by the exchange of halides. The ^{1}H-NMR spectrum clearly revealed a mixture of the two halides, with the chloromethyl protons resonating further downfield at δ=4.80ppm (bromomethyl was at δ=4.73ppm) due to chlorine's greater electronegativity. The `doublet' in the aromatic region at δ=7.82ppm (bromide was at δ=7.8ppm) assigned to the protons *ortho* to the bromomethylene group showed some doubling up due to the mixture of halides, thus supporting the assignment at step 3. A small amount of pure sample was prepared for characterisation purposes and in the ^{1}H-NMR spectrum the diastereotopic protons adjacent to the chiral centre (ABX system) showed up as two doublet of doublets at δ=3.27ppm with vicinal and geminal coupling constants of J=5.7, 5.8Hz and 14.0Hz respectively. The chiral proton resonated as a triplet of doublets at 5.00ppm with J values of 1.6Hz, 5.7Hz and 5.7Hz i.e with a small coupling to the N-H proton. Since the rest of the molecule had retained its character, it was decided to continue using this mixture in the following step of the synthesis.

In retrospect, the use of acetyl bromide in place of acetyl chloride would have avoided this complication or alternatively, the tyrosine part of the molecule could have been protected before coupling. Both of these possibilities would have alleviated the analysis problems encountered. Time limitations, however, precluded exploring these options.

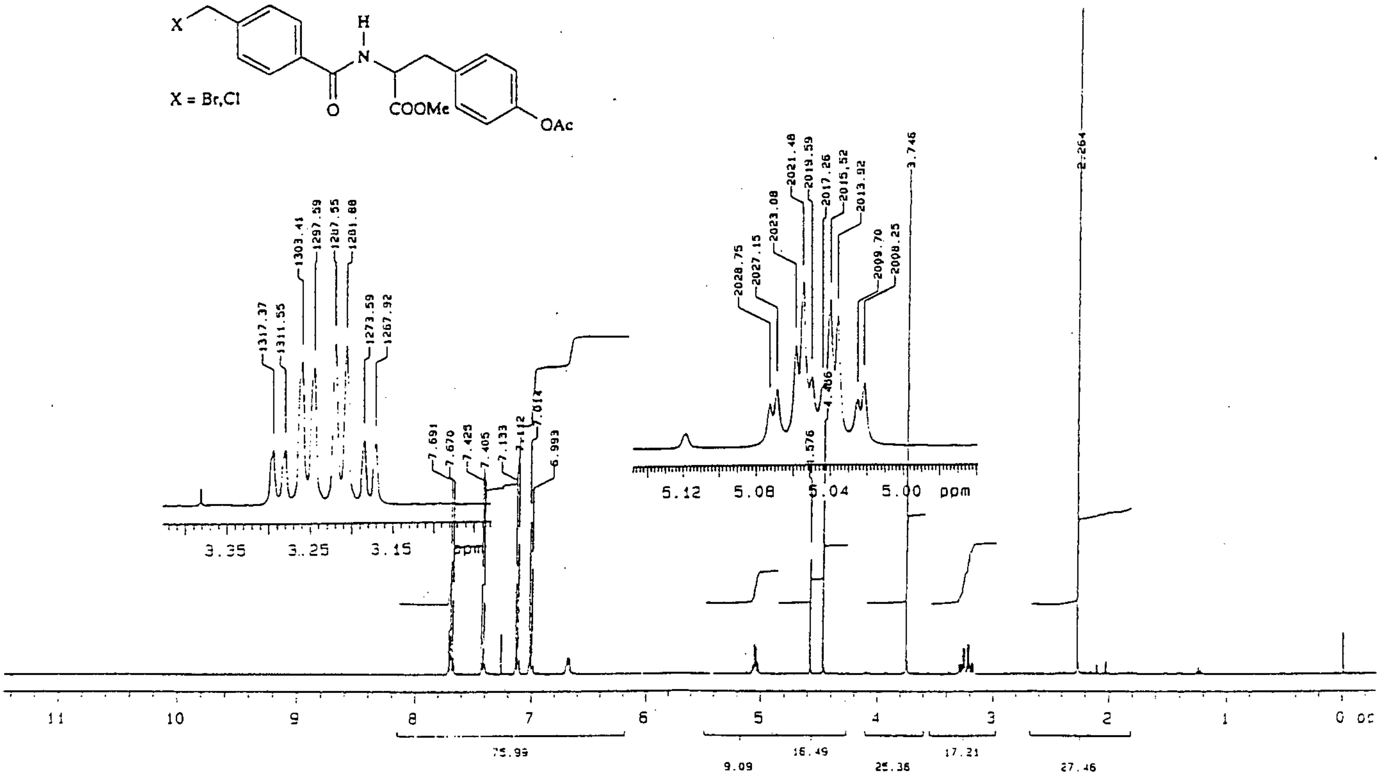


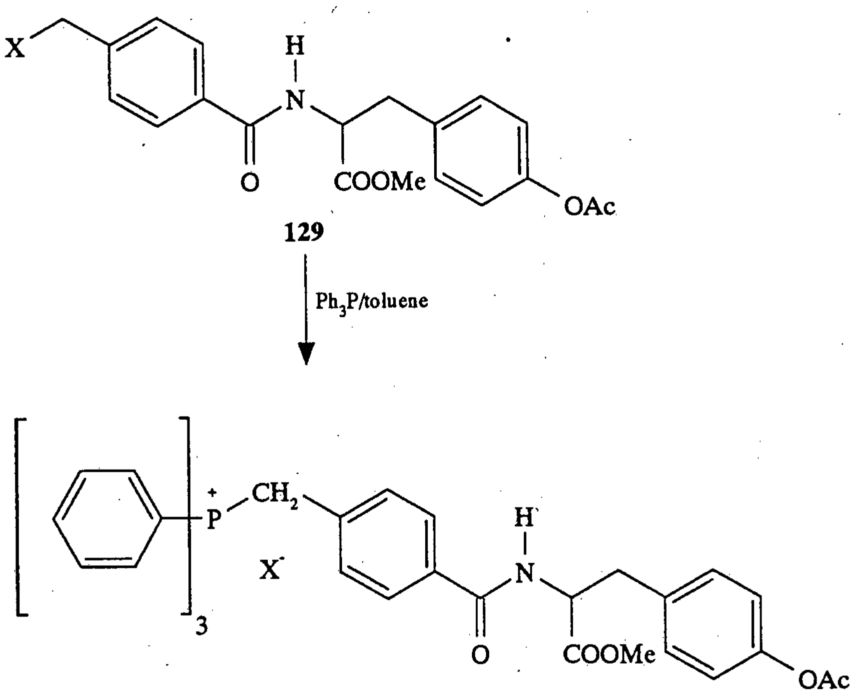
Figure 35

At this stage **129** consisted of a bulky chain between two phenyl rings which showed interesting solvent dependent behaviour. Both the ^{1}H-NMR spectra and the $[\alpha]_D$ were run in different solvents and gave remarkably different results. The NMR spectra were run in deuteriochloroform and in deuterated DMSO. The signal which showed the biggest shift was the N-H proton which appeared at δ=8.90ppm in d_6-DMSO compared to δ=6.68ppm in $CDCl_3$. (Figure 35) This shift may be explained by a change in conformation influencing the electronic environment of this proton. Since conformational effects alone provide insufficient explanation, it is likely that DMSO takes part in hydrogen bonding causing some deshielding of the proton attached to nitrogen.

Similarly, solvation effects could be reflected in the $[\alpha]_D$ values of the compound. While it is not unusual to see a change in $[\alpha]_D$ from one solvent to another, it is exceptional to see a change from (+) to (-) for a compound run in different solvents. Both *l*-tyrosine-methyl ester **127** starting material and the phenol **128** gave negative values for $[\alpha]_D$. Both were determined in polar solvents, such as water and ethyl acetate which have varying hydrogen bonding capabilities. When the rotation of the acetate **129** was taken in ethyl acetate, it also gave a minus result of $[\alpha]_D$ -15.45°. However, when taken in chloroform, the molecule gave a dextrorotatory reading of $[\alpha]_D$ +65.09°. No comparison was made with the first two compounds because they were insoluble in chloroform. This phenomenon has been documented[12] for another compound, atrolactic acid ($C_6H_5C(CH_3)OHCO_2H$), which is dextrorotatory in benzene and levorotatory in ether.

The explanation has interesting implications for inclusion coordination. Optical rotation is a function of the polarisability of a molecule around its asymmetric centre, and in general can be weighted according to the atomic/molecular masses of the groups around it. When a molecule forms a complex or weak bond with the solvent, the weightings around the chiral centre are altered, resulting in a change in the effect of plane polarised light. The acetate's **129** behaviour indicates that a hydrogen (amide hydrogen) on or close to the chiral carbon is involved in some way in hydrogen bonding/association with the solvent. This would increase the likelihood of inclusion being stereospecific.

The final step in the cation synthesis was carried out by refluxing the halide mixture **130** with triphenylphosphine in toluene for 48 hours. (Scheme 75) The precipitated salt was filtered and after recrystallisation from ethyl acetate/methanol gave a compound with spectroscopic data consistent with the desired product. In particular, the resonance of the methylene protons adjacent to phosphorus appeared as a doublet at δ=5.32ppm (J=8.5Hz) due to H-P coupling.



129

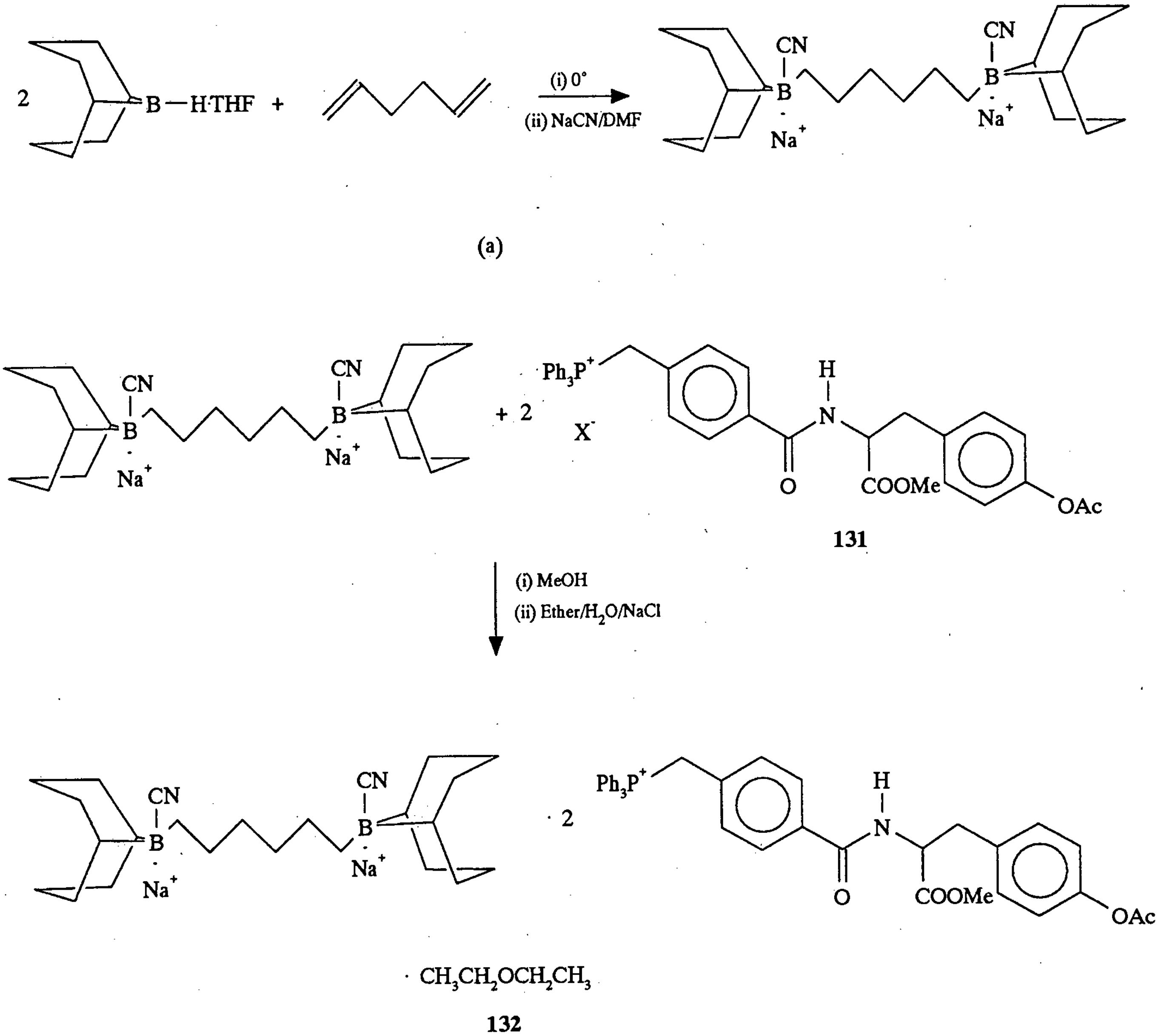
130

Scheme 75

A sample of **129** was dissolved in water and precipitated out as its hexafluorophosphate salt **131** to circumvent the problem of mixed halide counter-ions. This sample gave a correct analysis.

The borate anion was synthesised as before by hydroboration of 1.5-hexadiene with two equivalents of 9-(borabicyclo[3.3.1]nonane) followed by the cyanidation[14] (Scheme 76(a)) and the exchange of sodiums for the phosphonium cation (Scheme 76(b)). After the work-up a pale yellow gum formed, which was not unexpected due to the size and flexibilty of the tyrosine side chain of the cation. Upon drying rigorously *in vacuo* with gentle heating a solid resulted. Besides having a vitreous appearance under the microscope, the compound had no real melting point indicating heterogeneity.

Phosphonium Cyanoborate salt (VI)



(a)

131

132

(b)

Scheme 76

NMR studies showed that the borate salt displayed all of the relevant signals indicative of both anion and cation. The methylene peak for the benzylic group bonded to phosphorus and the chiral proton had overlapping signals at δ=4.83ppm integrating for six protons. From the ^{1}H-NMR spectrum it could be seen that ether was included from the extraction in a host-guest ratio of approximately 1:1. Thus, the compound was similar to the benzyltriphenylphosphonium salt **102** in this regard, except as hoped for the *para*-substituent helped to increase the inclusion ratio.

The infra red spectrum of the borate **132** displayed a peak at 3056cm^{-1} indicating that it also included water from the extraction. However, the ^{1}H-NMR spectrum showed many unexpected peaks, one of which was the doubling up of the methyl peak of the ester. This also appeared in the ^{13}C-NMR spectrum. Purification presented a major problem with this salt and since it was washed in hot water, it is conceivable that some hydrolysis of the anion took place to form a cyanoborinate (Chapter 4). With the cyanoborate salts discussed in chapter 4, washing with ethyl-acetate or petroleum ether had been sufficient to clean them up, but in this case the solid did not respond favourably to either.

In retrospect, the use of warm water in place of hot water followed by precipitation from dichloromethane would have been a much safer purification option and seemed to work on a small scale.

5.4 NMR SHIFT EXPERIMENT

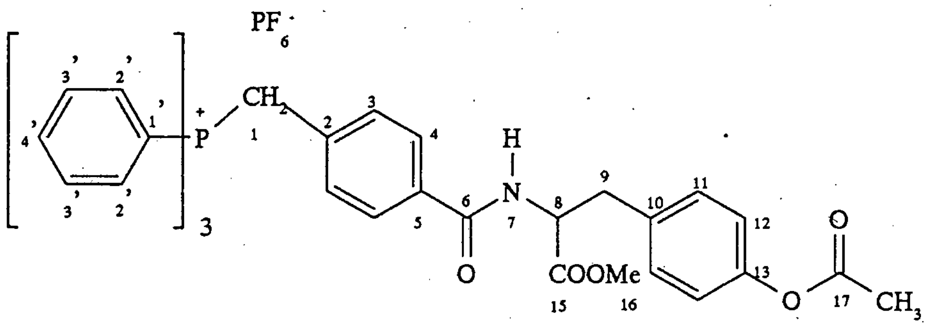
The ^{1}H-NMR spectra of complex molecules are often difficult to interpret because of overlapping resonances[15]. A cheap and efficient way to increase chemical shift differences is to use rare earth metals such as europium which are paramagnetic and in certain complexes, e.g. β-diketonates can provide a local magnetic field suitable for use in NMR experiments. The molecule in question can then reversibly coordinate to the metal complex at the OH group, and the local field due to the metal ion spreads out the peaks in the spectrum. In polyfunctional molecules, each functional group competes for the shift reagent according to its relative binding ability. An optically active shift reagent binds to R and S forms of a substrate with different binding constants. Thus, if the binding is sufficiently strong, the resonances of R and S forms are shifted to different extents. In this manner, the optical purity of R, S mixtures can be determined.

In order to ascertain the stereochemical purity of the chiral phosphonium salt **131** a NMR shift experiment was carried out using the six-coordinate chiral shift reagent, tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato]ytterbium(III), which was titrated against a solution of the phosphonium hexafluorophosphate **131**. It was hoped that the chiral lanthanide shift reagent would co-ordinate with a Lewis basic site in the molecule concerned and thus form diastereomeric complexes with each of any enantiomers present. The lanthanide reagent could in principle bind to four possible sites in this molecule, namely to the amide, the carbonyl, the methoxyl or the acetate group. In practice however, it was hoped that the shift reagent would bind to the amide functionality, which being close in proximity to the chiral centre would result in observable differences in the shifts of the two enantiomers that might be present. Table 26 summarises the results.

TABLE 26
NMR shift data.

<table>
<tr><th colspan="5">δ(ppm) of **131** without L.R.S.</th></tr>
<tr><th colspan="5">proton</th></tr>
<tr><th>1</th><th>8</th><th>9</th><th>16</th><th>18</th></tr>
<tr><td>5.24(d)</td><td>4.65(m)</td><td>2.97-3.25(br.m.)</td><td>3.63(s)</td><td>2.24(s)</td></tr>
<tr><th colspan="5">δ(ppm) of **131** with L.S.R.</th></tr>
<tr><th>1</th><th>8</th><th>9</th><th>16</th><th>18</th></tr>
<tr><td>1. 4.8(br.m.)</td><td>4.6(br.s.)</td><td>3.52(d)</td><td>3.73</td><td>2.33</td></tr>
<tr><td>2. 4.96(m)</td><td>5.74(br.s.)</td><td>3.60(br.s.)</td><td>3.77</td><td>2.41</td></tr>
<tr><td>5.10(m)</td><td></td><td>3.84(br.s.)</td><td></td><td></td></tr>
<tr><td>3. 5.06(t)</td><td>6.40(br.s.)</td><td>3.60(br.s.)</td><td>3.80</td><td>2.45</td></tr>
<tr><td>5.20(t)</td><td></td><td>4.00(br.s.)</td><td></td><td></td></tr>
</table>

L.S.R. Lanthanide shift reagent
1. run 1: 0.0017mol(L.R.S.)/ml
2. run 2: 0.0034mol(L.R.S.)/ml
3. run 3: 0.0051mol(L.S.R.)/ml



131

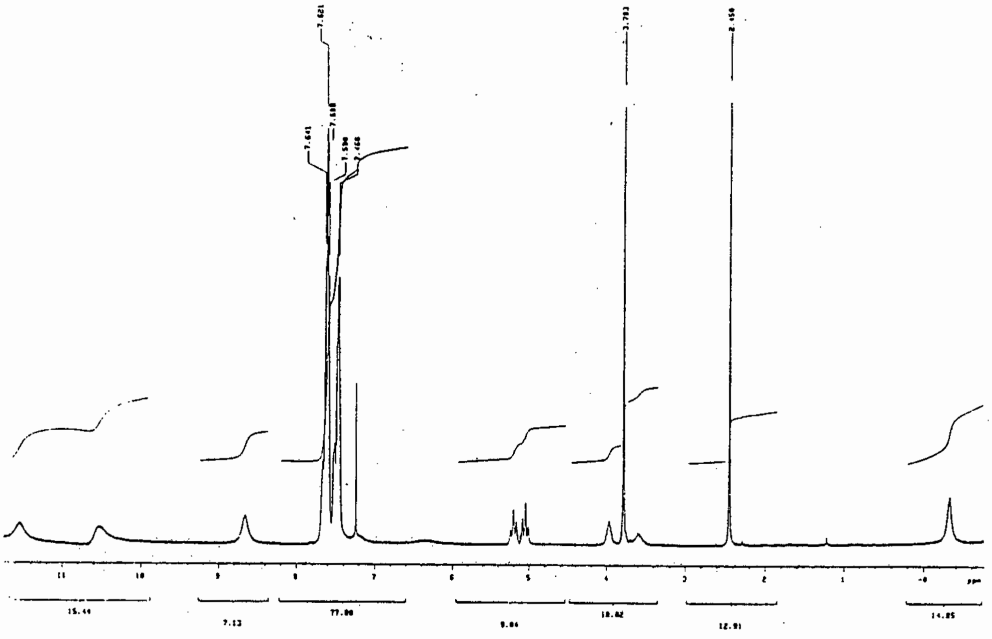


Figure 36

Consistent with the idea that the shift reagent binds the most strongly to the amide group, the largest shift was observed for the proton at the chiral centre (H-8) of up to about 2ppm downfield, followed by the two sets of benzylmethylene protons (H-1 and H-9) boded to phosphorus and the chiral centre respectively. In the former, the starting multiplet quickly collapsed to a broad singlet. By comparison, the diastereotopic protons close to phosphorus, which initially appeared as only a doublet due to P-H coupling, eventually separated into two well-resolved triplets showing geminal coupling as a result of enhanced diastereotopicity. Similarly, the methylene protons vicinal to the proton at the chiral centre eventually also separated into two signals but as broad singlets. The two singlets for the acetate and methyl ester groups were shifted to a lesser extent. These results, particularly once resonances appeared separated (Figure 36) strongly suggests the presence of one enantiomer only, but further studies using decoupling experiments are needed for unambiguous assignment. Another spectroscopic study (^{1}H-NMR) that might be done in principle, is to exchange the anion PF_6^- for a chiral one in the hope of observing any diastereomers arising from an enantiomeric mixture. Degradation of the phosphonium salt **131** to obtain the tyrosine auxiliary was inappropriate in this case because of the risk of racemisation during hydrolysis. More studies are indeed required, even to the extent of chosing an auxiliary which cannot racemise during the synthesis.

5.5 INCLUSION EXPERIMENTS

In view of the problems associated with the synthesis and purification of the chiral salt () as well as the assessment of its optical purity, it was not possible to undertake a comprehensive study of the inclusion of chiral guests. However, in order to justify initiating a comprehensive study of these issues, it was decided to undertake an exploratory investigation into the potential inclusion activity of the salt with a range of solvents as done previously with the other salts. This appeared justified in view of the compound's inclusion activity with ether. All investigations were carried out on the crude borate (typically 100mg) dissolved in dichloromethane with the guest as before. Compound **132** did not dissolve in neat toluene nor *t*-butanol. All samples were left to evaporate until solid appeared which was vacuum dried for 30 min. and characterised by ^{1}H-NMR and TGA. The ratios determined for the inclusion of ether were calculated from the crude product from the extraction. Table 27 summarises the results.

TABLE 27

Results of inclusion experiments with $[(C_8H_{14})(CN)B^-(C_6H_{12})B^-(CN)(C_8H_{14})\cdot 2Ph_3P^+CH_2PhCONH\text{-}CH(COOMe)(CH_2C_6H_4OAc]\cdot$ether

Guest	^{1}H-NMR
Acetonitrile	1.0
Acetone	decomposes
Methanol	decomposes
Toluene	3.5
t-Butanol	2.6
Dichloromethane	1
Pyridine	dissolves
Ether	1

These preliminary results show that the guest inclusion spectrum has been shifted into a more polar range compared with that of the prototype host **47**. Moreover, the inclusion ratios are much higher than those of **47**. The inclusion of *t*-butanol, probably via hydrogen bonding, suggests that other hindered alcohols may be candidates for inclusion by this host compound. As expected methanol resulted in decomposition. Thus, it would appear that preliminary aspirations for inclusion activity have been met based on the idea that a substituted benzyltriphenylphosphonium salt could meet the lattice requirements as suggested by studies in chapter 4.

Preliminary observations of the behaviour of this salt with furan showed the same colour changes and similar dissolution behaviour as for the bis(methyltriphenylphosphonium) cyanoborate. However, the sample of host investigated was too small to give conclusive results as to whether a liquid clathrate had formed. These observations, together with the inclusion data, show that this compound has a wide range of inclusion possibilities, which may be ascribed to the molecule possessing a variety of donor and acceptor sites for association[8]. Furthermore, they justify an in-depth study being undertaken on the use of chiral substituted benzyltriphenylphosphonium cyanoborates as optical resolving agents.

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CHAPTER 6

CONCLUSION

Supramolecular chemistry is a topical subject in chemistry and focuses on intermolecular bonding between substrates. It has had great influence on the development of separation technology, biomimetic systems, molecular devices and even synthesis, and transcends the borders of physical, organic, inorganic and analytical chemistry.

Molecular recognition forms an integral part of supramolecular chemistry and complementarity of substrates is the determining factor of recognition. In the case of clathrates, this is seen as a strictly steric consideration, so steric and spatial factors are very important. Aromatic rings rigidify and organise binding sites, participate in specific aromatic binding interactions, and serve as points of attachment for functional groups for recognition and even catalysis. Moreover, they are very useful in the creation of spaces within the lattice. In the design of hosts it is thus important to combine the steric and electronic factors in such a way as to optimize the binding capabilities of the receptors. Besides increased selectivity, co-ordination assisted host-guest interactions increase the stability of the complex. Complementary placement of binding sites and careful consideration of spatial requirements in the host and guest leads to a high degree of recognition.

During synthetic studies on developing an electrolyte for the Zebra battery, a novel class of cyanoborate compound was discovered, which constitutes the first, air-stable cyanoborate host family. The prototype, methyltriphenylphosphonium cyanoborate salt **47**, forms coordinatoclathrates with a fairly modest inclusion activity, and this led to the exciting discovery of its water-dependent solid and liquid clathrate behaviour. In general, the anhydrous host **47** formed solid clathrates with mainly nonpolar aromatic guests which was exemplified by its X-ray structure with *p*-xylene. Liquid clathrate formation was observed with the guests furan thiophene and benzene, but only in the presence of a certain amount of water. Crystalline clathrates were obtained from all three liquid clathrate systems, and an X-ray analysis carried out on the furan clathrate gave invaluable information on the interactional forces operating within the lattice structure. The structure of this clathrate, as well as that of *p*-xylene with **47** are examples of coordinatoclathrates in a coordination assisted lattice. Coordination is provided by hydrogen bonding between a nitrogen of a cyano group and a hydrogen of a phosphonium methyl. The borate anion is in its preferred zig-zag conformation in which the two cyano groups are trans with respect to the B-B axis, whereas in the guest-free host the anion takes on a cisoid conformation. With both guests C-H$\cdots\pi\cdots$H-C interactions are prominent features involving a hydrogen of a methyl on a phosphonium group and a hydrogen from the *ortho* position of a phenyl group. The two hydrogens originate from different phosphonium cations. These anion-cation interactions were crucial for promoting guest inclusion. From these structures it became apparent that the phosphonium cation plays a pivotal structural role in this clathrate family and this species became a focal point of subsequent modifications. Moreover, these interactions were used as a guideline for the structure-activity study.

Studies on structurally modifying the spacer indicated that its length and flexibility were crucial factors in ensuring that the compounds were workable solid cyanoborates. In this regard, a hexamethylene chain proved to be the most promising spacer but further studies with spacers incorporating substituted phenyl groups would also be worthwhile. The introduction of heteroatoms into the spacer resulted in oils as products, which were undesirable for host-guest experiments. Similarly, changing the primer of the anion did not lead to viable, workable materials either. Thus, the focus of attention in the study centered predominantly on varying the cation. Changing the central cation to sulfur or nitrogen but keeping the substituents as one methyl and phenyl groups proved synthetically difficult and the alternative derivatives synthesised did not meet the steric and electronic requirements for establishing a coordination assisted lattice for guest inclusion. Thus, changing the phosphonium ligands, especially the methyl group proved to be the best option. The tetraphenylphosphonium and ethyltriphenylphosphonium derivatives were both inactive, while the cinnamyltriphenylphosphonium showed a very modest and highly restricted activity. This led to the important conclusion that benzyltriphenylphosphonium might meet the requirements as suggested from X-ray data, and indeed this was the case. This was rationalised in terms of retaining the hydrogen bonding features of the coordination assisted lattice as well as the larger size of the cation leading to larger lattice voids for inclusion. This watershed development in the structure-activity study resulted in a number of substituted benzyltriphenylphosphonium salts being evaluated. In this regard, substitution of the phenyl rings on phosphorus by a methoxyl group at the *para* position proved to be the most successful shift the inclusion range towards guests of higher polarity, e.g. CH_2Cl_2, and bodes well for future studies. Similarly, substituted phenyl-based substitution on the benzyl ring also has potential for modifying the inclusion activity. Finally, the wealth of information regarding the implications of substituent changes was put to good effect using the larger arsenic as the central atom. Methyl- and benzyltriphenylarsonium salts both gave promising results and empirically confirmed the validity of the structural model. Further X-ray analyses are required to validate this.

In summary, the various studies have established that a certain basic structural type of onium cyanoborate constitutes a new class of clathrand family and the first based on boron. Furthermore, they have opened up several areas for future investigation, particularly regarding further substitution studies for the inclusion of polar guests as well as the synthesis and evaluation of chiral salts in both the solid and liquid clathrate areas.

CHAPTER 7

EXPERIMENTAL

7.1 General

7.1.1 Characterisation of compounds

All melting points (m.p.) were determined on a Reichert Jung hot stage microscope and are uncorrected.

Infra-red spectra were recorded in chloroform, dichloromethane or carbon tetrachloride using a Perkin-Elmer 983 Spectrophotometer.

Routine proton nuclear magnetic resonance spectra (^{1}H-NMR) were recorded on a Varian EM 360 (60MHz spectrometer) or a Bruker90 (90MHz spectrometer). High resolution proton (^{1}H-NMR) and carbon-13 (^{13}C-NMR) spectra were recorded on a Varian VXR-200 (200.057MHz) and 50.31Mhz respectively) in deuteriochloroform, unless otherwise stated. The chemical shifts (δ) are given in ppm relative to the signal of tetramethylsilane TMS (δ=0.00) or the residual chloroform in the deuteriochloroform (δ=7.24).

Microanalyses for C, H and N were carried out using a Heraeus CHN-rapid combustion analyser (UCT).

Mass spectra were recorded on a VG micromass 16F mass-spectrometer (UCT).

Reactions that were monitored by thin layer chromatography (TLC) were carried out on Merck TLC aluminium sheets, silica gel 60 F_{254}, layer thickness 0.2mm. Detection was done by one of the following methods:
(a) using an ultraviolet lamp (wavelength 254nm),
(b) by placing the plate in iodine vapour for 5-10min,
(c) by heating the plate at 100°C after spraying with a mixture of 1ml conc. sulfuric acid and 10ml 2.5% anisaldehyde in ethanol or
(d) by heating the plate at 100°C after spraying with a 1% solution of cerium ammonium sulfate in 6N sulfuric acid.

Column chromatography was carried out on silica gel (merck, Silica gel 60, particle size 0.063-0.200mm (70-230 mesh ASTM)). Usually the amount of silica gel used was 100 fold of the crude product weight. The eluents are specified in each experiment.

7.1.2 Solvents

Commonly used solvents were purified as described below:

Tetrahydrofuran: Dried over sodium wire and then distilled from sodium and benzophenone under a nitrogen atmosphere immediately before use.

Benzene: Distilled from sodium wire and stored over sodium wire.

Dichloromethane: Stored over phosphorus pentoxide and distilled immediately before use.

Diethyl ether: Distilled from sodium and stored over sodium wire.

Dimethylformamide: Distilled from calcium hydride and stored over molecular sieves (4Å).

Pyridine: Distilled from potassium hydroxide and stored over molecular sieves (4Å).

Pet. ether (boiling range 60-70°C), hexane and ethyl acetate for column chromatography were distilled.

7.1.3 Experimental conditions

All non-aqueous reactions were done under a nitrogen atmosphere and the reagents were introduced into the reaction flask via syringe.

After the standard work-up procedure as specified, the organic fractions were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo*, which refers to the removal of solvent under reduced pressure on a Büchi rotary evaporator.

7.1.4 NMR Shift Experiment

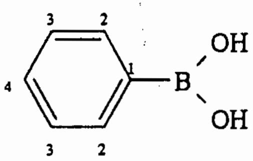
A shift experiment was carried out on the phosphonium hexafluorophosphate salt (32mg in 0.7ml $CDCl_3$). The chiral lanthanide shift reagent (34.2mg in 0.5ml $CDCl_3$) was titrated in 0.05ml aliquots and the spectra were recorded on the 400MHz instrument.

7.1.5 Inclusion Compound Formation

Inclusion compounds were formed by dissolving the host compound in either dichloromethane, which had been dried over phosphorus pentoxide or THF, which had been dried over benzophenone and sodium wire. A small amount of guest liquid, in at least ten times molar excess of the host, was then added. The resulting solution was allowed to evaporate slowly at room temperature until solid had formed. This was then filtered, washed with diethyl ether and air dried. In cases, where the host included ether, it was filtered, washed with pet. ether and air dried. The host-guest ratios were determined by ^{1}H-NMR and by TGA.

7.2 Synthesis of Triorganylboranes

Phenylboronic acid 3[1]



To a solution of dry ether (50ml) under nitrogen, was added tripropylborane (21.9ml, 100mmol) and the solution cooled to -70°C. Phenylmagnesiumbromide (prepared from bromobenzene (10.5ml, 100mmol) and Mg turnings (2.6g, 110mmol)) was then added dropwise and the solution stirred for 30min. at -70°C, after which time the temperature was left to rise slowly to 0°C. Addition of dilute sulfuric acid (60ml, 1M) resulted in the formation of two layers which was extracted in the normal way (3 x 100ml ether), dried ($MgSO_4$), filtered and the solvent removed. The solid was then washed with hot distilled water and hexane to remove borinic acid and the aqueous layer separated to give boronic acid crystals after reduction of volume. The solid was filtered and dried *in vacuo* to afford **3** (10.9g, 44.7%) as colourless crystals, m.p. 210°C. (Lit. m.p. 214-216°C) (Phenylborinic acid was obtained from evaporation of the hexane layer.)
Phenylboronic acid was alternatively prepared from trimethylborate using the same method as above, but in an improved yield of 65%.

δ_H(d_6-DMSO) 7.24-7.47 (3H, m, H-3, H-4), 7.76-7.89 (2H, m, H-2), 8.04 (2H, br.s., OH)

δ_C 127.4 (C-2), 130.0 (C-4), 134.1 (C-3)

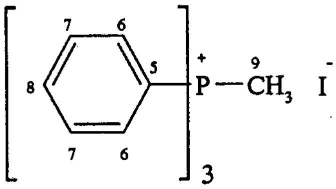
δ_H 3.33-3.46 (2H, m, H-3, H-4), 3.40 (3H, s, H-1'), 3.62-3.74 (4H, m, H-2, H-5, H-6), 3.93-4.44 (8H, m, H-2', H-3', H-4', H-6'), 4.78 (1H, d, J 6Hz, H-1), 5.11-5.35 (8H, m, H-2''', H-3''', H-4''', H-6'''), 5.82-6.09 (8H, m, H-2'', H-3'', H-4'', H-6'')

δ_C 54.9 (C-1'), 68.4 (C-6), 69.9 (C-4), 72.4 (C-2, C-5), 73.7 (C-3), 74.1 (C-3'), 77.3 (C-4'), 79.4 (C-2'), 81.4 (C-6'), 98.2 (C-1), 116.2, 116.5, 117.0, 117.4 (C-2''', C-3''', C-4''', C-6'''), 134.5, 134.8, 134.9, 135.3 (C-2'', C-3'', C-4'', C-6'')

m/z 323 (M^+ -31, 1%), 265 (8%), 71 (13%), 101 (32%), 140 (37%), 153 (51%), 41 (100%).

7.4 Synthesis of onium salts[4]

Methyltriphenylphosphonium iodide **15A**

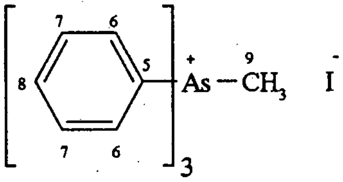


Triphenylphosphine (6.56g, 25mmol) dissolved in benzene (40ml) and methyl iodide (3.55g, 30mmol) were stirred overnight. The resultant solid was then filtered, washed with benzene and dried to afford (23) (9.75g, 96.5%) as a colourless solid, m.p. 182-184°C (Lit. m.p. 183-185°C), which was recrystallised from a mixture of ethyl acetate and MeOH (3:1).

δ_H 3.17 (3H, d, $J_{H\text{-}P}$ 13.2Hz, H-9), 7.65-7.95 (15H, m, H-6, H-7, H-8)

δ_C 11.3 ($J_{C\text{-}P}$ 56.8Hz, C-9), 118.5 ($J_{C\text{-}P}$ 88.2Hz, C-5), 130.3 ($J_{C\text{-}P}$ 12.9Hz, C-6), 133.1 ($J_{C\text{-}P}$ 10.7Hz, C-7), 135.0 (C-8)

Methyltriphenylarsonium iodide **115**

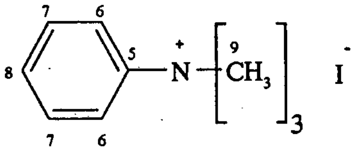


Triphenylarsine (3.67g, 12mmol) and methyl iodide (1.68ml, 27mmol) were heated in a pressure tube to 80°C for 3 hours. The resultant solid was then filtered, washed with acetone and dried to afford **115** (3.4g, 63.2%) as colourless crystals, m.p. 176-178°C, after recrystallising from acetone.

δ_H 2.89 (3H, s, H-9), 7.39-7.62 (15H, m, H-6, H-7, H-8)

δ_C 9.8 (J_{C-P} 1.5Hz, C-9), 120.8 (C-5), 130.3 (C-6), 131.6 (C-7), 133.6 (C-8)

Phenyltrimethylammonium iodide **90**

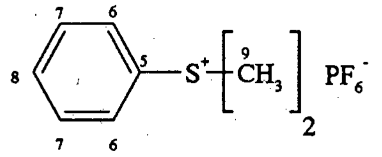


A mixture of N,N-dimethylaniline (10ml, 78.4mmol) in DMF (50ml) and methyl iodide (5.3ml, 85mmol) was stirred overnight at room temperature. The resultant solid was then filtered, washed with ether and dried to afford **90** (20.3g, 98.4%) as a colourless solid, m.p. 223-225°C (Lit. m.p. 227°C), which was recrystallised from ethyl acetate and MeOH (3:1).

δ_H 3.66 (9H, s, H-9), 7.50-7.72 (3H, m, H-7, H-8), 7.95-8.07 (2H, m, H-6)

δ_C 56.4 (C-9), 120.3 (C-6), 123.8 (C-5), 129.9 (C-7), 147.1 (C-8)

Dimethylphenylsulfonium hexafluorophosphate **86**

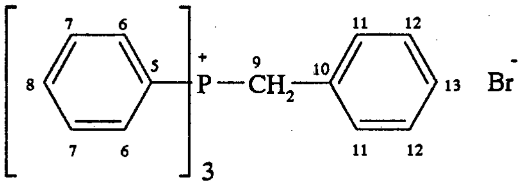


To a solution of thiophenol (10.2ml, 100mmol) in degased MeOH (150ml) was added KOH (6.2g, 110mmol) and the mixture cooled to 0°C before adding methyl iodide (6.85ml, 110mmol) dropwise via a pressure equilibrating dropping funnel. The mixture was stirred for 5min. at 0°C, allowed to warm up to room temperature and stirred for 48hrs. MeOH was removed *in vacuo* and the resulting solution extracted with water and ether (3 x 75ml). The organic layer was dried over $MgSO_4$ and the volume reduced to afford **86** (8.7g, 69.9%). Methylthiophenol (3g, 24.2mmol) dissolved in benzene (50ml) and dimethyl sulfate (2.9ml, 30mmol) were heated to 100°C for 3hrs. Benzene was then removed *in vacuo* and a solid slowly precipitated out, which was washed with ether, filtered and dried to afford the methyl sulfite salt (4.95g, 87.3%) as a beige solid, which was recrystallised from benzene and ethyl acetate. Ammonium hexafluorophosphate (0.03g, 20mmol) dissolved in water (1ml) was added to the sulfite (4.7g, 20mmol) dissolved in hot water (20ml). A white precipitate formed immediately and was filtered, washed with water and dried to afford **86** (7.4g, 90%), m.p. 154-157°C.

δ_H 3.26 (H-9), 7.83-7.91 (3H, m, H-7, H-8), 8.01-8.17 (2H, m, H-6)

δ_C 28.2 (C-9), 126.7 (C-5), 129.8 (C-6), 130.5 (C-7), 133.8 (C-8)

Benzyltriphenylphosphonium bromide **101**

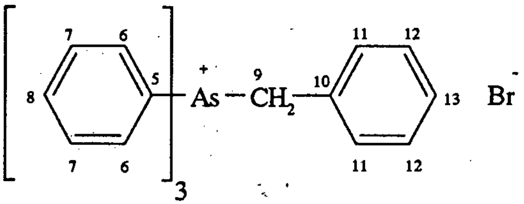


A mixture of triphenylphosphine (10g, 38mmol) dissolved in benzene and benzylbromide (5.0ml, 42mmol) was refluxed for 24 hours. The resultant solid was filtered, washed with benzene and dried to afford **101** (15.7g, 95.3%) as a colourless solid, m.p. 283-285°C, which was recrystallised from ethyl acetate and MeOH (3:1).

δ_H (d_6-DMSO) 5.22 (2H, d, $J_{H\text{-}P}$ 14Hz, H-9), 6.94-7.07 (2H, m, H-11), 7.08-7.34 (3H, m, H-12, H-13), 7.60-7.99 (15H, m, H-6, H-7, H-8)

δ_C 28.3 ($J_{C\text{-}P}$ 48Hz, C-9), 117.8 ($J_{C\text{-}P}$ 84.9Hz, C-5), 127.8 ($J_{C\text{-}P}$ 8.5Hz, C-10), 128.3 ($J_{C\text{-}P}$ 3.7Hz, C-13), 128.7 ($J_{C\text{-}P}$ 3.1Hz, C-12), 130.1 ($J_{C\text{-}P}$ 12.3Hz, C-6), 130.8 ($J_{C\text{-}P}$ 5.4Hz, C-11), 134.0 ($J_{C\text{-}P}$ 9.8Hz, C-7), 135.0 (C-8)

Benzyltriphenylarsonium bromide **118A**

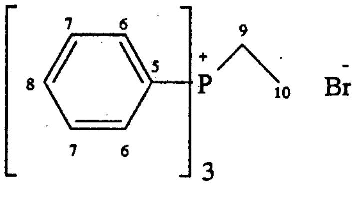


Triphenylarsine (3.0g, 9.8mmol) and benzylbromide (4ml, mmol) were heated to 90°C for 6 hours in a pressure tube. The resultant solid was filtered, washed with acetone and dried to afford **118A** (4.3g, 92%) as colourless crystals, m.p. 169-171°C.

δ_H 5.17 (2H, H-9), 6.83-7.10 (5H, m, H-11, H-12, H-13), 7.33-7.60 (15H, m, H-6, H-7, H-8)

δ_C 32.8 (C-9), 120.1 (C-5), 127.6 (C-10), 128.0 (C-13), 128.3 (C-12), 130.1 (C-6), 130.3 (C-11), 132.7 (C-7), 133.5 (C-8)

Ethyltriphenylphosphonium bromide **97**

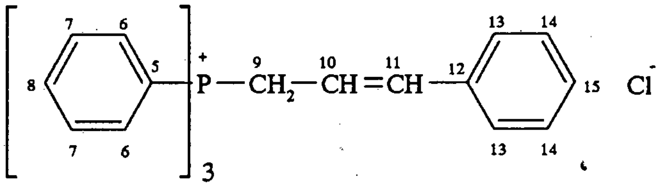


A mixture of triphenylphosphine (7.87g, 30mmol) dissolved in benzene (40ml) and bromoethane (2,98ml, 40mmol) was refluxed for 24 hours. The resultant solid was filtered, washed with benzene and dried to afford **97** (4.7g, 41.8%) as a colourless solid, m.p. 205-207°C (Lit. m.p. 206.5-207.5°C).

δ_H 1.14-1.38 (3H, dt, J_{H-H} 7.4Hz, J_{H-P} 19.9HZ, H-10), 3.56-3.78 (2H, m, H-9), 7.51-7.78 (15H, m, H-6, H-7, H-8)

δ_C 6.6 (J_{C-P} 5.2Hz, C-10), 16.9 (J_{C-P} 51.4Hz, C-9), 117.7 (J_{C-P} 85.5Hz, C-5), 130.2 (J_{C-P} 12.4Hz, C-6), 133.3 (J_{C-P} 9.8Hz, C-7), 134.8 (C-8)

1-(E)-3-phenylprop-2-enyltriphenylphosphonium chloride **104**

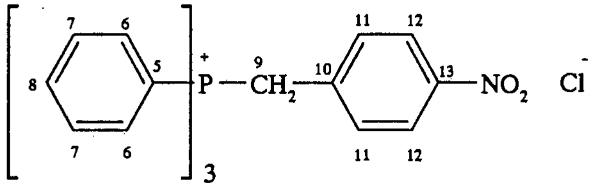


Cinnamyl chloride (3.05g, 20mmol) and triphenylphosphine (3.93g, 15mmol) were heated together without solvent until a homogeneous mixture had formed. After 1 hour the solution was allowed to cool whereupon a colourless solid precipitated out, which was filtered, washed with ethyl acetate and dried to afford **104** (5.77g, 92.7%),.m.p. 219-221°C.

δ_H 4.90 (2H, dd, J_{H-P} 15.5Hz, J_{H-H} 7.5Hz, H-9), 5.72-5.98 (1H, m, H-10), 6.62 (1H, dd, J_{H-H} 15.8Hz, J_{H-P} 5.6Hz, C-11), 7.08 (5H, m, H-13, H-14, H-15), 7.46-7.88 (15H, m, H-6, H-7, H-8)

δ_C 27.8 (J_{C-P} 48.7Hz, C-9), 113.6 (J_{C-P} 10.9Hz, C-11), 117.8 (J_{C-P} 85.0Hz, C-5), 126.2 (C-13), 128.1 (C-15), 128.3 (C-14), 130.1 (J_{C-P} 12.4Hz, C-6), 133.7 (J_{C-P} 9.8Hz, C-7), 134.7 (C-8), 135.5 (C-12), 139.8 (J_{C-P} 13.4Hz, C-10)

4-Nitrobenzyltriphenylphosphonium chloride **105**

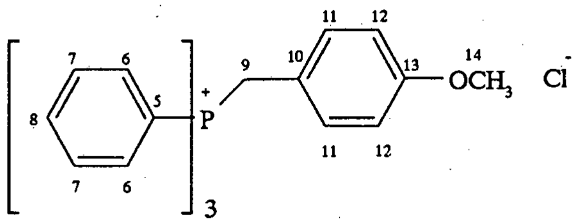


A mixture of triphenylphosphine (4.46g, 17mmol) and 4-nitrobenzyl chloride (3.25g, 19mmol) in benzene (25ml) was refluxed for 96 hours. The resultant solid was filtered, washed with benzene and dried to afford **105** (4.66g, 63.2%) as a beige solid, m.p. 258-260°C.

δ_H 6.13 (2H, d, J_{H-P} 16Hz, H-9), 7.40-7.90 (19H, m, H-6, H-7, H-8, H-11, H-12)

δ_C 29.7 (J_{C-P} 46.5Hz, C-9), 117.5 (J_{C-P} 85.6Hz, C-5), 123.2 (J_{C-P} 3.2Hz, C-), 130.1 (J_{C-P} 12.6Hz, C-6), 132.8 (J_{C-P} 5.3Hz, C-), 134.5 (J_{C-P} 9.9Hz, C-7), 134.9 (C-8), 136.2 (J_{C-P} 8.7Hz, C-), 147.3 (C-13)

4-Methoxybenzyltriphenylphosphonium chloride **107**

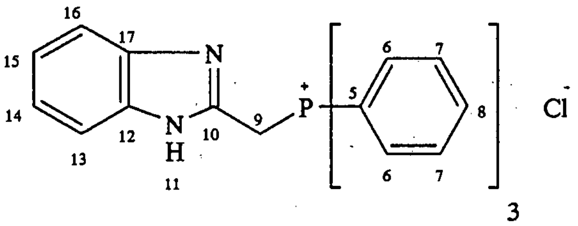


A mixture of triphenylphosphine (7.86g, 30mmol) (40ml) and 4-methoxybenzyl chloride (4.71g, 30mmol) in toluene was refluxed for 120 hours. The resultant solid was filtered, washed with toluene and dried to afford **107** (8.76g, 70%) as a colourless solid, m.p. 237-238°C.

δ_H 3.47 (3H, s, H-14), 5.06 (2H, d, J_{H-P} 13.8Hz, H-9), 6.38 (2H, d, J_{H-P} 8.8Hz, H-12), 6.76 (2H, dd, J_{H-H} 8.7Hz, J_{H-H} 2.5Hz, H-11), 7.32-7.64 (15H, m, H-6, H-7, H-8)

δ_C 29.6 (J_{C-P} 46.6Hz, C-9), 54.9 (C-14), 113.8 (J_{C-P} 3.1Hz, C-12), 117.5 (J_{C-P} 84.9Hz, C-5), 118.3 (J_{C-P} 8.6Hz, C-10), 129.9 (J_{C-P} 12.4Hz, C-6), 132.2 (J_{C-P} 5.4Hz, C-11), 133.9 (J_{C-P} 9.8Hz, C-7), 134,8 (C-8), 159.4 (C-13)

2-Benzimidazolylmethyltriphenylphosphonium chloride **108B**

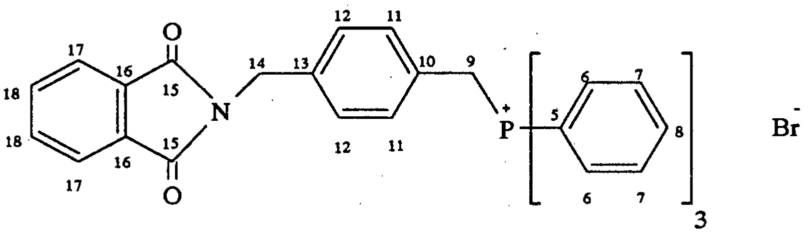


A mixture of triphenylphosphine (7.86g 30mmol) and 2-chloromethylbenzimidazol (5.0g, 30mmol) in benzene and acetonitrile (30:10ml) was refluxed for 24 hours. The resultant solid was filtered, washed with benzene and ether and dried to afford **108B** (12.3g, 95.8%) as a beige solid, m.p. 283-285°C.

δ_H 5.76 (2H, d, J_{H-P} 15.7Hz, H-9), 7.12 (2H, m, H-14, H-15), 7.45 (2H, t, J 7.3Hz, H-13, H-16), 7.62-7.98 (15H, m, H-6, H-7, H-8)

δ_C 23.8 (J_{C-P} 53.8Hz, C-9), 118.5 (C-16), 118.6 (J_{C-P} 86.9Hz, C-5), 121.5 (C-15), 122.6 (C-14), 129.9 (J_{C-P} 12.8Hz, C-6), 133.7 (C-17), 133.9 (J_{C-P} 10.6Hz, C-7), 134.8 (C-8), 142.7 (J_{C-P} 1.1Hz, C-12), 143.6 (J_{C-P} 6.8Hz, C-10)

Phthalimidetriphenylphosphonium bromide **108A**

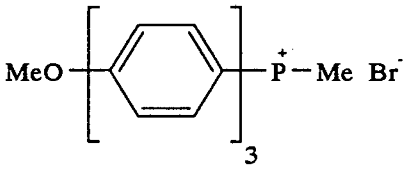


A mixture of triphenylphosphine (2.6g, 10mmol) and α,α'-dibromo-*p*-xylene (2.6g, 10mmol) in benzene (50ml) was stirred for 7 days at room temperature. The precipitated solid was then filtered, washed with benzene and dried to afford the monosubstituted product (45g, 85%) as a colourless solid. To this product (21g, 40mmol) dissolved in DMF (200ml) was added anhydrous K_2CO_3 (3g, 20mmol) and phthalimide (6g, 40mmol), and the mixture stirred and heated at 60°C for 48 hours. The mixture was then stirred at room temperature for 24 hours, before removing DMF *in vacuo* and adding ice/water (250ml). The resulting liquid was filtered, washed several times with water and dried to afford **108A** (17g, 72%) as a solid, m.p. 162-164°C.

δ_H 4.67 (2H, s, H-14), 5.12-5.18 (2H, d, $J_{H\text{-}P}$ 12Hz, H-9), 6.86-7.04 (4H, m, H-11, H-12), 7.38-7.80 (19H, m, H-6, H-7, H-8, H-17, H-18)

δ_C 30.2 (J 47Hz, C-9), 40.9 (C-14), 117.4 (J 85.2Hz, C-5), 123.2 (C-17), 126.6 (C-10), 128.2 (C-11), 130.1 (J 12.5Hz, C-6), 131.6 (C-12), 131.7 (C-16), 134.0 (C-18), 134.1 (J 9.6Hz, C-7), 134.8 (C-8), 136.5 (C-13), 167.7 (C-15)

Methyl-tris(4-methoxyphenyl)phosphonium iodide **109A**

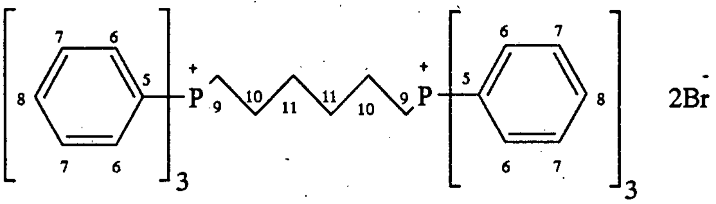


To a solution of 4-bromoanisole (15ml, 108mmol) in dry THF cooled to -100°C was added BuLi (1.6M in hexane, 90ml, 140mmol) dropwise via a pressure equilibrating dropping funnel under nitrogen. The mixture was stirred at -100°C for 30min. Freshly distilled PCl_3 (3.15ml, 36mmol) was then added, the mixture stirred for 30min. and then allowed to warm to room temperature and stirred overnight. The solution was neutralised by adding dilute sodium bicarbonate and extracted with ethyl acetate and water. The organic layer was dried over $MgSO_4$ and ethyl acetate removed *in vacuo* resulting in a colourless solid together with an oil. This crude mixture was purified by washing copiously with MeOH, filtering and drying to afford tris-(4-methoxyphenyl)phosphine (7.43g, 59%) as a colourless solid, m.p. 127-130°C. Tris-(4-methoxyphenyl)phosphine (1.0g, 2.8mmol) dissolved in benzene and methyl iodide (0.25ml, 4.0mmol) were stirred at 0°C overnight at room temperature. The precipitated product was filtered and washed with benzene to afford **109A** (1.3g, 94%) as a colourless solid, m.p. 213-215°C.

δ_H 2.85 (3H, d, J 13.1Hz, H-9), 3.84 (3H, s, H-10), 7.05-7.15 (6H, m, H-6), 7.45-7.60 (6H, m, H-7)

δ_C 12.1 (J 59.3Hz, C-9), 55.9 (C-10), 109.6 (J 96.3Hz, C-5), 116.0 (J 13.9Hz, C-6), 134.8 (12.2Hz, C-7), 164.5 J 2.7Hz, C-8), 148.8 (C-4)

1,6-Hexanediylbis(triphenylphosphonium)dibromide **111**

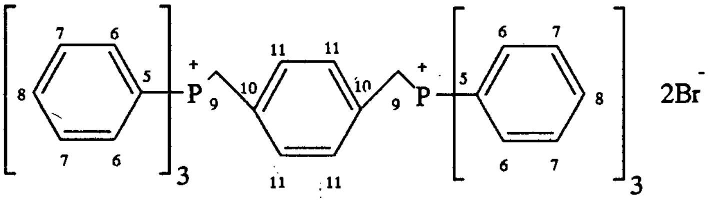


A mixture of triphenylphosphine (13.7g, 52mmol) dissolved in DMF (60ml) and 1,6-dibromohexane (6.1g, 25mmol) was refluxed for 24 hours and the resultant solid filtered, washed with ether and dried to afford **111** (13.6g, 70.8%) as a colourless solid, m.p. 75-80°C, which was recrystallised from EtOH.

δ_H 1.34-1.67 (8H, m, H-10, H-11), 3.50-3.75 (4H, m, H-9), 7.62-8.10 (30H, m, H-6, H-7, H-8)

δ_C 20.1 (J_{C-P} 49.5 Hz, C-9), 21.4 (J_{C-P} 3.4Hz, C-11), 28.7 (J_{C-P} 16.9Hz, C-10),118.4 (J_{C-P} 85.0Hz, C-5), 130.1 (J_{C-P} 12.3Hz, C-6), 133.5 (J_{C-P} 10.1Hz, C-7), 134.8 (C-8)

α,α'-Dibromo *p*-xylenediyl bis-triphenylphosphonium **112**



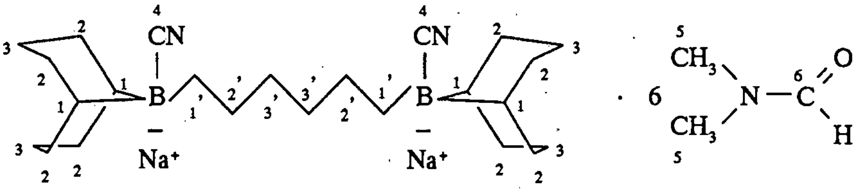
A mixture of triphenyl phosphine (13.5g, 50mmol) and α,α'-dibromo-*p*-xylene (6.64g, 25mmol) dissolved in benzene and DMF (40:20ml) was refluxed for 24 hours to afford **112** (18.8g, 95.4%) as a colourless solid, m.p. > 300°C.

δ_H 5.26 (4H, d, J_{H-P} 14.6Hz, H-9), 6.81 (4H, s, C-11), 7.52-8.01 (30H, m, H-6, H-7, H-8)

δ_C 27.7 ($J_{C\text{-}P}$ 47.2Hz, C-9), 117.6 ($J_{C\text{-}P}$ 85.7Hz, C-5), 128.1 ($J_{C\text{-}P}$ 4Hz, C-10), 130.1 ($J_{C\text{-}P}$ 11.1Hz, C-6), 131.1 (C-11), 133.8 ($J_{C\text{-}P}$ 10Hz, C-7), 135.1 (C-8)

7.5 Synthesis of cyanoborate salts

Disodium 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl) hexane•DMF clathrate **15**



To a solution of 9-BBN (0.5M in THF, 40ml, 20mmol) cooled to 0°C was added 1,5-hexadiene (1.2ml, 10mmol) via syringe. The mixture was stirred overnight at room temperature before removing the THF by distillation at atmospheric pressure followed by pumping *in vacuo*. To the resulting liquid was added dry, deoxygenated DMF (1ml per 10mmol of diene), dry sodium cyanide (1.2g, 24.5mmol) and the mixture stirred until the reaction had cooled to room temperature. The clear solution was then pipetted into a dry sample tube leaving residual sodium cyanide behind. Over a period of time the sodium cyanoborate · 6 DMF salt crystallised out and this was filtered and washed with dry ether to afford **15** (2.34g, 29%) as a colourless solid, m.p. 79-81°C (Found:C,57.9; H,9.4; N,12.3; $C_{42}H_{82}B_2N_8Na_2O_2$ requires C,58.5; H,9.6; N,12.9%).

ν_{max} 2909, 2859, 2833, 2149, 1670, 1094cm^{-1}

δ_H 0.2 (4H, m, H-1'), 0.37 (4H, br.s., H-1), 1.05-1.9 (32H, m, H-2, H-3, H-2', H-3'), 2.82 (3H, s, H-5), 2.93 (3H, s, H-5), 7.96 (1H, s, H-6)

δ_C 23.6 (C-1'), 24.4 (C-1), 25.4 (C-3), 26.4 (C-3), 27.0 (C-2'), 30.3 (C-2), 31.7 (C-5), 34.2 (C-3'), 34.6 (C-2), 36.9 (C-5), 152.0 (C-4), 163.7 (C-6)

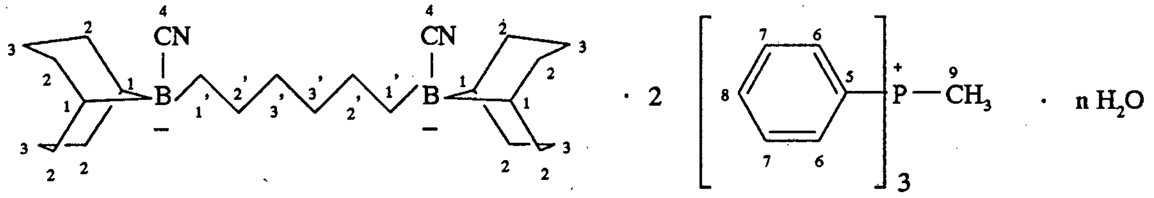
The onium salts were synthesised by the following method:

(This procedure applies to a 15mmol scale of diene)

For the onium salt formation Na^+ ion exchange was carried out by adding the respective salt (2eq.) dissolved in methanol to the borate mixture and stirring until a homogeneous mixture had formed. Methanol was then removed *in vacuo* and ether and water were added resulting in the formation of three layers. Addition of solid NaCl (0.1g) assisted in salting out the borate. The lower aqueous phase was separated and extracted twice with ether (2x15ml). The combined ether extracts together with the oily middle layer from the first extraction were then washed three times with water (3x15ml) usually resulting in the formation of crystals from the middle layer. The combined ether extracts together with the oily middle layer and the crystals were kept at room temperature for all the precipitate to form. If solid did not form, all the aqueous and organic extracts were combined and left at 0°C to precipitate out. The solid was filtered, washed with ether and water twice and vacuum dried.

The following salts were prepared in this manner:

Bis-methyltriphenylphosphonium 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane• H_2O **47**



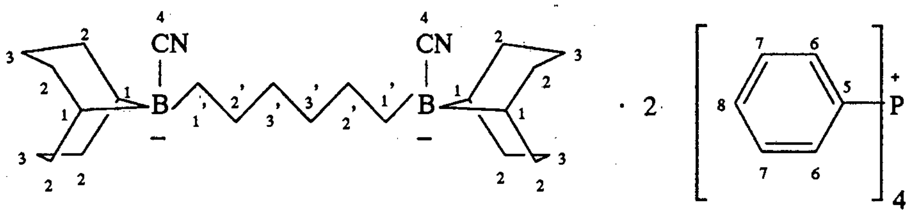
On a 15mmol scale using diene (1.8ml, 15mmol), 9-BBN (60ml, 30mmol), NaCN (1.8g, 36.7mmol), DMF (1.5ml) and methyltriphenylphosphonium bromide (10.72g, 30.0mmol in 25ml MeOH), **47** (10.56g, 76%) was obtained as clear crystals, m.p. 110-113°C (Found: C,78.0; H,8.3; N,2.9; $C_{62}H_{78}B_2N_2O_1P_2$ requires C,78.3; H,8.3; N,3.0%).
The included H_2O was removed under vacuum (0.5mmHg) at 70°C for 16 hrs, m.p. 110-112°C (Found:C,80.6; H,8.5; N,2.6; $C_{62}H_{76}B_2N_2P_2$ requires C,80.5; H,8.2; N,3.0%).

ν_{max} 2906, 2826, 2146, 1437, 1114cm^{-1}

δ_H 0.14 (4H, m, H-1'), 0.35 (4H, br.s., H-1), 0.95-2.12 (32H, m, H-2, H-3, H-2', H-3'), 2.89 (6H, d, $J_{P\text{-}H}$ 13.3Hz, H-9), 7.48-7.87 (30H, m, H-6, H-7, H-8)

δ_C 9.9 ($J_{C\text{-}P}$ 58Hz, C-9), 24.6 (C-1, C-1'), 25.6 (C-3), 26.5 (C-3), 28.7 (C-2'), 30.7 (C-2), 34.6 (C-2), 35.9 (C-3'), 118.6 ($J_{C\text{-}P}$ 88Hz, C-5), 130.5 ($J_{C\text{-}P}$ 12.9Hz, C-6), 132.9 ($J_{C\text{-}P}$ 10.8Hz, C-7), 135.2 (C-8), 150.0 (C-4)

Bis-tetraphenylphosphonium 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane **96**



On a 10mmol scale using diene (1.2ml, 10mmol), 9-BBN (40ml, 20mmol), NaCN (1.2g, 24.5mmol), DMF (1.0ml) and tetraphenylphosphonium bromide (8.34g, 20mmol in 25ml MeOH), **96** (7.65g, 72.4%) was obtained as a colourless solid, m.p. 183-187°C (Found:C,81.5; H,7.6; N,3.0; $C_{72}H_{80}B_2N_2P_2$ requires C,81.8; H,7.6; N,2.7%).

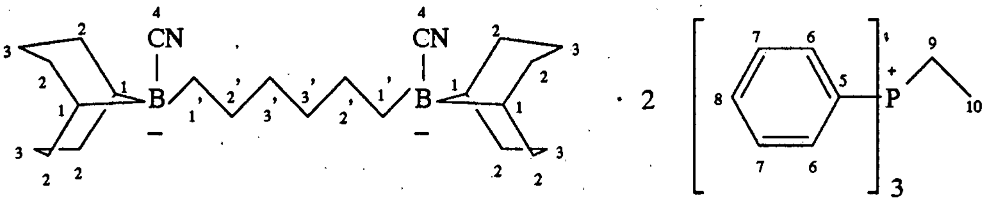
ν_{max} 2907, 2825, 2147, 1487, 1435, 1107cm^{-1}

δ_H(d_6-DMSO) 0.14 (4H, m, H-1'), 0.35 (4H, br.s., H-1), 1.00-2.05 (32H, m, H-2, H-3, H-2', H-3'), 7.65-8.05 (40H, m, H-6, H-7, H-8)

δ_C 24.0 (C-1, C-1'), 25.2 (C-3), 26.2 (C-3), 28.1 (C-2'), 30.4 (C-2), 34.0 (C-2), 35.4 (C-3'), 117.6 ($J_{C\text{-}P}$ 89Hz, C-5), 130.4 ($J_{C\text{-}P}$ 12.8Hz, C-6), 134.5 ($J_{C\text{-}P}$ 10.5Hz, C-7), 135.3 (C-8), 150.3 (C-4)

Bis-(ethyltriphenylphosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane

97A



On a 10mmol scale using diene (1.18ml, 10mmol), 9-BBN (40ml, 20mmol), NaCN (1.18g, 24mmol), DMF (1.0ml) and ethyltriphenylphosphonium bromide (7.42g, 20mmol in 25ml MeOH), **97A** (5.3g, 54.1%) was obtained as a colourless solid, m.p. 130-138°C after washing with ethyl acetate (Found: C,79.8; 8.7; N,3.3; $C_{64}H_{80}B_2N_2P_2$ requires C,79.99; H,8.98; N,2.91%).

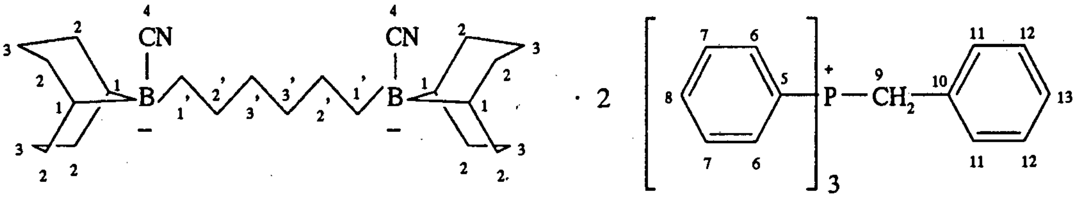
ν_{max} 2907, 2825, 2146, 1437, 1112cm^{-1}

δ_H 0.17 (4H, m, H-1'), 0.41 (4H, br.s., H-1), 1.00-2.18 (38H, m, H-2, H-3, H-2', H-3', H-10), 3.22-3.49 (4H, m, H-9), 7.57-7.90 (30H, m, H-6, H-7, H-8)

δ_C 6.7 ($J_{C\text{-}P}$ 5.3Hz, C-10), 16.7 ($J_{C\text{-}P}$ 52.3Hz, C-9), 24.8 (C-1, C-1'), 25.7 (C-3), 26.6 (C-3), 28.9 (C-2'), 30.9 (C-2), 34.7 (C-2), 36.2 (C-3'), 117.6 ($J_{C\text{-}P}$ 85.6Hz, C-5), 130.6 ($J_{C\text{-}P}$ 12.4Hz, C-6), 133.4 ($J_{C\text{-}P}$ 9.7Hz, C-7), 135.3 (C-8), 150.0 (C-4)

Bis(benzyltriphenylphosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane

102



$n\ C_2H_5OC_2H_5$

On a 10mmol scale using diene (1.18ml, 10mmol), 9-BBN (40ml, 20mmol), NaCN (1.18g, 24mmol), DMF (1.0ml) and benzyltriphenylphosphonium bromide (8.67g, 20mmol in 25ml MeOH), **102** (9.09g,78-84%) was obtained as a colourless solid, with included ether (n=0.3-0.8).

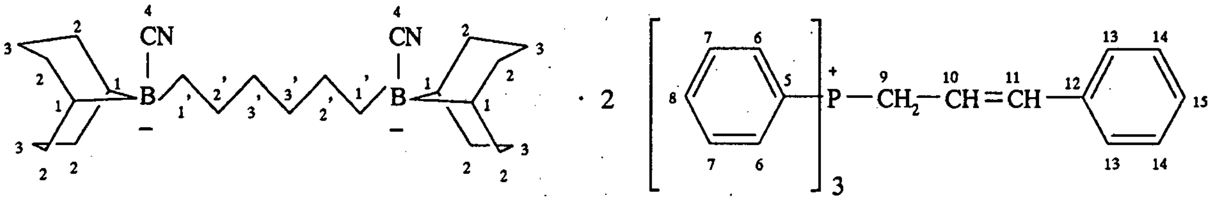
The included ether was removed under vacuum (0.5mmHg) at 80°C for 16 hours to give pure (9), m.p. 135-139°C (Found: C,82.4; H,7.9; N,2.6; $C_{74}H_{84}B_2N_2P_2$ requires C,81.91; H,7.80; N,2.58%).

ν_{max} 2907, 2826, 2145, 1436, 1110cm^{-1}

δ_H 0.18 (4H, m, H-1'), 0.45 (4H, br.s., H-1), 0.91-2.18 (32H, m, H-2, H-3, H-2', H-3'), 4.85 (4H, d, J_{H-P} 14.2Hz, H-9), 6.94 (4H, m, H-11), 7.02-7.30 (6H, m, H-12, H-13), 7.41-7.87 (30H, m, H-6, H-7, H-8)

δ_C 24.8 (C-1, C-1'), 25.7 (C-3), 26.7 (C-3), 29.0 (C-2'), 30.9 (J_{C-P} 47.6Hz, C-9), 30.9 (C-2), 34.8 (C-2), 36.2 (C-3'), 117.2 (J_{C-P} 85.5Hz, C-5), 126.6 (J_{C-P} 8.5Hz, C-10), 128.7 (J_{C-P} 3.8Hz, C-13), 129.0 (J_{C-P} 3.3Hz, C-12), 130.3 (J_{C-P} 12.5Hz, C-6), 131.15 (J_{C-P} 5.45Hz, C-11), 134.0 (J_{C-P} 9.6Hz, C-7), 135.2 (C-8), 150.2 (C-4)

Bis(1-[(E)-3-phenylprop-2-enyl]triphenylphosphonium) 1,6-bis(9-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane **103**



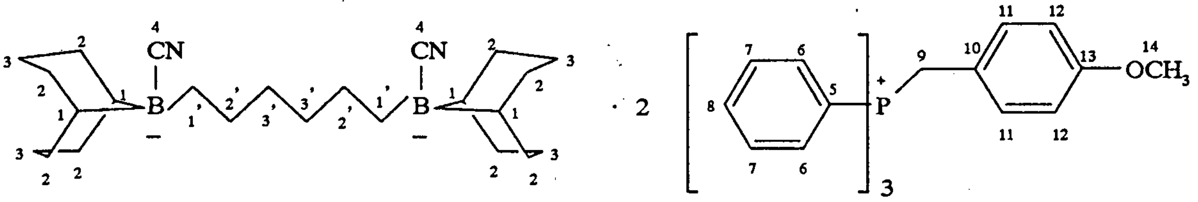
On a 10mmol scale using diene (1.18ml, 10mmol), 9-BBN (40ml, 20mmol), NaCN (1.18g, 24mmol), DMF (1.0ml) and cinnamyltriphenylphosphonium chloride (8.29g, 20mmol in 25ml MeOH), **103** (9.23g, 88.7%) was obtained as a pink solid, which was washed with ethyl acetate to afford a colourless solid, m.p. 137-144°C (Found: C,82.1; H,7.7; N,2.5; $C_{78}H_{88}B_2N_2P_2$ requires C,82.39; H,7.80; N,2.46%).

ν_{max} 2906, 2826, 2146, 1709, 1436, 1220, 1111cm^{-1}

δ_H (d_6-DMSO) 0.13 (4H, m, H-1'), 0.36 (4H, br.s., H-1), 1.03-2.05 (32H, m, H-2, H-3, H-2', H-3'), 4.80 (4H, dd, J_{H-P} 16.5Hz, J_{H-H} 7.3Hz, H-9), 6.12 (2H, m, H-10), 6.60 (2H, dd, J_{H-H} 15.8Hz, J_{H-P} 5.3Hz, H-11), 7.27 (10H, s, H-13, H-14, H-15), 7.64-8.03 (30H, m, H-6, H-7, H-8)

δ_C 24.0 (C-1, C-1'), 25.3 (C-3), 26.0 (J_{C-P} 45Hz, C-9), 26.2 (C-3), 28.1 (C-2'), 30.4 (C-2), 34.0 (C-2), 35.4 (C-3'), 115.1 (J_{C-P} 10.5Hz, C-11), 118.2 (J_{C-P} 85Hz, C-5), 126.3 (C-13), 128.3 (C-15), 128.7 (C-14), 130.1 (J_{C-P} 12.5Hz, C-6), 133.8 (J_{C-P} 9.8Hz, C-7), 134.9 (C-8), 135.5 (C-12), 138.6 (J_{C-P} 13.7Hz, C-10), 149.0 (C-4)

Bis(4-methoxybenzyltriphenylphosphonium) 1,6-bis(9-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane **107**



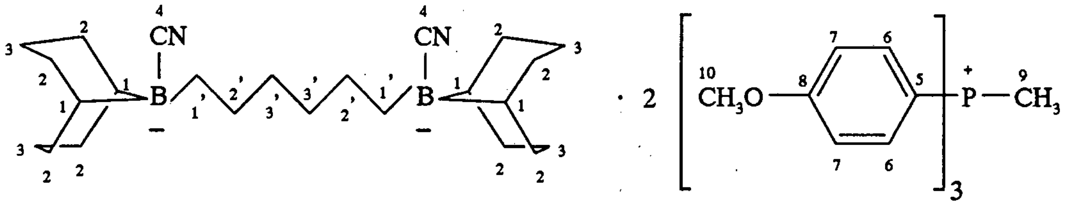
On a scale of 7.5mmol using diene (0.89ml, 7.5mmol), 9-BBN (30ml, 15mmol), NaCN (0.88g, 18mmol), DMF (0.75ml) and 4-methoxybenzyltriphenylphosphonium chloride (6.3g, 15mmol in 20ml MeOH), **107** (6.93g, 83%) was obtained as a colourless solid, m.p. 133-145°C (Found: C,79.5; H,7.4; N,2.9; $C_{74}H_{84}B_2N_2O_2P_2$ requires C,79.77; H,7.58; N,2.51%).

ν_{max} 2908, 2837, 2146, 1708, 1607, 1586, 1510, 1436, 1356, 1302, 1247, 1178, 1110cm^{-1}

δ_H(d_6-DMSO) 0.17 (4H, m, H-1'), 0.39 (4H, br.s., H-1), 1.01-2.12 (32H, m, H-2, H-3, H-2', H-3'), 3.67 (6H, s, H-14), 5.15 (4H, d, J_{H-P} 15Hz, H-9), 6.76 (4H, d, J_{H-H} 8.6Hz, H-12), 6.92 (4H, dd, J_{H-H} 8.8Hz, J_{H-H} 2.2Hz, H-11), 7.41-8.02 (30H, m, H-6, H-7, H-8)

δ_C 23.9 (C-1, C-1'), 25.3 (C-3), 26.3 (C-3), 27.6 (J_{C-P} 47Hz, C-9), 28.1 (C-2'), 30.4 (C-2), 34.0 (C-2), 35.5 (C-3'), 55.0 (C-14), 114.1 (J_{C-P} 2.9Hz, C-12), 117.8 (J_{C-P} 84.6Hz, C-5), 119.0 (J_{C-P} 8.6Hz, C-10), 129.9 (J_{C-P} 12.2Hz, C-6), 132.0 (J_{C-P} 5.5Hz, C-11), 133.9 (J_{C-P} 9.6Hz, C-7), 134.9 (C-8), 146.3 (C-4), 159.1 (C-13)

Bis(methyl-tris[4-methoxyphenyl]phosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane 110



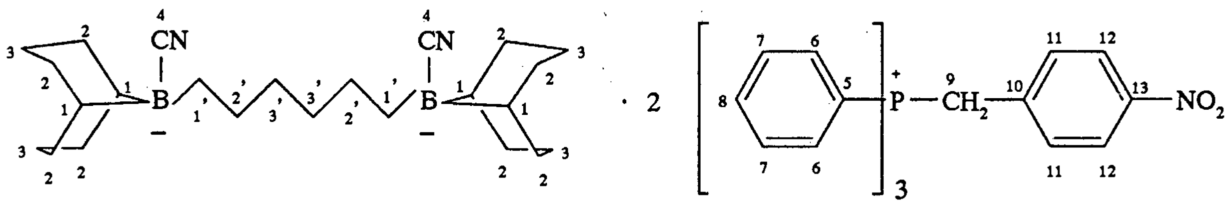
On a 9mmol scale using diene (1.07ml, 9mmol), 9-BBN (36ml, 18mmol), NaCN (1.1g, 22mmol), DMF (0.9ml) and tris(4-methoxyphenyl)methylphosphonium iodide (8.9g, 18mmol in 20ml MeOH), **110** was obtained as a waxy solid. This was washed with a mixture of ethyl acetate and pet. ether (1:1) to afford a colourless solid (4.65g, 58.7%), m.p. 76-84°C (Found: C,77.0; H,8.7; N,3.0; $C_{68}H_{88}B_2N_2O_6P_2$ requires C,77.39; H,8.65; N,2.73%).

ν_{max} 2907, 2840, 2146, 1593, 1565, 1501, 1302, 1182, 1116, 1022cm^{-1}

δ_H(d_6-DMSO) 0.13 (4H, m, H-1'), 0.35 (4H, br.s., H-1), 0.98-1.07 (32H, m, H-2, H-3, H-2', H-3'), 2.94 (6H, d, J_{H-P} 13.2Hz, H-9), 3.87 (18H, s, H-10), 7.20-7.35 (12H, m, H-7), 7.54-7.73 (12H,m, H-6)

δ_C 8.5 (J_{C-P} 57.2Hz, C-9), 24.0 (C-1, C-1'), 25.3 (C-3), 26.2 (C-3), 28.1 (C-2'), 30.4 (C-2), 34.0 (C-2), 35.5 (C-3'), 55.8 (C-10), 110.9 (J_{C-P} 95.4Hz, C-5), 115.7 (J_{C-P} 13.7Hz, C-6), 135.0 (J_{C-P} 12.2Hz, C-7), 146.1 (C-4), 163.9 (C-8)

Bis(4-nitrobenzyltriphenyl phosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane 106



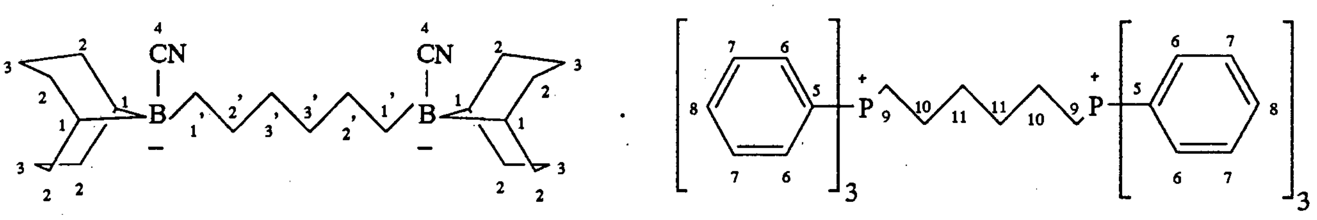
On a 2.5mmol scale using diene (0.3ml, 2.5mmol), 9-BBN (10ml, 5mmol), NaCN (0.3g, 6mmol), DMF (0.3ml) and 4-nitrobenzyltriphenylphosphonium chloride (2.17g, 5mmol in 8ml MeOH), **106** (1.21g, 42%) was obtained as a pink solid, which after washing with chloroform resulted in a beige solid, m.p. 143-147°C (Found: C,80.4; H,7.1; N,2.6; $C_{74}H_{82}B_2N_2O_4P_2$ requires C,80.35; H,7.18; N,2.43%).

ν_{max} 2908, 2829, 2143, 1523, 1435, 1346, 1109cm^{-1}

δ_H 0.1 (4H, m, H-1'), 0.35 (4H, br.s., H-1), 1.0-2.05 (32H, m, H-2, H-3, H-2', H-3'), 5.36 (4H, d, J_{H-P} 16.5Hz, H-9), 7.24 (4H, dd, J_{H-H} 8.8Hz, J_{H-P} 2.2Hz, H-11), 7.6-8.0 (30H, m, H-6, H-7, H-8), 8.11 (4H, d, J_{H-H} 8.7Hz, H-12)

δ_C 23.9 (C-1, C-1'), 25.3 (C-3), 26.2 (C-3), 28.0 (J_{C-P} 47.5Hz, C-9), 28.1 (C-2'), 30.4 (C-2), 34.0 (C-2), 35.4 (C-3'), 117.1 (J_{C-P} 85.4Hz C-5), 123.8 (J_{C-P} 2.5Hz, C-12), 130.2 (J_{C-P} 12.6Hz, C-6), 132.0 (J_{C-P} 5.3Hz, C-11), 134.0 (J_{C-P} 9.9Hz, C-7), 135.3 (C-8), 136.0 (J_{C-P} 8.5Hz, C-10), 147.3 (C-13), 149.8 (C-4)

1,6-Hexanediylbis(triphenyl phosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane 111A



On a 10mmol scale using diene (1.18ml, 10mmol), 9-BBN (40ml, 20mmol), NaCN (1.18g, 24mmol), DMF (1.0ml) and 1,6-hexanediylbis(triphenylphosphonium) dibromide (7.68g, 10mmol in 25ml MeOH), **111A** (9.82g,99.6%) was obtained as a colourless solid, m.p. 175-179°C (Found: C,80.5; H,8.5; N,2.8; $C_{66}H_{82}B_2N_2P_2$ requires C,80.32; H,8.37; N,2.84%).

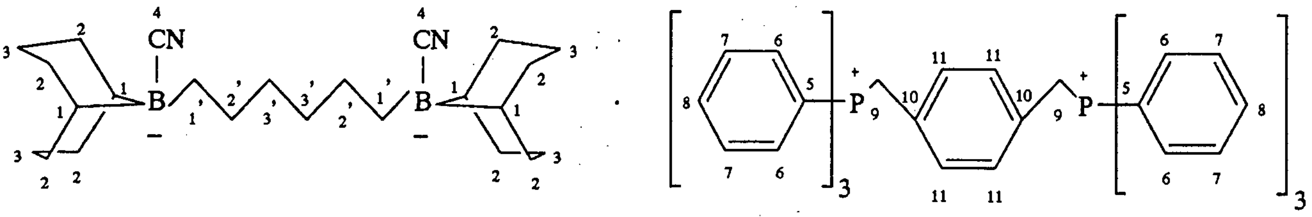
ν_{max} 3565, 3501, 2149, 1640, 1435, 1112, 1044cm^{-1}

δ_H 0.12 (4H, m, H-1'), 0.35 (4H, br.s., H-1), 1.10-2.05 (40H, m, H-2, H-3, H-2', H-3', H-10, H-11), 3.50 (4H, m, H-9), 7.68-8.00 (30H, m, H-6, H-7, H-8)

δ_C 19.8 (J_{C-P} 49.5Hz, C-9), 21.3 (J_{C-P} 3.4Hz, C-11), 24.0 (C-1, C-1'), 25.2 (C-3), 26.2 (C-3), 28.1 (C-2'), 29.0 (J_{C-P} 16.9Hz, C-10), 30.4 (C-2), 34.0 (C-2), 35.4 (C-3'), 118.4

($J_{C\text{-}P}$ 85.3Hz, C-5), 130.2 ($J_{C\text{-}P}$ 12.5Hz, C-6), 133.5 ($J_{C\text{-}P}$ 10.0Hz, C-7), 134.8 (C-8), 146.3 (C-4)

[1,4-Phenylenebis(methylene)]bis(triphenylphosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane **113**



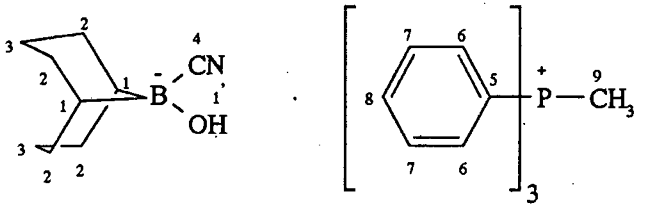
On a 10mmol scale using diene (1.18ml, 10mmol), 9-BBN (40ml, 20mmol), NaCN (1.18g, 24mmol), DMF (1.0ml) and 1,4-phenylenebis(methylene)bis-triphenylphosphonium dibromide (7.89g, 10mmol in 25ml MeOH), **113** (9.44g, 93.7%) was obtained as a colourless solid, m.p. 156-162°C (Found: C,80.9; H,7.6; N,2.9; $C_{68}H_{78}B_2N_2P_2$ requires C,81.11; H,7.80; N,2.78%).

ν_{max} 3564, 3496, 2809, 2149, 1640, 1435, 1109, 1031cm^{-1}

δ_H 0.13 (4H, m, H-1'), 0.38 (4H, br.s., H-1), 1.05-2.05 (32H, m, H-2, H-3, H-2', H-3'), 5.14 (4H, d, $J_{H\text{-}P}$ 14.7Hz, H-9), 6.80 (4H, s, H-11), 7.56-7.96 (30H, m, H-6, H-7, H-8)

δ_C 23.9 (C-1, C-1'), 25.3 (C-3), 26.2 (C-3), 27.7 ($J_{C\text{-}P}$ 40.8Hz, C-9), 28.1 (C-2'), 30.4 (C-2), 34.0 (C-2), 35.4 (C-3'), 117.5 ($J_{C\text{-}P}$ 86Hz, C-5), 128.1 ($J_{C\text{-}P}$ 4.3Hz, C-10), 130.1 ($J_{C\text{-}P}$ 12.5Hz, C-6), 131.1 (C-11), 133.8 ($J_{C\text{-}P}$ 10.1Hz, C-7), 135.1 (C-8), 146.2 (C-4)

Methyltriphenylphosphonium B-Cyano-B-hydroxy-9-boratabicyclo[3.3.1]nonane **68**



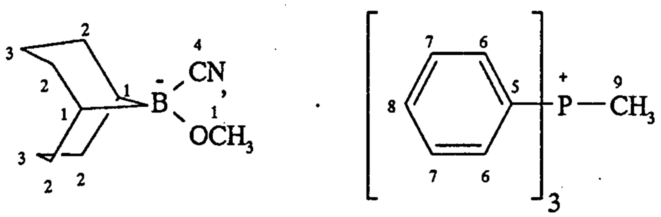
On a 14mmol scale using 9-methoxy-9-borabicyclo[3.3.1]nonane (2.15g, 14mmol), H_2O (0.25g, 14mmol), NaCN (0.73g, 15mmol), DMF (1.5ml) and methyltriphenylphosphonium bromide (5.05g, 14mmol in 25ml MeOH), **68** (2.84g, 45.5%) was obtained as a colourless solid, m.p. 101-115°C (Found: C,76.1; H,7.5; N,3.4; $C_{28}H_{33}B_1N_1P_1O_1$ requires C,76.19; H,7.53; N,3.17%).

ν_{max} 3656, 3370, 2804, 2155, 1585, 1436, 1198, 1114cm^{-1}

δ_H(d_6-DMSO) -0.18 (1H, br.s., H-1'), 0.39 (2H, br.s., H-1), 1.20-1.95 (12H, m, H-2, H-3), 3.19 (3H, d, J_{H-P} 7.2Hz, H-9), 7.72-7.91 (15H, m, H-6, H-7, H-8)

δ_C 7.3 (J_{C-P} 27.7Hz, C-9), 25.1 (C-3), 25.4 (C-3), 26.4 (C-1), 29.8 (C-2), 32.9 (C-2), 119.8 (J_{C-P} 43.8Hz, C-5), 130.0 (J_{C-P} 6.3Hz, C-6), 133.2 (J_{C-P} 5.4Hz, C-7), 134.7 (C-8), 144.0 (C-4)

Methyltriphenylphosphonium B-Cyano-B-methoxy-9-borabicyclo[3.3.1]nonane 69



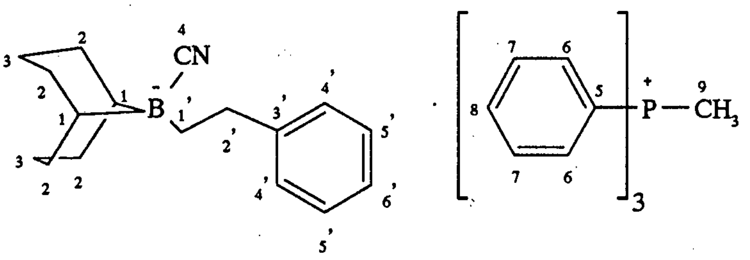
On a 14.3mmol scale using 9-methoxy-9-borabicyclo[3.3.1]nonane (2.17g, 14.3mmol), NaCN (0.73g, 15mmol), DMF (1.5ml) and methyltriphenylphosphonium bromide (5.1g, 14.3mmol in 25ml MeOH), **69** (4.47g, 68.7%) was obtained as a colourless solid, m.p. 118-134°C (Found: C,76.7; H,7.5; N,3.0; $C_{29}H_{35}B_1N_1O_1P_1$ requires C,76.49; H,7.75; N,3.08%).

ν_{max} 2929, 2160, 1587, 1482, 1436, 1196, 1114cm^{-1}

δ_H 0.56 (2H, br.s., H-1), 1.21-1.90 (12H, m, H-2, H-3), 2.92 (3H, d, J_{H-P} 6.6Hz, H-9), 3.12 (3H, s, H-1'), 7.54-7.80 (15H, m, H-6, H-7, H-8)

δ_C 9.5 (J_{C-P} 28.8Hz, C-9), 23.4 (C-1), 25.0 (C-3), 25.6 (C-3), 29.8 (C-2), 33.0 (C-2), 50.5 (C-1'), 118.5 (J_{C-P} 44.2Hz, C-5), 130.3 (J_{C-P} 6.1Hz),132.7 (J_{C-P} 5.4Hz, C-7), 135.1 (C-8), 150.0 (C-4)

Methyltriphenylphosphonium B-Cyano-B-[2-phenethyl]-9-boratabicyclo[3.3.1]nonane 74



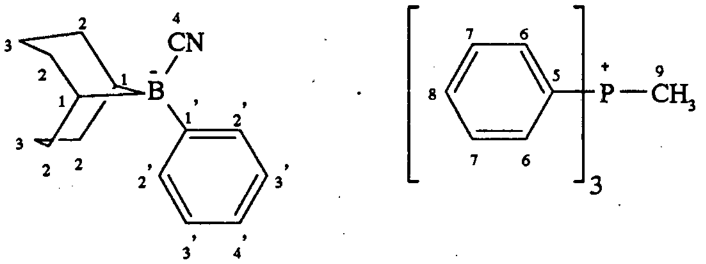
On a 15mmol scale using styrene (1.7ml, 15mmol), 9-BBN (30ml, 15mmol), NaCN (0.88g, 18mmol), DMF (1.5ml) and methyltriphenylphosphonium bromide (5.36g, 15mmol in 25ml MeOH), **74** (2.3g, 28.9%) was obtained as a colourless solid by precipitation of the oil from the extraction using ethyl acetate, m.p. 138-143°C (Found: C,82.0; H,7.7; N,2.5; $C_{36}H_{41}B_1N_1P_1$ requires C,81.66; H,7.80; N,2.65%).

ν_{max} 2799, 2153, 1489, 1436, 1114cm^{-1}

δ_H 0.38-0.62 (4H, m, H-1, H-1'), 1.14-2.13 (12H, m, H-2, H-3), 2.38-2.56 (2H, m, H-2'), 2.76 (3H, d, J_{H-P} 13.3Hz, H-9), 6.87-7.15 (5H, m, H-4', H-5', H-6'), 7.40-7.81 (15H, m, H-6, H-7, H-8)

δ_C 9.9 (J_{C-P} 57.9Hz, C-9), 24.5 (C-1, C-1'), 25.6 (C-3), 26.6 (C-3), 30.7 (C-2), 34.5 (C-2), 34.7 (C-2'), 118.6 (J_{C-P} 88.2Hz, C-5), 123.8 (C-3'), 127.7 (C-4'), 128.2 (C-5'), 130.6 (J_{C-P} 13.1Hz, C-6), 132.9 (J_{C-P} 10.6Hz, C-7), 135.4 (C-8), 149.2 (C-4), 150.6 (C-6')

Methyltriphenylphosphonium B-Cyano-B-phenyl-9-boratabicyclo[3.3.1]nonane 73A



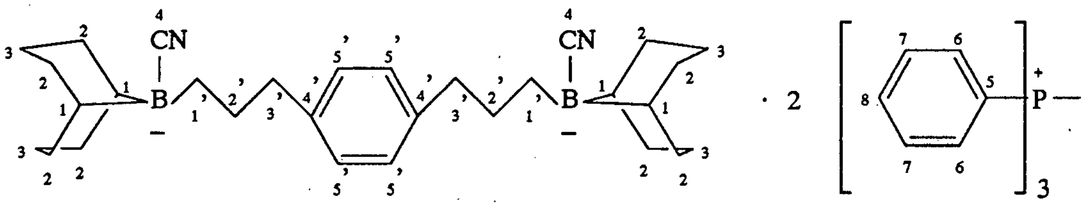
On a 4.3mmol scale using 9-phenyl-9-borabicyclo[3.3.1]nonane (0.85g, 4.3mmol), NaCN (0.24g, 5.0mmol), DMF (0.5ml) and methyltriphenylphosphonium bromide (1.54g, 4.3mmol in 10ml MeOH), **73A** (0.56g, 26.0%) was obtained as a colourless solid, m.p. 150-158°C (Found: C,81.3; H,7.3; N,2.6; $C_{34}H_{37}N_1B_1P_1$ requires C,81.44; H,7.44; N,2.79%).

ν_{max} 2803, 2155, 1436, 1114cm^{-1}

δ_H 1.12 (2H, br.s., H-1), 1.30-2.46 (12H, m, H-2, H-3), 2.35 (3H, d, J_{P-H} 13.0Hz, H-9), 6.80 (2H, t, J_{H-H} 7.2Hz, H-2'), 6.98 (3H, t, J_{H-H} 7.2Hz, H-3', H-4'), 7.32-7.88 (15H, m, H-6, H-7, H-8)

δ_C 8.7 (J_{C-P} 57.6Hz, C-9), 23.4 (C-1), 25.5 (C-3), 25.7 (C-3), 30.3 (C-2), 34.0 (C-2), 118.6 (J_{C-P} 88.2Hz, C-5), 122.7 (C-2'), 126.4 (C-3'), 130.2 (J_{C-P} 12.8Hz, C-6), 132.8 (J_{C-P} 10.7Hz, C-7), 133.3 (C-4'), 135.0 (C-8), 148.1 (C-4), 158.0 (C-1')

Bis(methyltriphenylphosphonium) 1,4-bis(3-[B-cyano-9-boratabicyclo[3.3.1]non-9-yl)propyl)benzene **63**



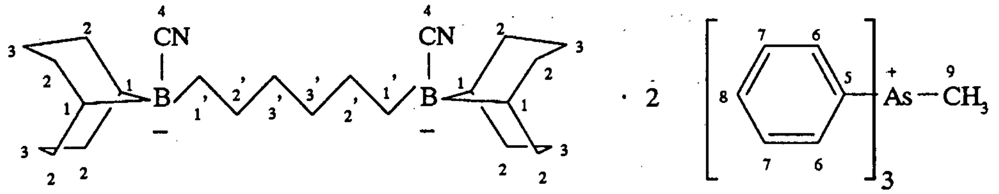
On a 10mmol scale using 1,4-bis(allyl)benzene (1.58g, 10mmol), 9-BBN (40ml, 20mmol), NaCN (1.18g, 24mmol), DMF (1.0ml) and methyltriphenylphosphonium bromide (7.14g, 20mmol in 20ml MeOH), **63** was obtained as an oil. After a few weeks the addition of ethyl acetate to the oil was successful in precipitating it out (20) as a colourless solid (3.98g, 39.5%), m.p. 122-126°C (Found: C,80.5; H,8.1; N,2.9; $C_{68}H_{80}B_2N_2P_2$ requires C,80.95; H,7.99; N,2.78%).

ν_{max} 2925, 2220, 1669, 1587, 1437, 1114cm^{-1}

δ_H 0.10-0.46 (4H, br.s., H-1), 0.93-2.62 (36H, m, H-1', H-2, H-3, H-2', H-3'), 2.84 (6H, d, J_{H-P} 13.2Hz, H-9), 6.80 (4H, s, H-5'), 7.32-7.81 (30H, m, H-6, H-7, H-8)

δ_C 9.9 ($J_{C\text{-}P}$ 57.5Hz, C-9), 24.8 (C-1, C-1'), 25.5 (C-3), 26.4 (C-3), 30.6 (C-2), 33.2 (C-2'), 34.5 (C-2), 40.7 (C-3'), 118.6 ($J_{C\text{-}P}$ 88.3Hz, C-5), 128.0 (C-5'), 130.3 ($J_{C\text{-}P}$ 12.9Hz, C-6), 132.9 ($J_{C\text{-}P}$ 10.7Hz, C-7), 135.2 (C-8), 141.5 (C-4'), 149.2 (C-4)

Bis(methyltriphenylarsonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane **116**



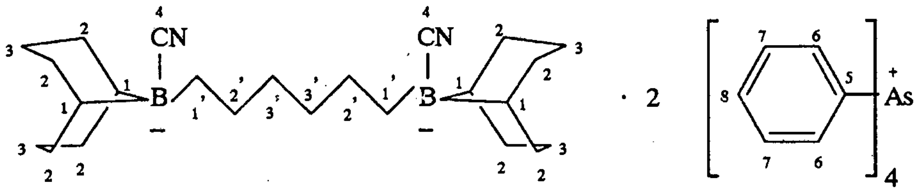
On a 10mmol scale using diene (1.18ml, 10mmol), 9-BBN (40ml, 20mmol), NaCN (1.2g, 24mmol), DMF (1.0ml) and methyltriphenylarsonium iodide (8.96g, 20mmol in 20ml MeOH), **116** (6.9g, 68.5%) was obtained as a colourless solid, m.p. 151-161°C (Found: C,73.0; H,7.7; N,2.9; $C_{62}H_{76}As_2B_2N_2P_2$ requires C,72.95; H,7.50; N,2.74%).

ν_{max} 2906, 2826, 2146, 1435, 1109cm^{-1}

δ_H 0.15 (4H, m, H-1'), 0.36 (4H, br.s., H-1), 0.98-2.10 (32H, m, H-2, H-3, H-2', H-3'), 2.84 (6H, s, H-9), 7.51-7.85 (30H, m, H-6, H-7, H-8)

δ_C 8.8 (C-9), 24.4 (C-1, C-1'), 25.7 (C-3), 26.6 (C-3), 28.8 (C-2'), 30.8 (C-2), 34.7 (C-2), 36.0 (C-3'), 121.5 (C-5), 131.1 (C-6), 132.1 (C-7), 134.4 (C-8), 150.0 (C-4)

Bis-tetraphenylarsonium 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane **117**



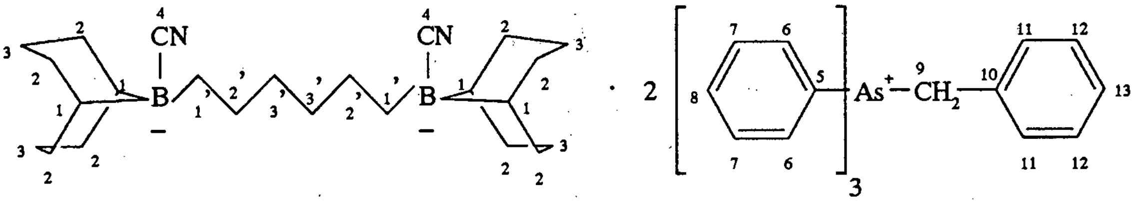
On a 5mmol scale using diene (0.6ml, 5mmol), 9-BBN (20ml, 10mmol), NaCN (0.6g, 12.2mmol), DMF (0.5ml) and tetraphenylarsonium chloride hydrate (4.2g, 10mmol in 15ml MeOH), **117** was obtained as a yellow solid, which after washing with ethyl acetate yielded a colourless solid (4.12g, 72.0%), m.p. 181-191°C (Found:C, $C_{72}H_{80}B_2N_2As_2$ C,75.3; H,6.9; N,2.9% requires C,75.6; H,7.0; N,2.5%).

ν_{max} 2906, 2825, 2147, 1481, 1080cm^{-1}

δ_H 0.05 (4H, m, H-1'), 0.34 (4H, br.s., H-1), 0.85-2.15 (32H, m, H-2, H-3, H-2', H-3'), 7.52-7.65 (16H, m, H-6), 7.65-7.90 (24H, m, H-7, H-8)

δ_C 24.3 (C-1, C-1'), 25.7 (C-3), 26.6 (C-3), 28.8 (C-2'), 30.9 (C-2), 34.6 (C-2), 36.1 (C-3'), 120.2 (C-5), 131.4 (C-6), 132.7 (C-7), 134.8 (C-8), 149.0 (C-4)

Bis(benzyltriphenylarsonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl) hexane **118**



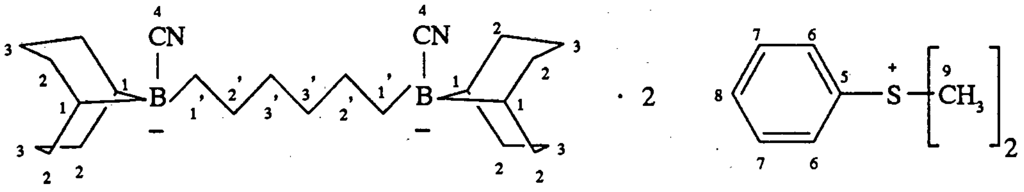
On a 10mmol scale using diene (1.2ml, 10mmol), 9-BBN (40ml, 20mmol), NaCN (1.2g, 24mmol), DMF (1ml) and benzyltriphenylarsonium bromide (9.54g, 20mmol in 25ml MeOH), **118** (13.8g, %) was obtained as a colourless solid, m.p. 160-162°. (Found: C,75.6; H,7.3; N,2.5; $C_{74}H_{84}As_2B_2N_2$ requires C,75.77; H,7.22; N,2.39%).

ν_{max} 2907, 2825, 2145, 1438, 1081cm^{-1}

δ_H 0.13-0.36 (4H, m, H-1'), 0.49 (4H, br. s., H-1), 0.95-2.3 (32H, m, H-2, H-2', H-3, H-3'), 4.87 (4H, s, H-9), 6.99-7.23 (10H, m, H-11, H-12, H-13), 7.36-7.73 (30H, m, H-6, H-7, H-8)

δ_C 24.8 (C-1, C-1'), 25.7 (C-3), 26.6 (C-3), 28.9 (C-2'), 30.9 (C-2), 33.0 (C-9), 34.7 (C-2), 36.1 (C-3'), 120.3 (C-5), 127.6 (C-10), 128.7 (C-13), 129.1 (C-12), 130.6 (C-6), 130.8 (C-11), 132.9 (C-7), 134.2 (C-8), 151.0 (C-4)

Bis(dimethylphenylsulfonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane **87**



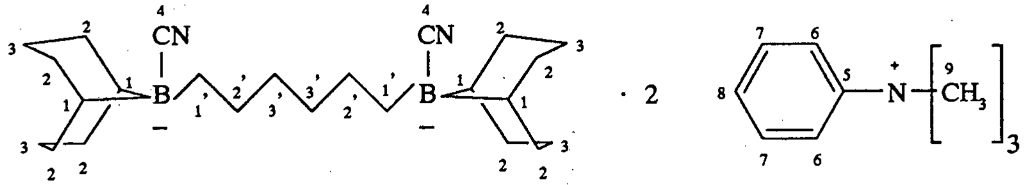
On a 5mmol scale using diene (0.6ml, 5mmol), 9-BBN (20ml, 10mmol), NaCN (0.6g, 12mmol), DMF (0.5ml) and dimethylphenylsulfonium hexafluorophosphate (3.4g, 12mmol in 10ml MeOH), **87** (3.22g, 98.2%) was obtained as a colourless solid, m.p. 140-155°C (Found: C,73.3; H,9.4; N,4.5; $C_{40}H_{62}B_2N_2S_2$ requires C,73.16; H,9.51; N,4.26%).

ν_{max} 2904, 2804, 2148, 1445, 996cm^{-1}

δ_H 0.13 (4H, m, H-1'), 0.38 (4H, br.s., H-1), 1.02-2.07 (32H, m, H-2, H-3, H-2', H-3'), 3.27 (12H, s, H-9), 7.64-7.85 (6H, m, H-7, H-8), 8.01-8.13 (4H, m, H-6)

δ_C 23.9 (C-1, C-1'), 25.3 (C-3), 26.2 (C-3), 28.2 (C-2', C-9), 30.4 (C-2), 34.1 (C-2), 35.5 (C-3'), 126.7 (C-5), 129.7 (C-6), 130.4 (C-7), 133.6 (C-8), 146.6 (C-4)

Bis(phenyltrimethylammonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane **91**



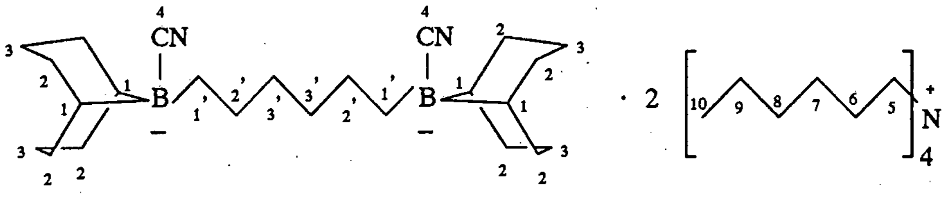
On a 5.5mmol scale using diene (0.67ml, 5.5mmol), 9-BBN (22ml, 11mmol), NaCN (0.7g, 14.3mmol), DMF (0.5ml) and phenyltrimethylammonium iodide (3.0g, 11mmol in 15ml MeOH), **91** (1.6g, 44.7%) was obtained as a colourless solid, m.p. 162-167°C (Found:C,77.5; H,10.6; N,8.6; $C_{42}H_{68}B_2N_4$ requires C,77.5; H,10.5; N,8.6%).

ν_{max} 2906, 2825, 2147, 1494cm^{-1}

δ_H(d_6-DMSO) 0.14 (4H, m, H-1'), 0.38 (4H, br.s., H-1), 1.05-2.1 (32H, m, H-2, H-3, H-2', H-3'), 3.62 (18H, s, H-9), 7.54-7.70 (6H, m, H-7, H-8), 7.92-8.02 (4H, m, H-6)

δ_C 23.9 (C-1, C-1'), 25.3 (C-3), 26.2 (C-3), 28.1 (C-2'), 30.4 (C-2), 34.0 (C-2), 35.5 (C-3'), 56.4 (C-9), 120.3 (C-6), 123.8 (C-5), 130.0 (C-7), 147.4 (C-8), 150.2 (C-4)

Bis(tetrahexylammonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane **88**



On a 5mmol scale using diene (0.6ml, 5mmol), 9-BBN (20ml, 10mmol), NaCN (0.6g, 12mmol), DMF (0.5ml) and tetrahexylammonium bromide (4.3g, 10mmol in 10ml MeOH), **88** (3.9g, 71.5%) was obtained as a colourless waxy solid, m.p. 93-103°C (Found: C,79.3; H,13.5; N,5.3; $C_{72}H_{144}B_2N_4$ requires C,79.51; H,13.35; N,5.15%).

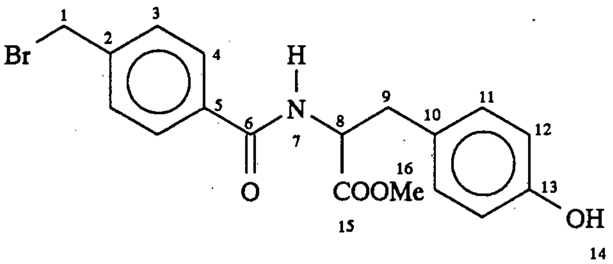
ν_{max} 2800, 2151, 1463, 1043cm^{-1}

δ_H 0.29 (4H, m, H-1'), 0.48 (4H, br.s., H-1), 0.91 (24H, m, H-10), 1.02-2.15 (96H, m, H-6, H-7, H-8, H-9), 3.22 (16H, m, H-5)

δ_C 13.6 (C-10), 22.0 (C-9), 22.4 (C-8), 24.8 (C-1, C-1'), 25.8 (C-3), 26.0 (C-3), 26.7 (C-7), 29.0 (C-2'), 30.9 (C-2), 31.1 (C-6), 34.8 (C-2), 36.5 (C-3'), 59.1 (C-5), 149.3 (C-4)

7.6 Synthesis of the chiral phosphonium cyanoborate salt

p-Bromomethyl-N[1'-(S)-methoxycarbonyl-2'-*p*-hydroxyphenethyl]benzamide **128**



To a solution of sodium bicarbonate (9.50g) in water (100 ml) at 0°C was added THF (300ml) and L-tyrosine methyl ester hydrochloride (4.5309g, 19.42mmol) and stirred for ca. 3 minutes. To this was added **126** (4.27g) and stirred at 0°C for 30 minutes. The mixture was then extracted into ethyl acetate (2 x 50 ml) and the organic layer washed with water (3 x 15ml) and brine (3 x 5ml). The extracts were dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to afford a creamy yellow powder **128** (6.76g, 93.55%). This was recrystallised from ethyl acetate/methanol yielding colourless crystals, m.p. 174-175°C, $[\alpha]_D$ -4.74° (c=2.47, ethyl acetate). (Found: C, 55.2; H, 4.7; N, 3.8; $C_{18}H_{18}BrO_4N$ requires C, 55.11; H, 4.63; N, 3.57%).

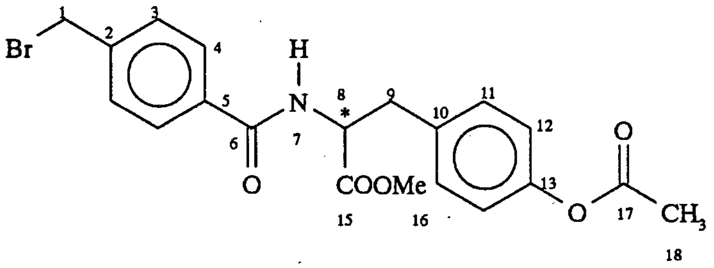
ν_{max} (nujol) 3419, 3306, 1725, 1638, 1569, 1514, 808 cm^{-1}.

δ_H (d_6-DMSO) 3.01 (2H, m, W=40 Hz, H-9), 3.63 (3H, s, H-16), 4.58 (1H, td, J 7.73 Hz, 8.66 Hz, H-8), 4.73 (2H, s, H-1), 6.66 (2H, d, J 8.47Hz, H-12), 7.08 (2H, d J 8.46Hz, H-11), 7.52 (2H, d, J 8.20Hz, H-4), 7.79 (2H, d, J 8.06Hz, H-3), 8.80 (1H, d, J 7.79Hz, H-7), 9.20 (1H, s, H-13).

δ_C 33.4 (C-1), 35.5 (C-9), 51.9 (C-16), 54.6 (C-8) 115.0 (C-12), 127.6 (C-10), 127.8 (C-4), 129.1 (C-3), 129.9 (C-11), 133.5 (C-5), 141.4 (C-2), 155.9 (C-13), 165.9 (C-6), 172.2 (C-15).

m/z 312 (M^+-80, 3%), 214 (11%), 197 (18%), 119 (28%), 107 (52%), 178 (100%).

p-Bromomethyl-N[1'-(S)-methoxycarbonyl-2'-*p*-acetoxyphenethyl]benzamide **129**



To a solution of **128** (5.44g, 13.87mmol) in dichloromethane (50ml) at -79°C was added Hünig's base (4.75ml) followed by a further 1ml (total: 33.58mmol) after 6 hours. To this was added acetyl chloride (2ml) followed by a further 2ml (total:56.25mmol) after 6 hours. The reaction mixture was then extracted with dichloromethane and water and the organic layer washed with cold dilute hydrochloric acid (10ml) followed by sodium carbonate. Dichloromethane was removed *in vacuo* to afford a solid **129** (5.56g, 92.37%) which purified by slow evaporation of ethyl acetate, m.p. 144-145°C, $[\alpha]_D$ -15.45° (c=2.68, ethyl acetate), $[\alpha]_D$ +65.09° (c=3.45, $CHCl_3$).

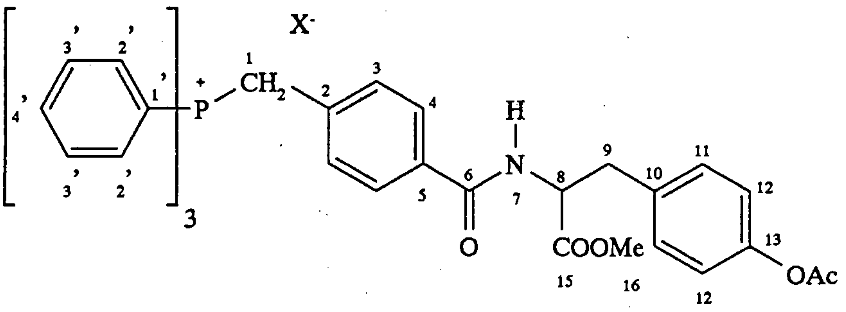
ν_{max} (nujol) 3294, 1741, 1629, 1569, 804 cm^{-1}.

δ_H (400MHz) 2.26 (3H, s, H-18), 3.23 (1H, dd, J 5.7Hz, 5.8Hz, 14.07Hz, H-9, X=Br), 3.75 (3H, s, H-16), 4.47 (1.24H, s, H-1, X=Br), 5.03 (1H, dq, J 1.6Hz, 5.7Hz, 5.7Hz, H-8) 6.68 (1H, d, J 7.41, H-7), 7.00 (2H, d, J 8.4Hz, H-12), 7.12 (2H, d, J 8.4Hz, H-11),l7.42 (2H, d, J 8.0Hz, H-4), 7.68 (2H, t, J 8.4Hz, H-3)

δ_C 21.0 (C-18), 32.1 (C-8), 37.1 (C-1, X=Br), 52.4 (C-9), 53.5 (C-16), 121.7 (C-12), 127.4 (C-4, X=Br), 128.7 (C-3, X=Br), 130.2 (C-11), 133.4 (C-10), 133.6 (C-5, X=Br), 141.1 (C-2, X=Br), 149.8 (C-13), 166.2 (C-6), 169.3 (C-17), 171.8 (C-15)

m/z 354 (M^+-80, 3%), 220 (33%), 197 (15%), 178 (100%), 153 (23%), 119 (26%), 107 (49%).

4[N(1'-(S)-Methoxycarbonyl-2'-*p*-acetoxyphenethyl)amidobenzyl]triphenylphosphonium halide 130



The acetate **129** (4.81g, 11.08mmol) and triphenylphosphine (2.94g, 11.20mmol) were dissolved in toluene (150ml) and heated under reflux for 65 hours to afford the insoluble phosphonium salt **130** (5.45g, 7.82mmol, 70.60%). It was recrystallised from ethyl acetate/methanol to give colourless feathery crystals, m.p. 224-225°C, $[\alpha]_D$ -38.77° (c=1.05, Methanol).

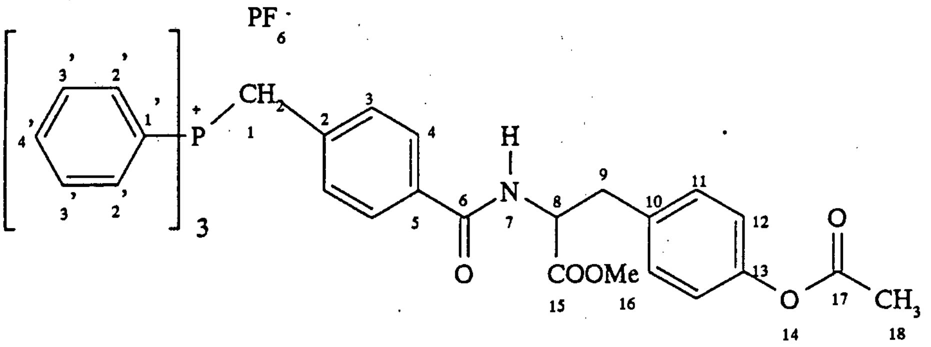
ν_{max} (nujol) 3622, 3200, 3100, 1741, 1640, 1610, 1541 cm^{-1}.

δ_H (d_6-DMSO) 2.23 (3H, s, H-18), 3.14 (2H, br. m., W=16.9Hz, H-9) 3.62 (3H, s, H-16), 4.62 (1H, br. m., W=22.9Hz, H-8), 5.32 (2H, d, J 8.5Hz, H-1), 7.02 (2H, d, J 8.5Hz, H-12), 7.07 (3H, dd, J 2.2Hz, 8.5Hz, H-4') 7.31 (2H, d, J 8.5Hz, H-11), 7.65-7.95 (16H, br. m., W=60.9Hz, H-2', H-3', H-4', H-3), 8.91 (1H, d, J 7.6Hz, H-7)

δ_C 20.8 (C-18), 28.0 (d, J_{C-P} 45.7Hz, C-1), 35.4 (C-8), 51.9 (C-16), 54.2 (C-9), 117.6 (J_{C-P} 85Hz, C-1'), 121.5 (C-12), 127.7 (J_{C-P} 3Hz, C-11), 130.1 (J 12.6Hz, C-2'), 130.7 (J 5.3Hz, C-4), 131.6 (J 8Hz, C-2), 133.2 (J 3.9Hz, C-5), 134.0 (J 9.85Hz, C-3'), 135.0 (C-4'), 135.1 (J 2.7Hz, C-3), 149.1 (C-13), 165.7 (C-6), 169.1 (C-17), 171.9 (C-15)

m/z 277 (19%), 262 (100%), 183 (62%), 178 (10%), 153 (6%), 119 (71%), 107 (9%)

4[N(1'-(S)-Methoxycarbonyl-2'-*p*-acetoxyphenethyl)amidobenzyl]triphenylphosphonium hexafluorophosphate **131**[5]



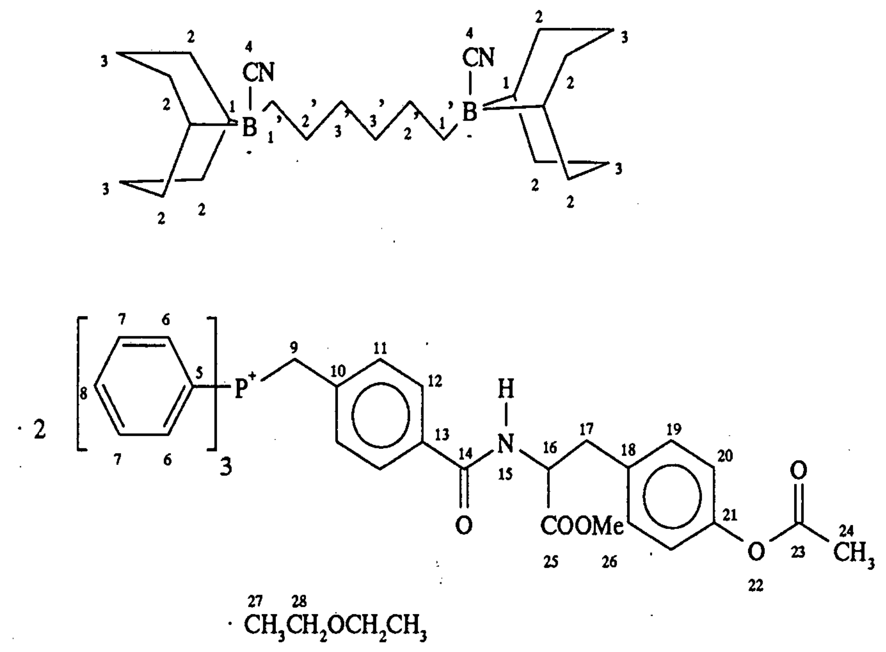
Ammonium hexafluorophosphate (0.11g, 0.68mmol) was dissolved in water (2ml) and added to a solution of the phosphonium salt (0.46g, 0.68mmol) dissolved in hot water (120ml) to afford a white precipitate **131** (0.33g, 64%) which was dried in an oven for 1 hour, m.p. 117-118°C. (Found: C,59.4; H,4.5; N,1.9; $C_{38}H_{35}F_6NO_5P_2$ requires C,59.92; H,4.63; N,1.84%).

ν_{max} (CH_2Cl_2) 3674, 3421, 3060, 1745, 1662, 1611, 1571, 1436 cm^{-1}.

δ_H (400MHz) 2.24 (3H, s, H-18), 2.97-3.25 (1H, br. m., H-9), 3.63 (3H, s, H-16), 5.24 (2H, d, J 16.1Hz, H-1), 6.98-7.13 (4H, m, H-11, H-12), 7.25-7.40 (2H, d, J 8.5Hz, H-2), 7.60-7.86 (15H, m, H-2', H-3', H-4') 7.7.86-8.11 (2H, m, H-4), 8.86 (1H, d, J 7.8Hz, H-7)

δ_C 20.8 (C-18), 28.0 (J 45Hz, C-1), 35.5 (C-8), 51.9 (C-16), 54.2 (C-9), 117.6 (J_{C-P} 85.2Hz, C-1'), 121.5 (C-12), 127.7 (J_{C-P} 2.7Hz, C-11), 130.1 (J_{C-P} 12.6Hz, C-2'), 130.8 (J_{C-P} 5.3Hz, C-4), 131.6 (J_{C-P} 8.9Hz, C-2), 133.3 (J_{C-P} 3.4Hz, C-5), 134.0 (J_{C-P} 9.9Hz, C-3'), 135.0 (C-4'), 135.1 (C-3), 149.1 (C-13), 165.8 (C-6), 169.1 (C-17), 172.0 (C-15)

Bis-4[N(1'-(S)-methoxycarbonyl-2'-*p*-acetoxyphenethyl)amidobenzyl]triphenylphosphonium 1,6-bis(B-cyano-9-borabicyclo[3.3.1]non-9-yl)hexane **132**



On a scale using 1,5-hexadiene (1ml, 8.33mmol), 9-BBN (33.8ml, 16.9mmol), NaCN (0.88g, 18mmol), DMF (1ml) and the phosphonium halide salt **130** (4.0g in MeOH), **132** was obtained as a viscous oil, which when dried *in vacuo* afforded a pale yellow solid (0.5g, 39%).

ν_{max} (CH_2Cl_2) 3675, 3412, 3056, 2909, 2857, 2147, 1740, 1661, 1611, 1571, 1436 cm^{-1}.

δ_H 0.24 (4H, br.s., H-1') 0.46 (4H, m, H-1) 1.19 (6H, t, J 6.98Hz, H-27) 1.2-2.2 (32H, m, H-2, H-3, H-2', H-3'), 2.25 (3H, s, H-24), 3.33 (2H, m, H-17), 3.46 (4H, q, J 6.96Hz, H-28) 3.58 (3H, s, H-26), 3.63 (3H, s, H-16?), 4.83 (3H, br.m, H-9, H-16), 6.69-7.78 (46H, m, H-6, H-7, H-8, H-11, H-12, H-19, H-20), 8.12 (2H, d, H-15)

δ_C 15.21 (C-27), 21.1 (C-24), 24.8 (C-1, C-1', C-17), 25.6 (C-3), 26.6 (C-3), 29.0 ($J_{C\text{-}P}$ 45.7Hz, C-9), 30.8 (C-2), 34.8 (C-2), 35.0 (C-16), 36.4 (C-3'), 52.2 (C-26), 54.5 (C-17), 65.8 (C-28), 117.2 ($J_{C\text{-}P}$ 84Hz, C-5), 121.4 (C-20), 127.9 ($J_{C\text{-}P}$ 15.4Hz, C-19), 130.3 ($J_{C\text{-}P}$ 13.0Hz, C-6), 130.4 ($J_{C\text{-}P}$ 10.0Hz, C-12), 131.2 ($J_{C\text{-}P}$ 5Hz, C-10), 133.4 ($J_{C\text{-}P}$ 3.9Hz, C-13), 134.1 ($J_{C\text{-}P}$ 9.6Hz, C-7), 134.6 (C-8), 135.3 ($J_{C\text{-}P}$ 5.5Hz, C-11), 144.3 (C-4), 149.5 (C-21), 150.4 (C-20), 166.7 (C-14), 169.5 (C-23), 172.5 (C-25)

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