Arsenium Ions in Asymmetric Synthesis

Michelle Louise Weir

Bachelor of Biotechnology (Hons) *ANU*

A thesis submitted for the degree of Doctor of Philosophy of

The Australian National University

THE AUSTRALIAN NATIONAL UNIVERSITY

December 2009

The work described in this thesis is the author's own unless stated otherwise.

Michelle L. Weir

December 2009

I not only use all the brains I have, but all that I can borrow- Woodrow Wilson

Acknowledgements

First and foremost, I would like to thank my supervisor Prof. Bruce Wild. Bruce's seemingly boundless knowledge and enthusiasm was vital for the success of my work, just as his good nature and sense of humour was for my day-to-day life. I have no doubt that without his encouragement and support, I would not have made it through the last 4 years. It was a true privilege to work for someone that I respect so much professionally, and like so much personally.

I was fortunate to work with many good people within the Wild Group: Paul Gugger, Nathan Kilah, Heather Kitto, Illham Maulana, Jörg Steinbach and Di Lu. A huge thank you to Paul for all his technical assistance, to Nathan for his part in our very enjoyable discussions and debates, and to Di for her friendship and company in the final 18 months of my degree. My thanks also go to Dr Geoff Salem and Roy Doyle for kindly offering me their assistance during the last few months. I acknowledge Keith Porter, Elizabeth Krenske and Xiangting Zhou for establishing the methodologies on which my project was based.

Thank you to Prof. Martin Bennett, Prof. Tony Hill and all the members of the Hill Group for providing the feeling of an Inorganic community, particularly during tea breaks! A special mention to Horst Neumann for his cheerful smile and affable manner, even when I was continually borrowing chemicals and equipment; and to Ian Cade for his good humour and for being a great travelling companion in Paris.

I am very grateful to the Research School of Chemistry for providing me with a scholarship to study at a world-class establishment as well as the opportunity to present my work at conferences in France and around Australia. Thank you to the many

administrative and technical staff who have assisted me along the way, particularly to Tony Willis of the X-ray Crystallography Unit, to Chris Blake and Peta Simmonds of the NMR Centre, and to Vicki Withers and Sasha Melnitchenko of the Microanalytical Unit.

To my friends Alex, Anna, Conor, Doug, Heather, Peter, Phil, Stephen and Tim for supporting me in different, and invaluable ways, at times you were single-handedly responsible for my sanity. A very special mention to Alison, for sharing her home and love of baseball with me; and to Emily and Nick for all the wine, conversations and dinners throughout my entire time at university. To my friends around the RSC, particularly Andrew, Leaf, Junming and Tanya, thank you for the lunchtime conversation, it was often the best part of my day. Thank you also, to Chris, who unexpectedly made the last few months of my PhD nicer than I could have hoped.

And finally, my most loving thanks to my family, who supported me in every way possible and only ever asked that I do my best in return.

Abstract

The asymmetric synthesis of tertiary arsines by nucleophilic addition to chiral phosphine-stabilised arsenium salts has been investigated. The addition at –95 °C of *n*-butyllithium in hexanes to a dichloromethane solution of the phosphine-stabilised arsenium salt (±)-[(R_3P)AsMePh]PF_6, where R_3P is an enantiomerically pure, atropisomeric phosphepine, furnishes (S_{As})-(+)-(*n*-butyl)methylphenylarsine in 85% enantioselectivity (70% enantiomeric excess) with displacement of the (aR_P)-phosphepine. The enantioselectivity of the synthesis is lower than the diastereoselectivity of coordination of the (aR_P)-phosphepine to the prochiral methylphenylarsenium ion with which it is in equilibrium in solution by As–P bond dissociation, as determined by NMR spectroscopy at –95 °C. The excess of the *S* enantiomer of the arsine is consistent with the S_N2 mechanism proposed for the reaction and the solid-state structure of the predominant diastereomer of the phosphepine–arsenium complex.

The methodology has been extended to the asymmetric synthesis of chiral bis(tertiary arsines). The addition of RLi (R = Me, *n*-Bu) to an equilibrating mixture of diastereomers of the (aR_P)-phosphepine-stabilised 1,2-ethanediyl*bis*(phenylarsenium triflate) generates unequal mixtures of diastereomers and enantiomers of chelating bis(tertiary arsines), chiral at arsenic. Thus, the addition of methyllithium in diethyl ether at –95 °C to a dichloromethane solution of the complex (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-1,2-[(R_3P)PhAsCH_2CH_2AsPh(PR_3)]$(OTf)_2$ (where PR_3 = (aR_P)-phosphepine), generates (R^*_{As},R^*_{As})-(±)-1,2-*bis*(methylphenylarsino)ethane in 78% diastereoselectivity (together with the corresponding (R^*_{As},S^*_{As}) diastereomer in 22% diastereoselectivity) and 95% enantioselectivity in favour of the (R_{As},R_{As}) enantiomer. Under similar conditions, the addition of *n*-butyllithium in hexanes to a solution of the bis[(aR_P)-phosphepine-stabilised]-diarsenium triflate at –95 °C produces (R^*_{As},R^*_{As})-

(±)-1,2-*bis*[(*n*-butyl)phenylarsino)ethane in 77% diastereoselectivity and 93% enantioselectivity in favour of the (R_{As},R_{As}) enantiomer.

Two novel chiral phosphines have been synthesised as auxiliaries for the potential asymmetric synthesis of tertiary arsines. Thus, ($1R_C$,$2S_C$,$5R_C$)-(8-phenylmenthyl)diphenylphosphine and ($1S_C$,$2S_C$,$5R_C$)-(8-phenyl*neo*menthyl)diphenylphosphine were prepared by the addition of potassium diphenylphosphide to the menthanesulfonates of the appropriate menthyl alcohols. The phosphines were obtained in low yield (13% and 7%, respectively) because of a competing elimination reaction that generates 8-phenylmenthene and diphenylphosphine. The attempted synthesis of phosphine-stabilised arsenium salts from the two phosphines by the two-phase and chloride-abstraction methods failed, apparently because of the steric bulk of the phosphine.

The first tertiary arsine-stabilised arsenium salts, (±)-[(L)AsMePh]OTf (L = Ph_3As, Me_2PhAs, [2-($MeOCH_2$)C_6H_4]Ph_2As, [2-($MeOCH_2$)C_6H_4]Me_2As), have been prepared by chloride abstraction from chloromethylphenylarsine with trimethylsilyl triflate in the presence of the arsine. The complexes were characterised by crystallography and ^1H NMR spectroscopy. The NMR spectroscopic data for the complexes in dichloromethane-d_2 are consistent with rapid exchange of the arsine on the arsenium ion, even at –90 °C. The corresponding phosphine-stabilised complexes are considerably more stable than their arsine counterparts in dichloromethane-d_2 with the free energy of activation $\Delta G^{\ddagger}_c$= ca. 60 kJ mol^{-1} being calculated for phosphine exchange in [(Me_2PhP)AsMePh]OTf at 8 °C; for [(Me_2{2-($MeOCH_2$)C_6H_4}P)AsMePh]OTf in the same solvent, $\Delta G^{\ddagger}_c$= ca. 70 kJ mol^{-1} at 50 °C.

Table of contents

Abbreviations

a	axial
amu	atomic mass units
Ar*H*	aromatic protons
aq.	aqueous
BCS	(+)-bromocamphor-π-sulfonate
BINOL	1,1′-bi-2-naphthol
bp	boiling point
br	broad
Bu	butyl
c	concentration (grams per 100 mL)
ca.	circa
cat.	catalytic amount
CIP	Cahn–Ingold–Prelog
COSY	correlation spectroscopy
Cy	cyclohexyl
d	doublet
d	deuterated
dd	doublet of doublets
de	diastereomeric excess
dec.	decomposition
deg	degrees

DFT	density functional theory
δ	chemical shift (parts per million)
$\Delta G^{\ddagger}_{c}$	free energy of activation
E	pnictogen
ee	enantiomeric excess
EI MS	electron impact mass spectrum
en	ethane-1,2-diamine
Eq	equation
equiv.	equivalents
es	enantioselectivity
ES MS	electrospray ionisation mass spectrometry
Et	ethyl
h	hours
Hx	hexyl
HSQC	heteronuclear single-quantum correlation
IUPAC	International Union of Pure and Applied Chemistry
$^{n}J_{AB}$	*n*-bond coupling between nuclei A and B (Hz)
lit.	literature
m	multiplet
m/z	mass-to-charge-ratio
M^{+}	molecular ion (a.m.u)
Me	methyl
min	minutes

mmHg	millimetres of mercury
mp	melting point
MS	mass spectrum
NMR	nuclear magnetic resonance
NOE	Nuclear Overhauser Effect
NOESY	Nuclear Overhauser Effect Spectroscopy
Np	naphthyl
ORTEP	Oak Ridge Thermal Ellipsoid Plot
OTf^-	trifluoromethanesulfonate (triflate), $CF_3SO_3^-$
Ph	phenyl
ppm	parts per million
Pr	propyl
py	pyridine
q	quartet
R	aryl or alkyl group
R	right-handed (clockwise) CIP sequence
S	left-handed (anticlockwise) CIP sequence
s	singlet
sept.	septet
t	triplet
$t_{1/2}$	half-life
T_c	coalescence temperature
THF	tetrahydrofuran

TMEDA	*N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine
Tol	tolyl
UV–Vis	Ultraviolet–visible spectroscopy
X	halogen

Chapter 1:

Introduction

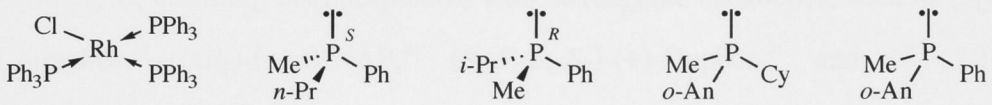
1.1 Chirality of arsenic and phosphorus

The interest in arsenic and phosphorus as stereogenic centres followed from the successful resolution of a simple ammonium ion by fractional crystallisation of the *D*-camphorsulfonate salts in 1899.[1] The first resolution of an acyclic phosphonium ion was achieved in 1959 by the fractional crystallisation of the (*D*)-(–)-dibenzoylhydrogentartrate salts.[2] Subsequently, the isolation the first optically active, monodentate tertiary phosphines were isolated by the electrolytic cleavage of benzyl, allyl, or benzhydryl groups from resolved phosphonium salts, which proceeded with retention of configuration at phosphorus.[3, 4] Resolved arsonium salts were converted into optically active arsines by applying the same technique.[5] These results confirmed the configurational stability of a resolved non-cyclic tertiary phosphine or arsine. A comprehensive review of the resolution of tertiary arsines follows in Section 1.3.

A sufficient condition for the resolution of a chiral compound is that the barrier to intramolecular inversion be greater than ca. 24 kcal mol^{-1}.[6, 7] Acyclic tertiary amines have very low barriers to inversion, ca. 6–7 kcal mol^{-1} and thus are unresolvable under normal laboratory conditions.[8] The thermal rates of racemisation for series of acyclic tertiary phosphines was found to be in the range 29.1–35.6 kcal mol^{-1} in decalin at 130 ± 0.3 °C.[9] Interestingly, the presence of a phenyl group in (±)-PMePh(*n*-Pr) resulted in a 78-fold decrease in thermal stability compared to the similar compound having a cyclohexyl group.[9] Tertiary arsines have much higher barriers to intramolecular inversion than tertiary phosphines: the free energy of activation for (±)-ethylmethylphenylarsine of 42.4 ± 0.5 kcal mol^{-1} in decalin at 217.6 ± 0.3 °C, which corresponds to a half-life of racemisation of ca. 740 h at this temperature.[10] This means that *As*-chiral arsines, unlike similar phosphines, can be distilled at elevated temperatures without loss of optical activity.[6]

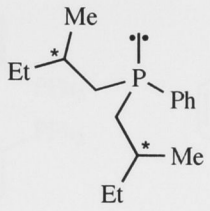
1.2 Phosphines and arsines as chiral auxiliaries

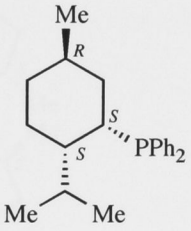
Chiral tertiary phosphines are of great importance in organic and inorganic chemistry, especially as auxiliaries for homogeneous, metal-catalysed asymmetric synthesis. Pioneering work in the field by Horner[11] and Knowles[12] indicated that substitution of the triphenylphosphine ligands in Wilkinson's catalyst, **1**[13], with the optically active *P*-chiral monophosphines (S_P)-(+)-**2**[11] and (R_P)-(–)-**3**[12] gave modest enantioselectivities for the hydrogenation of certain prochiral olefins (3–15% ee). The moderate successes of these reactions led Knowles to the development of chiral phosphines containing an *o*-anisyl group, such as CAMP and PAMP, which gave 55–90% enantioselectivities for selected hydrogenations.[14] Para-substituted aromatic groups on phosphorus, such as *p*-anisyl or *p*-dimethylaminophenyl, did not increase the selectivities of the reactions.[15]



1 (S_P)-(+)-**2** (R_P)-(–)-**3** CAMP PAMP

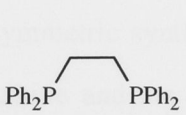
Difficulty of synthesis and resolution of phosphines chiral at phosphorus led to a shift in focus from *P*-chiral tertiary phosphines to phosphines in which the chirality was engineered into the carbon backbone of the ligand. Initial experiments involved the use of a phosphine containing chiral *i*-pentyl groups, as in **4**, but the catalyst showed negligible selectivity (ca. 1%) for the hydrogenation of α-phenylacrylic acid.[12] Despite these results, Morrison and coworkers showed that the use of ($1S_C$,$2S_C$,$5R_C$)-(+)-neomenthyldiphenylphosphine, NMDPP, as a chiral auxiliary gave (*S*)-3-butanoic acid in 61% ee following hydrogenation of (*E*)-β-methylcinnamic acid with the appropriate rhodium(I) catalyst.[16]



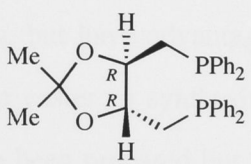


4 $(1S_C,2S_C,5R_C)$-(+)-NMDPP

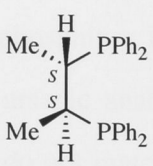
The use of chiral bis(tertiary phosphines) as chiral auxiliaries was initially avoided as it had been shown that the substitution of the triphenylphosphine ligands in Wilkinson's catalyst with 1,2-*bis*(diphenylphosphino)ethane (dppe) significantly reduced the turnover rate for hydrogenation due to the stabilisation of the catalytic intermediates by the chelate effect.[17] The use of (R_C,R_C)-(–)-DIOP, however, which is derived from (R_C,R_C)-tartaric acid, was found to be an efficient auxiliary that gave high selectivities (ees up to 88%) for certain hydrogenations.[18] This development led to the synthesis of a great variety of chelating bis(phosphines) with stereogenic backbones, such as (S_C,S_C)-(–)-Chiraphos,[19] (aR_P)-(+)-BINAP,[20] (S_C,S_C,S_C,S_C)-(+)-Duphos,[21] and (R)-(S_C)-(–)-Josiphos.[22] Many of these phosphines can be synthesised efficiently from enantiomerically pure tosylates of readily prepared diols.[23] There are now phosphine-containing catalysts available for nearly every standard reaction for converting achiral organic precursors into chiral products.



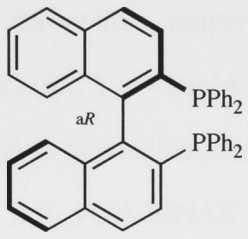
dppe



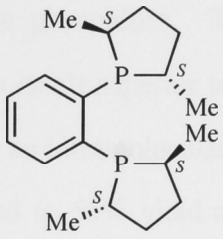
(R_C,R_C)-(–)-DIOP



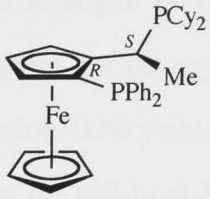
(S_C,S_C)-(–)-Chiraphos



(aR_P)-(+)-BINAP

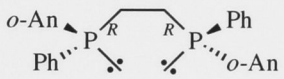


(S_C,S_C,S_C,S_C)-(+)-Duphos

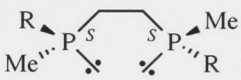


(*R*)-(S_C)-(−)-Josiphos

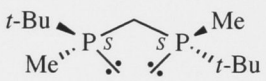
Despite the effectiveness of bis(phosphines) containing chiral backbones for asymmetric synthesis, there are reactions that proceed with greater efficiency when the phosphorus stereocentre is itself chiral.[24] The first industrial, metal-catalysed asymmetric synthesis employed the *P*-chiral bis(phosphine) (R_P,R_P)-(−)-DIPAMP for the production of *L*-DOPA in 95% ee.[25] Enantiomeric excesses of greater than to 99% have since been achieved for the hydrogenation of dehydroamino acids and their methyl esters using rhodium catalysts containing (S_P,S_P)-BisP* and (S_P,S_P)-*t*-Bu-MiniPHOS.[26]



(R_P,R_P)-(−)-DIPAMP



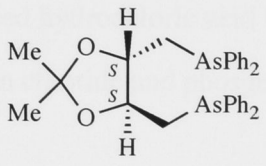
(S_P,S_P)-BisP*
R = *t*-Bu, 1-adamantyl, 1-methylcyclohexyl



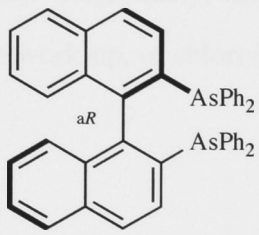
(S_P,S_P)-*t*-Bu-MiniPHOS

Resolved *As*-chiral arsines are less frequently employed as chiral auxiliaries for catalytic asymmetric syntheses, but have advantages over phosphines in that they are less air-sensitive and are often easier to synthesise. The arsenic analogues of some known phosphine ligands have been prepared but typically do not match the reactivity or selectivity of the phosphine in the chosen reaction.[6] Interestingly, the asymmetric hydrogenation of α-acetamidocinnamic acid using a rhodium(I) catalyst containing (S_C,S_C)-(−)-DIARSOP gave (*S*)-(−)-*N*-acetylphenylalanine in 39% ee, whereas (S_C,S_C)-(−)-DIOP gave the opposite enantiomer in 88% ee.[27] There are some examples, however,

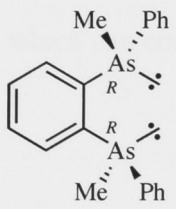
where the arsines outperform the phosphines. The arsenic analogue of (aR_P)-(+)-BINAP, (aR_{As})-(+)-BINAs, gave a result superior to the phosphine for the asymmetric cyclisation of an alkenyl iodide by an intramolecular Heck reaction: 90% yield and 82% ee for (aR_{As})-(+)-BINAS compared to 55% yield and 32% ee for (aR_P)-(+)-BINAP.[28] Rhodium(I) catalysts containing (R_{As},R_{As})-(+)-1,2-*bis*(methylphenylarsino)benzene, (R_{As},R_{As})-(+)-**5**, gave higher selectivities than the phosphorus isostere for certain catalytic asymmetric hydrogenations[29] and hydrosilylations.[30] The resolution of tertiary arsines has been comprehensively reviewed.[6,31]



(S_C,S_C)-(−)-DIARSOP



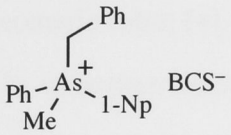
(aR_{As})-(+)-BINAs



(R_{As},R_{As})-(+)-**5**

1.3 Resolution of chiral arsines

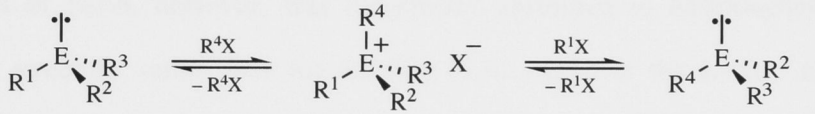
The first evidence of optical activity in an arsenic compound was published in 1921 by Burrows and Turner: one diastereomer of (±)-benzylmethyl(1-naphthyl)phenylarsonium (+)-bromocamphor-π-sulfonate (BCS) was enriched by fractional crystallisation of the salt **6**.[32] The enriched diastereomer of the salt was converted into the iodide, which exhibited transitory optical activity in certain organic solvents, particularly chloroform.[32]



(±)-**6**

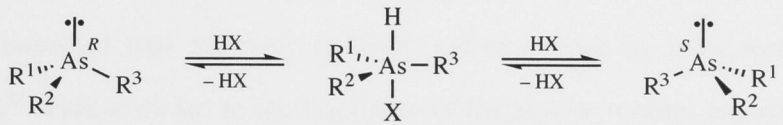
The initial inability of the leaders in the field to resolve acyclic, chiral phosphonium and arsonium salts was attributed to the dissociative equilibrium shown in Scheme 1.1.[33] It is now known, however, that chiral tertiary arsines are rapidly racemised by traces of haloacids, especially hydrogen iodide, presumably by Berry pseudorotation of 5-coordinate intermediates (Scheme 1.2). Regrettably, much of the pioneering work in the field used hydrochloric acid in the work-up, or chloroform, which can contain traces of hydrogen chloride and phosgene.[6]

Scheme 1.1



E = As, P
R = alkyl, aryl

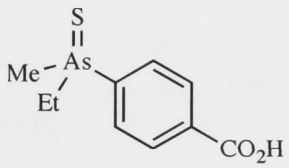
Scheme 1.2



1.3.1 Resolutions with salt-forming agents

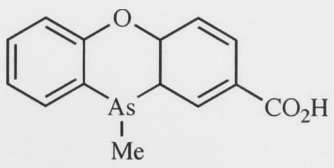
The first complete resolution of an arsenic compound, the tertiary arsine sulfide (±)-**7**, was achieved in 1925.[34] Both enantiomers of the chiral arsine sulfide were isolated by

fractional crystallisation of diastereomeric salts; (+)-**7** was obtained with (–)-morphine and (–)-**7** with (–)-brucine. The salts were then converted back into the optically active carboxylic acids by treatment with dilute acid. The optical stability of the arsine sulfide was attributed to the presence of the sulfur, which prevented intramolecular inversion at arsenic.[34]

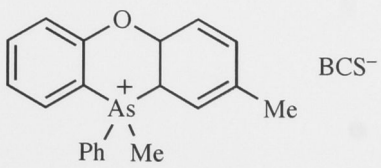


(±)-**7**

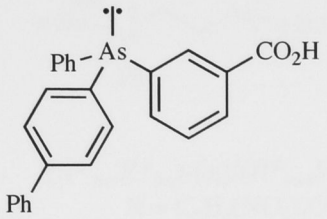
Successful resolution of the heterocylic phenoxoarsine (±)-**8** constituted the first resolution of a three-coordinate, tertiary arsine.[35] The optical stability of the enantiomers of (±)-**8**, however, was incorrectly attributed to atropisomerism of the folded ring structure, rather than the stability to inversion of the arsenic stereocentre. This view was supported by the failure to successfully separate the diastereomers of the related arsonium salt (±)-**9**.[36] This notion was refuted, however, by the successful resolution of the acyclic arsine (±)-**10**; (+)-**10** was obtained with use of (–)-1-phenylethylamine and (–)-**10** with (+)-amphetamine. The pure diastereomers of the salts were converted into the free, optically active arsines by treatment with dilute *sulfuric* acid.[37] This work led to the resolution of the acyclic tertiary arsines **11–15** with salt-forming agents.[38-49]



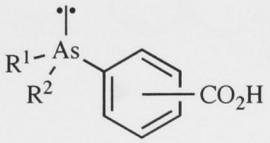
(±)-**8**



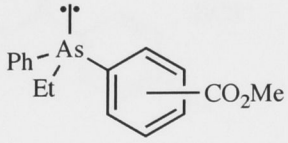
9



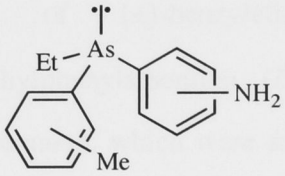
(±)-**10**



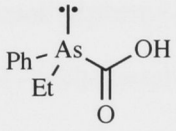
(±)-**11**[38-43]
R = Alkyl, Aryl



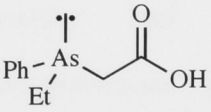
(±)-**12**[43]



(±)-**13**[44-47]



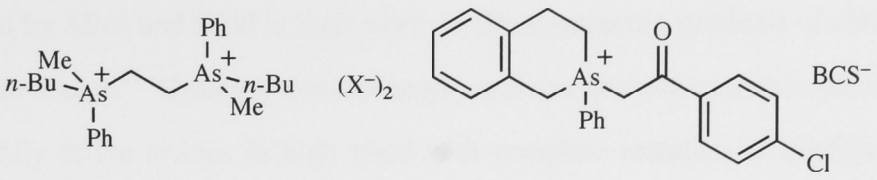
(±)-**14**[48]



(±)-**15**[49]

1.3.2 Resolutions of arsonium salts

The diastereomers of the diarsonium picrates (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**16** were separated by fractional crystallisation from ethanol.[50] This result confirmed the configurational stability of the arsonium stereocentres, but the stabilities of the separate salts were incorrectly attributed to the impossibility of the dissociative equilibrium between the arsonium salts and the pyramidally unstable free arsine and an alkyl picrate ether.[51] It was also considered that a heterocyclic arsonium salt would be resolvable because dissociative equilibrium was unlikely. Accordingly, the first successful resolution of an arsonium ion was achieved by the fractional crystallisation of the (±)-arsinolinium salt **17**. The diastereomerically pure salts of **17** were subsequently converted into the picrates and iodides; the iodide racemised in chloroform.[51]

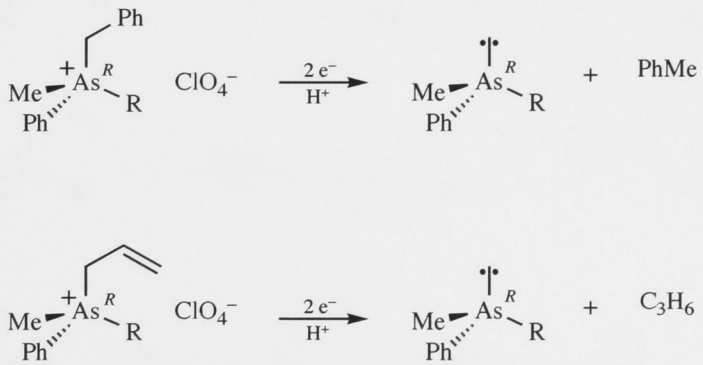


(R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**16** (±)-**17**

X = $C_6H_2(NO_2)_3O^-$

The first resolution of an *acylic* arsonium salt was reported in 1962.[5] The fractional crystallisation of (±)-benzylethylmethylphenylarsonium and (±)-benzyl(*n*-butyl)ethylmethylphenylarsonium (*D*)-(–)-dibenzoylhydrogentartrates gave the less soluble diastereomers, which were subsequently converted into the perchlorates. The reductive cleavage of the benzyl groups from the arsonium perchlorates at a mercury cathode gave the optically active arsines in quantitative yield, with retention of configuration at arsenic.[5] Allyl groups could be cleaved similarly from resolved arsonium salts with retention of configuration (Scheme 1.3).[52]

Scheme 1.3

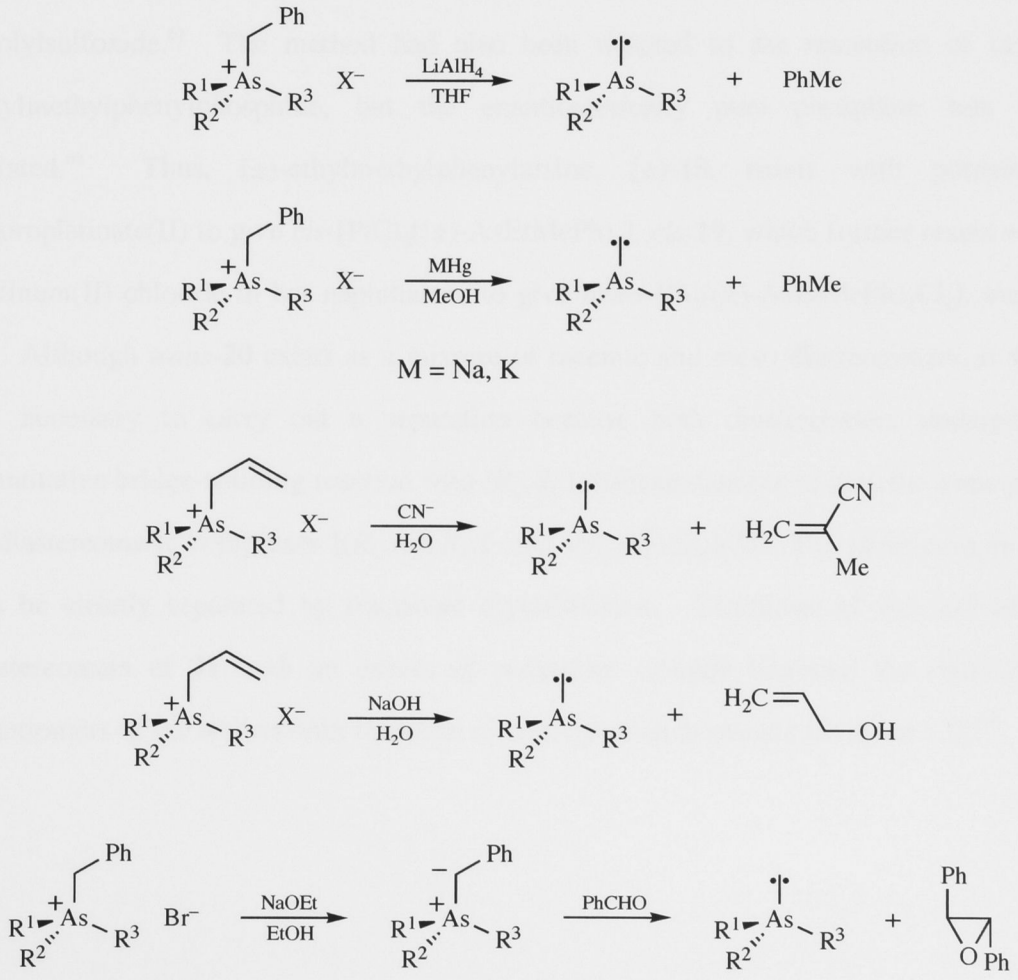


R = Et, *n*-Bu

Benzyl groups could also be cleaved from arsonium ions with retention of configuration with use of alkali metal amalgams[53] or lithium aluminium hydride;[54] allyl groups can be stereoselectively cleaved from arsonium ions by cyanolysis[55] or hydrolysis.[56] Another clean method for removing a benzyl group from a resolved benzylarsonium ion was

developed by Allen and Wild in their work on the asymmetric synthesis of chiral *trans*-1,2-diaryloxiranes.[57] Optically active benzyl arsonium bromides can be converted into the optically active arsines in high yield with complete retention of configuration at arsenic by transfer of a benzylidene group from an arsonium ylide to benzaldehyde (Scheme 1.4).

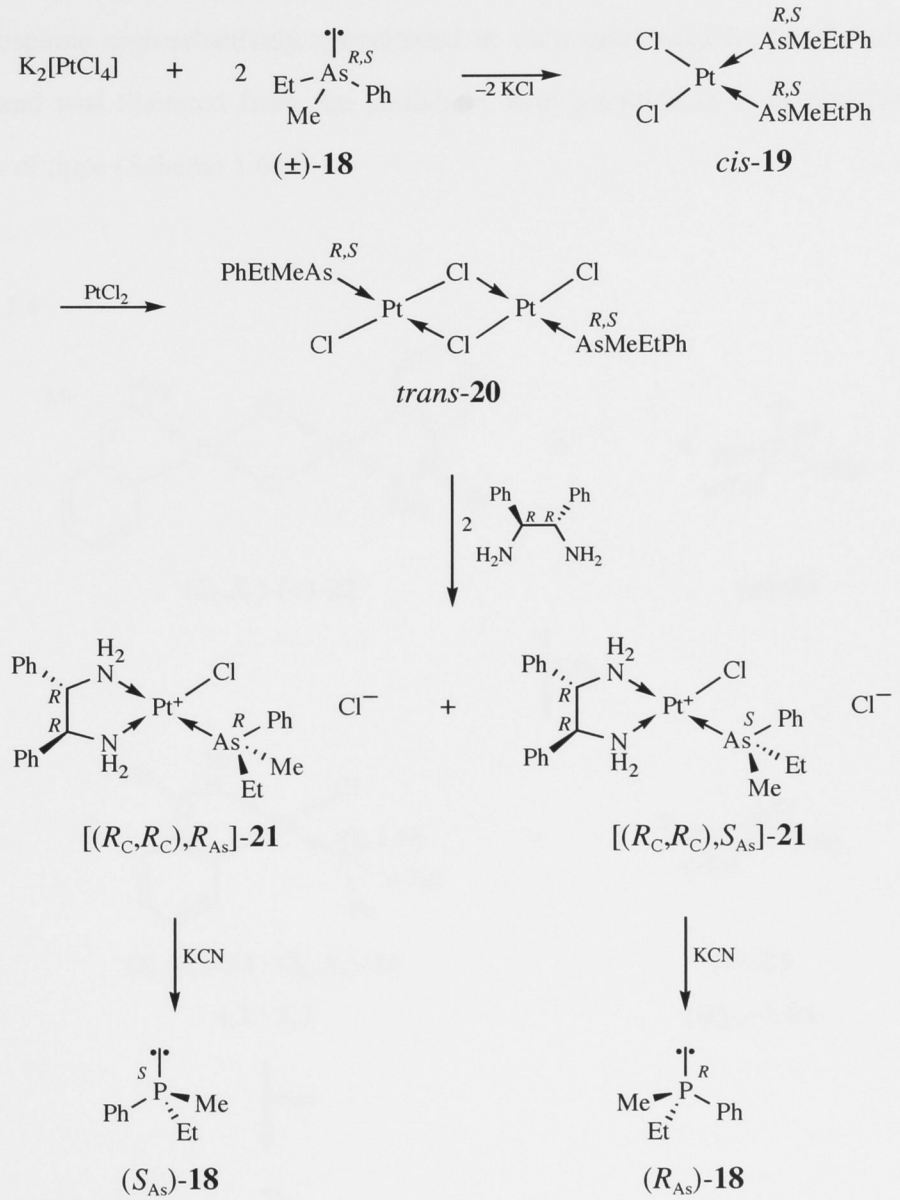
Scheme 1.4



1.3.3 Resolutions of tertiary arsines by metal complexation

The resolution of chiral arsines by the separation of internally diastereomeric metal complexes is the preferred method for obtaining *As*-chiral arsines of high enantiomeric purity.[6] The first resolution of a tertiary arsine–metal complex was achieved by Bosnich and Wild in 1970[58] following a modification of a procedure used for the resolutions of (±)-*trans*-cyclooctene,[59] (±)-*cis,trans*-1,5-cyclooctadiene,[60] and (±)-ethyl-*p*-tolylsulfoxide.[61] The method had also been adapted to the resolution of (±)-*t*-butylmethylphenylphosphine, but the enantiomerically pure phosphine was not isolated.[62] Thus, (±)-ethylmethylphenylarsine, (±)-**18**, reacts with potassium chloroplatinate(II) to give *cis*-[$PtCl_2$((±)-AsEtMePh)$_2$], *cis*-**19**, which further reacts with platinum(II) chloride in hot naphthalene to give *trans*-[Pt_2((±)-AsEtMePh)$_2Cl_4$], *trans*-**20**. Although *trans*-**20** exists as a mixture of racemic and meso diastereomers, it was not necessary to carry out a separation because both diastereomers undergo a quantitative bridge-splitting reaction with (R_C,R_C)-stilbene diamine to give the same pair of diastereomeric complexes [(R_C,R_C),R_{As}]- and [(R_C,R_C),S_{As}]-**21**. The latter complexes can be cleanly separated by fractional crystallisation. Treatment of the individual diastereomers of **21** with an excess of potassium cyanide liberated the individual enantiomers of the arsines with retention of configuration at arsenic (Scheme 1.5).[58]

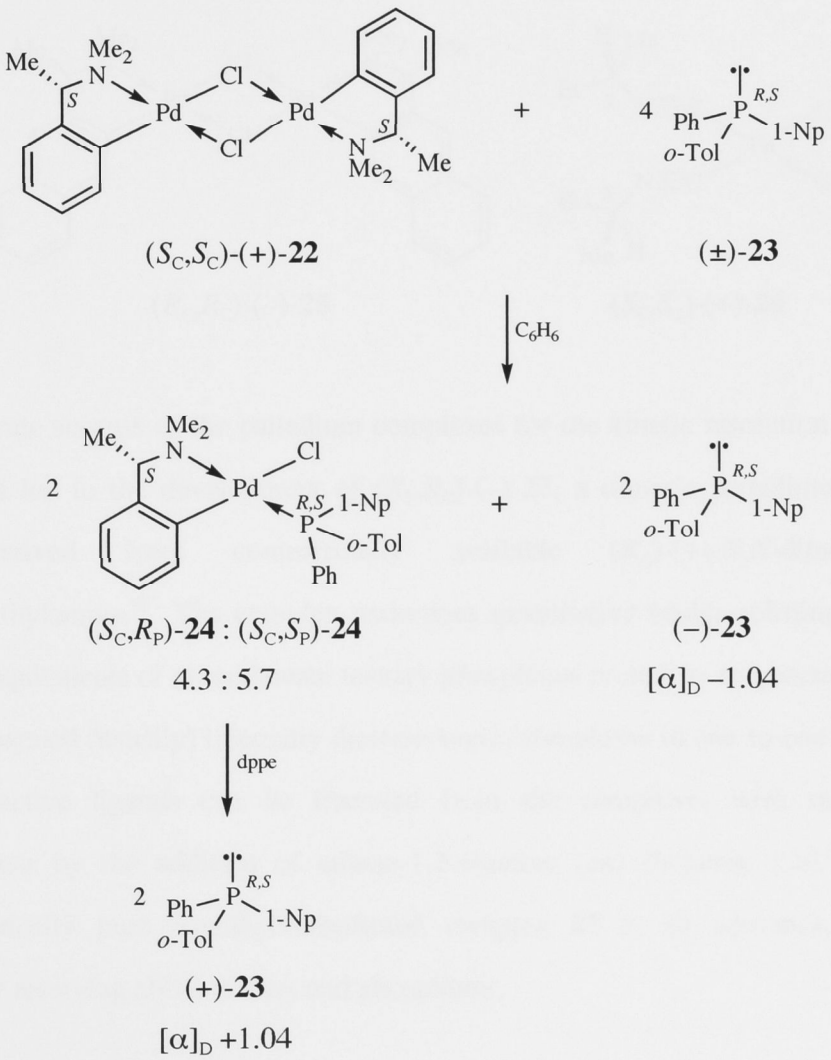
Scheme 1.5



Another advance in the field came when Otsuka and coworkers employed the dimeric palladium complex (S_C,S_C)-(+)-**22** for the partial kinetic resolution of several chiral triarylphosphines.[63] The palladium dimer underwent a bridge-splitting reaction with *four* equivalents of (±)-1-naphthylphenyl(*o*-tolyl)phosphine, (±)-**23**, to give the internally diastereomeric complexes (S_C,S_P)- and (S_C,R_P)-**24** in the ratio 5.7:4.3 (^{1}H NMR integration) and two equivalents of the free phosphine. Concentration of the solution led to the precipitation of the complexes; the opposite enantiomer of the

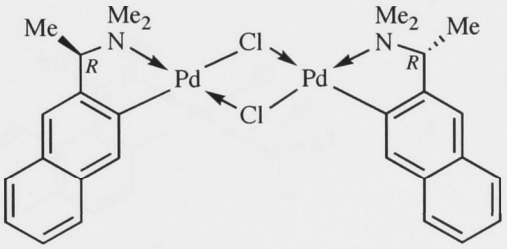
phosphine was enriched in the mother liquor and isolated by evaporation of the solvent. The phosphine regioselectively coordinated in each case *trans* to the dimethylamino group, and was liberated from the palladium with retention of configuration by the addition of dppe (Scheme 1.6).[63]

Scheme 1.6

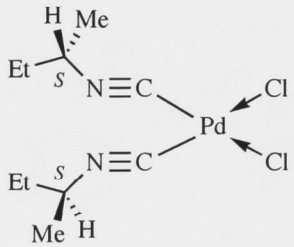


Although the benzylamine complex (S_C,S_C)-**22** is an effective resolving agent for chiral triarylphosphines, (R_C,R_C)-(–)-**25**, which was prepared from (R_C)-(+)-*N*,*N*-dimethyl-1-(2-naphthyl)ethylamine, gave superior results for the partial kinetic resolution of dialkylarylphosphines in the manner described above. This paper also describes the use

of the optically active *sec*-butylisocyanide palladium complex (S_C,S_C)-(+)-**26**, which, when reacted with two equivalents of a racemic (±)-triarylphosphine, gave a diastereomerically enriched solution of the *trans*-isocyanide–phosphine complex. The efficiency of (S_C,S_C)-(+)-**26** for the reaction, however, depended greatly on the nature of the phosphine substituents.[64]



(R_C,R_C)-(−)-**25**

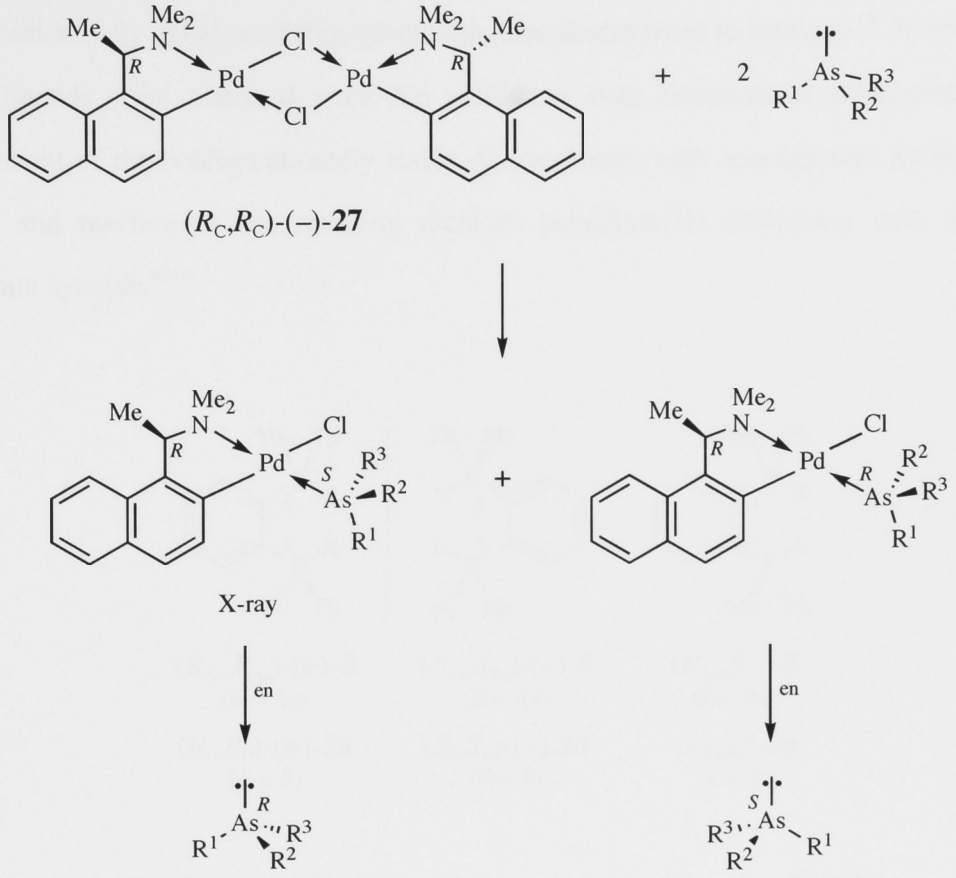


(S_C,S_C)-(+)-**26**

The moderate success of the palladium complexes for the kinetic resolution of tertiary phosphines led to the development of (R_C,R_C)-(−)-**27**, a dimeric palladium resolving agent derived from commercially available (R_C)-(+)-*N*,*N*-dimethyl-1-(1-naphthyl)ethylamine.[65] The complex undergoes quantitative bridge-splitting reactions with two equivalents of monodentate tertiary phosphines or arsines to generate pairs of readily separated (usually) internally diastereomeric complexes in one-to-one ratio. The optically active ligands can be liberated from the complexes with retention of configuration by the addition of ethane-1,2-diamine (en) (Scheme 1.7).[†6, 31] The enantiomerically pure naphthyl-substituted complex **27** is an extremely effective reagent for resolving chiral arsines and phosphines.

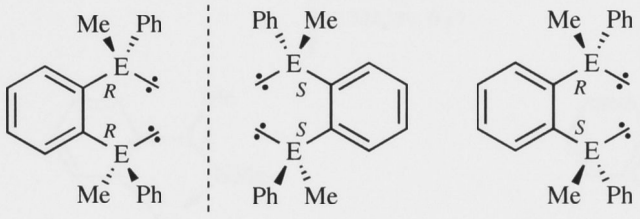
[†] Coordination of an *As*-chiral arsine to a metal is stereospecific: the apparent inversion of configuration that takes place at arsenic when a chiral arsine coordinates to an element of higher atomic number than 12 is a consequence of the Cahn–Ingold–Prelog (CIP) rules.[7, 66] Upon coordination to the palladium, the lone pair on the free arsine of CIP priority 4 is replaced by a ligand (the metal) of CIP priority 1.

Scheme 1.7



The resolution of tertiary arsines by metal complexation has been comprehensively reviewed in the literature and some salient examples are described below.[6, 31] The benzyl-substituted complex (S_C,S_C)-**22** has been successfully employed for the resolution of (*R**,*R**)-(±)-1,2-*bis*(methylphenylarsino)benzene, (±)-**5**,[67] and the phosphorus analogue (±)-**28**[68] after initial separation of the racemic and meso diastereomers of the ligands by fractional crystallisation. The related *As*,*P*-bidentate (*R**,*R**)-(±)/(*R**,*S**)-(±)-**29** exists as a pair of chiral diastereomers.[69] The threo diastereomer, (*R**,*R**)-(±)-**29,** was isolated by fractional crystallisation of the mixture from hot methanol and was resolved with (R_C,R_C)-(–)-**22**; the erythro diastereomer, (*R**,*S**)-(±)-**29**, was purified as the (thiocyanato)nickel(II) complex and was resolved

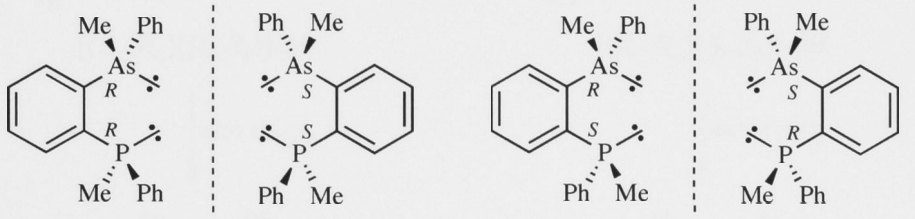
with (R_C,R_C)-(–)-**27**.[‡] The threo and erythro diastereomers of the ligand coordinate regioselectively to the resolving agent with phosphorus *trans* to nitrogen.[69] In each case the ligands were liberated from the palladium with retention of configuration by treatment of the configurationally stable diastereomers with concentrated hydrochloric acid and reaction of the resulting dichloro palladium(II) complexes with aqueous sodium cyanide.[67-69]



(R_{As},R_{As})-(+)-**5** (E = As)
(R_P,R_P)-(+)-**28** (E = P)

(S_{As},S_{As})-(–)-**5** (E = As)
(S_P,S_P)-(–)-**28** (E = P)

(R_{As},S_{As})-**5** (E = As)
(R_P,S_P)-**28** (E = P)



(R_{As},R_P)-(+)-**29**

(S_{As},S_P)-(–)-**29**

(R_{As},S_P)-(–)-**29**

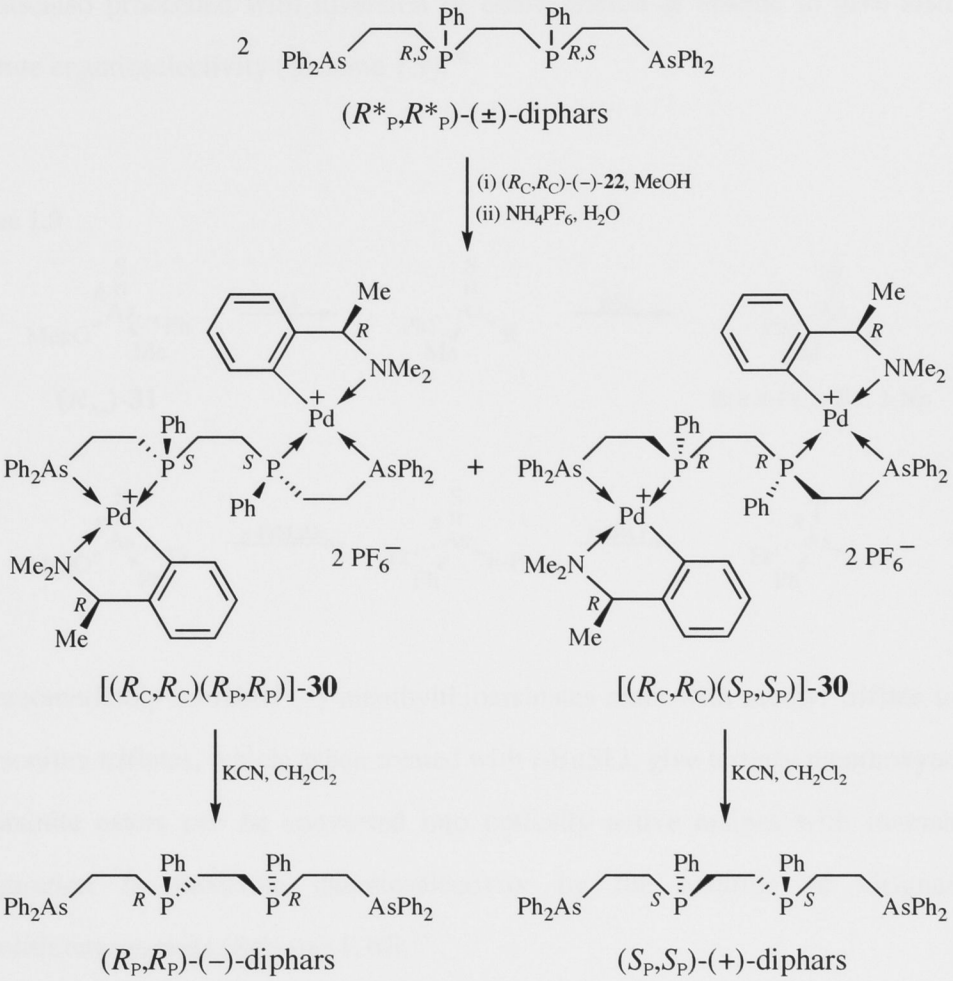
(S_{As},R_P)-(+)-**29**

The bis(tertiary phosphine)–bis(tertiary arsine) (R^*_P,R^*_P)-(±)/(R^*_P,S^*_P)-diphars was separated into the racemic and meso diastereomers by fractional crystallisation from dichloromethane and ethanol.[70] The racemate was resolved with use of an equimolar quantity of (R_C,R_C)-(–)-**22** and exchange of chloride with excess ammonium hexafluorophosphate to give the pair of complexes [(R_C,R_C)(R_P,R_P)]-**30** and [(R_C,R_C)(S_P,S_P)]-**30** that were separated by fractional crystallisation. The pure

[‡] The reaction of (*R**,*S**)-(±)-**29** with (R_C,R_C)-(–)-**27** produced an inseparable mixture of diastereomers.

enantiomers of diphars was recovered from the individual diastereomers of **30** by treatment with potassium cyanide (Scheme 1.8).[70]

Scheme 1.8

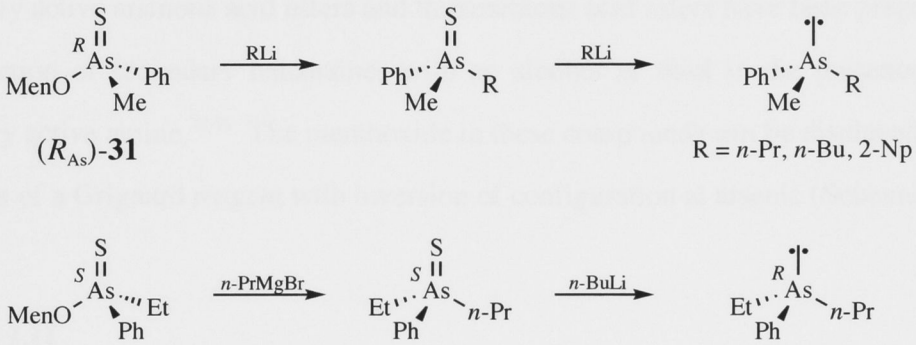


1.4 Enantioselective syntheses of chiral arsines

The first enantioselective synthesis of a chiral tertiary arsine was reported by Mislow and coworkers in 1973.[71] Displacement of (–)-menthoxide at low temperature from diastereomerically enriched (*O*-menthyl)methylphenylthioarsinate, (R_{As})-**31**, with alkyl-

or aryllithium reagents gave the corresponding tertiary arsine sulfides with inversion of configuration. Reductions of the arsine sulfides with a second equivalent of lithium reagent gave the tertiary arsines with moderate enantioselectivities, in one pot.[71] The displacement of (–)-menthoxide from the thioarsinates with the appropriate Grignard reagents also proceeded with inversion of configuration at arsenic to give arsines in moderate enantioselectivity (Scheme 1.9).[72]

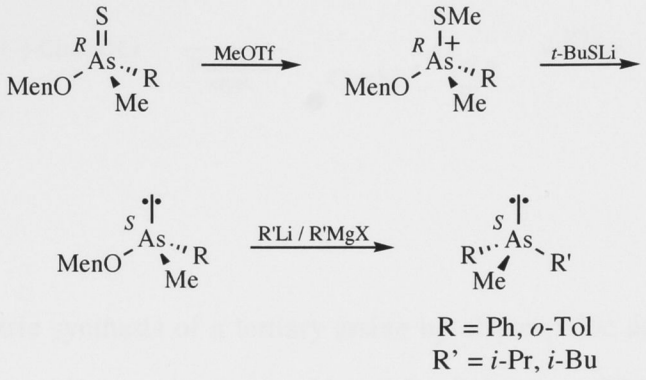
Scheme 1.9



(R_{As})-**31**

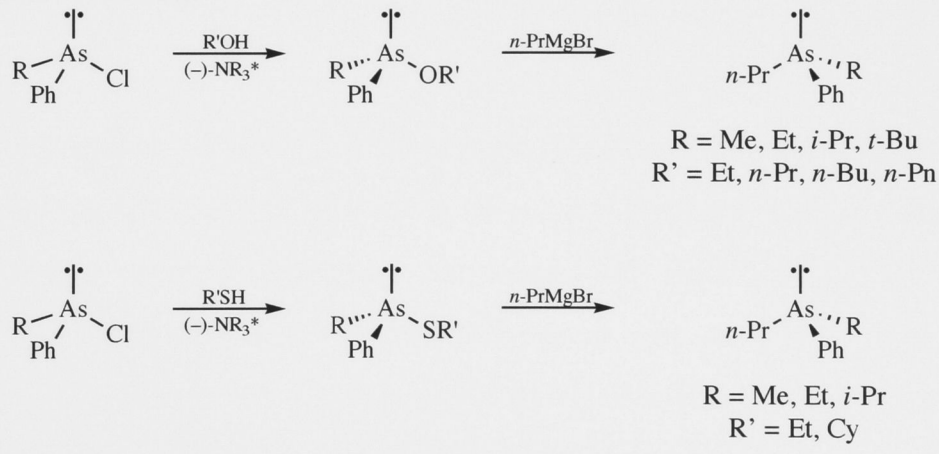
Diastereomerically enriched (–)-menthylthioarsinates react with methyl triflate to give thioarsonium triflates, which, when treated with *t*-BuSLi, give tertiary menthoxyarsines. The arsinite esters can be converted into optically active arsines with inversion of configuration in moderate enantioselectivity by the addition of Grignard or organolithium reagents (Scheme 1.10).[73]

Scheme 1.10



Optically active arsinous acid esters and thioarsinious acid esters have been prepared by the reaction of secondary haloarsines with an alcohol or thiol in the presence of an optically active amine.[74-76] The menthoxide in these compounds can be displaced by the addition of a Grignard reagent with inversion of configuration at arsenic (Scheme 1.11).

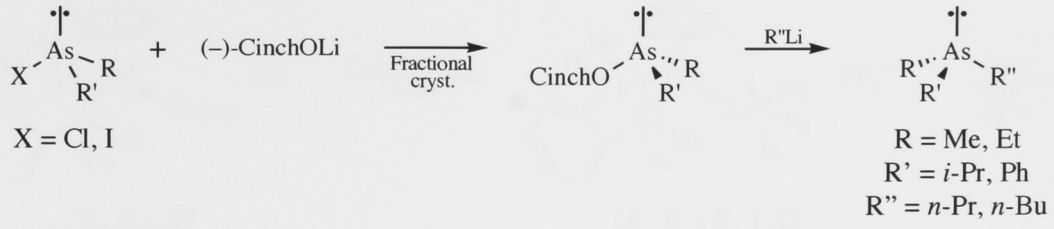
Scheme 1.11



NR_3* = (–)-*N*,*N*-diethyl-α-methylbenzylamine, (–)-brucine

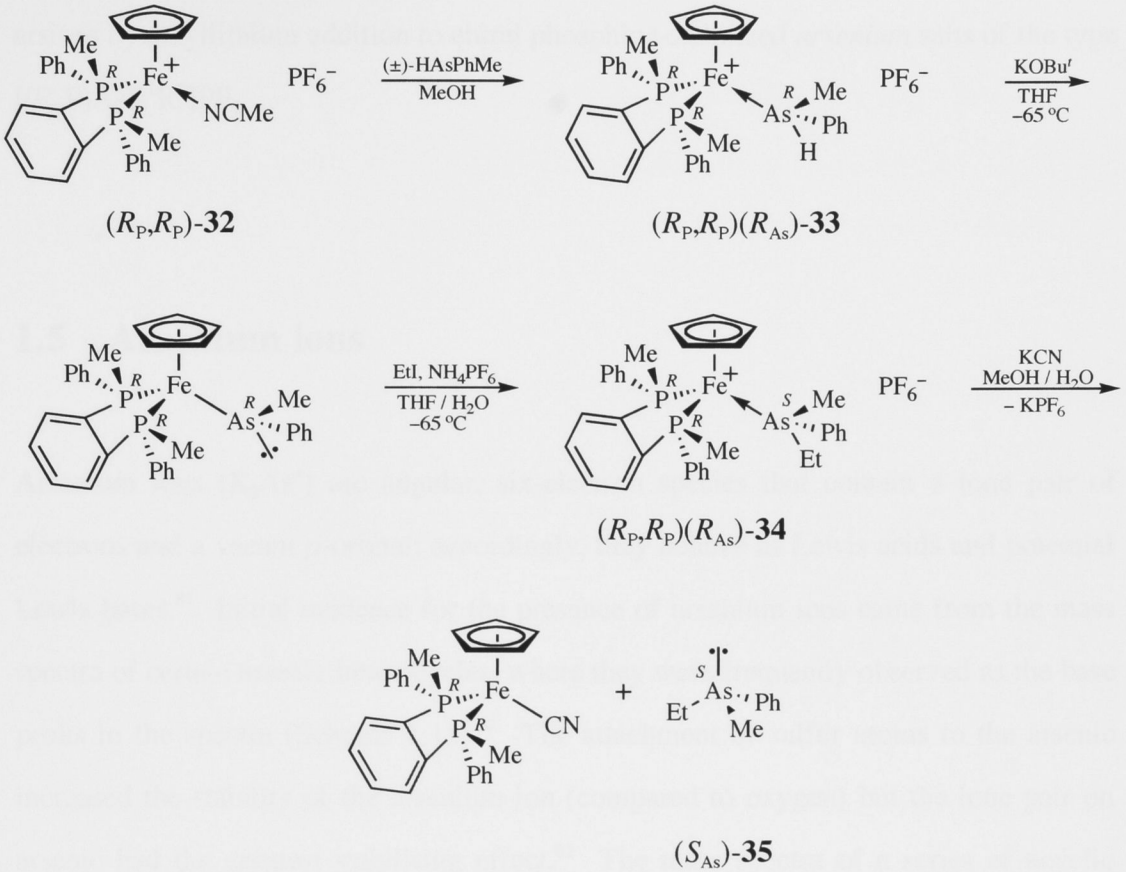
Secondary chloro- or iodoarsines react with the lithium reagent of (–)-cinchonidine to generate crystalline cinchonidine esters that can be fractionally crystallised; the cinchonidide is displaced with alkyllithium reagents to give enantiomerically enriched tertiary arsines with predominant inversion of configuration at arsenic (Scheme 1.12).[77]

Scheme 1.12



The first asymmetric synthesis of a tertiary arsine by electrophilic alkyl addition to an optically active arsenido complex was achieved by Salem and Wild in 1989.[78] The addition of (±)-HAsMePh to the optically active acetonitrile–iron complex (R_P,R_P)-**32** gave one diastereomer of the secondary arsine complex (R_P,R_P)(R_{As})-**33** by an asymmetric transformation of the second kind.[7] Deprotonation and subsequent addition of iodoethane at –65 °C to the intermediate arsenido–iron complex gave the (R_P,R_P)(S_{As})- diastereomer of the tertiary arsine complex **34** in 87% yield. Optically active (S_{As})-**35** was liberated from the complex with cyanide and had $[\alpha]_D$ –2.0 (*c* 0.751, Et_2O) (Scheme 1.13).[78]

Scheme 1.13



(R_P,R_P)-**32**

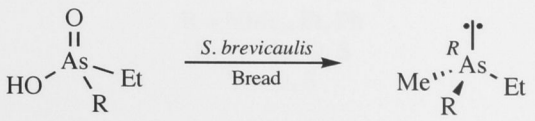
$(R_P,R_P)(R_{As})$-**33**

$(R_P,R_P)(R_{As})$-**34**

(S_{As})-**35**

Another interesting example of an asymmetric synthesis of a tertiary arsine was the enantioselective biotransformation of an arsinic acid with the yeast *Scopulariopsis brevicaulis*. Growing on moist bread impregnated with a prochiral arsinic acid, the yeast reductively methylates dialkylarsinic acids to give the corresponding chiral tertiary arsines in up to 70% ee, as determined by coordination of the evolved arsines to (R_C,R_C)-(–)-**27** and recording the ^{1}H NMR spectra (Scheme 1.14).[79, 80]

Scheme 1.14



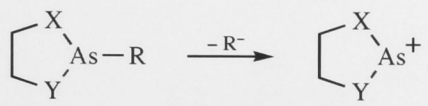
R = *n*-Pr, *i*-Pr, *n*-Bu, *n*-Hx

Recent work within our group has focussed on the asymmetric synthesis of tertiary arsines by alkyllithium addition to chiral phosphine-stabilised *arsenium* salts of the type $[(R_3P)AsR^1R^2]PF_6$.

1.5 Arsenium ions

Arsenium ions (R_2As^+) are angular, six-electron species that contain a lone pair of electrons and a vacant *p*-orbital; accordingly, they behave as Lewis acids and potential Lewis bases.[81] Initial evidence for the presence of arsenium ions came from the mass spectra of certain arsenic heterocycles, where they were frequently observed as the base peaks in the spectra (Scheme 1.15).[82] The attachment of sulfur atoms to the arsenic increased the stability of the arsenium ion (compared to oxygen) but the lone pair on arsenic had the greatest stabilising effect.[82] The mass spectra of a series of acyclic tertiary, secondary, and halogenoarsines have been recorded; in most cases, arsenium ions were the base peaks in the spectra where they resulted from the fragmentation of an As–C bond of an alkyl group (particularly methyl groups) rather than an aryl group. The methylphenylarsenium ion is the base peak in the mass spectrum of iodomethylphenylarsine through loss of iodide.[83]

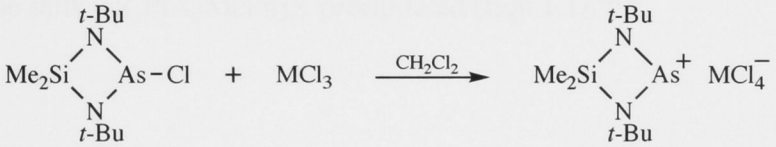
Scheme 1.15



R = NMe_2, Et, Ph
X = NMe, O, S
Y = O, S

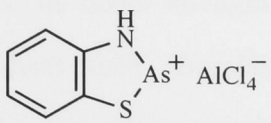
Direct syntheses of arsenium salts have been achieved from secondary chloroarsines with use of halide-abstracting agents; the first salts of this type, **36**, were prepared with the use of aluminium, gallium, and indium trichlorides (Scheme 1.16). The analogous phosphenium, stibenium, and bismuthenium salts were characterised by X-ray crystallography, but the arsenium salts were not crystalline and were characterised by UV–vis and ^{1}H NMR spectroscopy.[84]

Scheme 1.16

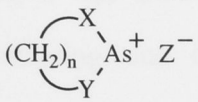


36
M = Al, Ga, In

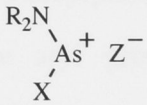
Subsequent work resulted in the first X-ray structure of an arsenium salt, **37**; the cation in the salt is almost planar and contains short As–N and As–S bonds, which is consistent with some double-bond character due to delocalisation of the charge across the conjugated backbone.[85, 86] This work led to the synthesis of a series of cylic, **38**, and acylic, **39**, arsenium salts; the electron-poor arsenium centres in the cations were considered to be stabilised by lone-pair donation from neighbouring heteroatoms.[87-90]



37



38
X, Y = NMe, NEt, S
Z = $AlCl_4$, $GaCl_4$, $InCl_4$
n = 2, 3



39
R = Me, Et, *i*-Pr
X = NEt_2, Cl
Z = $AlCl_4$, OTf

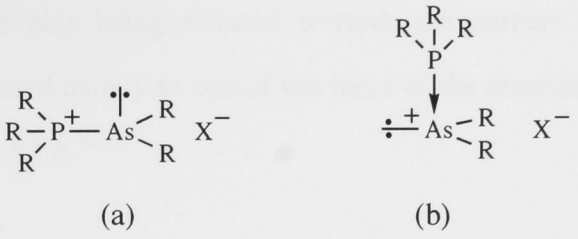
1.6 Phosphine-stabilised arsenium salts

Arsenium ions can be stabilised by neighbouring group interactions and by coordination of Lewis bases.[91] The first ligand-stabilised arsenium salts to be isolated were considered as *arsinophosphonium salts*, where the positive charge in each case was centred on phosphorus. The salts were prepared by the addition of a tertiary phosphine to a diethyl ether or cyclohexane solution of a secondary chloro-, bromo-, or iodoarsine, whereupon the salts $[(R_3P)AsMePh]X$ precipitated (Eqn 1.1).[92, 93]

$$R_3P + XAsR_2 \xrightarrow{Et_2O\ /\ CyH} [(R_3P)AsR_2]X \downarrow \qquad \text{(Eqn 1.1)}$$

R = alkyl, aryl
X = Cl, Br, I

The crystalline *iodides* sublimed on heating and had the characteristic odour of the parent iodoarsine when heated, which suggested an equilibrium involving the starting materials, although there was no evidence of this behaviour in solution. Triphenylphosphine-stabilised salts could not be synthesised by this method, but there was evidence of an unstable pyridine adduct of iododimethylarsine. Conductimetric analyses of the salts showed that the affinity of the ligand for the arsenic substrate was dependent on its donor strength. Thus, it was shown that trialkylphosphines from stronger adducts than phosphines containing one or more aryl groups.[93] The arsinophosphonium salts react with sodium alkoxides or *n*-butyllithium to give arsinous acid esters or tertiary arsines, respectively, with displacement of the phosphine. This observation indicated to us that significant positive charge resided on the arsenic, rather than the phosphorus (Figure 1.1). Accordingly, we now describe salts of this type as *phosphine-stabilised arsenium salts*.[91, 93]

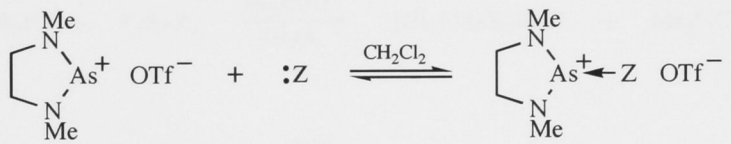


(a) (b)

Figure 1.1 Representations of the structures of (a) arsinophosphonium salts and (b) phosphine-stabilised arsenium salts.

Ligand-stabilised arsenium salts have also been prepared by the addition of Lewis bases to arsenium salts. The reactions can be monitored by NMR spectroscopy, where there is evidence of a rapid dissociative equilibrium between reactants and products in solution (Scheme 1.17). The focus of this work was to determine the Lewis acidity of phosphenium and arsenium ions, and there was no attempt to isolate the adducts.[89]

Scheme 1.17



Z = $HNEt_2$, py, P(*n*-Bu)$_3$

A series of phosphine-stabilised arsenium hexafluorophosphates was synthesised directly in a two-phase system in which a dichloromethane solution of the phosphine and the iodoarsine was exposed to a solution of ammonium hexafluorophosphate in water (Eqn 1.2).[81, 91] When the iodide is replaced by hexafluorophosphate, the equilibrium between the reactants and product is no longer possible. The colourless phosphine-stabilised arsenium salts were readily isolated from the organic phase and, in general, are air- and moisture-stable solid. In the solid state, the stereochemistry around arsenic in each case is based on the distorted trigonal pyramid; the six-electron arsenium ion has an angular geometry with the As–*C* carbons of the methyl and phenyl

groups and the lone pair being directed towards the corners of a triangle. The phosphine is coordinated axially to one of the faces of the arsenium ion, with a typical As–P bond length of 2.3 Å.[81, 91]

$$R_3P + IAsR_2 \underset{CH_2Cl_2}{\rightleftharpoons} [(R_3P)AsR_2]I \xrightarrow[H_2O]{NH_4PF_6} [(R_3P)AsR_2]PF_6 \quad \text{(Eqn 1.2)}$$

Phosphine-stabilised arsenium salts can also be prepared by the addition of a chloride abstracting agent, such as trimethylsilyl triflate (Eqn 1.3)[94] or thallium(I) hexafluorophosphate (Eqn 1.4),[95] to a solution of a chloroarsine and a phosphine. The by-products are easily removed, in vacuo (trimethylsilyl chloride) or by filtration (thallium(I) chloride); this method provides an effective route to moisture-sensitive complexes.[94, 95]

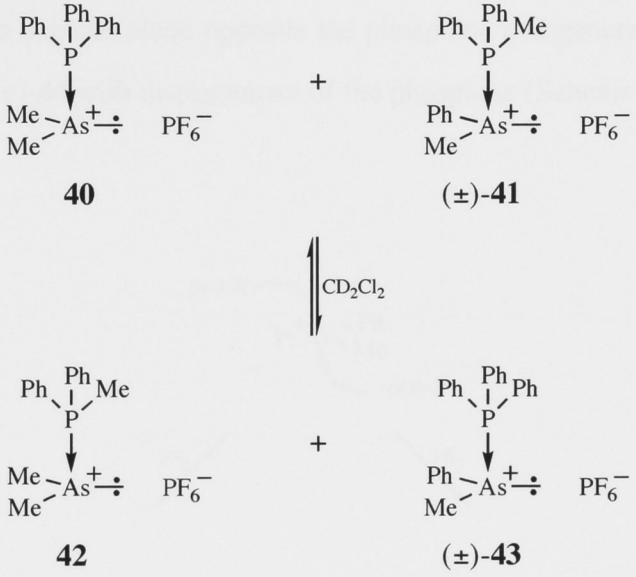
$$R_3P + ClAsR_2 \xrightarrow[CH_2Cl_2]{Me_3SiOTf} [(R_3P)AsR_2]OTf + Me_3SiCl \quad \text{(Eqn 1.3)}$$

$$R_3P + ClAsR_2 \xrightarrow[CH_2Cl_2]{TlPF_6} [(R_3P)AsR_2]PF_6 + TlCl \quad \text{(Eqn 1.4)}$$

Although phosphine-stabilised arsenium salts are thermodynamically stable, the As–P bonds in the complexes are labile and the complexes undergo facile phosphine exchange in solution. Ligand exchange is considerably slowed at low temperatures, which is evident from low temperature NMR spectroscopic investigations.[81, 91] The complex **40** has a free energy of activation for phosphine dissociation at 7 °C (T_C) of 67 kJ mol^{-1} in CD_2Cl_2 based on the observation of phosphorus coupling to the AsMe groups in the ^{1}H NMR spectrum at that temperature; this coupling was not evident in the spectrum at room temperature. Furthermore, the addition of an equimolar quantity of **40** to a CD_2Cl_2 solution of (±)-**41** at room temperature gives the crossover products

42 and (±)-**43** within the time of mixing and recording the $^{31}P\{^{1}H\}$ NMR spectrum, ca. 1 min (Scheme 1.18).[81, 91]

Scheme 1.18

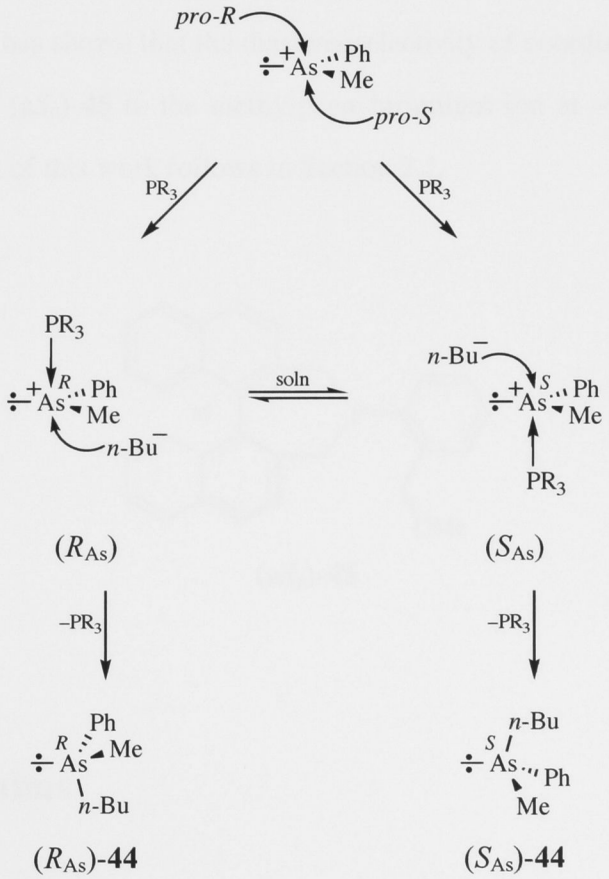


1.7 Asymmetric synthesis of chiral arsines from phosphine-stabilised arsenium salts

An arsenium ion of the type $[As^{+}R^{1}R^{2}]^{+}$, being planar and unsymmetrically substituted, is prochiral; the addition of a phosphine to the *pro-R* or *pro-S* face of the ion will generate the *R* or *S* enantiomer of the phosphine-stabilised arsenium cation.[91] The absolute configuration of each enantiomer of the cation can be assigned by viewing the structure down the axis containing the ligand of lowest Cahn–Ingold–Prelog (CIP) priority (the lone pair, priority number 4) and observing the direction of rotation of the remaining ligands 1→3 at the corners of the triangular face at the base of the pyramid.[7, 66] Due to the lability of the phosphorus–arsenic bond in the cation in solution, the enantiomers of the complex will be in equilibrium under ambient conditions through

dissociation of the phosphine. As previously indicated, the phosphine in the complex is readily displaced by anionic nucleophiles such as the *n*-butyl anion in an S_N2-type substitution reaction. Since the geometry about the arsenic in a chiral cation of this type is based on the trigonal pyramid, the nucleophile will attack the arsenic from the exposed side of the trigonal plane opposite the phosphine and generate a chiral tertiary arsine of the type (±)-**44** with displacement of the phosphine (Scheme 1.19).[81, 91]

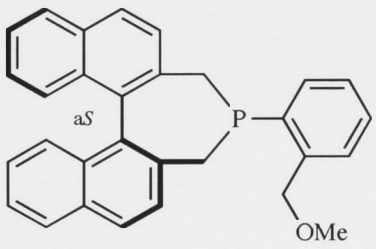
Scheme 1.19



The use of an enantiomerically pure phosphine will generate a phosphine-stabilised arsenium salt that exists as a pair of diastereomers, epimeric at the stereogenic arsenic stereocentre. The proportion of each diastereomer at equilibrium will be dependent on the relative free energies of the complexes. This phenomenon forms the basis of our

work on the asymmetric syntheses of chiral arsines by nucleophilic addition of an alkyllithium reagent to a chiral phosphine-stabilised arsenium salts.[91, 96] If the phosphine is enantiomerically pure and the negatively charged carbon nucleophile adds irreversibly to the arsenium centres of each of the equilibrating diastereomers at a rate that is faster than the rate of phosphine exchange between the diastereomers, the prevailing configuration of the product will correspond to the configuration of the arsenium ion in the more stable phosphine–arsenium diastereomer.[91, 96]

Work in our group has shown that the diastereoselectivity of coordination of the axially chiral phosphepine (aS_P)-**45** to the methylphenylarsenium ion at –90 °C is 86%.[91] A detailed description of this work follows in Section 2.1.



(aS_P)-**45**

1.8 Project aims

The work presented in this thesis consists of four separate, but related projects. The first project involves the asymmetric synthesis of (±)-(*n*-butyl)methylphenylarsine from the phosphine-stabilised methylphenylarsenium complex containing the phosphepine (aR_P)-**45** as the chiral auxiliary. The second project describes an extension of this methodology to the asymmetric synthesis of chelating bis(tertiary arsines). In the third

project, the synthesis of two novel phosphine auxiliaries based on ($1R_C$,$2S_C$,$5R_C$)-8-phenylmenthol and some preliminary work on the synthesis of arsenium adducts of these phosphines will be presented. The final project involves the synthesis of the first arsine-stabilised arsenium salts and examines their potential for the asymmetric synthesis of tertiary arsines.

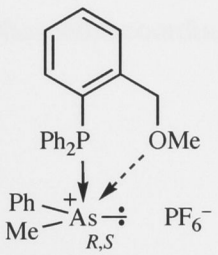
Chapter 2:

Asymmetric synthesis of a tertiary arsine

2.1 Introduction

Chiral phosphine-stabilised arsenium salts are usually air- and moisture-stable crystalline compounds that are potentially convenient intermediates for the asymmetric synthesis of tertiary arsines by nucleophilic addition.[81] The irreversible addition of a carbanionic nucleophile to the planar, prochiral arsenium ion in the trigonal pyramidal cation of the complexes is expected to occur at the trigonal face opposite the chiral phosphine to give an excess of one enantiomer of the chiral tertiary arsine with displacement of the phosphine auxiliary.[81, 97]

The effect at arsenic of an achimeric substituent on the phosphine was examined by the synthesis of (±)-**46**.[81] The destabilising chelate effect of the 2-methoxymethyl substituent on the phenyl group of the phosphine was apparent in the X-ray crystal structure. The As–P length in the substituted complex is 0.0223 Å longer than the corresponding bond in (±)-[(PPh_3)AsMePh]PF_6;[81] oxygen–arsenic interaction was also evident from the As···O distance of 2.878(1) Å, which is shorter than the sum of the van der Waals radii for the two atoms (3.37 Å).[98] The 2-methoxymethyl interaction at arsenic will hinder rotation about the As–P bond.

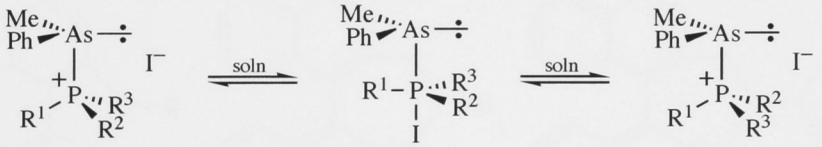


(±)-**46**

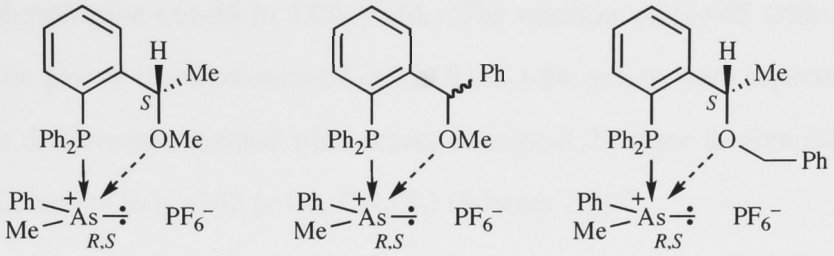
2.1.1 Chiral phosphine design

The *P*-chiral phosphine (±)-[2-(methoxymethyl)phenyl]methylphenylphosphine was synthesised by standard procedures; the (+)-enantiomer of the phosphine was reacted with iodomethylphenylarsine and ammonia hexafluorophosphate in the two-phase, dichloromethane–water system to give the expected phosphine–arsenium complex in 59% yield after recrystallisation.[91] Unfortunately, the product showed no optical activity and further investigations indicated that the *P*-chiral phosphine had epimerised in the presence of the iodoarsine (Scheme 2.1).[91, 99] Subsequent work in our group therefore focussed on the use of chiral phosphines in which the configurationally pure element of the ligand was a chiral substituent or formed the backbone of the phosphine auxiliary, rather than residing on phosphorus.

Scheme 2.1

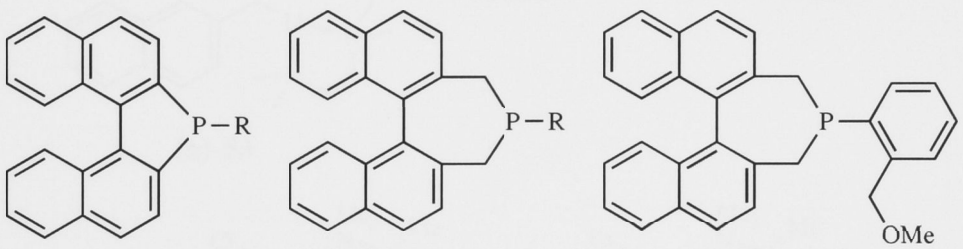


Accordingly, the phosphine-stabilised arsenium salts $(S_C,R_{As})/(S_C,S_{As})$-**47**, $(R^*_C,R_{As})/(R^*_C,S_{As})$-**48**, and $(S_C,R_{As})/(S_C,S_{As})$-**49** were prepared and shown by $^{31}P\{^1H\}$ NMR spectroscopy to have des of phosphine coordination of 35–40% at –80 °C.



$(S_C,R_{As})/(S_C,S_{As})$-**47** $(R^*_C,R_{As})/(R^*_C,S_{As})$-**48** $(S_C,R_{As})/(S_C,S_{As})$-**49**

Axially dissymmetric diphosphines, such as (aR_P)-BINAP, are extremely effective chiral auxiliaries for metal-catalysed asymmetric syntheses[100] and so the heterocycles (±)-**50** and (±)-**51** were considered attractive targets. Phosphafluorenes of the type (±)-**50**, however, are unsuitable for resolution because of rapid interconversion between the atropisomers at room temperature.[101]

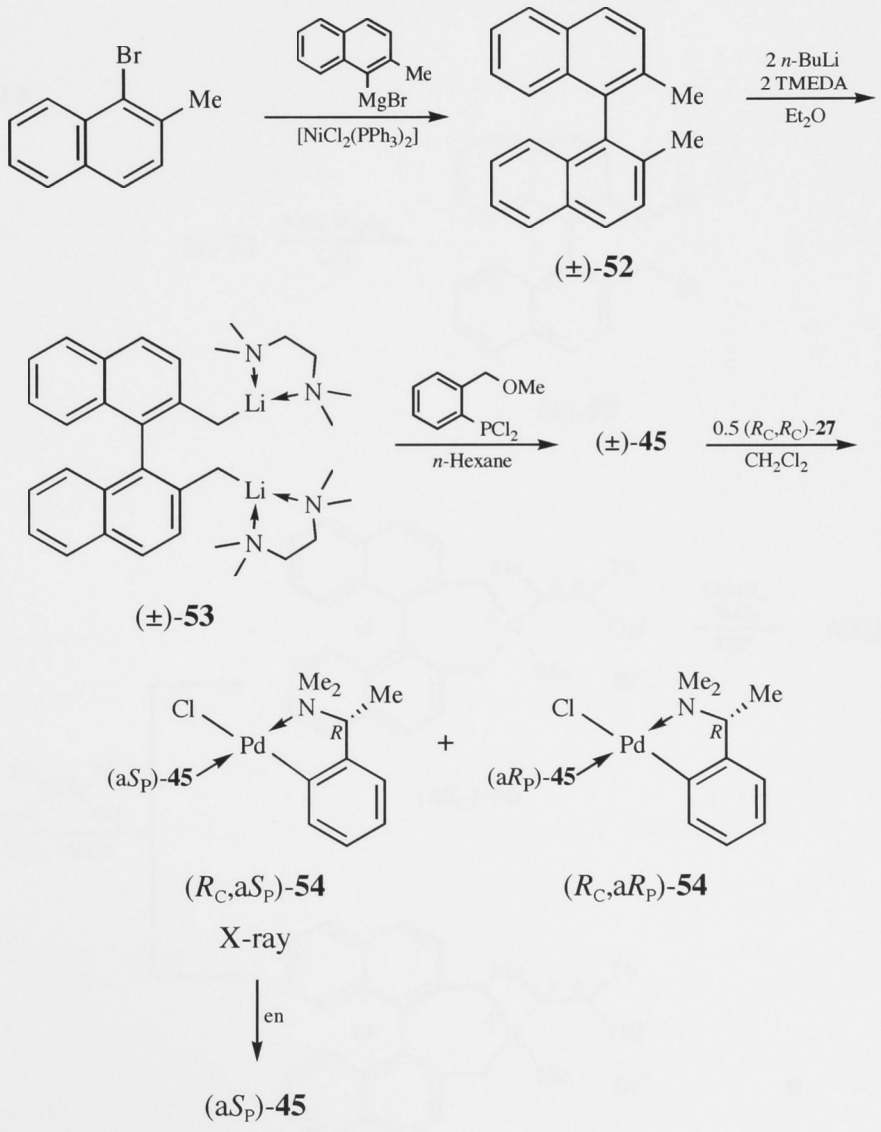


(±)-**50** (±)-**51** (±)-**45**

The phosphepine (±)-**45** was synthesised by the three routes described below. The 1,1′-binaphthyl intermediate (±)-**52** was obtained by coupling 1-bromo-2-methylnapthalene with the corresponding Grignard reagent in the presence of a nickel(II) catalyst;[102] the 2,2′-dimethyl-1,1′-binaphthyl intermediate (±)-**52** was metallated with *n*-BuLi in the presence of TMEDA to give the air- and moisture-sensitive dilithiated binaphthyl (±)-

53.[102, 103] Condensation of (±)-**53** with dichloro[2-(methoxymethyl)phenyl]phosphine[§] gave the phosphepine (±)-**45** in 18% yield. The reaction of (±)-**45** with (R_C,R_C)-**27** generated the pair of diastereomers (R_C,aR_P)/(R_C,aS_P)-**54**, which were separated and the less-soluble diastereomer treated with excess diamino-1,2-ethane to give (aS_P)-**45**, mp 239–240 °C, having $[\alpha]_D$ –152 (*c* 1.0, CH_2Cl_2) (Scheme 2.2).[91]

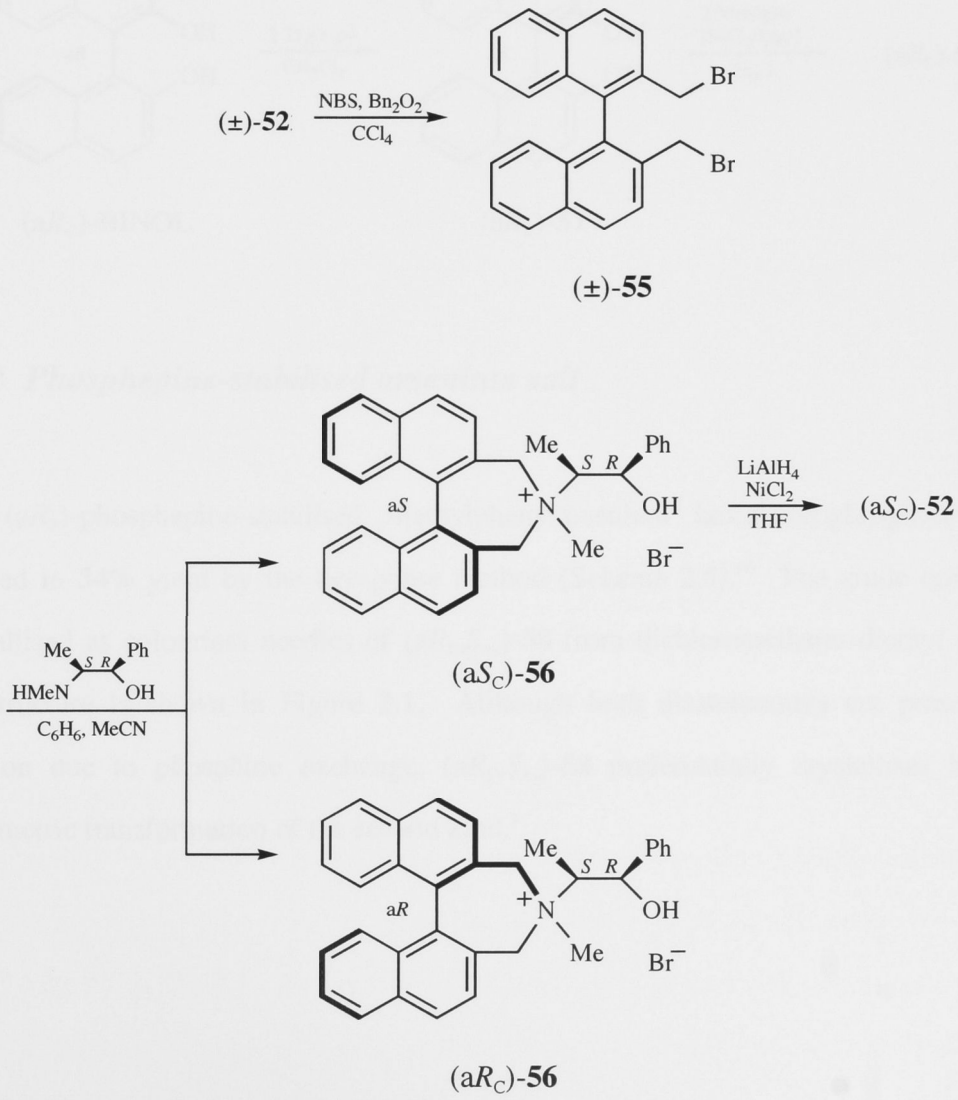
Scheme 2.2



[§] The phosphine was prepared by the addition of the Grignard reagent of 1-bromo-2-methoxymethyl-benzene to $ClP(NEt_2)_2$ followed by treatment with anhydrous hydrogen chloride.[91]

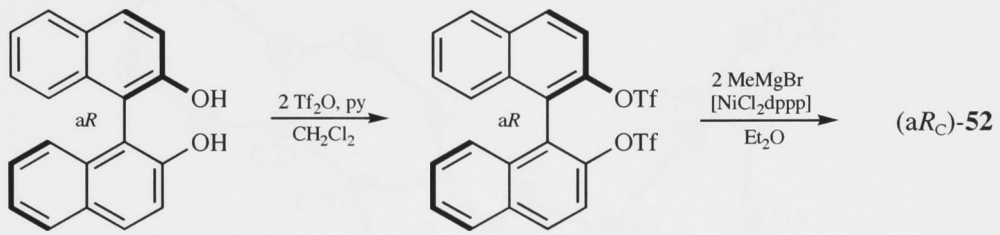
In another approach to (±)-**45**, (±)-**52** was brominated with *N*-bromosuccinimide (NBS) and the resulting dibromo compound (±)-**55** was treated with (–)-ephedrine in boiling acetonitrile/benzene, to give a quantitative yield of the diastereomeric ammonium salts (aR_C)- and (aS_C)-**56**.[102] Fractional crystallisation of this mixture gave the less soluble diastereomer that was reduced with $LiAlH_4$ to furnish (aS_C)-**52** (Scheme 2.3). Enantiomerically pure (aS_C)-**52** was then lithiated and treated with the dichlorophosphine to give (aS_P)-**45**, $[\alpha]_D$ –180 (*c* 1.0, CH_2Cl_2).[91]

Scheme 2.3



Limitations of the above methods include the number of synthetic steps required and the low-yielding resolution step. The use of commercially availability (aR_C)-BINOL, however, eliminates the need of resolving the 1,1′-binaphthyl backbone. Accordingly (aR_C)-**52** was synthesised in ca. 95% yield by cross-coupling of methylmagnesium bromide with the ditriflate of (aR_C)-BINOL, (aR_C)-**57**, (Scheme 2.4).[104] The phosphepine (aR_P)-**45** was isolated in 53% via (aR_C)-**52**, as indicated in Scheme 2.2.[96]

Scheme 2.4

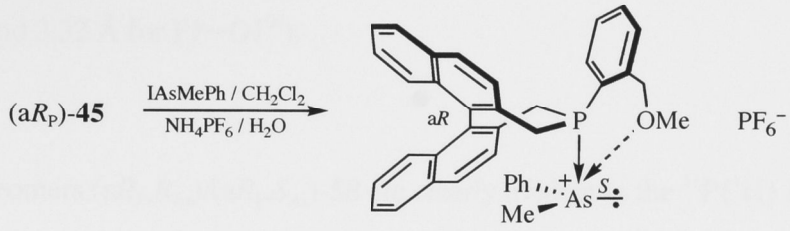


(aR_C)-BINOL (aR_C)-**57**

2.1.2 Phosphepine-stabilised arsenium salt

The (aR_P)-phosphepine-stabilised methylphenylarsenium hexafluorophosphate was isolated in 54% yield by the two-phase method (Scheme 2.5).[96] The crude complex crystallised as colourless needles of (aR_P,S_{As})-**58** from dichloromethane–diethyl ether; the structure is shown in Figure 2.1. Although both diastereomers are present in solution due to phosphine exchange, (aR_P,S_{As})-**58** preferentially crystallises by an asymmetric transformation of the second kind.[7]

Scheme 2.5



(aR_P,S_{As})-**58**

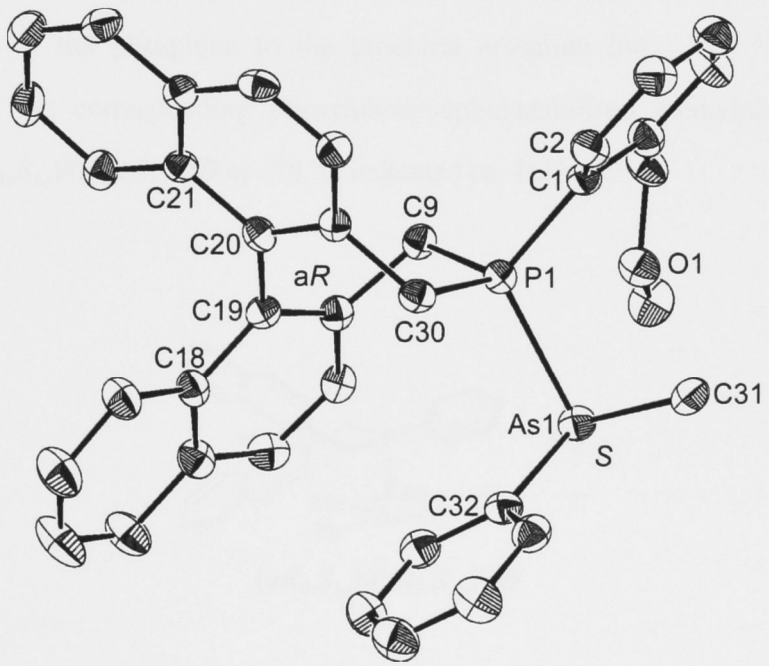
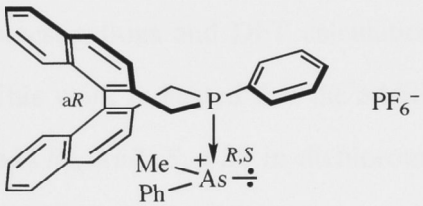


Figure 2.1 The structure of the cation of (aR_P,S_{As})-**58** showing 30% probability ellipsoids (hydrogen and solvent atoms omitted for clarity).

The As–P distance in (aR_P,S_{As})-**58** is 2.3579(12) Å, which is similar to the corresponding distances in related 2-(methoxymethyl)phenylphosphine–arsenium complexes.[81, 97] The phosphine in each case coordinates orthogonally to the arsenium plane, with P1–As1–C31 = 94.33(14)° and P1–As1–C32 = 98.61(13)°. The oxygen of the 2-(methoxymethyl) group interacts with arsenic and phosphorus, as is indicated by the As1···O1 and P1···O1 distances of 2.837 Å and 2.870 Å, respectively, which are

within the sum of the van der Waals radii for the two pairs of atoms (viz. 3.37 Å for As1···O1, and 3.32 Å for P1···O1[98]).

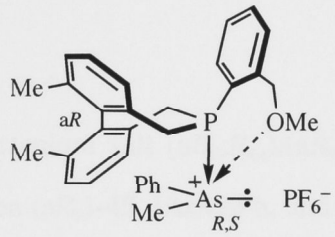
The diastereomers (aR_P,R_{As})/(aR_P,S_{As})-**58** are clearly evident in the $^{31}P\{^1H\}$ NMR spectra of the complex in dichloromethane-d_2; preliminary studies indicated a 54% excess of the major diastereomer at room temperature and an 86% de at –90 °C.[91] The 2-(methoxymethyl)phenyl group substantially increased the diastereofacial selectivity of coordination of the phosphine to the prochiral arsenium ion. The $^{31}P\{^1H\}$ NMR spectrum of the corresponding *phenyl*phosphepine-stabilised methylphenylarsenium complex (aR_P,S_{As})/(aR_P,S_{As})-**59** at –78 °C indicated ca. 16% de.[91]



(aR_P,S_{As})/(aR_P,S_{As})-**59**

The identity of the major diastereomer of (aR_P,S_{As})/(aR_P,S_{As})-**58** in solution was determined by low temperature NOESY.[7, 96] NOE correlations were observed for the 9-CH_{eq}, OCH_3 and AsC*H* protons, which indicated that the OCH_3 and AsCH_3 groups were situated at the rear of the molecule and the arsenium phenyl group directed to the front. Although these correlations did not decisively conclude which diastereomer of the complex was in excess, rotation about the As–P bond (apparent due to a room temperature NOE correlation between the AsCH_3 protons and 2-C*H*) is unfavourable for the (aR_P,R_{As}) diastereomer because of steric hindrance. Thus, (aR_P)-**45** appears to diastereoselectively coordinate to the *S* face of the prochiral methylphenylarsenium ion.

Subsequent DFT calculations on the model system (aR_P,R_{As})/(aR_P,S_{As})-**60** were consistent with the NMR spectroscopic results.[97]



(aR_P,R_{As})/(aR_P,S_{As})-**60**

2.2 Present work

The NMR spectroscopic investigations and DFT calculations were conducted by Drs Porter and Krenske.[91, 96] This work indicated that the addition of *n*-butyllithium to an equilibrating mixture of (aR_P,R_{As})/(aR_P,S_{As})-**58** in dichloromethane at low temperature would give (±)-(*n*-butyl)methylphenylarsine in an ee that corresponded to the de of the phosphine–arsenium complex at that temperature.[91, 96] Experimental conditions for the asymmetric synthesis were developed as part of my work, which also led to an improved syntheses of (aR_P)-**45** and (aR_P,R_{As})/(aR_P,S_{As})-**58**.

2.2.1 Synthesis

The syntheses of (aR_P)-**45** from (aR_C)-**53** was optimised to give 60% of the pure, colourless, crystalline product. The earlier work gave the phosphepine in 54% yield as a pale yellow powder after purification by column chromatography.[96] This procedure involved heating the mixture of (aR_C)-**53** and dichloro[2-

(methoxymethyl)phenyl]phosphine in *n*-hexane under reflux for 72 h. In the current work, the reaction time was reduced to 12 h, the chromatography step was omitted, and the crude product from the aqueous work-up was recrystallised from dichloromethane by the addition of *n*-hexane.

The phosphepine-stabilised arsenium salt (aR_P,R_{As})/(aR_P,S_{As})-**58** was isolated in 83% yield from the reaction between (aR_P)-**45**, IAsMePh, and KPF_6 in the two-phase system described above. The higher yield was attributed to the use of the Schlenk technique and purer (aR_P)-**45**. Although (aR_P,R_{As})/(aR_P,S_{As})-**58** is air- and moisture-stable, the phosphine is air-sensitive in solution. The ^1H and $^{31}P\{^1H\}$ NMR spectra of the complex indicated that it was of >98% purity.

2.2.2 Diastereoselectivity in (aR_P,R_{As})/(aR_P,S_{As})-58

The $^{31}P\{^1H\}$ NMR spectrum of (aR_P,R_{As})/(aR_P,S_{As})-**58** in CD_2Cl_2 at 25 °C contains singlet peaks for the each diastereomer in the ratio (aR_P,S_{As}):(aR_P,R_{As}) = 78:22; cooling the sample to –95 °C increased the proportion of (aR_P,S_{As})-**58** to 97% (Figure 2.2). Varying the concentration of the sample did not alter the ratio of diastereomers.

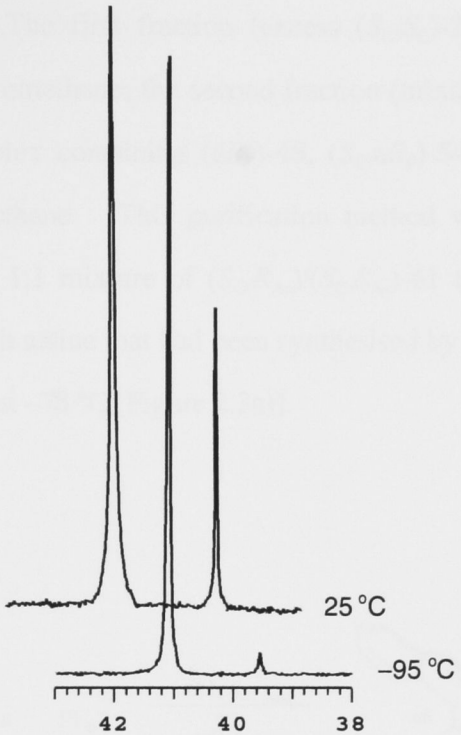


Figure 2.2 Variable temperature $^{31}P\{^{1}H\}$ NMR spectra (500 MHz, CD_2Cl_2) of (aR_P,R_{As})/(aR_P,S_{As})-**58**.

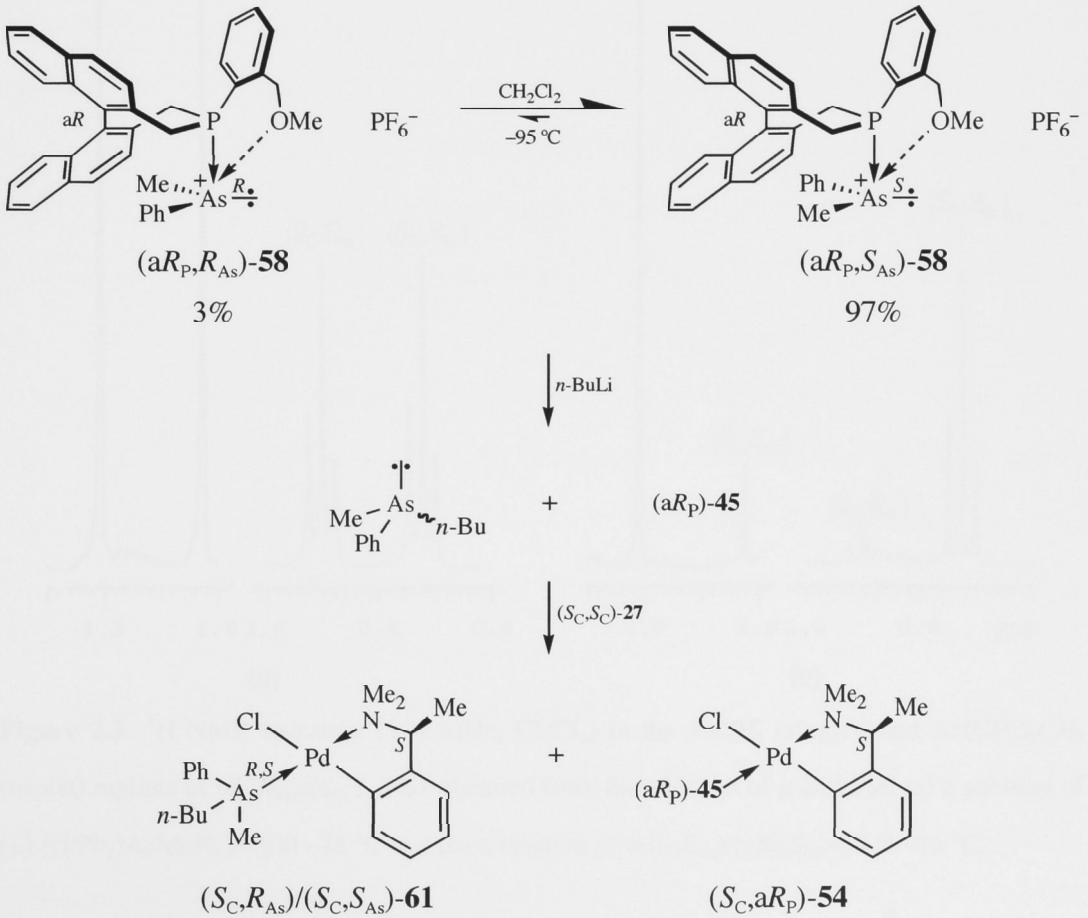
2.2.3 Asymmetric synthesis

The asymmetric synthesis of (±)-(*n*-butyl)methylphenylarsine was undertaken as indicated in Scheme 2.6. Thus, a solution of *n*-butyllithium (1.1 equiv, 1.4M in hexanes) was added to (aR_P,R_{As})/(aR_P,S_{As})-**58** (1 equiv) in dichloromethane at –95 °C.** The reaction mixture was stirred for ca. 5 min and then water was added to quench the excess lithium reagent. The cooling bath was removed and when the mixture had reached room temperature, the solvents were removed from the product in vacuo. The residue was dissolved in dichloromethane and a suspension containing an excess of (S_C,S_C)-**27**·CH_2Cl_2 in dichloromethane was added. After ca. 15 min, the yellow solution was concentrated to a small volume and transferred to a short silica column made up

** *n*-Butyllithium does not react appreciably with dichloromethane at temperatures below –74 °C.[105]

with dichloromethane. The first fraction (excess (S_C,S_C)-**27**) was eluted from the column with neat dichloromethane; the second fraction (mixture of (S_C,R_{As})/(S_C,S_{As})-**61** and the palladium complex containing (aR_P)-**45**, (S_C,aR_P)-**54**), was eluted with 10% diethyl ether–dichloromethane. [This purification method was shown not to enrich either diastereomer of a 1:1 mixture of (S_C,R_{As})/(S_C,S_{As})-**61** that was prepared by the reaction of (S_C,S_C)-**27** with arsine that had been synthesised by the addition of *n*-BuLi to (±)-[(PPh_3)AsMePh]PF_6 at –78 °C (Figure 2.3a)].

Scheme 2.6



Integration of the AsCH_3 singlets and As$(CH_2)_3CH_3$ triplets in the ^{1}H NMR spectrum of the second fraction eluted from the column indicated (S_C,R_{As})/(S_C,S_{As})-**61** = 85/15

(Figure 2.3b). This ratio corresponds to an enantioselectivity of 85% for the *S* arsine (70% ee). The absolute configuration of (S_{As})-As(*n*-Bu)MePh is consistent with the known spectroscopic properties of (S_C,R_{As})-**61** and the S_N2-type mechanism proposed for the reaction.[97]

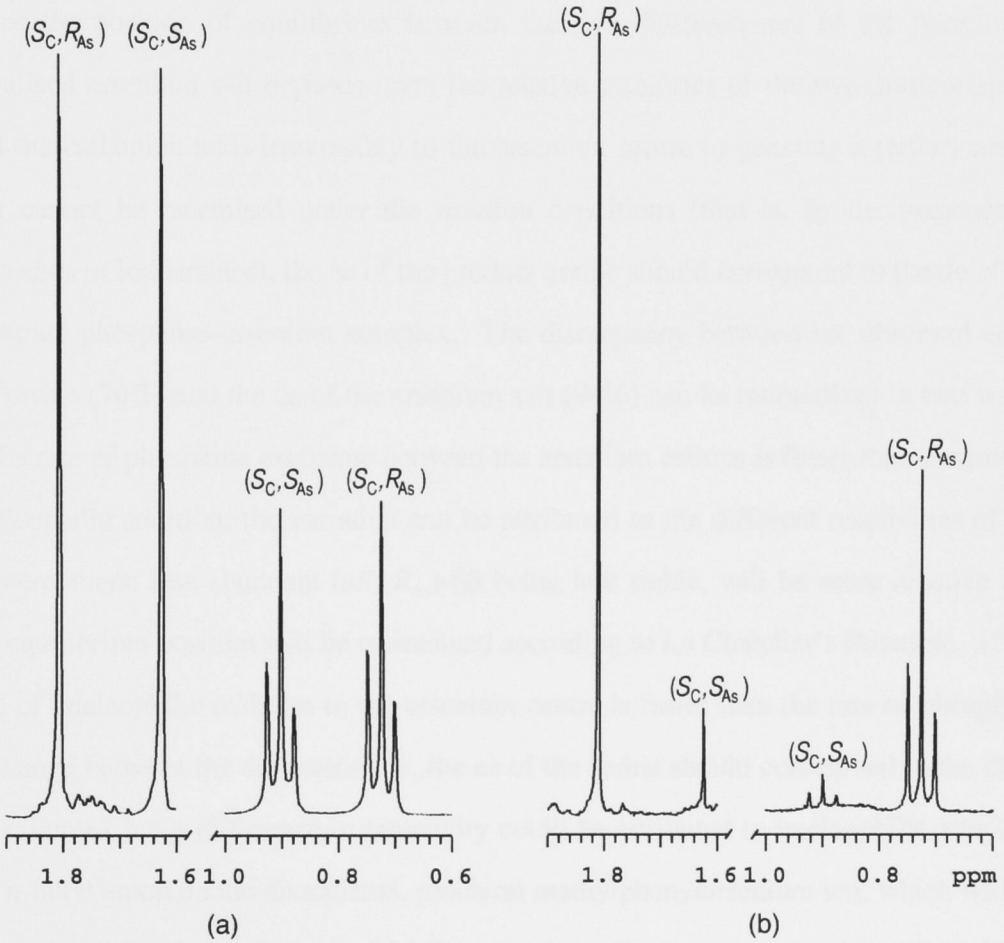


Figure 2.3 ^{1}H NMR spectrum (300 MHz, $CDCl_3$) in the AsCH_3 (singlet) and As$(CH_2)_3CH_3$ (triplet) regions of (S_C,R_{As})/(S_C,S_{As})-**61** obtained from the addition of *n*-BuLi to: (a) a solution of (±)-[(PPh_3)AsMePh]PF_6 at –78 °C and (b) a solution of (aR_P,R_{As})/(aR_P,S_{As})-**58** at –95 °C.

The experimental parameters for the reaction were altered in attempts to improve the enantioselectivity of the synthesis. Changes included adjusting the concentrations of the lithium reagent and the solution of the arsenium salt, cooling the *n*-butyllithium

prior to addition, changing the rate of addition of the *n*-butyllithium solution, and lowering the reaction temperature to –103 °C (10% 2-chloropropane in dichloromethane): none of these changes increased the enantioselectivity of the arsine synthesis.

Since the position of equilibrium between the two diastereomers of the phosphine-stabilised arsenium salt depends upon the relative stabilities of the two diastereomers, and the carbanion adds irreversibly to the arsenium centre to generate a tertiary arsine that cannot be racemised under the reaction conditions (that is, by the presence of haloacids or iodoarsines), the ee of the product arsine should correspond to the de of the substrate phosphine–arsenium complex. The discrepancy between the observed ee of the arsine (70%) and the de of the arsenium salt (94%) can be rationalised in two ways. If the rate of phosphine exchange between the arsenium cations is faster than the rate of nucleophilic addition, the variation can be attributed to the different reactivities of the diastereomers: less abundant (aR_P,R_{As})-**58** being less stable, will be more reactive and the equilibrium position will be maintained according to Le Chatelier's Principle. If the rate of nucleophilic addition to the arsenium centre is faster than the rate of phosphine exchange between the diastereomers, the ee of the arsine should correspond to the de of the complex but a difference in selectivity could be attributed to nucleophilic attack of the *n*-butyl anion on the dissociated, prochiral methylphenylarsenium ion, which will be non-enantioselective and more rapid than attack on the less electropositive phosphine-stabilised species. The latter scenario is supported by variable temperature ^{1}H NMR spectroscopic investigations, which showed that the slow exchange limit for phosphine-exchange in (aR_P,R_{As})/(aR_P,S_{As})-**58** is reached at –70 °C, as indicated by the ^{31}P coupling to the AsCH_3 protons.

The mechanism was further investigated by analysing the diastereoselectivity of phosphine coordination in the phosphine-stabilised arsenium salts to the enantioselectivity of the asymmetric synthesis at different temperatures. To ensure consistency in the findings, three asymmetric reactions were conducted at each temperature and the relevant peaks in the ^{1}H NMR spectra in chloroform-*d* were integrated three times, and averaged. The des for three samples of known concentration in dichloromethane-d_2 were measured at each temperature by integrating the resonances in the $^{31}P\{^{1}H\}$ NMR spectrum after long accumulation times. The results of the investigation are shown graphically in Figure 2.4 and the data are included in Appendix 1.

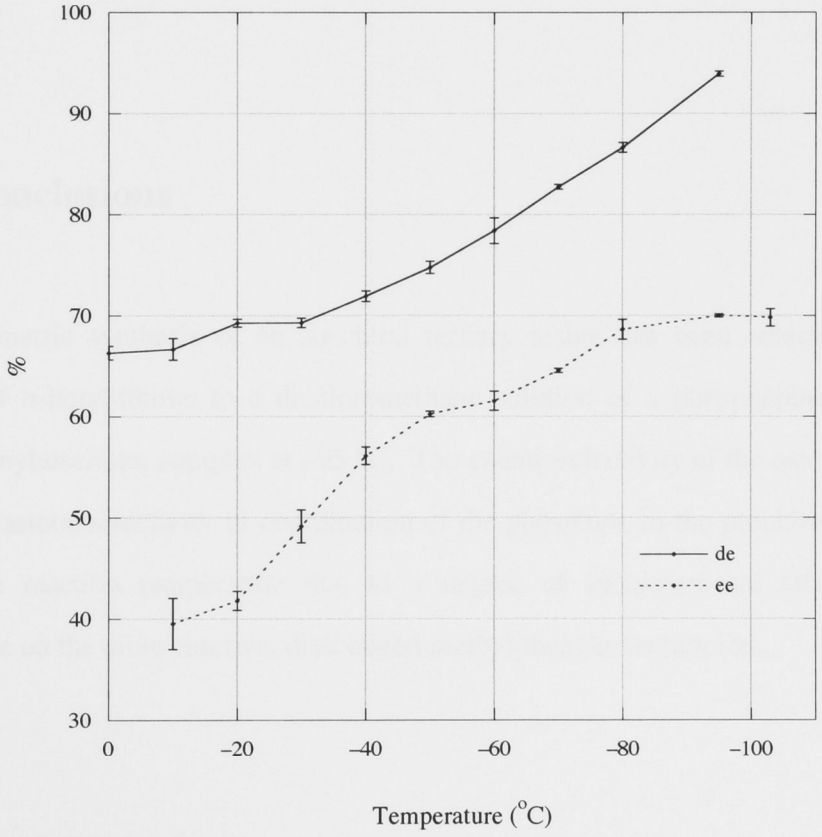


Figure 2.4 Averaged de of (aR_P,R_{As})/(aR_P,S_{As})-**58** ($^{31}P\{^{1}H\}$ NMR, CD_2Cl_2) and ee (^{1}H NMR, $CDCl_3$) resulting from the addition of *n*-BuLi to (aR_P,R_{As})/(aR_P,S_{As})-**58** at the corresponding temperatures indicated. Error bars indicate 1 standard deviation.

These data show that at each temperature examined, the de for (aR_P,R_{As})/(aR_P,S_{As})-**58** was at least 15% higher than the ee for the asymmetric synthesis. Phosphine-exchange in the complex is slow on the NMR timescale at temperatures below –70 °C, so it was concluded that the discrepancy between the des and ees below this temperature was due to non-specific nucleophilic addition to a dissociated, prochiral arsenium ion. Moreover, because the rate of phosphine-exchange between the diastereomers increases with increasing temperature, the variations between des and ees above –70 °C may be partly due to the increased reactivity of the less abundant diastereomer. It must be acknowledged, however, that the rate of nucleophilic addition at elevated temperatures will also increase.

2.3 Conclusions

The asymmetric synthesis of an *As*-chiral tertiary arsine has been achieved by the addition of *n*-butyllithium to a dichloromethane solution of a phosphepine-stabilised methylphenylarsenium complex at –95 °C. The enantioselectivity of the reaction is less than the diastereoselectivity of coordination of the phosphine to the prochiral arsenium ion at the reaction temperature due to a degree of indiscriminate attack of the nucleophile on the more reactive, dissociated methylphenylarsenium ion.

Chapter 3:

Asymmetric syntheses of bis(tertiary arsines)

3.1 Introduction

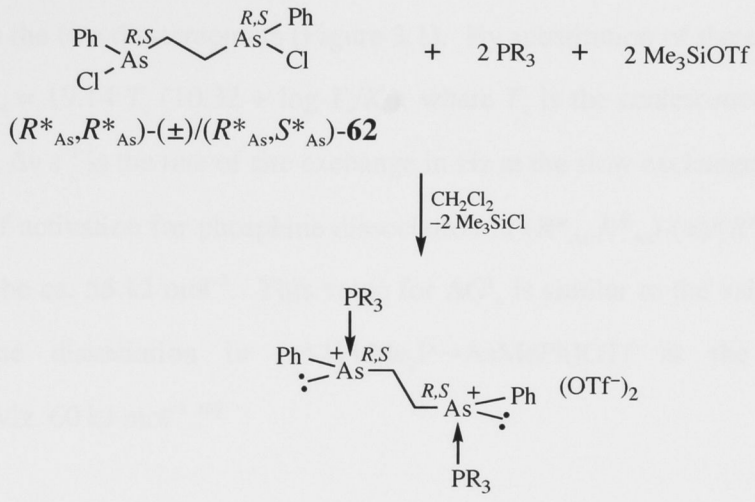
Chelating bis(tertiary arsines) in enantiomerically pure form are potentially important auxiliaries for metal-catalysed asymmetric synthesis.[6] It was therefore of interest to determine if the methodology described above for the asymmetric synthesis of mono(tertiary arsines) could be extended to the asymmetric synthesis of bis(tertiary arsines).

3.1.1 Model complexes

3.1.1.1 Syntheses

The attempted preparation of the bis(phosphine-stabilised) diarsenium hexafluorophosphate salts by the *two-phase method* resulted in the production of phosphine oxides and diarsinic acids, as evidenced by NMR spectroscopy. However, the addition of trimethylsilyl triflate to a dichloromethane solution of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-1,2-*bis*(chlorophenylarsino)ethane, (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62**, containing triphenylphosphine or methyldiphenylphosphine produced the bis(phosphine-stabilised) diarsenium triflates (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**63** and -**64** after evaporation of the solvent and trimethylsilyl chloride by-product (Scheme 3.1). The salts crystallised readily from dichloromethane upon the addition of diethyl ether, but were sensitive to hydrolysis, unlike the related mono-arsenium complexes.[81]

Scheme 3.1



$PR_3 = PPh_3$ (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**63**
$PR_3 = PPh_2Me$ (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**64**

3.1.1.2 NMR Spectroscopy

Because of the lability of the As–P bonds in (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**63** and -**64**, the complexes exist in solution as equilibrium mixtures of two diastereomers, the C_2 (R^*_{As},R^*_{As})-(±) diastereomer that exists as pairs of enantiomers, and the achiral C_S (R^*_{As},S^*_{As}) diastereomers in which the arsenic stereocentres in each case have opposite configurations. At around room temperature and above, As–P bond dissociation in the complexes is fast on the NMR time-scale and the resonances for the individual diastereomers are indistinguishable. As the temperature of the solution is lowered, however, the averaged resonances broaden and eventually split into the resonances for the individual diastereomers at the slow exchange limit. The $^{31}P\{^1H\}$ NMR spectra of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**63** and -**64** in dichloromethane-d_2 at 25 °C consists of sharp singlets at 17.45 and 12.91 ppm, respectively. Triphenylphosphine is a weak ligand for arsenium ions[92, 93] and at –95 °C only minor splitting of the singlet $^{31}P\{^1H\}$ NMR resonances for the equilibrating diastereomers (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**63** is evident. Alkylphosphines form more stable adducts, and the singlet $^{31}P\{^1H\}$ NMR resonance for (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**64** broadens and coalesces as the temperature is lowered and

separates into two peaks of equal intensity with baseline separation at –50 °C that correspond to the two diastereomers (Figure 3.1). By substitution of these data into the equation $\Delta G^{\ddagger}_{c} = 19.14\ T_c\ (10.32 + \log T_c/K_c)$, where T_c is the coalescence temperature and $K_c = 2.22\ \Delta\nu\ s^{-1}$ is the rate of site exchange in Hz at the slow exchange limit,[7, 106] the free energy of activation for phosphine dissociation in (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**64** is calculated to be ca. 55 kJ mol^{-1}. This value for $\Delta G^{\ddagger}_{c}$ is similar to the value calculated for phosphine dissociation in (±)-[$PhMe_2P$→AsMePh]OTf at the coalescence temperature, viz. 60 kJ mol^{-1}.[107]

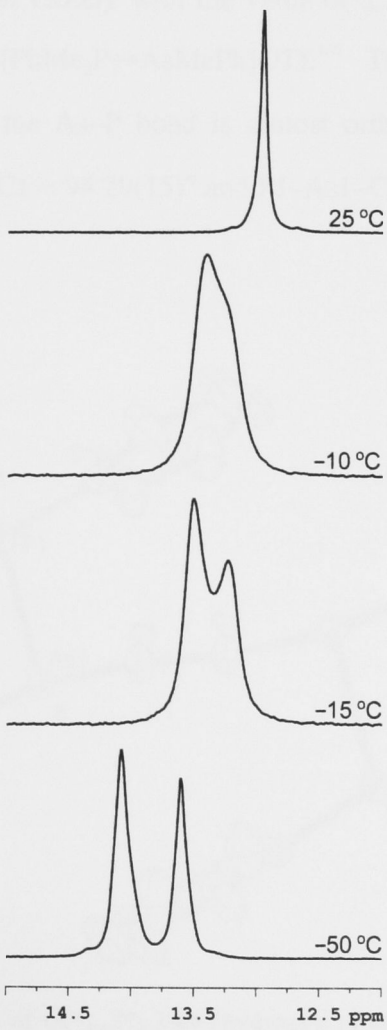


Figure 3.1 Variable temperature $^{31}P\{^1H\}$ NMR spectra (CD_2Cl_2) of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**64**.

3.1.1.3 Crystal Structure

The diastereomer (R^*_{As},S^*_{As})-**64** crystallises from dichloromethane–diethyl ether as colourless prisms in the monoclinic space-group $P2_1/c$ in a typical asymmetric transformation of the second kind;[7] the structure of the cation is shown in Figure 3.2 and relevant bond lengths and angles are given in Table 3.2. The crystallographic asymmetric unit consists of one half of the bis(phosphine-stabilised) diarsenium dication and one triflate ion related by a crystallographic inversion centre; the triflate counterion is disordered (Table 3.1). The As–P distance of 2.3239(12) Å in the complex is longer than the sum of the covalent radii for the two main group elements, viz. 2.29 Å,[108] and compares closely with the value of 2.3402(8) Å measured for the corresponding bond in (±)-[$PhMe_2P$→AsMePh]OTf.[107] The C1–As1–C2 angle in the cation is 100.15(18)° and the As–P bond is almost orthogonal to the plane of the arsenium ion, viz. P1–As1–C1 = 94.29(15)° and P1–As1–C2 = 97.22(13)°.

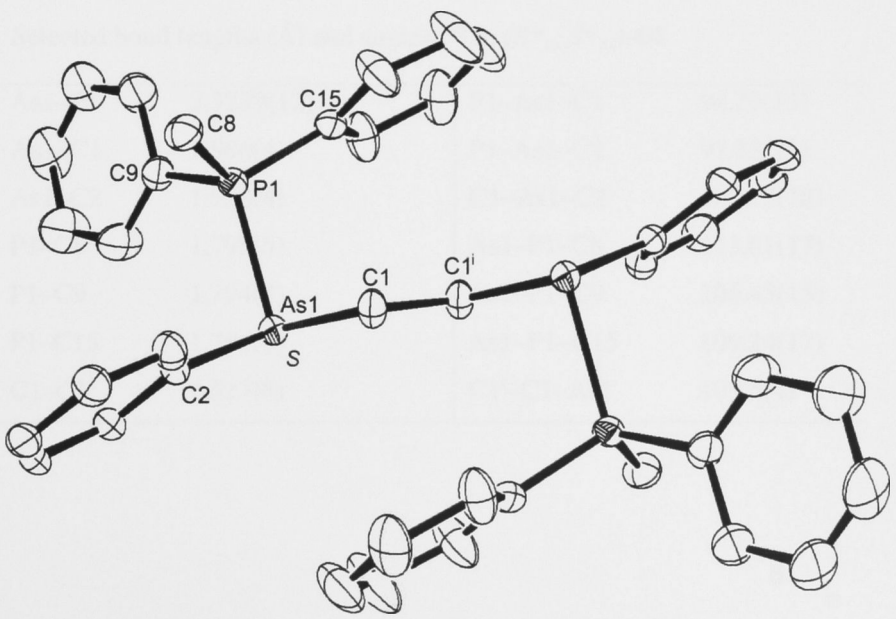


Figure 3.2 Structure of cation of (R^*_{As},S^*_{As})-**64** (hydrogen atoms omitted for clarity) showing 30% probability ellipsoids.

Table 3.1 Crystallographic and experimental details for the X-ray crystal structure analysis of (R^*_{As},S^*_{As})-**64**

empirical formula	$C_{42}H_{40}As_2F_6O_6P_2S_2$
formula weight (g mol^{-1})	1030.69
crystal colour, habit	colourless, prism
crystal size (mm)	0.35 × 0.20 × 0.19
space group	$P2_1/c$
crystal system	monoclinic
a (Å)	11.5468(2)
b (Å)	11.2427(2)
c (Å)	17.0825(3)
V (Å^3)	2206.74(7)
Z	2
D	1.438
no. unique reflections	5057
no. reflections observed	2863 ($I > 3.00u(I)$)
temperature (K)	200
final R_1, wR	0.0373, 0.0427

Table 3.2 Selected bond lengths (Å) and angles (°) in (R^*_{As},S^*_{As})-**64**

As1–P1	2.3239(12)	P1–As1–C1	94.29(15)
As1–C1	1.986(4)	P1–As1–C2	97.22(13)
As1–C2	1.958(4)	C1–As1–C2	100.15(18)
P1–C8	1.798(5)	As1–P1–C8	113.81(17)
P1–C9	1.794(4)	As1–P1–C9	106.45(15)
P1–C15	1.796(5)	As1–P1–C15	109.24(17)
C1–C1^i	1.527(8)	C1^i–C1–As1	109.6(4)

3.2 Bis(chiral phosphine-stabilised) diarsenium complex

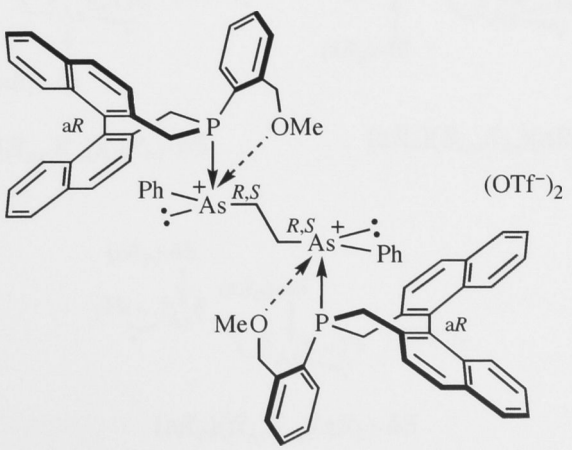
3.2.1 Synthesis

The bis(phosphine-stabilised) diarsenium complex (aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/(aR_P)(R_{As},S_{As})(aR_P)-**65** was isolated in 65% yield from the reaction between the phosphepine (aR_P)-**45** (2.1 equiv), (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62** (1 equiv), and trimethylsilyl triflate (2.1 equiv) in dichloromethane (Scheme 3.2). Moisture-sensitive (aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/(aR_P)(R_{As},S_{As})(aR_P)-**65** crystallises from dichloromethane–diethyl ether in 65% yield as fine, feather-like clumps of needles having mp 240–242 °C and $[\alpha]_D^{25}$ +76 (*c* 1.0, CH_2Cl_2). A number of attempts at growing crystals of this complex suitable for X-ray crystallography were unsuccessful.

Scheme 3.2

(R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62** + 2 (aR_P)-**45** + 2 Me_3SiOTf

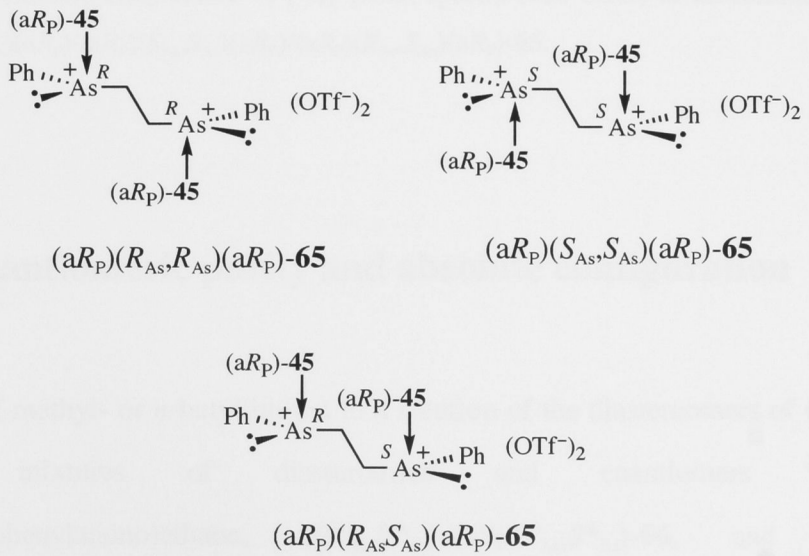
CH_2Cl_2
–2 Me_3SiCl



(aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/(aR_P)(R_{As},S_{As})(aR_P)-**65**

3.2.2 NMR spectra

The $^{31}P\{^{1}H\}$ NMR spectrum of (aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/ (aR_P)(R_{As},S_{As})(aR_P)-**65** in dichloromethane-d_2 at 25 °C contains three over-lapping peaks between 39.6 and 40.2 ppm and a singlet at 17.8 ppm for the three diastereomers of the complex (Figure 3.3). On cooling the solution, the intensity of the peak in the spectrum at 17.8 ppm decreased and at –25 °C the overlapping peaks at 39.6 and 40.0 ppm had coalesced. At –95 °C an intense peak was observed in the spectrum at 39.23 ppm, which was consistent with the presence of a single C_2 diastereomer in large excess (ca. 90%), together with several smaller peaks corresponding to the two other diastereomers (Figure 3.4). Comprehensive NMR spectroscopic investigations and DFT calculations on the mono-arsenium complex (aR_P,R_{As})/(aR_P,S_{As})-**58**, which crystallised by an asymmetric transformation of the second kind as the (aR_P,S_{As}) diastereomer, indicated that the (aR_P)-phosphepine preferentially binds to the *pro-S* face of the methylphenylarsenium ion.[97] Based on these considerations, it was presumed that the diastereomer in large excess in the diarsenium system was (aR_P)(R_{As},S_{As})(aR_P)-**65**.



(aR_P)(R_{As},R_{As})(aR_P)-**65**

(aR_P)(S_{As},S_{As})(aR_P)-**65**

(aR_P)(R_{As},S_{As})(aR_P)-**65**

Figure 3.3 Representation of the three diastereomers of **65**.

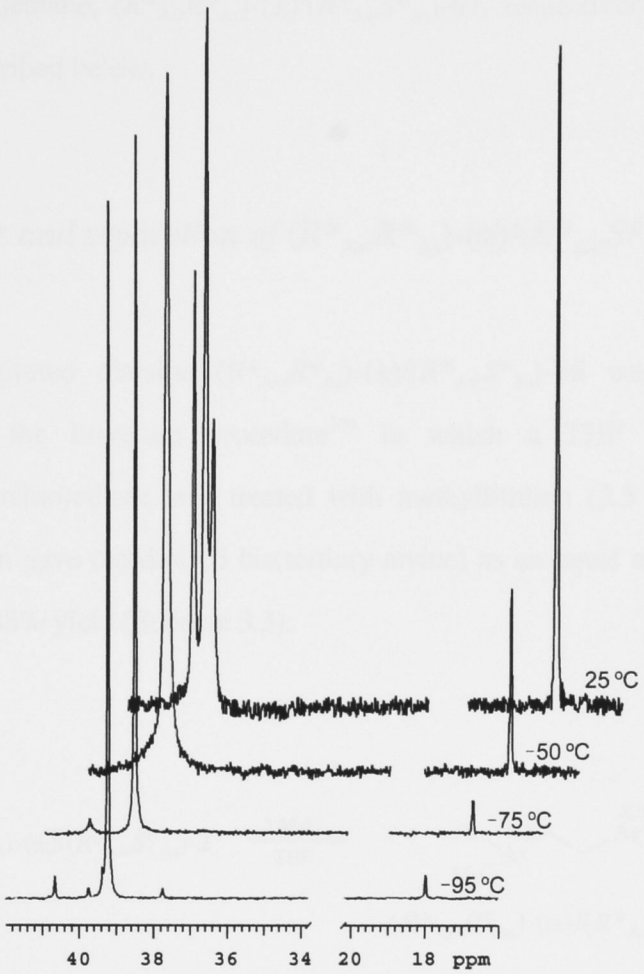


Figure 3.4 Variable temperature $^{31}P\{^{1}H\}$ NMR spectra (121 MHz) in dichloromethane-d_2 of (aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/(aR_P)(R_{As},S_{As})(aR_P)-**65**.

3.2 Enantiomeric purity and absolute configuration

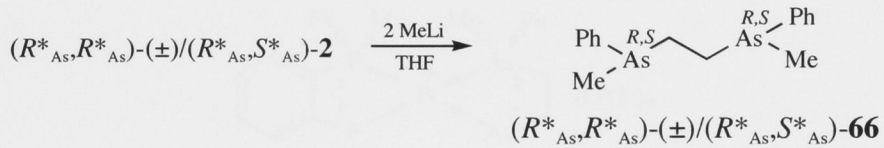
Addition of methyl- or *n*-butyllithium to a solution of the diastereomers of **65** afforded unequal mixtures of diasteromers and enantiomers of 1,2-*bis*(methylphenylarsino)ethane, (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**66**, and 1,2-*bis*(*n*-

butylphenylarsino)ethane, (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**67**, respectively. The results of this work are described below.

3.2.1 Synthesis and separation of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-*66*

The methyl-substituted diarsine (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**66** was prepared by a modification of the literature procedure[109] in which a THF solution of 1,2-*bis*(chlorophenylarsino)ethane was treated with methyllithium (2.5 equiv) in diethyl ether; this reaction gave the desired bis(tertiary arsine) as an equal mixture of the two diastereomers in 88% yield (Scheme 3.3).

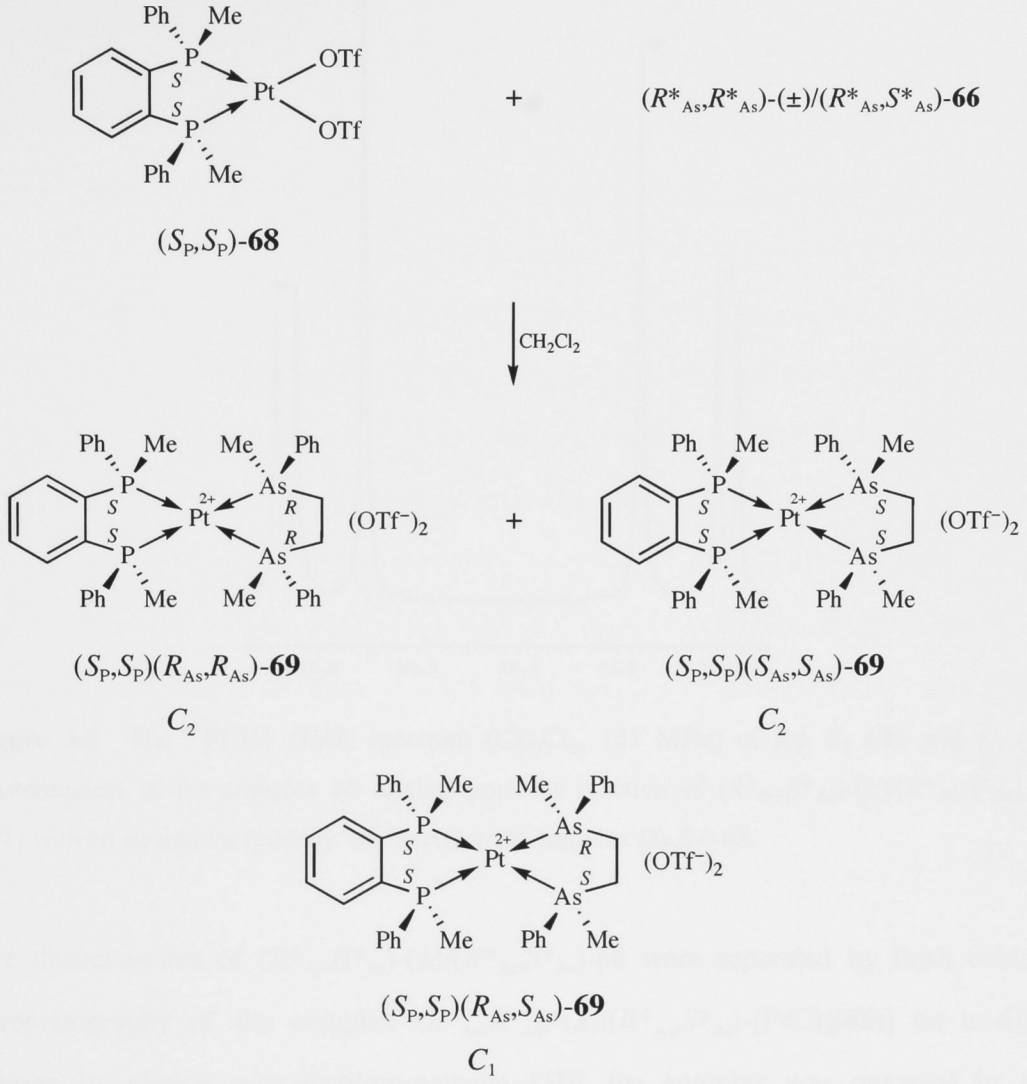
Scheme 3.3



(R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**66**

The stereoisomeric composition of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**66** was determined by reaction with enantiomerically pure (S_P,S_P)-[Pt(diphos)(OTf)$_2$], (S_P,S_P)-**68**.[110] The products of this facile displacement reaction are the diastereomeric salts (S_P,S_P)(R_{As},R_{As})- and (S_P,S_P)(S_{As},S_{As})-**69**, which are derived from (R^*_{As},R^*_{As})-(±)-**66** and have C_2 symmetry, and (S_P,S_P)(R_{As},S_{As})-**69**, which is derived from (R^*_{As},S^*_{As})-**66** and has C_1 symmetry (Scheme 3.4).

Scheme 3.4



The $^{31}P\{^1H\}$ NMR spectrum for each of the C_2 diastereomers will consist of a singlet resonance (along with the satellites due to the coupling with the ^{195}Pt nuclei of 33.8% abundance[111]), but the C_1 diastereomer of the complex will exhibit in its $^{31}P\{^1H\}$ NMR spectrum a pair of doublets for the two non-equivalent phosphorus nuclei. The $^{31}P\{^1H\}$ NMR spectrum in dichloromethane-d_2 of the mixture of diastereomers $(S_P,S_P)(R_{As},R_{As})$/$(S_P,S_P)(S_{As},S_{As})$/$(S_P,S_P)(R_{As},S_{As})$-**69** that were obtained from the reaction of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**66** (1/1) with (S_P,S_P)-**68** in dichloromethane is shown in Figure 3.5.

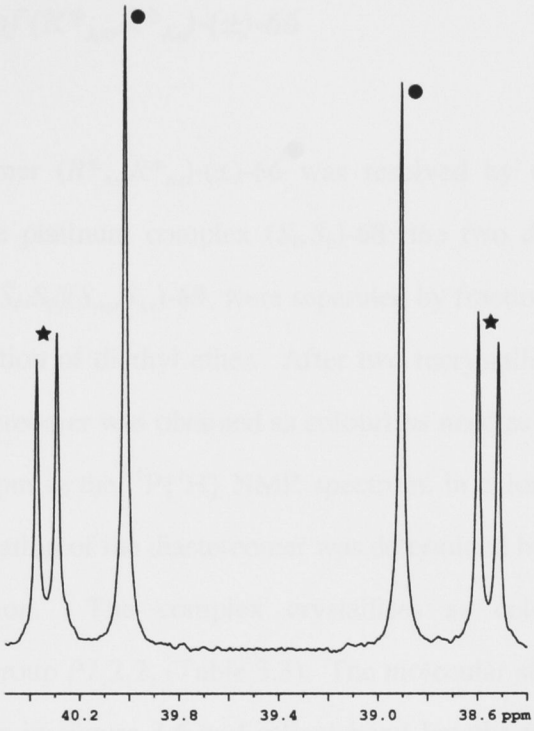


Figure 3.5 The $^{31}P\{^{1}H\}$ NMR spectrum (CD_2Cl_2, 121 MHz) of the C_2 (●) and C_1 (★) diastereomers of the complex **69** arising from the reaction of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**66** (1/1) with an equimolar quantity of the reference complex (S_P,S_P)-**68**.

The diastereomers of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**66** were separated by flash column chromatography of the complex (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-[$PdCl_2$(**66**)] on a silica column by elution with dichloromethane–THF; the complex was prepared by the reaction of the ligand with palladium(II) chloride in methanol containing excess lithium chloride.[58] The complex (R^*_{As},R^*_{As})-(±)-[$PdCl_2$(**66**)] was the first compound to be eluted from the silica column with dichloromethane–THF (95/5 v/v). The racemic diastereomer of the diarsine, (R^*_{As},R^*_{As})-(±)-**66**, was liberated from (R^*_{As},R^*_{As})-(±)-[$PdCl_2$(**66**)] by treatment with an aqueous sodium cyanide solution and was distilled with retention of configuration at arsenic, bp 168–170 °C (0.2 mmHg) [Lit.[58] 156–158 °C (0.1 mmHg)].

3.2.2 Resolution of (R^*_{As},R^*_{As})-(±)-66

The chiral diastereomer (R^*_{As},R^*_{As})-(±)-**66** was resolved by complexation with the enantiomerically pure platinum complex (S_P,S_P)-**68**; the two diastereomers resulting, (S_P,S_P)(R_{As},R_{As})- and (S_P,S_P)(S_{As},S_{As})-**69**, were separated by fractional crystallisation from methanol by the addition of diethyl ether. After two recrystallisations of the mixture, the less-soluble diastereomer was obtained as colourless needles that exhibited a singlet resonance of 39.48 ppm in the $^{31}P\{^1H\}$ NMR spectrum, in chloroform-*d*. The identity and absolute configuration of the diastereomer was determined by a single-crystal X-ray structure determination. The complex crystallises as colourless plates in the orthorhombic space group $P2_12_12_1$ (Table 3.3). The molecular structure of the cation of the complex is shown in Figure 3.6 and salient bond lengths and angles are given in Table 3.4. The absolute configurations of the arsenic stereocentres in the complex are (R_{As},R_{As}) based on the known absolute configuration of the resolving complex (S_P,S_P)-**68** and refinement of the Flack parameter. Thus, the free diarsine has the (S_{As},S_{As}) configuration.[††]

[††] Coordination of an *As*-chiral arsine to a metal is stereospecific: the apparent inversion of configuration that takes place at arsenic when a chiral arsine coordinates to an element of higher atomic number than 12 is a consequence of the Cahn–Ingold–Prelog (CIP) rules.[7, 66] Upon coordination to the palladium, the lone pair on the free arsine of CIP priority 4 is replaced by a ligand (the metal) of CIP priority 1.

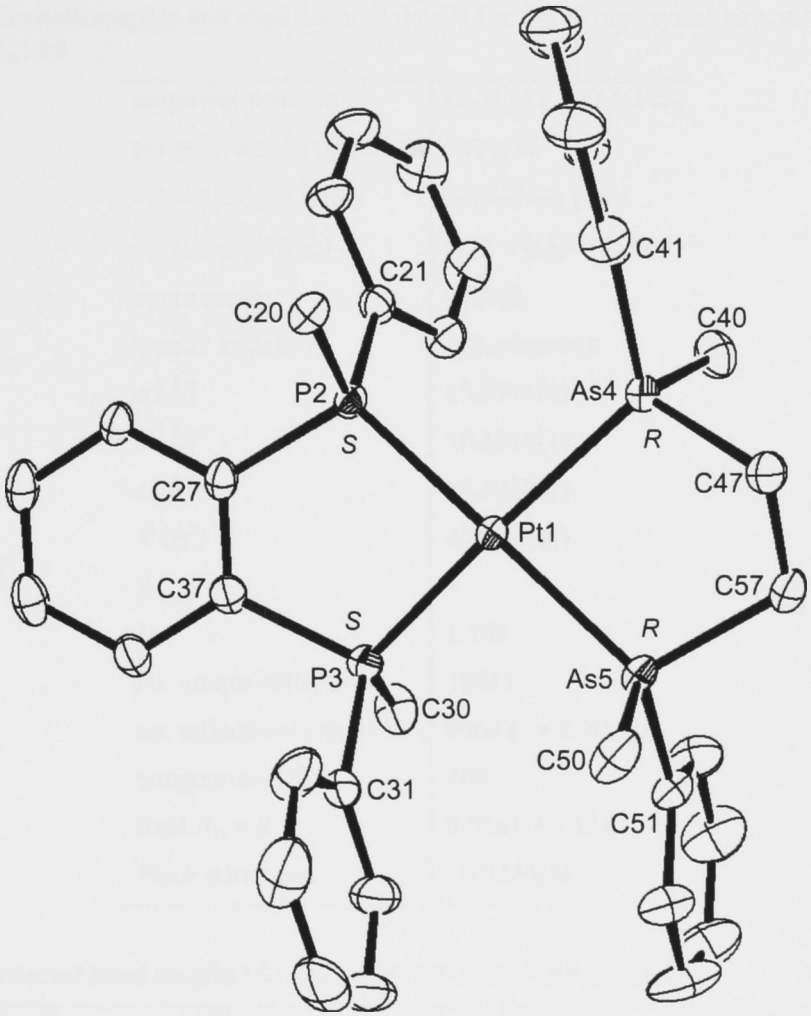


Figure 3.6 Structure of the cation of $(S_P,S_P)(R_{As},R_{As})$-**69** (hydrogen atoms omitted for clarity). Ellipsoids show 30% probability.

Table 3.3 Crystallographic and experimental details for the X-ray crystal structure analysis of $(S_P,S_P)(R_{As},R_{As})$-**69**

empirical formula	$C_{38}H_{40}As_2F_6O_6P_2PtS_2$
formula weight (g mol^{-1})	1171.71
crystal colour, habit	colourless, plate
crystal size (mm)	0.52 × 0.36 × 0.22
space group	$P2_12_12_1$
crystal system	orthorhombic
a (Å)	13.9541(2)
b (Å)	16.5910(1)
c (Å)	18.8238(2)
V (Å^3)	4357.94(8)
Z	4
D	1.795
no. unique reflections	10011
no. reflections observed	8962 ($I > 2.00u(I)$)
temperature (K)	200
final R_1, *wR*	0.0241, 0.0524
Flack parameter	–0.0244(4)

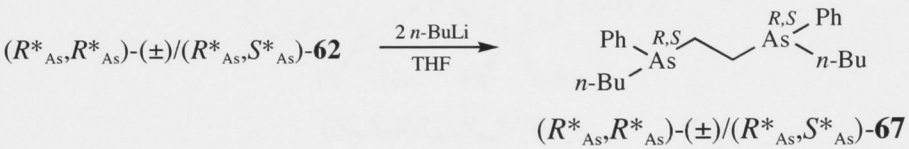
Table 3.4 Selected bond lengths (Å) and angles (°) in $(S_P,S_P)(R_{As},R_{As})$-**69**

Pt1–P2	2.2704(10)	P2–Pt1–P3	86.80(4)
Pt1–P3	2.2810(9)	P2–Pt1–As4	95.06(3)
Pt1–As4	2.4307(4)	P3–Pt1–As5	95.34(3)
Pt1–As5	2.4139(4)	As4–Pt1–As5	83.821(14)
P2–C27	1.820(4)	P2–Pt1–As5	172.65(3)
P3–C37	1.931(4)	P3–Pt1–As4	171.69(3)
As4–C47	1.963(5)		
As5–C57	1.963(4)		

3.2.3 Synthesis and attempted separation of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-*67*

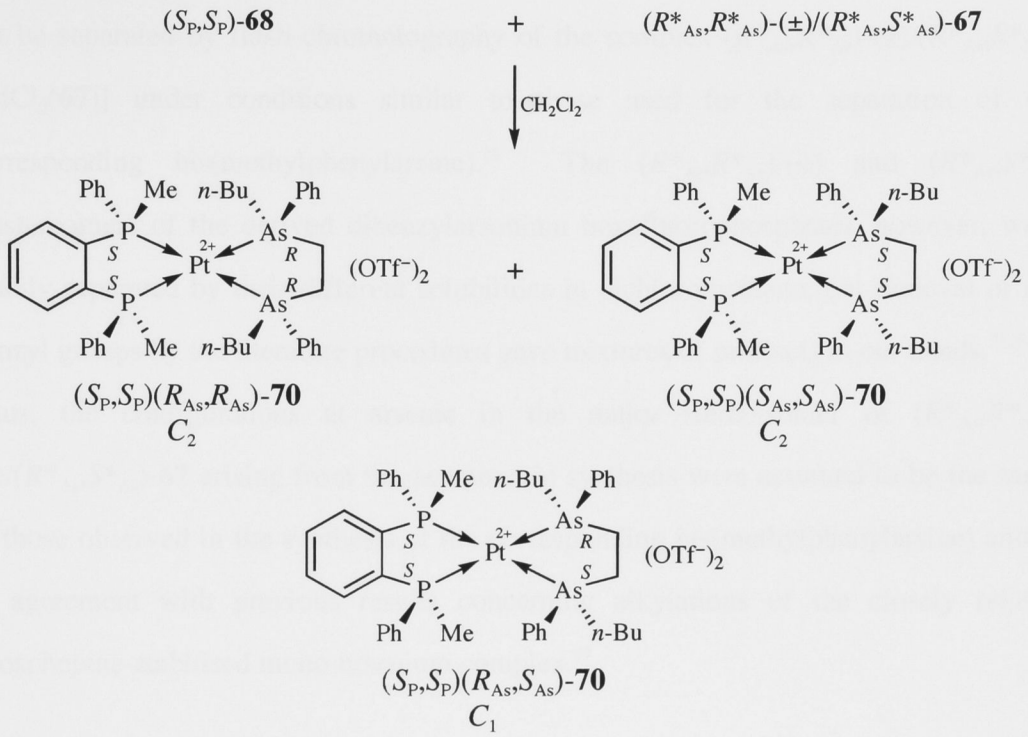
The diarsine (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**67** was also prepared by a modification of the literature procedure[50] in which a solution of *n*-butyllithium in hexanes (2.6 equiv) was added slowly to a solution of the chloroarsine (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62** in THF; this reaction gave the diarsine in 88% yield as an equimolar mixture of the two diastereomers (Scheme 3.5).

Scheme 3.5



The stereoisomeric composition of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**67** was determined in the manner described above for the methyl analogue. Thus, the reaction of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**67** with (S_P,S_P)-**68** in dichloromethane resulted in the diastereomeric mixture (S_P,S_P)(R_{As},R_{As})/(S_P,S_P)(S_{As},S_{As})/(S_P,S_P)(R_{As},S_{As})-**70** (Scheme 3.6), as indicated in the $^{31}P\{^1H\}$ NMR spectrum of the mixture in $CDCl_3$ (Figure 3.7).

Scheme 3.6



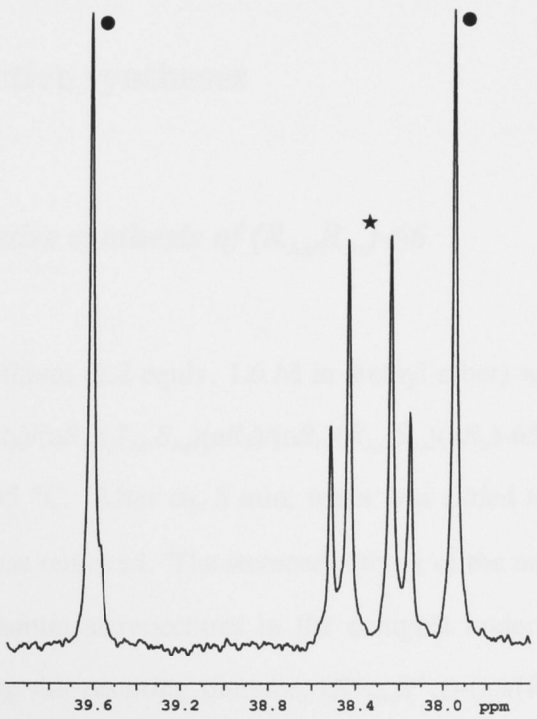


Figure 3.7 $^{31}P\{^{1}H\}$ NMR spectrum ($CDCl_3$, 121 MHz) of the C_2 (●) and C_1 (★) diastereomers of **70** arising from the reaction of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**70** (1/1) with an equimolar quantity of the reference complex (S_P,S_P)-**68**.

The diastereomers of the bis[(*n*-butyl)phenylarsine] (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**67** could not be separated by flash chromatography of the complex (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-[$PdCl_2$(**67**)] under conditions similar to those used for the separation of the corresponding bis(methylphenylarsine).[‡‡] The (R^*_{As},R^*_{As})-(±) and (R^*_{As},S^*_{As}) diastereomers of the derived dibenzylarsonium hexafluorophosphates, however, were readily separated by their different solubilities in dichloromethane, but removal of the benzyl groups by the literature procedures gave mixtures of products in our hands.[53, 54, 57] Thus, the configurations at arsenic in the major stereoisomer of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**67** arising from the asymmetric synthesis were assumed to be the same as those observed in the synthesis of the corresponding bis(methylphenylarsine) and is in agreement with previous results concerning alkylations of the closely related phosphepine-stabilised mono-arsenium complex.[97]

3.3 Stereoselective syntheses

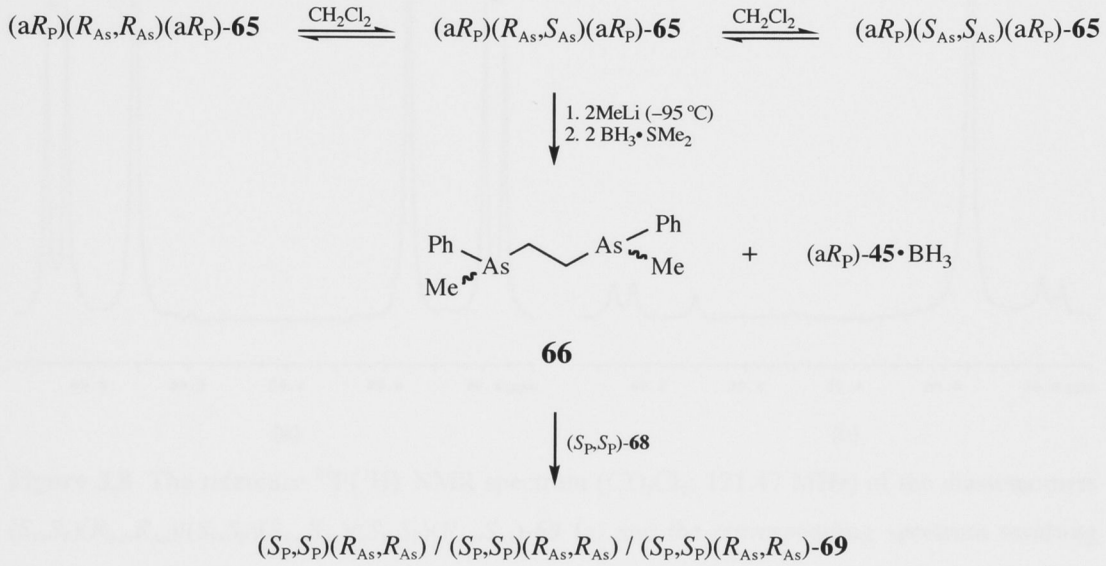
3.3.1 Enantioselective synthesis of (R_{As},R_{As})-66

A solution of methyllithium (2.2 equiv, 1.6 M in diethyl ether) was added to a solution of (aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/(aR_P)(R_{As},S_{As})(aR_P)-**65** (1 equiv) in dichloromethane at –95 °C. After ca. 5 min, water was added to the reaction mixture and the cooling bath was removed. The stereoselectivity of the nucleophilic additions at the two prochiral arsenium stereocentres in the complex under these conditions was determined by reacting the resulting diarsine, (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**66**, with the

[‡‡] The diastereomers of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**67** have been separated by tedious mechanical separation of the complexes (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-[Pd(**67**)Cl_2],[50] but we were unable to duplicate this result.

enantiomerically pure platinum complex (S_P,S_P)-**68** (after treatment of the reaction mixture with borane dimethyl sulfide to deactivate the phosphepine to coordination to the platinum) (Scheme 3.7).

Scheme 3.7



Integration of the peaks in the $^{31}P\{^1H\}$ NMR spectrum of the resulting complex in dichloromethane-d_2 gave the following result for the synthesis: (S_P,S_P)(R_{As},R_{As}):(S_P,S_P)(R_{As},S_{As}):(S_P,S_P)(S_{As},S_{As})-**69** = 4:22:74, Figure 3.8(b). Thus, the diastereoselectivity of the synthesis of the diarsine (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**66** is 78% in favour of the (R^*_{As},R^*_{As}) diastereomer, which consists of 95% of the (R_{As},R_{As}) enantiomer.

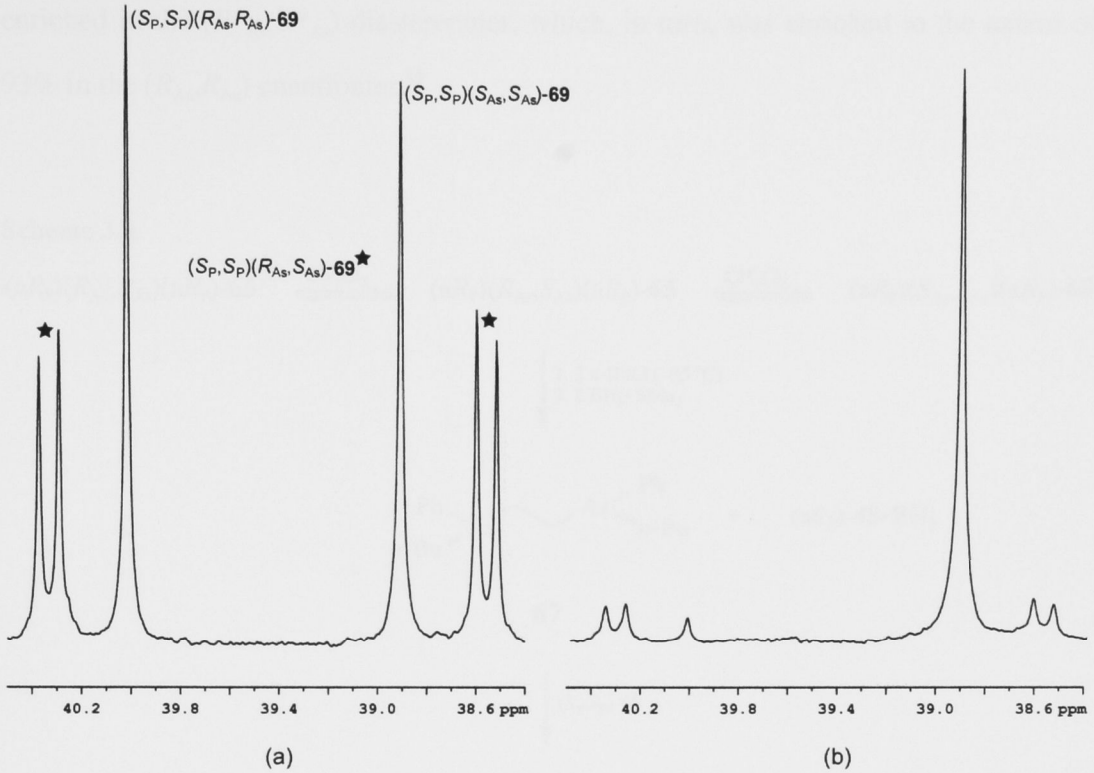


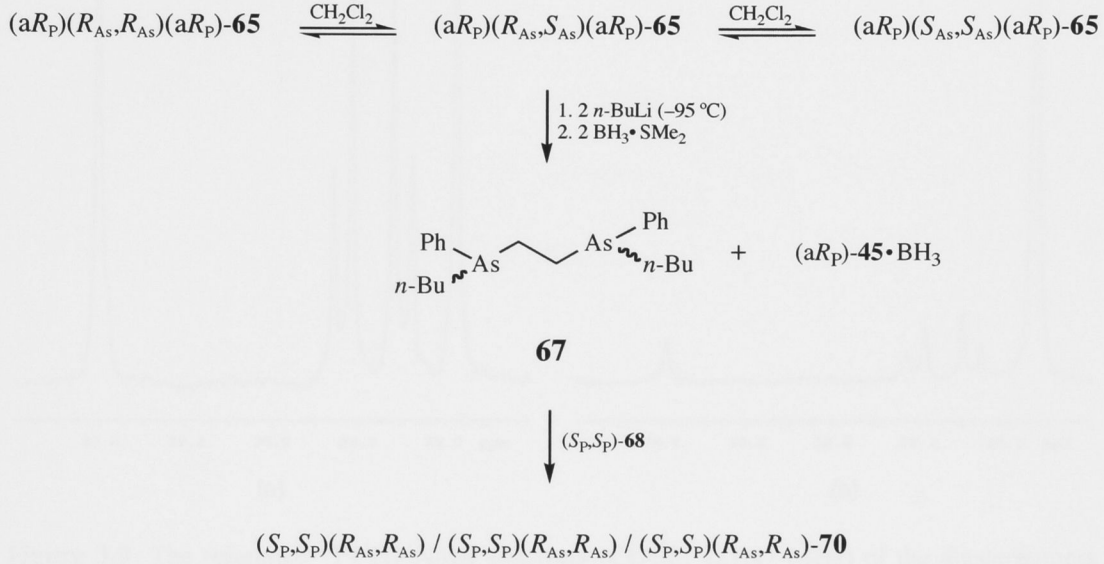
Figure 3.8 The reference $^{31}P\{^{1}H\}$ NMR spectrum (CD_2Cl_2; 121.47 MHz) of the diastereomers $(S_P,S_P)(R_{As},R_{As})/(S_P,S_P)(S_{As},S_{As})/(S_P,S_P)(R_{As},S_{As})$-**69** (a) and the corresponding spectrum resulting from the asymmetric synthesis (b).

3.3.2 Enantioselective synthesis of (R_{As},R_{As})-67

By the procedure described above for the synthesis of 1,2-*bis*(methylphenylarsino)ethane, the bis[(*n*-butyl)phenylarsine] (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**67** was synthesised by the addition of *n*-butyllithium (2.2 equiv, 1.5 M in hexanes) to a dichloromethane solution of $(aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/(aR_P)(R_{As},S_{As})(aR_P)$-**65** at –95 °C (Scheme 3.8). After workup and complexation with (S_P,S_P)-**68**, the $^{31}P\{^{1}H\}$ NMR spectrum shown in Figure 3.9(b) was obtained; integration of the resonances gave $(S_P,S_P)(R_{As},R_{As}):(S_P,S_P)(R_{As},S_{As}):(S_P,S_P)(S_{As},S_{As})$-**70** = 5:23:72. Thus, the diastereoselectivity of the *n*-butyllithium addition to the (aR_P)-phosphepine-stabilised bis(arsenium triflate) **65** led to (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**67** that was 77%

enriched in the (R^*_{As},R^*_{As}) diastereomer, which, in turn, was enriched to the extent of 93% in the (R_{As},R_{As}) enantiomer.[§§]

Scheme 3.8



[§§] The opposite configuration at arsenic obtained for the asymmetric synthesis of (S_{As})-As(*n*-Bu)MePh[97] to the (R_{As},R_{As})-diarsines is because of a reversal of the CIP priorities at arsenic in proceeding from the monoarsine to the diarsine, rather than inversions of configurations.

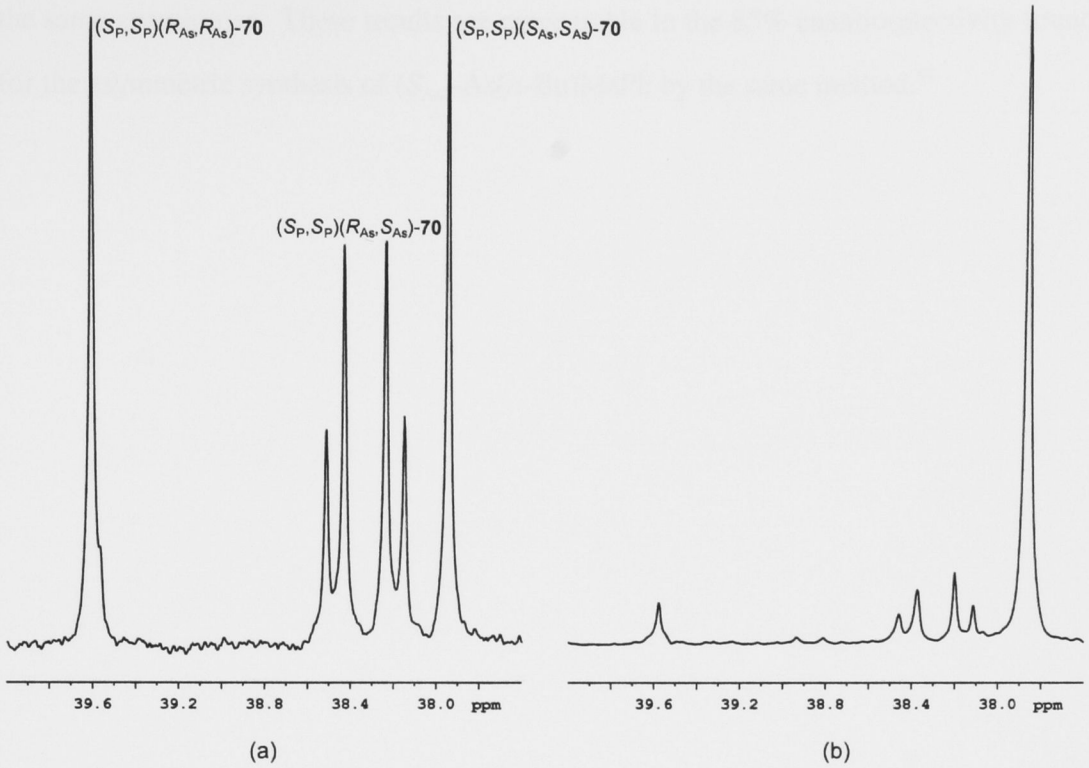


Figure 3.9 The reference $^{31}P\{^{1}H\}$ NMR spectrum ($CDCl_3$; 121.47 MHz) of the diastereomers $(S_P,S_P)(R_{As},R_{As})/(S_P,S_P)(S_{As},S_{As})/(S_P,S_P)(R_{As},S_{As})$-**70** (a) and the corresponding spectrum resulting from the asymmetric synthesis (b).

3.4 Conclusions

The addition of methyl- or *n*-butyllithium to solutions of a *bis*[(aR_P)-phosphepine-stabilised] diarsenium triflate at –95 °C in dichloromethane results in stereoselective syntheses of the corresponding diarsines: the methyllithium addition gave (R^*_{As},R^*_{As})-(±)-1,2-*bis*(methylphenylarsino)ethane with 78% diastereoselectivity and 95% enantioselectivity in favour of the (R_{As},R_{As}) enantiomer; the addition of *n*-butyllithium to the diarsenium salt under similar conditions gives (R^*_{As},R^*_{As})-(±)-1,2-*bis*[(*n*-butyl)phenylarsino]ethane with 77% diastereoselectivity and 93% enantioselectivity for

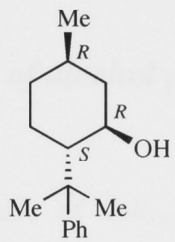
the same enantiomer. These results are comparable to the 85% enantioselectivity found for the asymmetric synthesis of (S_{As})-As(*n*-Bu)MePh by the same method.[97]

Chapter 4:

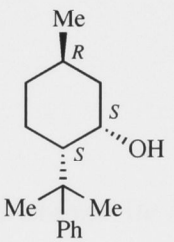
Synthesis and reactivity of 8-phenylmenthyl-substituted phosphines

4.1 Introduction

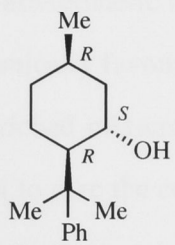
The syntheses of ($1R_C,2S_C,5R_C$)-(–)-8-phenylmenthol, ($1R_C,2S_C,5R_C$)-**71**, and its enantiomorph, ($1S_C,2R_C,5S_C$)-(+)-**71**, were reported by Corey and Ensley in 1975; the chiral alcohols are effective chiral auxiliaries for the asymmetric synthesis of certain prostaglandin intermediates.[112] It was also reported that the acrylate of ($1R_C,2S_C,5R_C$)-**71** gave a much superior induction than (–)-menthyl acrylate for the stannic chloride-catalysed, Diels–Alder cycloaddition of cyclopentadiene.[112] The four ($5R_C$)-stereoisomers of 8-phenylmenthol (Figure 4.1) can be synthesised from naturally occurring (R_C)-(+)-pulegone[113, 114] and behave as useful auxiliaries for asymmetric reactions, particularly those requiring diastereofacial selectivity.[115]



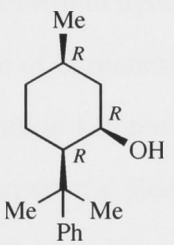
(–)-8-phenylmenthol
($1R_C,2S_C,5R_C$)-**71**



(+)-8-phenyl*neo*menthol
($1S_C,2S_C,5R_C$)-**71**



(+)-8-phenyl*iso*menthol
($1S_C,2R_C,5R_C$)-**71**



(–)-8-phenyl*isoneo*menthol
($1R_C,2R_C,5R_C$)-**71**

Figure 4.1 The stereoisomers of 8-phenylmenthol.

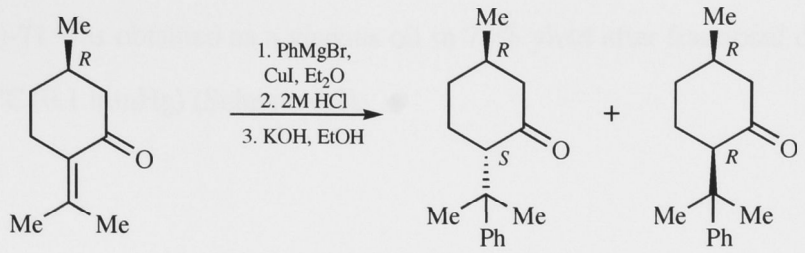
Recent work within our group showed that ($1R_C$,$2S_C$,$5R_C$)-(–)-menthyldiphenylphosphine and ($1S_C$,$2S_C$,$5R_C$)-(+)-*neo*menthyldiphenylphosphine gave very low diastereoselectivities of coordination to the prochiral methylphenylarsenium ion (ca. 15%).[116] It was therefore of interest to determine if the 8-phenyl-substituted menthylphosphines would show increased diastereoselectivity for the methylphenylarsenium ion and thus function as effective auxiliaries for the asymmetric synthesis of chiral arsines by nucleophilic additions to prochiral arsenium ions.

4.2 Syntheses of 8-phenylmenthyl-substituted tertiary phosphines

4.2.1 Preparation of alcohol precursors

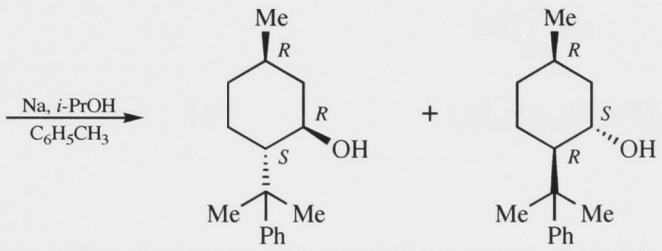
The literature synthesis of ($1R_C$,$2S_C$,$5R_C$)-**71** is shown in Scheme 4.1; copper(I) mediated conjugated addition of phenylmagnesium bromide to (R_C)-(+)-pulegone gave the kinetic mixture (1:1) of the *cis* and *trans* isomers of 8-phenylmenthone, **72**.[112, 113] Equilibration of the diastereomeric mixture with potassium hydroxide in boiling ethanol led to the thermodynamically favoured distribution of diastereomers, which is ca. 85:15 (*trans* : *cis*). The enriched mixture of diastereomeric ketones was then reduced with sodium and *i*-propanol to give the corresponding equatorial alcohols ($1R_C$,$2S_C$,$5R_C$)- and ($1S_C$,$2R_C$,$5R_C$)-**71** that were successfully separated by column chromatography. The isomers can also be separated by preparative HPLC[117] and by fractional crystallisation of the chloroacetate esters of the alcohols.[113]

Scheme 4.1



(R_C)-(+)-pulegone *trans*-**72** *cis*-**72**

85 : 15



($1R_C,2S_C,5R_C$)-**71** ($1S_C,2R_C,5R_C$)-**71**

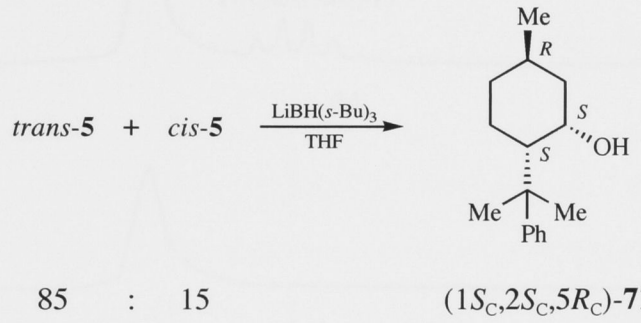
85 : 15

Reduction of *trans*/*cis*-**72** (85/15) with sodium and *i*-propanol gave ($1R_C,2S_C,5R_C$)/($1S_C,2R_C,5R_C$)-**71** (85/15) as a thick oil in 56% yield, bp 122–126 °C (0.05 mmHg) [Lit[113] 103–107 °C (0.01 mmHg)]. Several attempts at separating the mixture by fractional distillation and flash chromatography were unsuccessful and it was decided that the mixture of products would be used for the next step without separation.

The reduction of a substituted cyclohexanone with a bulky nucleophile gives the axial alcohol because the nucleophile can only add from the equatorial face of the ketone; conversely, reduction of the ketone with a less-hindered nucleophile gives the equatorial alcohol as addition occurs from the axial side.[7] Therefore, reduction of the ketones with L-Selectride® solution (lithium tri-*s*-butylborohydride in THF) gave the axial alcohols

($1S_C,2S_C,5R_C$)- and ($1R_C,2R_C,5R_C$)-**71** in an 85:15 ratio.[118] In this way, pure ($1S_C,2S_C,5R_C$)-**71** was obtained as a viscous oil in 78% yield after fractional distillation, bp 120–122 °C (0.1 mmHg) (Scheme 4.2).

Scheme 4.2



The C*H*OH protons of the diastereomeric menthols resonate at higher frequencies in the ^{1}H NMR spectra than the other alkyl protons; these regions of the spectra for the various reductions are shown in Figure 4.2. The axial protons in ($1R_C,2S_C,5R_C$)- and ($1S_C,2R_C,5R_C$)-**71** resonate as overlapping doublets of doublets of doublets centred at δ 3.52 and 3.76, respectively, due to three bond coupling to one equatorial proton and two inequivalent axial protons in an antiperiplanar arrangement (Figure 4.2a). The C*H*OH protons in ($1S_C,2S_C,5R_C$)- and ($1R_C,2R_C,5R_C$)-**71** are in the equatorial position and the resonance for ($1S_C,2S_C,5R_C$)-**71** is a broad apparent singlet at δ 3.83, whereas the proton in ($1R_C,2R_C,5R_C$)-**71** resonates as an apparent doublet of doublets centred at δ 3.71 (Figure 4.2b); the broadness of the peaks can be attributed to shielding effects from the three coupled protons in a gauche arrangement.[7]

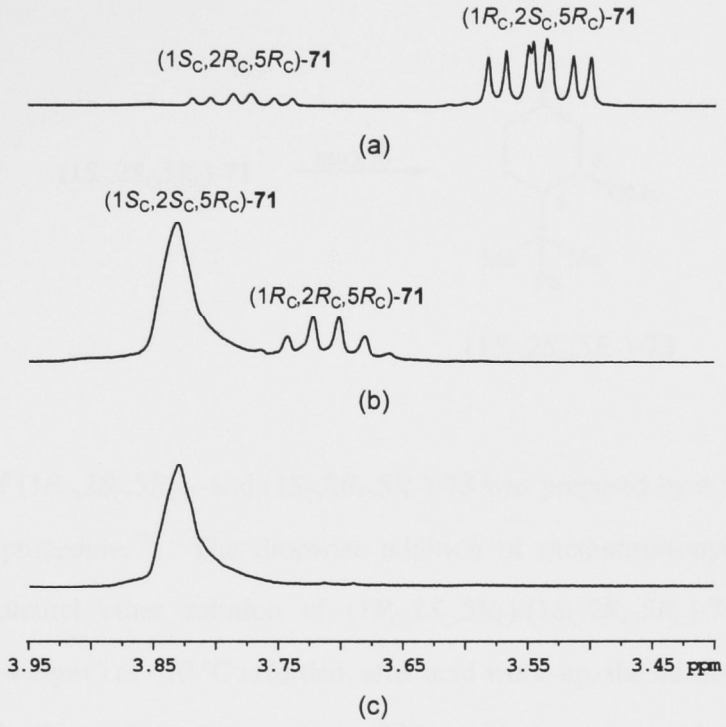
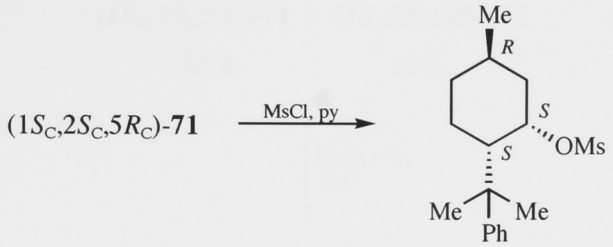


Figure 4.2 ^{1}H NMR spectra showing the C*H*OH resonances of (a) (1R_C,2S_C,5R_C)/(1S_C,2R_C,5R_C)-**71** (85:15) after reduction of *trans*, *cis*-**72** (85:15) with Na/*i*-PrOH, (b) (1S_C,2S_C,5R_C)/(1R_C,2R_C,5R_C)-**71** (85:15) after reduction with L-Selectride®, and (c) after fractional distillation of (b).

4.2.2 Preparation of methane sulfonate esters

The mesylate (1S_C,2S_C,5R_C)-**73** was prepared by the literature procedure.[118] A solution of (1S_C,2S_C,5R_C)-**71** in dry pyridine was added dropwise to a solution of methanesulfonyl chloride (1.4 equiv) in the same solvent at –10 °C; the suspension was stored overnight at low temperature to ensure complete crystallisation of the pyridinium hydrochloride by-product (Scheme 4.3). The thermally sensitive product was isolated as a pale yellow oil in 94% yield after dilute acid work-up of the filtrate and was used without further purification.

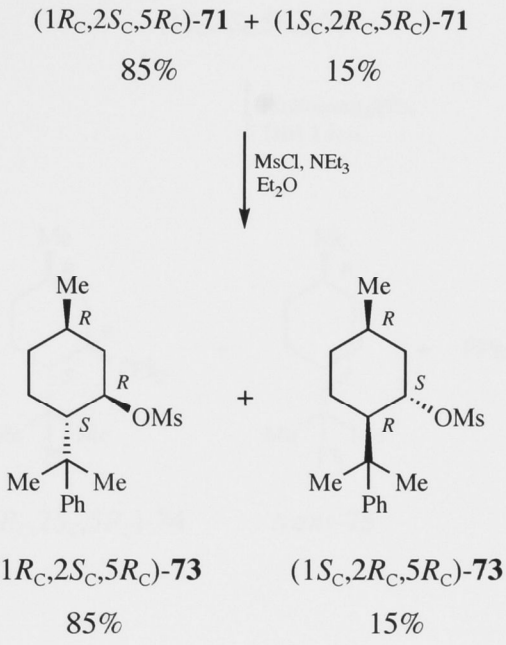
Scheme 4.3



$(1S_C,2S_C,5R_C)$-**73**

The mixture of $(1R_C,2S_C,5R_C)$- and $(1S_C,2R_C,5R_C)$-**73** was prepared by a modification of the literature procedure.[118] The dropwise addition of methansulfonyl chloride (1.5 equiv) to a diethyl ether solution of $(1R_C,2S_C,5R_C)$/$(1S_C,2R_C,5R_C)$-**71** (85:15) and triethylamine (4 equiv) at –10 °C afforded, after acid work-up, the mixture of mesylates as a pale pink, thermally-sensitive oil in 77% yield that was used without further purification (Scheme 4.4). The ^{1}H NMR resonances for the C*H*OMs protons of the diastereomers of the product are an overlapping apparent doublet of triplets ($^3J_{HH}$ = 10.5, 4.2 Hz) for $(1R_C,2S_C,5R_C)$-**73** and an unresolved multiplet for the minor product $(1S_C,2R_C,5R_C)$-**73**; integration of the peaks indictated an approximate 90:10 ratio of products.

Scheme 4.4

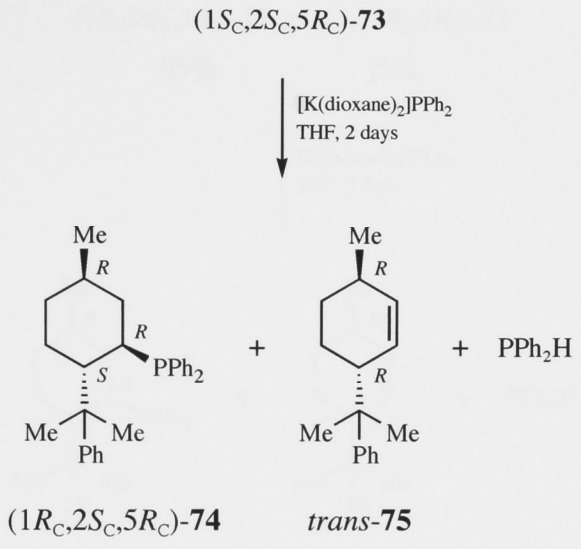


4.2.3 Preparation of 8-phenylmenthyl-substitued phosphines

The addition of phosphide of the type MPR_2 to a mesylate chiral at carbon proceeds with inversion of configuration by an S_N2 mechanism.[7] Thus, the addition of a solution of $[K(dioxane)_2]PPh_2$ to the *neo*menthyl mesylate $(1S_C,2S_C,5R_C)$-**73** gave the crude menthylphosphine $(1R_C,2S_C,5R_C)$-**74** as an oil. The presence of the bulky phenyl substituent on the *iso*-propyl group hinders the approach of the phosphide anion, slowing the reaction, and considerable amounts of the elimination products, cyclohexene *trans*-**75** and diphenylphosphine, are produced (Scheme 4.5). The elimination products are distilled off as a single fraction under vacuum and $(1R_C,2S_C,5R_C)$-**74** is identified by a single peak at –1.2 ppm in the $^{31}P\{^1H\}$ NMR spectrum of the residue.[***]

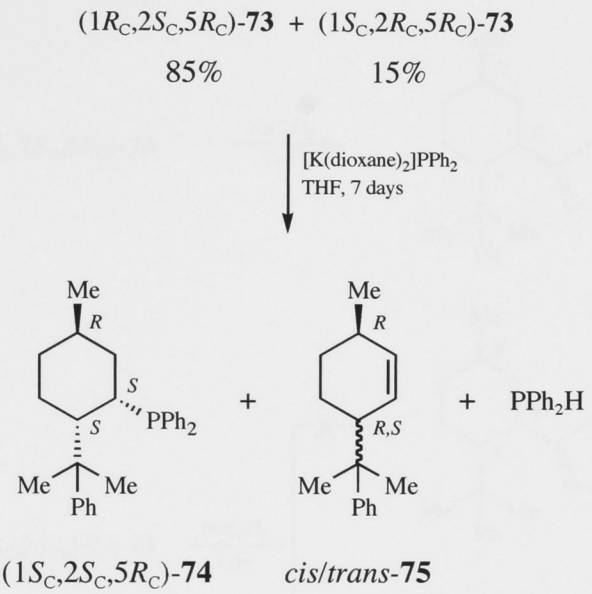
[***] $(1R_C,2S_C,5R_C)$-**74** is too high boiling to be purified by distillation.

Scheme 4.5



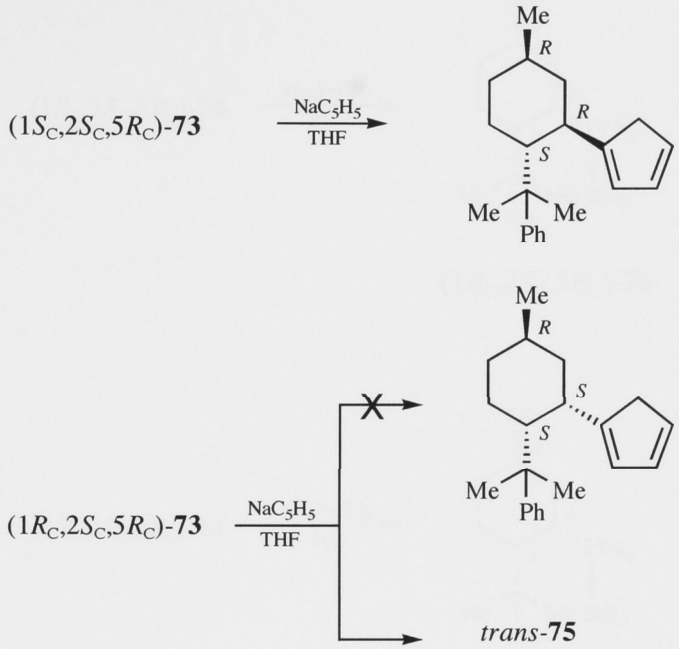
Similarly, a solution of the 85:15 mixture of the menthyl- and *iso*menthyl-mesylates in THF was added to a suspension of deep orange $[K(dioxane)_2]PPh_2$ in the same solvent (Scheme 4.6). This reaction was much slower than the one above, the orange colour of the diphenylphosphide still persisting after 7 days, when the reaction mixture was quenched with deoxygenated water. The elimination products, *cis/trans*-**75** and diphenylphosphine, were distilled from the product mixture after work-up and the $^{31}P\{^{1}H\}$ NMR spectrum of the crude product was recorded. Interestingly, the spectrum contained a single product peak at –11.4 ppm, rather than a pair of peaks in the starting material 85:15 ratio. An X-ray crystal structure determination on the borane adduct of the resulting phosphine confirmed the configuration of the phosphine as ($1S_C$,$2S_C$,$5R_C$)-**74**, Section 4.2.4.

Scheme 4.6



The phenyl ring of 8-phenyl-substituted menthyl mesylates profoundly affects their reactivities; this is apparent from the rates of phosphide substitution of the mesylate for the different diastereomers, which varies from ca. 2 days for $(1S_C,2S_C,5R_C)$-**73** to unreactive for $(1S_C,2R_C,5R_C)$-**73**. The similar reaction of lithium diphenylphosphide with $(1R_C,2S_C,5R_C)$-menthyl mesylate in THF at 30 °C gave $(1S_C,2S_C,5R_C)$-*neo*menthyldiphenylphosphine in 70% yield in 3 h.[119] This effect was also evident in published work on 8-phenylmenthyl substituted cyclopentadienyl complexes, where the addition of sodium cyclopentadienide to $(1S_C,2S_C,5R_C)$-**73** gave the desired cyclopentadienyl ligand; the reaction with $(1R_C,2S_C,5R_C)$-**73**, however, furnished only *trans*-**75** (Scheme 4.7).[118]

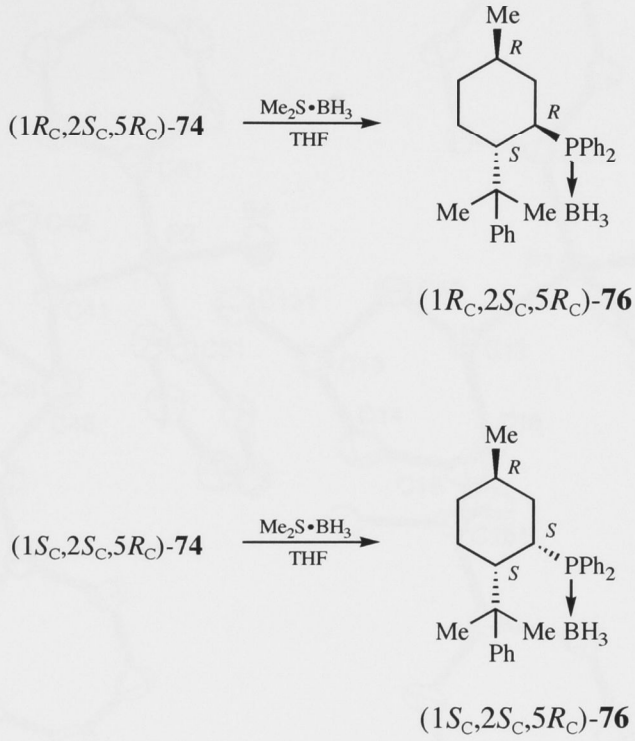
Scheme 4.7



4.2.4 Purification of 8-phenylmenthyl-substituted phosphine-borane adducts

Air-stable borane adducts of tertiary phosphines are especially useful for the purification of air-sensitive tertiary phosphines; the adducts can synthesised under mild conditions and are generally crystalline and can be purified by recrystallisation or chromatography.[120] The borane adducts of the 8-phenylmenthyl-substituted phosphines were prepared by the addition of an excess of borane dimethyl sulfide to a solution of the crude phosphine in THF at 0 °C (Scheme 4.8); the adducts were isolated after several hours by evaporation of the solvent and excess borane dimethyl sulfide.

Scheme 4.8



Pure $(1R_C,2S_C,5R_C)$-**76** was obtained in 21% yield after crystallisation from a dichloromethane–ethanol, mp 157–159 °C, $[\alpha]_D$ +101 (*c* 1.0, CH_2Cl_2). The adduct crystallised as colourless plates in the monoclinic space group $P2_1$ with 2 independent molecules in the asymmetric unit cell. The ORTEP diagram of the two independent units is shown in Figure 4.2 and crystallographic data and experimental details are given in Table 4.1; selected bond lengths and angles are given in Table 4.2. The absolute configuration of each molecule was confirmed as $(1R_C,2S_C,5R_C)$ by refinement of the Flack parameter. The P1–C11 and P2–C41 bonds in the molecule at 1.953(3) and 1.929(3) Å, respectively, are significantly longer than the remaining P–C bonds, presumably due to the steric bulk of the chiral alkyl group. The phosphorus atom has a distorted tetrahedral geometry with the boron atom being angled above the cyclohexyl group giving the C11–P1–B2 and C41–P2–B4 angles of 114.68(13)° and 113.84(14)°, respectively.

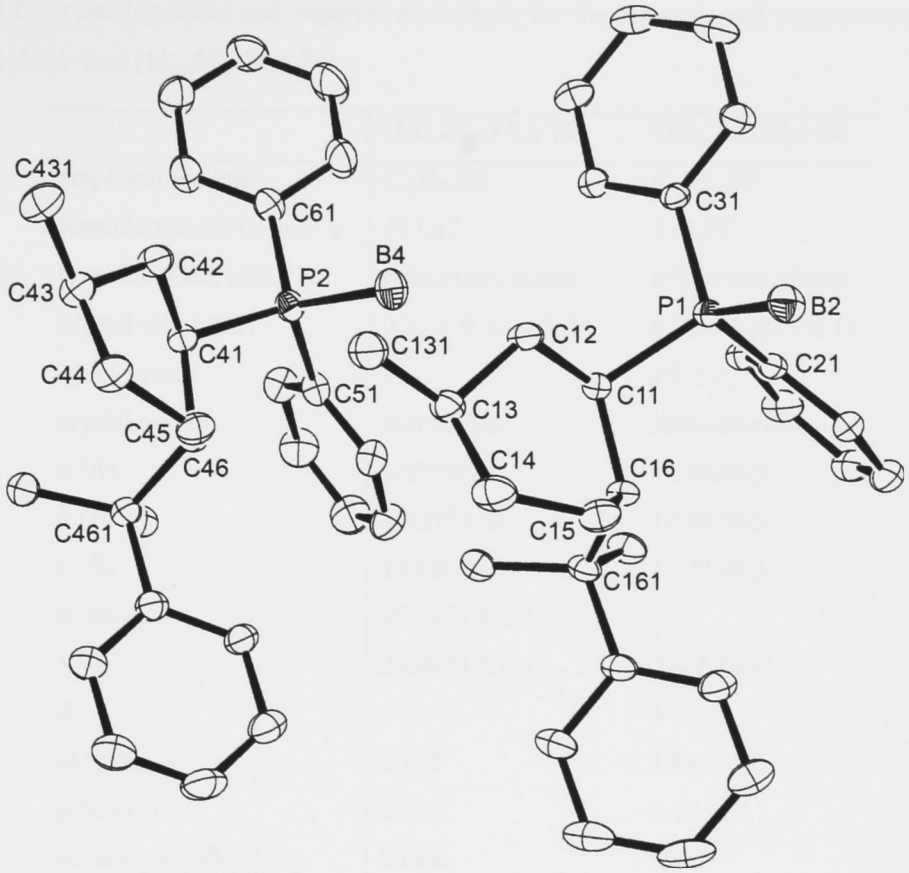


Figure 4.2 Structure of ($1R_C$,$2S_C$,$5R_C$)-**76** (hydrogen atoms omitted for clarity) showing 30% probability ellipsoids.

Table 4.1 Crystallographic and experimental details for the X-ray crystal structure analysis of ($1R_C$,$2S_C$,$5R_C$)- and ($1S_C$,$2S_C$,$5R_C$)-**76**

	($1R_C$,$2S_C$,$5R_C$)-**76**	($1S_C$,$2S_C$,$5R_C$)-**76**
empirical formula	$C_{28}H_{36}BP$	$C_{28}H_{36}BP$
formula weight (g mol^{-1})	414.37	414.37
crystal colour, habit	colourless, plates	colourless, plates
crystal size (mm)	0.31 × 0.25 × 0.08	0.33 × 0.20 × 0.15
space group	$P2_1$	$P2_12_12_1$
crystal system	monoclinic	orthorhombic
a (Å)	9.8779(2)	11.0528(2)
b (Å)	20.0534(4)	12.3929(3)
c (Å)	13.0002(2)	17.7250(3)
β (deg)	107.4719(10)	
V (Å^3)	2456.31(8)	2427.90(8)
Z	4	4
D (g cm^{-1})	1.120	1.134
μ (mm^{-1})	0.12	0.13
no. unique reflections	10964	5552
no. reflections observed	7574 ($I > 2.0\sigma(I)$)	4416 ($I > 2.0\sigma(I)$)
temperature (K)	200	200
final R_1, wR	0.036, 0.125	0.031, 0.102
Flack parameter	0.02(7)	–0.01(8)

Table 4.2 Selected bond lengths (Å) and angles (°) in ($1R_C$,$2S_C$,$5R_C$)- and ($1S_C$,$2S_C$,$5R_C$)-**76**

	($1R_C$,$2S_C$,$5R_C$)-**76**	($1S_C$,$2S_C$,$5R_C$)-**76**
P1–B2	1.935(3)	1.952(2)
P2–B4	1.929(3)	
P1–C11	1.849(2)	1.8790(16)
P2–C41	1.851(3)	
P1–C21	1.817(3)	1.8228(17)
P2–C51	1.815(3)	
P1–C31	1.818(2)	1.8243(19)
P2–C61	1.816(3)	
C11–P1–B2	114.68(13)	122.03(9)
C41–P2–B4	113.84(14)	
C11–P1–C21	104.87(11)	107.09(8)
C41–P2–C51	108.38(13)	
C11–P1–C31	107.87(11)	103.65(8)
C41–P2–C61	108.21(12)	

The neomenthylphosphine ($1S_C$,$2S_C$,$5R_C$)-**76** was obtained in 9.4% overall yield after recrystallisation from dichloromethane–ethanol, and had mp 156–158 °C, $[\alpha]_D$ +106 (*c* 1.0, CH_2Cl_2). The compound crystallises as colourless plates in the orthorhombic space group $P2_12_12_1$ with one molecule in the unit cell. The structure is shown in Figure 4.3; crystallographic data and experimental details are given in Table 4.1 and selected bond lengths and angles are given in Table 4.2. The absolute configuration of the molecule was confirmed as ($1S_C$,$2S_C$,$5R_C$) by refinement of the Flack parameter. As in ($1R_C$,$2S_C$,$5R_C$)-**76**, the P1–C11 bond in ($1S_C$,$2S_C$,$5R_C$)-**76** is 0.052 Å longer than the other P–C bonds. The phosphorus atom has a distorted tetrahedral geometry (C11–P1–B2 = 122.03(9)°) due to repulsion between the borane protons and the axial protons on C13 and C15.

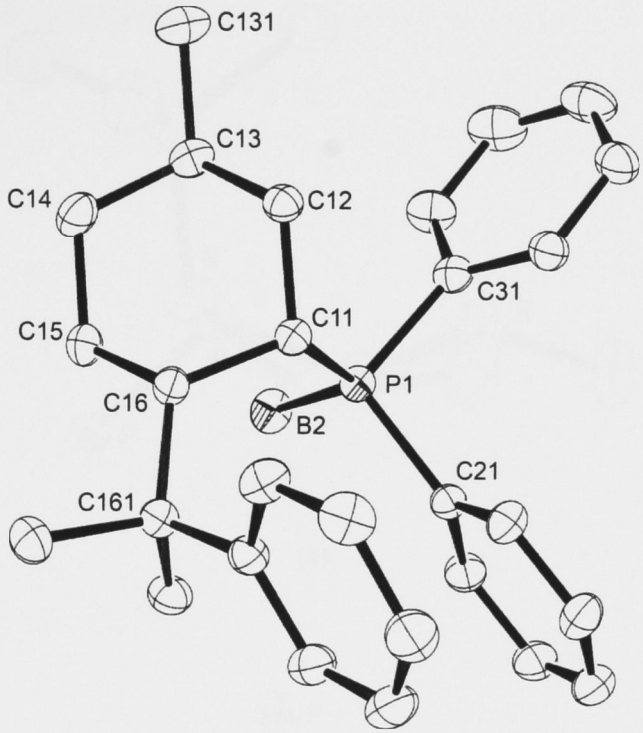
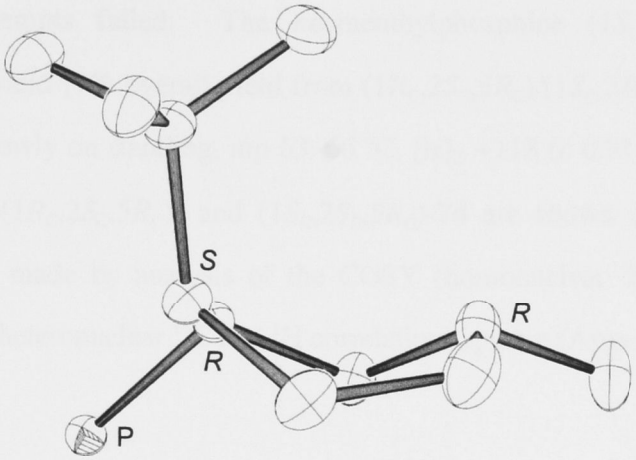
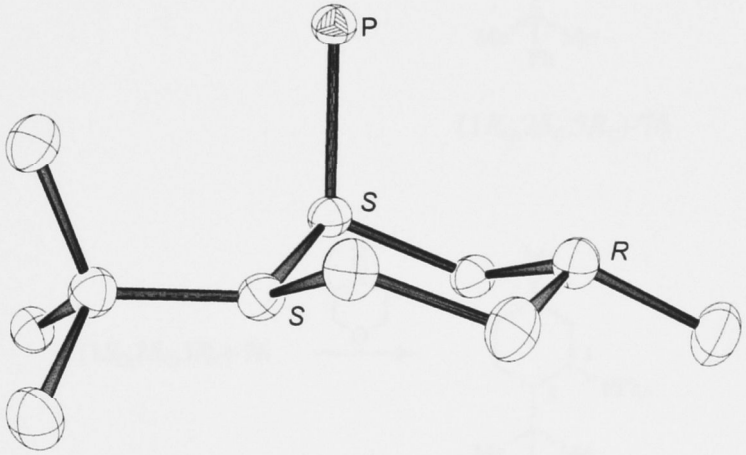


Figure 4.3 Structure of ($1S_C$,$2S_C$,$5R_C$)-**76** (hydrogen atoms omitted for clarity) showing 30% probability ellipsoids.

The simplified structures of the cyclohexyl rings in ($1R_C$,$2S_C$,$5R_C$)- and ($1S_C$,$2S_C$,$5R_C$)-**76** are shown in Figure 4.4. The internal geometry of ($1S_C$,$2S_C$,$5R_C$)-**76** shows the expected chair conformation with the methyl and substituted *iso*-propyl groups in equatorial positions and the phosphorus in an axial arrangement. Interestingly, the structure of ($1R_C$,$2S_C$,$5R_C$)-**76** shows the cyclohexyl ring in a twisted boat conformation with the phosphorus and methyl group in the equatorial position and the substituted *iso*-propyl group in the axial position. If the cyclohexyl ring in ($1R_C$,$2S_C$,$5R_C$)-**76** adopted the chair conformation, all of the substituents would have favourable equatorial positions, but the PPh_2 and $C(Me_2Ph)$ groups are too bulky to allow this arrangement to occur, so the cyclohexane ring adopts the less thermodynamically favoured boat conformation.



(a)



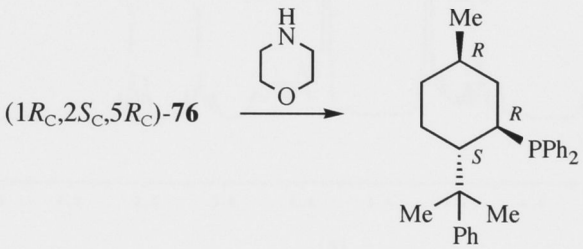
(b)

Figure 4.4 The simplified structure of the cyclohexyl rings in ($1R_C$,$2S_C$,$5R_C$)-**76** (a) and ($1S_C$,$2S_C$,$5R_C$)-**76** (b).

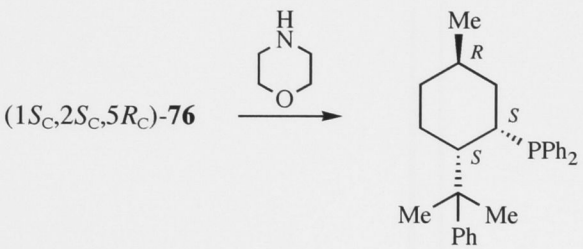
The phosphine–borane adducts were converted into the corresponding phosphines by heating in neat morpholine (Scheme 4.9); aqueous work-up of the reaction mixtures furnished the phosphines as gums that were shown to be pure by ^{1}H and ^{31}P{^{1}H} NMR spectroscopy. The menthylphosphine ($1R_C$,$2S_C$,$5R_C$)-**74** was obtained in a 68% yield (overall yield of 13% from ($1S_C$,$2S_C$,$5R_C$)-**71**), $[\alpha]_D$ –26 (*c* 0.98, CH_2Cl_2), but

crystallisation attempts failed. The *neo*menthylphosphine ($1S_C,2S_C,5R_C$)-**74** was obtained in 97% yield [7% overall yield from ($1R_C,2S_C,5R_C$)/($1S_C,2R_C,5R_C$)-**71** (85:15)] and crystallised slowly on standing, mp 63–66 °C, $[\alpha]_D$ +118 (*c* 0.91, CH_2Cl_2). The ^1H NMR spectra of ($1R_C,2S_C,5R_C$)- and ($1S_C,2S_C,5R_C$)-**74** are shown in Figure 4.5; the assignments were made by analysis of the COSY (homonuclear ^1H correlation) and gHSQC (gradient heteronuclear ^{13}C and ^1H correlation) spectra (Appendix 2).

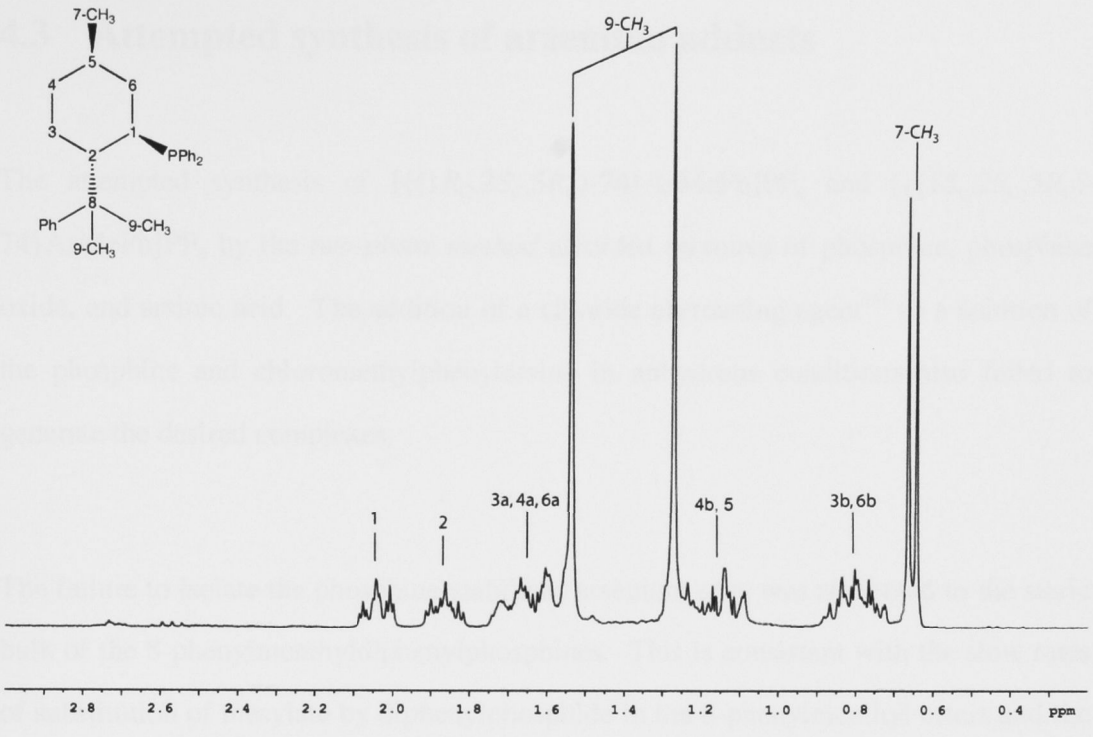
Scheme 4.9



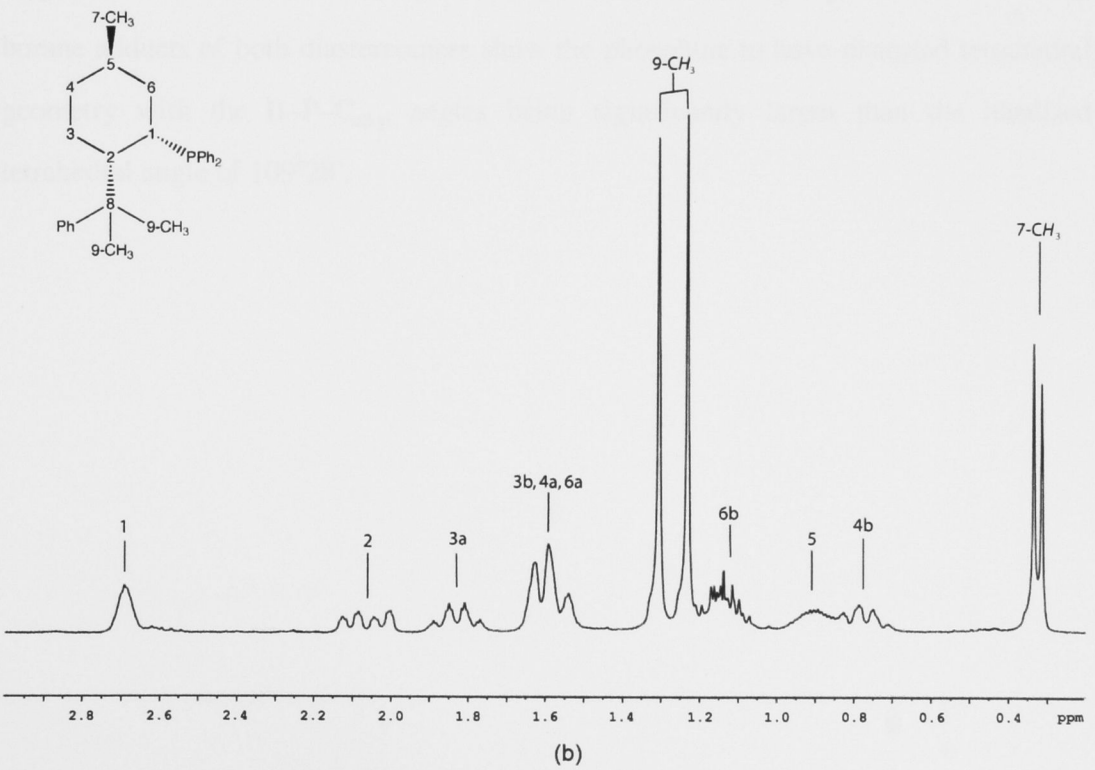
($1R_C,2S_C,5R_C$)-**74**



($1S_C,2S_C,5R_C$)-**74**



(a)



(b)

Figure 4.5 The aliphatic region of the ^{1}H NMR spectra ($CDCl_3$, 300 MHz) of ($1R_C$,$2S_C$,$5R_C$)-**74** (a) and ($1S_C$,$2S_C$,$5R_C$)-**74** (b).

4.3 Attempted synthesis of arsenium adducts

The attempted synthesis of [{(1R_C,2S_C,5R_C)-**74**}AsMePh]PF_6 and [{(1S_C,2S_C,5R_C)-**74**}AsMePh]PF_6 by the *two-phase method* afforded mixtures of phosphine, phosphine oxide, and arsinic acid. The addition of a chloride abstracting agent[†††] to a solution of the phosphine and chloromethylphenylarsine in anhydrous conditions also failed to generate the desired complexes.

The failure to isolate the phosphine-stabilised arsenium salts was attributed to the steric bulk of the 8-phenylmenthyldiphenylphosphines. This is consistent with the slow rates of substitution of mesylate by diphenylphosphide in the 8-phenylmenthyl esters and the large amounts of the elimination products observed. The X-ray crystal structures of the borane adducts of both diastereomers show the phosphine to have distorted tetrahedral geometry with the B–P–C_{alkyl} angles being significantly larger than the idealised tetrahedral angle of 109°28′.

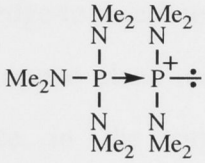
[†††] Chloride abstracting reagents used were trimethylsilyl triflate, trimethylsilyl tosylate, silver(I) triflate, silver(I) hexafluorophosphate, silver(I) hexafluoroantimonate, and silver(I) tosylate.

Chapter 5:

Tertiary arsine-stabilised arsenium salts

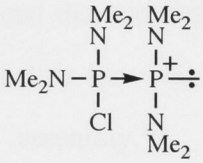
5.1 Introduction

The first syntheses of phosphine-stabilised phosphenium salts were reported in 1969 by Sisler and coworkers following reactions of several trialkylphosphines with chlorodimethylphosphine in the presence of aluminium(III) chloride.[121] The complexes isolated were $[(R_3P)PMe_2]Cl$ (R = ethyl, *n*-propyl, *n*-butyl and *n*-octyl). The attempted synthesis of similar aminophosphine adducts unexpectedly gave the phosphenium salts **77** and **78**, as determined by conductivity and NMR spectroscopic studies.[122, 123]



$AlCl_4^-$

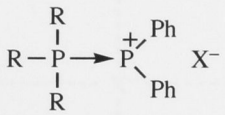
77



$AlCl_4^-$

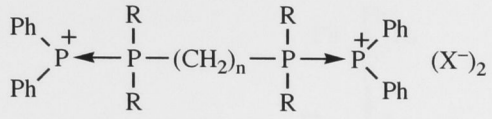
78

The field of phosphenium chemistry further developed with the synthesis of a series of phosphine-stabilised phosphenium salts of the type **79**, and the bis(phosphine-stabilised) diphosphenium salts **80** and **81** by chloride-abstractions from chlorophosphines in the presence of trimethylsilyl triflate, aluminium-, or gallium trichloride.[124-127]



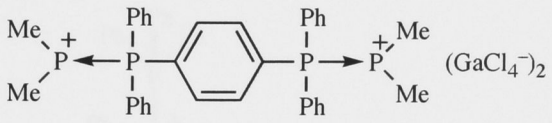
79

R = Me, Cy, Ph
X = OTf^-, $AlCl_4^-$, $GaCl_4^-$



80

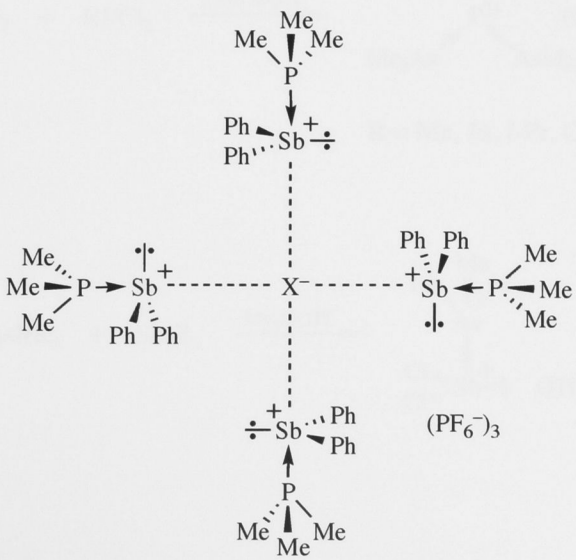
R = Me, Ph
X = OTf, $AlCl_4$, $GaCl_4$
n = 1, 2, 6



81

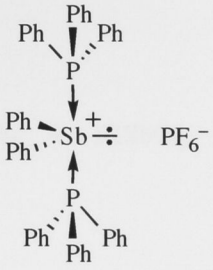
R = Me, Ph

The stibine-stabilised stibenium complex $[(Me_3Sb)SbMe_2][(MeSbBr_3)_2]$ was isolated from a redistribution of bromodimethylstibine and was structurally characterised.[128] The phosphine-stabilised stibenium complex $[(Me_3P)SbPh_2]PF_6$ self-assembles around halide ions to give complexes of the type $[\{(Me_3P)SbPh_2\}_4X](PF_6)_3$ (X = Cl, Br), **82**, with attractive edge-to-face interactions between the two sets of phenyl groups above and below the square plane containing the halide ion which appear to be a crucial stabilising force in the supramolecular assembly.[129] Coordination of two triphenylphosphine ligands to a central stibenium or bismuthenium ion has been observed in the complexes **83** and **84**, which have structures based on the distorted trigonal bipyramid.[95]

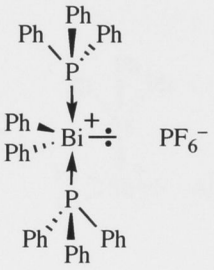


82

X = Br^-, Cl^-



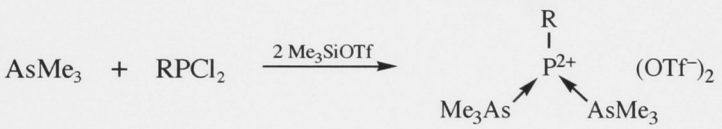
83



84

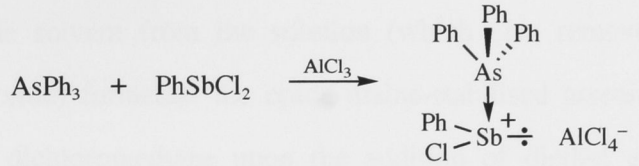
Prior to the publication of this work,[107] there were no reported syntheses of arsine-stabilised salts. Subsequently, however, reports detailing the syntheses of arsine-stabilised phosphenium,[130] stibenium[131] and bismuthenium[131] salts, as well as bis(stibine-stabilised phosphenium salts[132] and diarsonium salts,[130] were published (Scheme 5.1). A series of *arsine*-stabilised arsenium triflates has now been synthesised and the properties of the complexes compared with those of the analogous phosphine complexes by variable temperature ^{1}H NMR spectroscopy and X-ray crystallography.

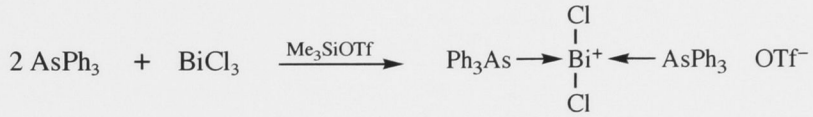
Scheme 5.1

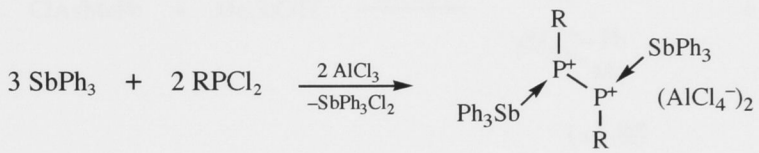


R = Me, Et, *i*-Pr, Cy, Ph

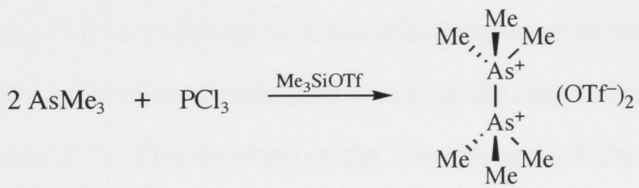
Scheme 5.1 cont.







R = *i*-Pr, Ph



5.2 Model Complexes

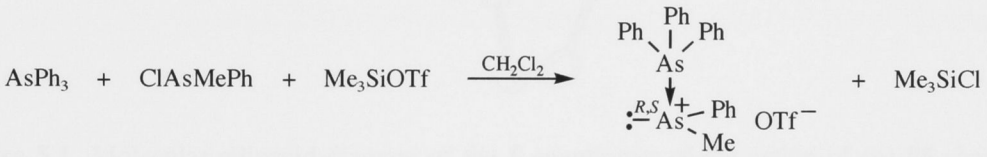
5.2.1 Triphenylarsine adduct

5.2.1.1 Synthesis

The attempted two-phase synthesis of (±)-[(Ph_3As)AsMePh]PF_6 from iodomethylphenylarsine and triphenylarsine in dichloromethane and potassium hexafluorophosphate in water, gave methylphenylarsinic acid, as verified by ^1H NMR and IR spectroscopy. Subsequently, (±)-[(Ph_3As)AsMePh]OTf [(±)-**85**] was prepared by the reaction of a dichloromethane solution of chloromethylphenylarsine with

triphenylarsine (1.1 equiv.) in the presence of trimethylsilyl triflate (1.1 equiv.); evaporation of the solvent from the solution (which also removed the by-product trimethylsilyl chloride) furnished the crude arsine-stabilised arsenium triflate, which crystallised from dichloromethane upon the addition of diethyl ether as colourless prisms in 51% yield (Scheme 5.2).

Scheme 5.2



(±)-**85**

5.2.1.2 Crystal structure

The arsine complex (±)-**85** crystallises as a racemic compound in the monoclinic space group $P2_1/c$ with two molecules of each enantiomer of the cation and associated anions in the unit cell (Table 5.1). The structure of the *S* enantiomer of the complex is shown in Figure 5.1 and important distances and angles in the cation are given in Table 5.2. The As1–As2 distance of 2.4518(5) Å is longer than the sum of covalent radii for the two arsenic atoms, viz. 2.40 Å,[108] and the arsine coordination is essentially orthogonal to the plane of the arsenium ion, with As2–As1–C11 = 91.21(12)° and As2–As1–C21 = 94.95(9)°. This compares closely with the corresponding angles in the analogous phosphine complex (±)-[(Ph_3P)AsMePh]PF_6, P–As–C_{Me} = 92.31(8)° and P–As–C_{Ph} = 97.04(6)°.[81] The coplanarity of the phenyl group with the arsenium ion is evident from the torsion angle C11–As1–C21–C22, which is –2.6(3)°.

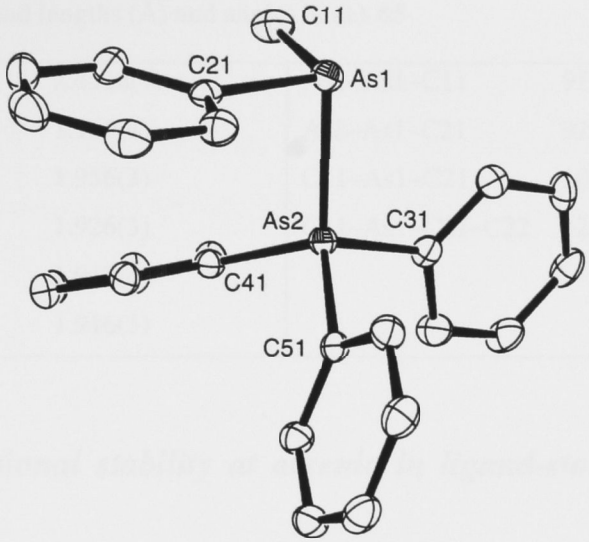


Figure 5.1 Molecular ellipsoid diagram of the *S* enantiomer of the cation of (±)-**85** showing 30% probability ellipsoids. Hydrogen atoms omitted for clarity.

Table 5.1 Crystallographic and experimental details for the X-ray crystal structure analysis of (±)-**85**

empirical formula	$C_{26}H_{23}As_2F_3O_3S$
formula weight (g mol^{-1})	622.37
crystal colour, habit	colourless, prism
crystal size (mm)	0.26 × 0.21 × 0.16
space group	$P2_1/c$
crystal system	monoclinic
a (Å)	11.1040(2)
b (Å)	17.8688(3)
c (Å)	13.5567(3)
β (°)	106.5477(12)
V (Å^3)	2578.45(8)
Z	4
D	1.438
μ (mm^{-1})	2.721
no. unique reflections	5927
no. reflections observed	2287 ($I > 3.00\sigma(I)$)
temperature (K)	200
final R_1, wR	0.0215, 0.024

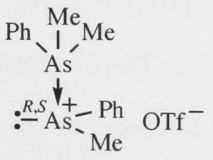
Table 5.2 Selected bond lengths (Å) and angles in (±)-**85**

As1–As2	2.4518(5)	As2–As1–C11	91.21(12)
As1–C11	1.961(4)	As2–As1–C21	92.95(9)
As1–C21	1.956(3)	C11–As1–C21	102.33(17)
As2–C31	1.926(3)	C11–As1–C21–C22	–2.6(3)
As2–C41	1.917(4)		
As2–C51	1.916(3)		

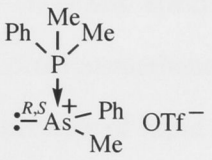
5.2.2 Configurational stability at arsenic in ligand-stabilised arsenium complexes

5.2.2.1 Syntheses

Dimethylphenylarsine is a useful model ligand for the synthesis of arsine-stabilised arsenium salts because the methyl groups of the arsine become diastereotopic in a chiral environment; thus the exchange of arsine in an arsine-stabilised arsenium complex can be investigated by ^{1}H NMR spectroscopy. Trimethylsilyl triflate was added to a dichloromethane solution of chloromethylphenylarsine and dimethylphenylarsine in dichloromethane; evaporation of the solvent from the almost colourless solution gave the crude arsine-stabilised arsenium triflate (±)-**86**, which crystallised from dichloromethane–diethyl ether as colourless needles in 75% yield. For comparison, the dimethylphenylphosphine analogue (±)-**87** was prepared in the same manner and was obtained as colourless prisms in 85% yield from dichloromethane–diethyl ether.



(±)-**86**



(±)-**87**

5.2.2.2 NMR spectroscopy

The ^{1}H NMR spectrum of the arsine-stabilised arsenium salt (±)-**86** did not show the expected diastereotopic splitting for the As*Me*$_2$ groups, even at –90 °C (Figure 5.2), which indicated that the slow-exchange limit had not been reached although there was some broadening of the As*Me* resonance for the arsenium group at this temperature.

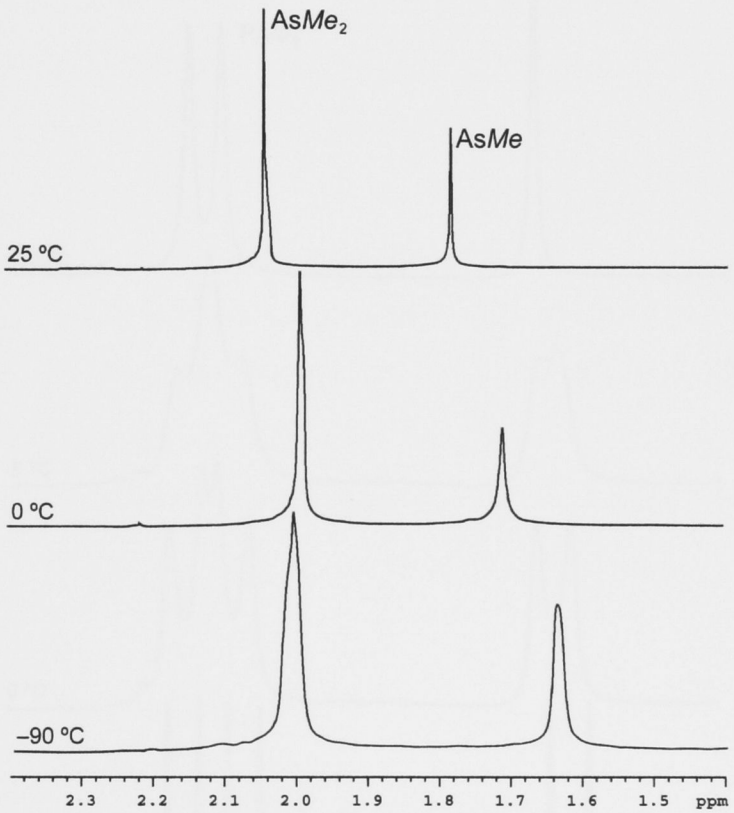


Figure 5.2 Variable temperature ^{1}H NMR spectra of (±)-**86** in dichloromethane-d_2.

The resonance for the PPh*Me*$_2$ groups in the ^{1}H NMR spectrum of the phosphine-stabilised arsenium complex (±)-**87** at 35 °C in dichloromethane-d_2 appear as a doublet (J_{HP} = 13.2 Hz) and the As*Me* peak as a singlet because of rapid phosphine exchange on the NMR time scale. On cooling the solution to 8 °C, the coalescence temperature for the P*Me* signals was reached; further cooling of the solution to –20 °C resulted in baseline separation of the P*Me* doublets (Figure 5.3). The free energy of activation for

phosphine dissociation ($\Delta G^{\ddagger}_{c}$) in (±)-**87** was calculated from the NMR data to be ca. 60 kJ mol^{-1} from the expression $\Delta G^{\ddagger}_{c} = 19.14\ T_{c}(10.32 + \log\ T_{c}/K_{c})$, where T_{c} is the coalescence temperature and $K_{c} = 2.22\ \Delta\nu\ s^{-1}$ is the rate of site exchange in Hz at the slow exchange limit.[7, 106]

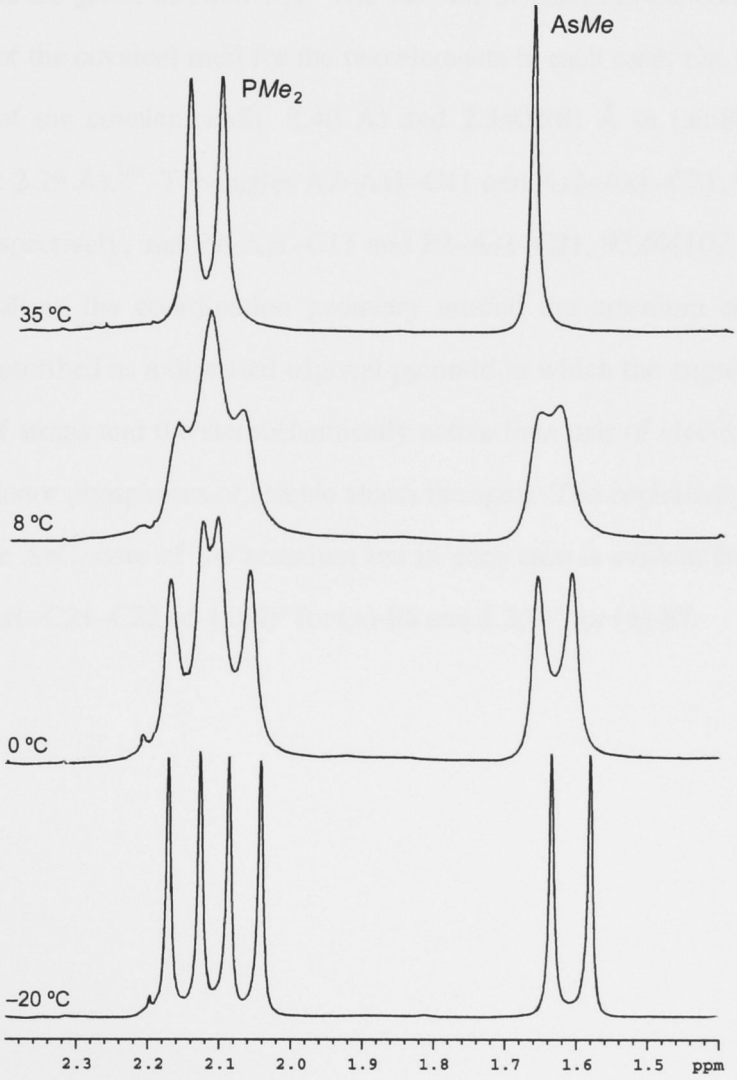


Figure 5.3 Variable temperature ^{1}H NMR spectra of (±)-**87** in dichloromethane-d_2.

5.2.2.3 Crystal structures

The complexes (±)-**86** and (±)-**87** are isomorphous with both compounds crystallising in the monoclinic space group $P2_1/n$ with two molecules of each enantiomer and associated anions in the unit cell (Table 5.3). The structures of the *S* enantiomers of (±)-**86** and (±)-**87** are shown in Figure 5.4; important distances and angles in the cations of the two salts are given in Table 5.4. The E2–As1 distances in the cations are longer than the sum of the covalent radii for the two elements in each case, viz. 2.4448(6) Å in (±)-**86** (sum of the covalent radii: 2.40 Å) and 2.3402(8) Å in (±)-**87** (sum of the covalent radii: 2.29 Å).[108] The angles A2–As1–C11 and As2–As1–C21, 94.94(14)° and 96.05(12)°, respectively, and P2–As1–C11 and P2–As1–C21, 95.69(10)° and 96.54(8)°, respectively, allow the coordination geometry around the arsenium centres in each cation to be described as a distorted trigonal pyramid in which the angular six-electron AsC_2 group of atoms and the stereochemically active lone pair of electrons occupy the base and the donor phosphorus or arsenic atoms the apex. The coplanarity of the phenyl group with the AsC_2 core of the arsenium ion in each case is evident from the torsion angles C11–As1–C21–C22 of 4.0(4)° for (±)-**86** and 5.2(3)° for (±)-**87**.

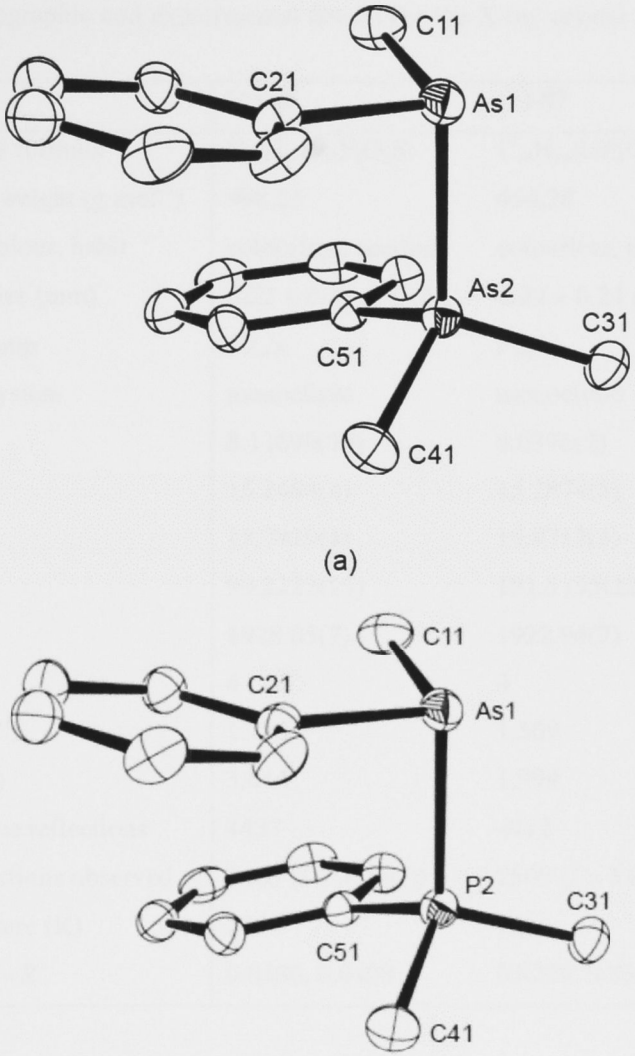


Figure 5.4 Molecular ellipsoid diagram for *S* enantiomer of the cation of (±)-**86** (a) and (±)-**87** (b) showing 30% probability ellipsoids. Hydrogen atoms omitted for clarity.

Table 5.3 Crystallographic and experimental details for the X-ray crystal structure analysis of (±)-**86** and (±)-**87**

	(±)-**86**	(±)-**87**
empirical formula	$C_{16}H_{19}As_2F_3O_3S$	$C_{16}H_{19}AsF_3O_3PS$
formula weight (g mol^{-1})	498.23	454.28
crystal colour, habit	colourless, needles	colourless, prisms
crystal size (mm)	0.22 × 0.13 × 0.12	0.29 × 0.24 × 0.23
space group	$P2_1/n$	$P2_1/n$
crystal system	monoclinic	monoclinic
a (Å)	8.13690(10)	8.0376(2)
b (Å)	15.2484(4)	15.2874(3)
c (Å)	15.7429(4)	15.9712(3)
β (deg)	99.2222(15)	101.5155(12)
V (Å^3)	1928.05(7)	1922.94(7)
Z	4	4
D (g cm^{-1})	1.716	1.569
μ (mm^{-1})	3.614	1.999
no. unique reflections	4437	4412
no. reflections observed	2463 ($I > 3.0\sigma(I)$)	2569 ($I > 3.0\sigma(I)$)
temperature (K)	200	200
final R_1, wR	0.0386, 0.0408	0.0294, 0.0346

Table 5.4 Selected bond lengths (Å) and angles (°) in (±)-**86** and (±)-**87**

	(±)-**86**	(±)-**87**
As1–E2	2.5558(6)	2.340(8)
As1–C11	1.969(5)	1.965(3)
As1–C21	1.959(9)	1.953(3)
E2–C31	1.914(4)	1.790(3)
E2–C41	1.918(4)	1.792(3)
E2–C51	1.910(4)	1.794(3)
E2–As1–C11	94.94(14)	95.69(10)
E2–As1–C21	96.05(12)	96.54(8)
C11–As1–C21	99.9(2)	100.65(14)
C11–As1–C21–C22	4.0(4)	5.2(3)

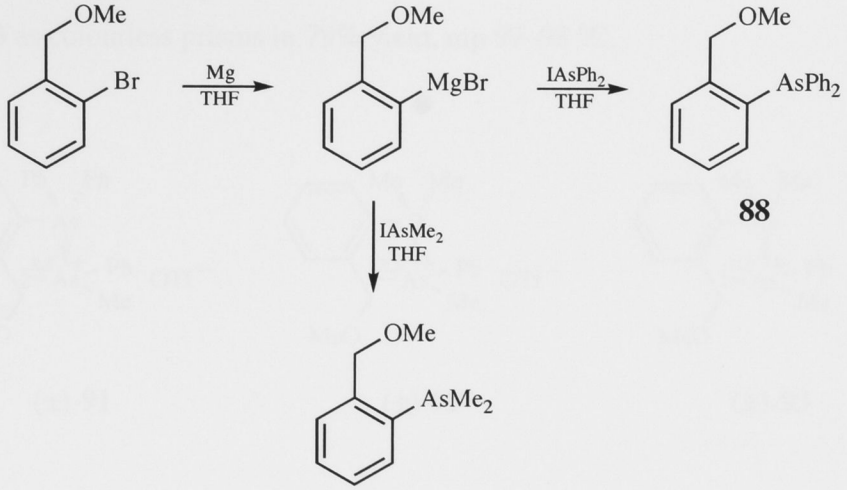
5.2 Anchimeric stabilising effect

The presence of a 2-(methoxymethyl)phenyl group in a phosphine has been shown to be an important factor in increasing the diastereoselectivity of coordination of tertiary phosphines to prochiral arsenium ions because the oxygen atom interacts with the arsenic and phosphorus atoms and hinders rotation around the arsenic–phosphorus bond.[97] This anchimeric interaction weakens the arsenic–phosphorus bond by a destabilising chelate effect, which is evident in X-ray crystal structures of complexes containing 2-(methoxymethyl)phenyl-substituted phosphines.[81, 97] Thus a 2-(methoxymethyl)phenyl substituted arsine was expected to slow arsine exchange on an arsenium ion and increased the diastereoselectivity would be observed at low temperatures by ^{1}H NMR spectroscopy.

5.2.1 Ligand synthesis

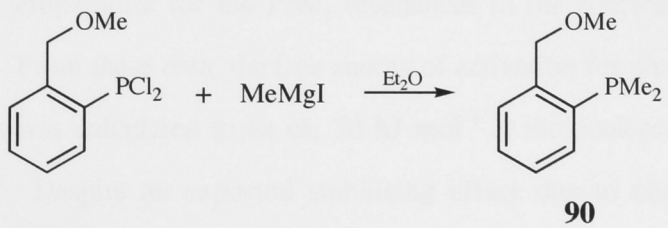
The 2-(methoxymethyl)phenyl-substituted arsines **88** and **89** were prepared by the addition of a solution of the Grignard reagent of 1-bromo-2-(methoxymethyl)benzene in THF to a solution of iododimethylarsine or iododiphenylarsine in the same solvent at 0 °C (Scheme 5.3). The crude products were purified to give **88** as colourless needles in 74% yield from hot ethanol, mp 84–86 °C, and **89** as a colourless oil in 64% yield by vacuum distillation, bp 62–63 °C (0.05 mmHg) [Lit.[133] bp 70–72 °C (0.1 mmHg)].

Scheme 5.3



The synthesis of [2-(methoxymethyl)phenyl]dimethylphosphine, **90**, was achieved by the reaction of an excess of methylmagnesium iodide with dichloro[2-(methoxymethyl)phenyl]phosphine in diethyl ether at 0 °C; the product was isolated in 70% yield, bp 78 °C (0.7 mmHg) (Scheme 5.4).

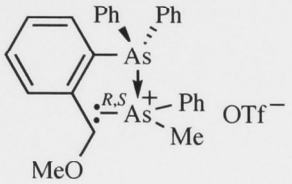
Scheme 5.4



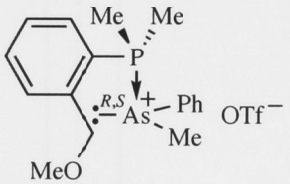
5.2.2 Arsenium complexes

A dichloromethane solution of chloromethylphenylarsine and the tertiary arsine or phosphine (1.1 equiv.) was treated with trimethylsilyl triflate (1.1 equiv.); evaporation of the solvent in each case gave the crude triflates that were recrystallised from dichloromethane–diethyl ether. The complex (±)-**91** was isolated as colourless prisms

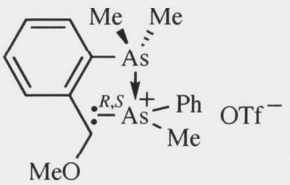
in 66% yield, mp 104–107 °C, (±)-**92** as colourless plates in 72% yield, mp 107–108 °C, and (±)-**93** as colourless prisms in 79% yield, mp 97–98 °C.



(±)-**91**



(±)-**92**



(±)-**93**

5.2.3 NMR spectroscopy

The anchimeric stabilising effect of a 2-(methoxymethyl)phenyl group attached to the arsine or phosphine was investigated by comparing the variable temperature ^{1}H NMR spectra of (±)-**92** and (±)-**93** with those obtained for the parent complexes. At 25 °C, the slow exchange limit was reached for the phosphine-stabilised arsenium salt (±)-**92**, evident by the baseline separation of the resonances for the diastereotopic P*Me*$_2$ groups. The coalescence temperature for the P*Me*$_2$ resonances in the spectrum of (±)-**92** was reached at 50 °C. From these data, the free energy of activation for phosphine exchange in the complexes was calculated to be ca. 70 kJ mol^{-1} at the coalescence temperature (Figure 5.5).[7, 106] Despite an expected stabilising effect due to chelation of the 2-(methoxymethyl)phenyl group in the arsine complex (±)-**93**, the ^{1}H NMR spectrum showed no splitting for the As*Me*$_2$ resonances at –90 °C in dichloromethane-d_2 (Figure 5.6).

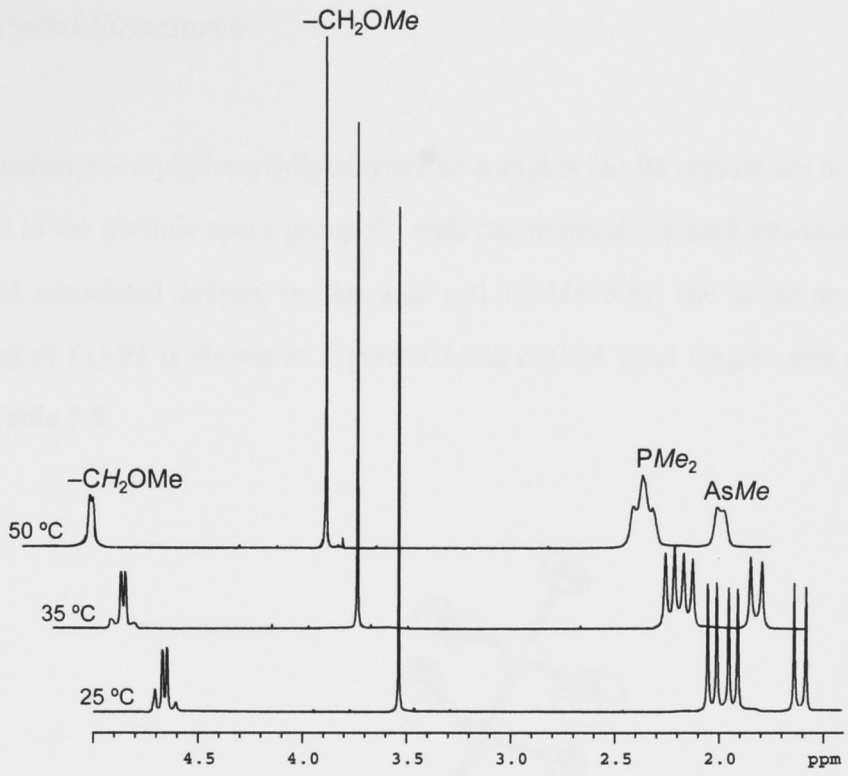


Figure 5.5 Variable temperature ^{1}H NMR spectra of (±)-**92** in dichloromethane-d_2.

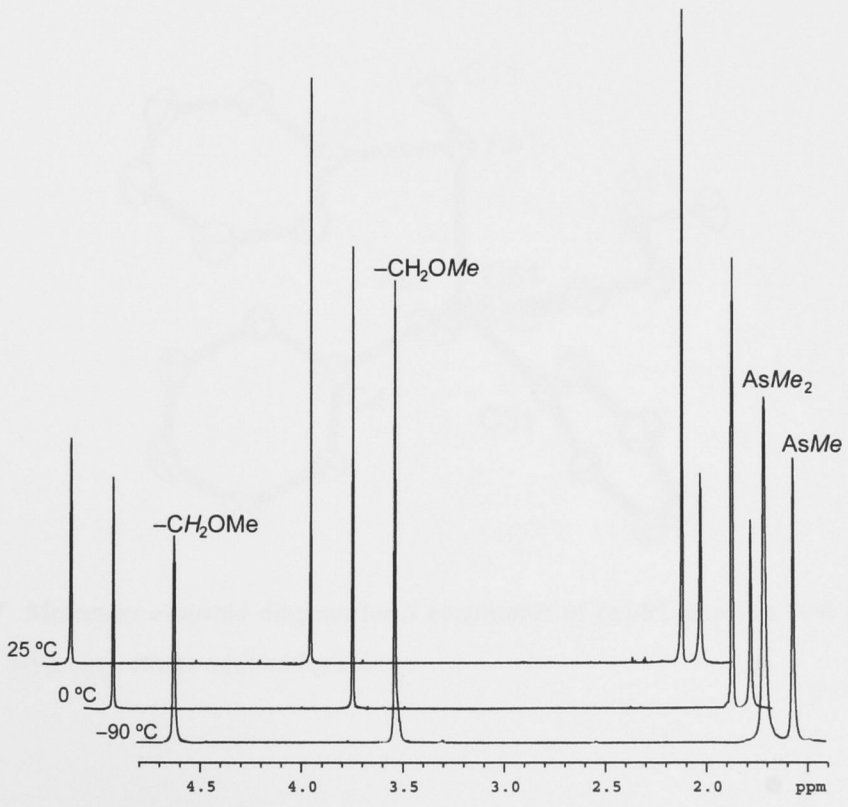


Figure 5.6 Variable temperature ^{1}H NMR spectra of (±)-**93** in dichloromethane-d_2.

5.2.4 Crystal Structures

The [2-(methoxymethyl)phenyl]diphenylarsine complex (±)-**91** crystallises as a racemic compound in the triclinic space group $P\bar{1}$ with one molecule of each enantiomer of the cation and associated anions in the unit cell (Table 5.5); the structure of the *S* enantiomer of (±)-**91** is shown in Figure 5.7 and critical bond lengths and angles are listed in Table 5.6.

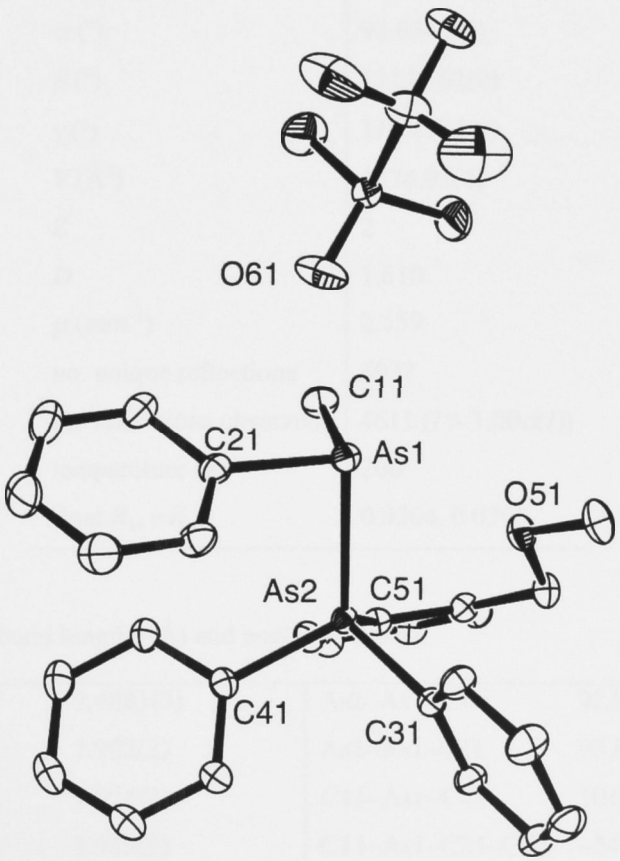


Figure 5.7 Molecular ellipsoid diagram for *S* enantiomer of (±)-**91** showing 30% probability ellipsoids. Hydrogen atoms omitted for clarity.

Table 5.5 Crystallographic and experimental details for the X-ray crystal structure analysis of (±)-**91**

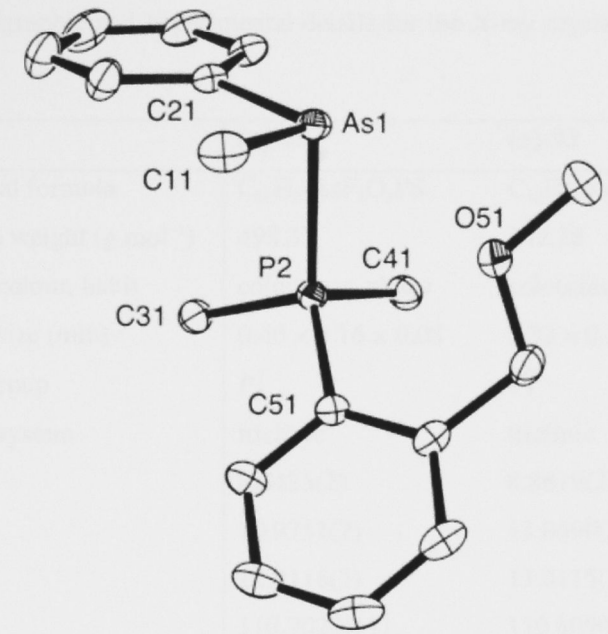
empirical formula	$C_{28}H_{27}As_2F_3O_3S$
formula weight (g mol^{-1})	666.42
crystal colour, habit	colourless, prisms
crystal size (mm)	0.20 × 0.19 × 0.16
space group	$P\bar{1}$
crystal system	triclinic
a (Å)	11.0285(5)
b (Å)	11.4661(2)
c (Å)	13.0560(2)
α (°)	93.6545(9)
β (°)	111.8762(9)
γ (°)	112.4184(9)
V (Å^3)	1374.93(4)
Z	2
D	1.610
μ (mm^{-1})	2.559
no. unique reflections	5927
no. reflections observed	4611 ($I > 3.00\sigma(I)$)
temperature (K)	200
final R_1, wR	0.0264, 0.0305

Table 5.6 Selected bond lengths (Å) and angles in (±)-**91**

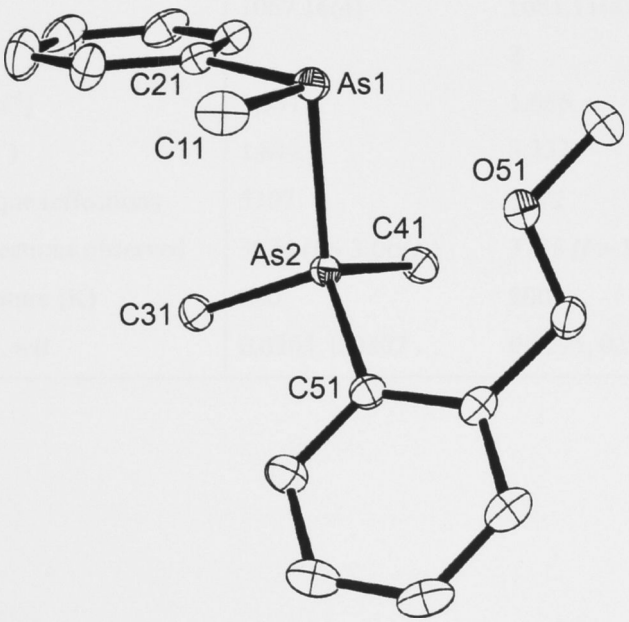
As1–As2	2.4881(3)	As2–As1–C11	92.06(7)
As1–C11	1.962(2)	As2–As1–C21	93.86(6)
As1–C21	1.954(2)	C11–As1–C21	101.45(10)
As2–C31	1.923(2)	C11–As1–C21–C22	–24.7(2)
As2–C41	1.938(2)		
As2–C51	1.941(2)		
As1···O51	3.065(2)		
As2···O51	2.855(2)		

The chelating interaction of the 2-(methoxymethyl)phenyl group results in a lengthening of the As–P bond in the model complex [({2-(MeOCH$_2$)C$_6$H$_4$}Ph$_2$P)AsMePh]PF$_6$ compared to the same bond in the triphenylphosphine adduct, 2.3703(5) Å and 2.3480(5) Å, respectively. There is also lengthening of the As–As bond from 2.4518(5) in (±)-**85** to 2.4881(3) in (±)-**91** (Table 5.2 and 5.6). The As···O distances are significantly less than the sum of the van der Waals radii for the two atoms (3.36 Å).[98] The As1–As2 bond in the cation is orthogonal to the plane containing the methyl (As2–As1–C11 = 92.06(7)°) and ipso-phenyl-*carbon* (As2–As1–C21 = 93.83(6)°) atoms.

The 2-(methoxymethyl)phenyl-substituted phosphine and arsine complexes (±)-**92** and (±)-**93** are isomorphous and crystallise as racemic compounds in the triclinic space group $P\bar{1}$ with one molecule of each enantiomer of the complex in the unit cell (Table 5.7). The structure of the *R* enantiomer of the cation of (±)-**92** and (±)-**93** are depicted in Figure 5.8; critical bond lengths and angles are listed in Table 5.8.



(a)



(b)

Figure 5.8 Molecular ellipsoid diagram for *R* enantiomer of the cation of (±)-**92** (a) and (±)-**93** (b) showing 30% probability ellipsoids. Hydrogen atoms omitted for clarity.

Table 5.7 Crystallographic and experimental details for the X-ray crystal structure analysis of (±)-**92** and (±)-**93**

	(±)-**92**	(±)-**93**
empirical formula	$C_{18}H_{23}AsF_3O_3PS$	$C_{18}H_{23}As_2F_3O_3S$
formula weight (g mol^{-1})	498.33	542.28
crystal colour, habit	colourless, plates	colourless, prisms
crystal size (mm)	0.40 × 0.16 × 0.08	0.33 × 0.27 × 0.25
space group	$P\bar{1}$	$P\bar{1}$
crystal system	triclinic	triclinic
a (Å)	8.8425(2)	8.8619(2)
b (Å)	10.9751(2)	11.0590(2)
c (Å)	12.9116(3)	13.0115(3)
α (°)	110.7028(11)	110.8090(13)
β (°)	93.8352(10)	93.8889(14)
γ (°)	110.9885(11)	111.3757(12)
V ($Å^3$)	1067.16(4)	1081.11(4)
Z	2	2
D (g cm^{-1})	1.551	1.666
μ (mm^{-1})	1.812	3.233
no. unique reflections	5107	5172
no. reflections observed	3274 ($I > 3.0\sigma(I)$)	3785 ($I > 3.0\sigma(I)$)
temperature (K)	200	200
final R_1, wR	0.0265, 0.0307	0.0275, 0.0305

Table 5.8 Selected bond lengths (Å) and angles (°) in (±)-**92** and (±)-**93**

	(±)-**92**	(±)-**93**
As1–E2	2.340(8)	2.5558(6)
As1–C11	1.965(3)	1.969(5)
As1–C21	1.953(3)	1.959(9)
E2–C31	1.790(3)	1.914(4)
E2–C41	1.792(3)	1.918(4)
E2–C51	1.794(3)	1.910(4)
As1···O51	2.947(2)	3.027(2)
E2···O51	2.965(2)	2.942(2)
E2–As1–C11	95.69(10)	94.94(14)
E2–As1–C21	96.54(8)	96.05(12)
C11–As1–C21	100.65(14)	99.9(2)
C11–As1–C21–C22	5.2(3)	4.0(4)

As observed for the parent compounds (±)-**86** and (±)-**87**, the E2–As1 distances in the 2-(methoxymethyl)phenyl-substituted compounds are longer than the sums of the covalent radii, viz. 2.3482(6) for P2–As1 and 2.4394(3) for As2–As1 compared to 2.29 Å and 2.40 Å, respectively.[108] The orthogonal coordination of the P or As donor atom to the arsenium is evident from the angles P2–As1–C11 of 97.68(8)° and P2–As1–C21 of 92.23(7)° in (±)-**92** and As2–As1–C11 of 97.25(9)° and As2–As1–C11 of 91.06(7)° in (±)-**93**. Incorporation of the 2-(methoxymethyl)phenyl group into the aryldimethyl-phosphine and -arsine ligands influences the length of the E2–As1 bonds to a lesser extent than it does for the triaryl-phosphine and -arsine ligands. The As1–P2 bond in (±)-**92** is 0.0080 Å longer than the corresponding bond in the PMe_2Ph adduct (±)-**87**. Interactions were observed between As1 and O51 at 3.027(2) Å and P2 and O51 at 2.965(2) Å in (±)-**92**. These distances are longer than the corresponding covalent distances but shorter than the sums of the corresponding van der Waals radii.[98] The As1–As2 bond in (±)-**93** of 2.4394(3) Å is 0.0054 Å *shorter* than the corresponding distance in the $AsMe_2Ph$ adduct. Interactions of the [2-($MeOCH_2$)C_6H_4]-*O* atom at

As1···O51 3.027(2) Å and As2···O51 2.942(2) in (±)-**93** place the oxygen closer to the arsenic atom of the tertiary arsine than the methylphenylarsenium ion, which could indicate that crystal packing effects are important in these complexes.

5.3 Conclusions

The first tertiary arsine-stabilised arsenium complexes have been prepared by chloride abstraction from secondary chloroarsines with trimethylsilyl triflate in the presence of tertiary arsines. The complexes have structures based on the trigonal pyramid and undergo ligand exchange in solution at faster rates than the corresponding phosphine-stabilised arsenium complexes.

Chapter 6:

Experimental

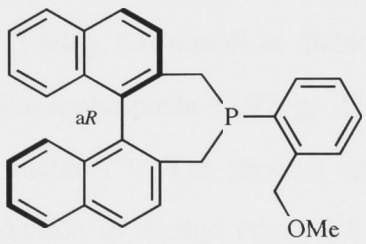
6.1 General

Reactions involving air-sensitive compounds were performed under a positive pressure of nitrogen with use of standard Schlenk techniques. Solvents were dried over appropriate drying agents and distilled before use.[134] Reaction temperatures of –78 °C and –95 °C refer, respectively, to acetone–dry ice and ethanol–liquid nitrogen slush baths. NMR spectra were recorded at 25 °C, unless otherwise stated, on Varian Mercury 300, and Inova 300 and 500 spectrometers. ^{1}H NMR chemical shifts are reported relative to residual solvent peaks; ^{31}P{^{1}H} NMR chemical shifts are quoted relative to external 85% aq. H_3PO_4 with positive shifts lying downfield of the standard. All chemical shifts (δ) are reported in parts per million (ppm). Staff within the Research School of Chemistry recorded elemental analyses and mass spectroscopic measurements. EI mass spectra were performed on a VG Autospec M series sector instrument. Optical rotations were measured on the specified solutions with a Perkin–Elmer Model 241 spectropolarimeter; specific rotations are within ±0.05 deg cm^2 g^{-1}. Melting points were measured on a Reichert Hot Stage melting point apparatus. X-ray crystallographic data were collected and the structures were solved by Dr Nathan Kilah [(R^*_{As},S^*_{As})-**64**, (±)-**85**, (±)-**86**, (±)-**87**, (±)-**91**, (±)-**92**, and (±)-**93**] and Dr Ian Cade [(S_P,S_P)(R_{As},R_{As})-**69**, (1R_C,2S_C,5R_C)- and (1S_C,2S_C,5R_C)-**76**].

6.2 Experimental: Chapter 2

The compounds dichloro[2-(methoxymethyl)phenyl]phosphine,[91] (aR_C)-**53**,[103] and iodomethylphenylarsine[135] were prepared by the literature methods. (S_C,S_C)-**27**·CH_2Cl_2[65] was synthesised by Paul Gugger of our group and had $[\alpha]_D$ +171.2 (*c* 1.0, CH_2Cl_2). *n*-Butyllithium was purchased from Aldrich Chemicals and standardised prior to use.[136]

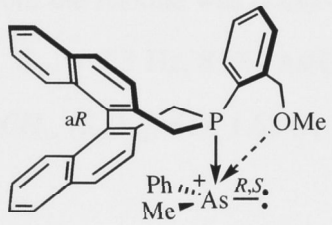
(aR_P)-(+)-4-[(2-Methoxymethyl)phenyl])-4,5-dihydro-3*H*-dinaphtho[2,1-c;1',2'-e]phosphepine, (aR_P)-45



This compound was prepared by a modified literature procedure.[96] A solution of dichloro[(2-methoxymethyl)phenyl]phosphine (2.32 g, 10.4 mmol) in *n*-hexane (25 mL) was added dropwise over 0.5 h to a suspension of the lithiated (aR_C)-**53** (4.83 g, 9.17 mmol) in *n*-hexane (50 mL) at 0 °C, and the mixture was heated under reflux overnight. The yellow suspension was cooled to room temperature and toluene (25 mL) and water (50 mL) were added. The two phases were separated and the aqueous phase was extracted with dichloromethane (4 × 30 mL). The organic layers were combined, dried over $MgSO_4$, and freed of solvent under vacuum. The crude product was recrystallised from dichloromethane–*n*-hexane to give the pure product as colourless needles: 2.40 g (60%); mp 254 °C (dec.). $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$): δ –9.66. ^1H NMR (300 MHz, $CDCl_3$) δ 2.69–3.02 (m, 4H, PCH_2), 3.43 (s, 3H, OCH_3), 4.59 (d, $^2J_{HH}$ = 11.1 Hz,

1H, CH_2OMe), 4.85 (dd, $^2J_{HH}$ = 10.8 Hz, J_{PH} = 2.7 Hz, 1H, CH_2OMe), 6.78 (m, 16H, Ar*H*).‡‡‡

(aR_P,S_{As})-(–)-{[4-(2-Methoxymethyl)phenyl]-4,5-dihydro-3*H*-dinaphtho[2,1-c;1',2'-e]phosphepine}methylphenylarsenium hexafluorophosphate, (aR_P,S_{As})-58



This complex was prepared by treatment of a solution of (aR_P)-**45** (3.00 g, 6.94 mmol) and iodomethylphenylarsine (1.94 g, 6.6 mmol) in dichloromethane (100 mL) with a solution of potassium hexafluorophosphate (4.97 g, 27 mmol) in water (100 mL) according to the published method.[81] The product gave colourless needles from dichloromethane upon the addition of diethyl ether: 4.1 g (83%); mp 155–159.0 °C. $^{31}P\{^1H\}$ NMR (202 MHz, CD_2Cl_2, –95 °C): δ 40.28 (br. s, minor, 3%), 38.81 (s, major, 97%), –144.14 (sept, $^1J_{PF}$ = 712.5 Hz, PF_6). ^1H NMR (500 MHz, CD_2Cl_2): δ 1.40 (s, 3H, AsCH_3), 2.48 (br. s, 1H, PCH_2), 3.57–3.92 (m, 3H, PCH_2), 3.71 (s, 3H, OCH_3), 4.50 (d, $^2J_{HH}$ = 12.7 Hz, 1H, H19a), 4.58 (d, $^2J_{HH}$ = 12.7 Hz, 1H, H19b), 7.04–8.27 (m, 21H, Ar*H*).‡‡‡

Enantioselective synthesis of (S_{As})-As(*n*-Bu)MePh

To a solution of (aR_P,S_{As})/(aR_P,S_{As})-**58** (ca. 10 μmol) in dichloromethane (1 mL) at –95 °C was added 1.0–1.1 equiv. of *n*-butyllithium (ca. 1.4 M in hexanes). The mixture was stirred for 5 min and then quenched with water (10 μL). The cooling bath was removed, and, once the mixture had warmed to room temperature, a suspension of

‡‡‡ Complete assignments of the 500 and 600 MHz ^1H NMR spectra were carried out by Dr E. H. Krenske.[97]

(S_C,S_C)-**27**·CH_2Cl_2 (1.3 equiv.) in dichloromethane was added. After a further 0.25 h, the solution was concentrated to a small volume and transferred to a short silica/dichloromethane column. The first fraction (excess (S_C,S_C)-**27**) was eluted with neat dichloromethane; the second fraction (mixture of (S_C,R_{As})/(S_C,S_{As})-**61** and (S_C,aR_P)-**54**) was eluted with 10% diethyl ether–dichloromethane. After evaporation of the solvent from the second fraction, the residue was dissolved in chloroform-*d*. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.74 (t, $^3J_{HH}$ = 7.3 Hz, 85%, As$(CH_2)_3CH_3$, (S_C,R_{As})-**61**), 0.91 (t, $^3J_{HH}$ = 7.3 Hz, 15%, As$(CH_2)_3CH_3$, (S_C,S_{As})-**61**), 1.62 (s, 15%, AsCH_3, (S_C,S_{As})-**61**) 1.83 (s, 85%, AsCH_3, (S_C,R_{As})-**61**).

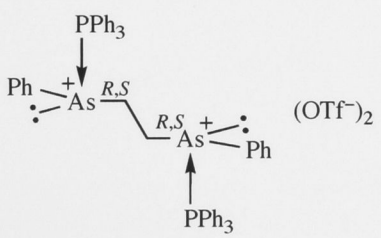
6.3 Experimental: Chapter 3

(R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62**,[50] methyldiphenylphosphine,[137] and (S_P,S_P)-**68**[110] were prepared by the literature methods. Triphenylphosphine, trimethylsilyl triflate, palladium(II) chloride, and borane dimethyl sulfide were obtained from commercial sources. Solutions of methyl- and *n*-butyllithium were purchased from Aldrich Chemicals and standardised prior to use.[136]

General procedure for preparation of bis(phosphine-stabilised) diarsenium triflates.

The tertiary phosphine (2.0–2.1 equiv) was added to a solution of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62** (1.0 equiv) in dichloromethane containing Me_3SiOTf (2.0–2.1 equiv). After ca. 0.5 h, the solvent and Me_3SiCl were removed in vacuo. The residues were dissolved in small quantities of dichloromethane and the crude products were precipitated by the addition of diethyl ether to separate them from the excess phosphine. The crude product in each case was dried and crystallised from dichloromethane–diethyl ether.

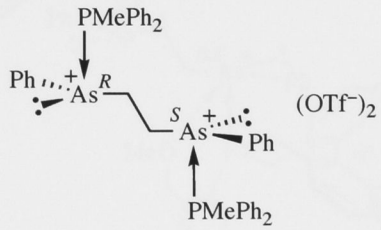
(R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-1,2-Ethanediyl*bis*[(triphenylphosphine-*P*)phenylarsenium triflate], (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-63



(R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62** (1.0 g, 2.5 mmol), PPh_3 (1.4 g, 5.2 mmol), Me_3SiOTf (1.0 mL, 5.2 mmol). Colourless prisms: 2.05 g (71%); mp 157–159 °C. Anal. Calcd

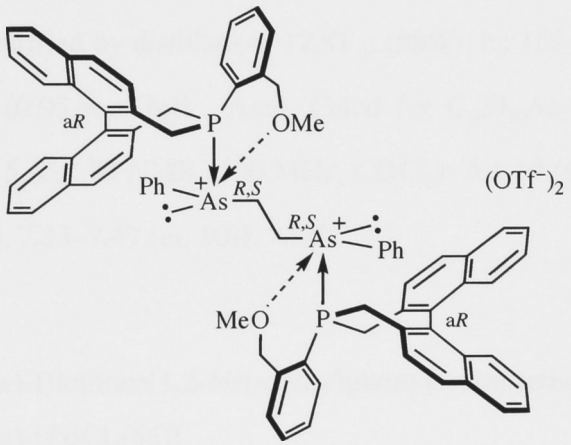
$C_{52}H_{44}As_2F_6O_6P_2S_2$: C, 54.08; H, 3.84. Found: C, 53.89; H, 3.91. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$): δ 17.45 (s). ^1H NMR (300 MHz, $CDCl_3$): δ 2.45 (br. s, 4H, AsCH_2), 6.22–7.73 (m, 40H, Ar*H*).

(R^*_{As},S^*_{As})-1,2-Ethanediyl*bis*[(methyldiphenylphosphine-*P*)phenylarsenium triflate], (R^*_{As},S^*_{As})-64



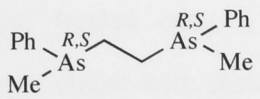
(R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62** (0.79 g, 2.0 mmol), $PMePh_2$ (0.8 g, 4.1 mmol), Me_3SiOTf (0.8 mL, 4.1 mmol). Colourless prisms: 1.58 g (77%); mp 136–138 °C. Anal. Calcd for $C_{42}H_{40}As_2F_6O_6P_2S_2$: C, 48.94; H, 3.91. Found: C, 49.21; H, 3.98. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$): δ 12.91 (s). ^1H NMR (300 MHz, $CDCl_3$): δ 2.33 (d, $^2J_{HP}$ = 13.2 Hz, 6H, PCH_3), 2.47 (br. s, 4H, AsCH_2), 7.15–7.68 (m, 30H, Ar*H*).

(aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/(aR_P)(R_{As},S_{As})(aR_P)-1,2-Ethanediyl*bis*{[(4-(2-methoxymethyl)phenyl)-4,5-dihydro-3*H*-dinaphtho(2,1-*c*;1',2'-*e*)phosphepine-*P*]phenylarsenium triflate}, (aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/ (aR_P)(R_{As},S_{As})(aR_P)-65



(R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62** (0.2 g, 0.6 mmol), (aR_P)-**45** (0.6 g, 1.2 mmol), Me_3SiOTf (0.2 mL, 1.2 mmol). Colourless needles: 0.57 g (65%); mp 240–242 °C, $[\alpha]_D^{25}$ +76 (*c* 1.0, CH_2Cl_2). Anal. Calcd for $C_{76}H_{64}As_2F_6O_8P_2S_2$: C, 61.05; H, 4.31. Found: C, 60.84; H, 4.47. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 202 MHz): δ 17.76 (s), 39.68 (s), 39.80 (s), 40.20 (s). $^{31}P\{^1H\}$ NMR (CD_2Cl_2, –95 °C, 202 MHz): 17.97 (s), 37.74 (s), 39.23 (s), 39.74 (s), 40.66 (s). ^1H NMR (CD_2Cl_2, 300 MHz): δ 1.53–2.38, 3.36–4.44 (m, 22H, aliphatic H), 6.94–8.54 (m, 42H, Ar*H*).

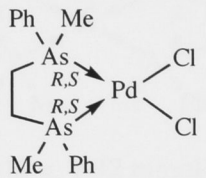
(R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-1,2-*Bis*(methylphenylarsino)ethane, (R^*_{As},R^*_{As})-(±)/ (R^*_{As},S^*_{As})-66



This compound was prepared by a modification of the literature method.[109] Methyllithium (1.6 M in diethyl ether, 63 mL) was slowly added to a solution of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62** (16.17 g, 40.0 mmol) in dry THF (300 mL) at 0 °C. The reaction mixture was stirred for 0.5 h before the unreacted methyllithium was quenched

with water (50 mL); the volatiles were removed and replaced with dichloromethane (250 mL) and water (200 mL). The organic phase was separated and the aqueous phase was extracted with dichloromethane (2 × 50 mL) and the combined organic fractions were dried ($MgSO_4$) and filtered. The solvent was removed from the filtrate to leave a cloudy oil that was purified by distillation: 12.81 g (88%); bp 158–164 °C (0.5 mmHg) [Lit.[109] 140–155 °C (0.05 mmHg)]. Anal. Calcd for $C_{16}H_{20}As_2$: C, 53.06; H, 5.57. Found: C, 52.87; H, 5.65. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.19 (s, 6H, AsCH_3), 1.69–1.85 (m, 4H, AsCH_2), 7.33–7.47 (m, 10H, Ar*H*).

[*SP*-4-(*R$_{As}$,*R**$_{As}$)]-(±)-Dichloro[1,2-*bis*(methylphenylarsino)ethane]palladium(II), [*SP*-4-(*R**$_{As}$,*R**$_{As}$)]-(±)-[$PdCl_2$(66)]**

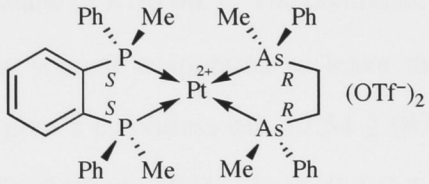


This compound was prepared by the published procedure.[58] Palladium(II) chloride (6.14 g, 34.6 mmol), lithium chloride (8.00 g, 188.7 mmol), (*R**$_{As}$,*R**$_{As}$)-(±)/(*R**$_{As}$,*S**$_{As}$)-**66** (12.57 g, 34.7 mmol). Yellow solid: 16.36 g (88%). ^{1}H NMR (300 MHz, $CDCl_3$): 1.76 (dd, $^2J_{HH}$ = 21.6 Hz, $^3J_{HH}$ = 13.8 Hz, 2H, (*R**$_{As}$,*R**$_{As}$)-C*H*HC*H*H), 2.02 (s, 6H, AsCH_3), 2.08 (s, 6H, AsCH_3), 2.24–2.34 (m, 2H, (*R**$_{As}$,*S**$_{As}$)-C*H*HC*H*H), 2.38–2.48 (m, 2H, (*R**$_{As}$,*S**$_{As}$)-CH*H*CH*H*), 2.75 (dd, $^2J_{HH}$ = 21.6 Hz, $^3J_{HH}$ = 13.8 Hz, 2H, (*R**$_{As}$,*R**$_{As}$)-CH*H*CH*H*), 7.36–7.87 (m, 20H, Ar*H*). The complex was dissolved in the minimum quantity of dichloromethane and loaded onto a silica column made up with dichloromethane; the first band was eluted with dichloromethane/THF (95/5 v/v) and contained the (*R**$_{As}$,*R**$_{As}$)-(±) diastereomer of the complex. Yellow microcrystals: 6.49 g (79%); mp 285–287 °C (dec). [Lit.[58] 287–288 °C (dec)]. ^{1}H NMR (300 MHz, $CDCl_3$): 1.76 (dd, 2H, $^2J_{HH}$ = 21.6 Hz, $^3J_{HH}$ = 13.8 Hz, C*H*HC*H*H), 2.02 (s, 6H, AsCH_3), 2.75 (dd, 2H, $^2J_{HH}$ = 21.6 Hz, $^3J_{HH}$ = 13.8 Hz, CH*H*CH*H*), 7.45–7.87 (m, 10 H, Ar*H*).

(R^*_{As},R^*_{As})-(±)-1,2-*Bis*(methylphenylarsino)ethane, (R^*_{As},R^*_{As})-(±)-66

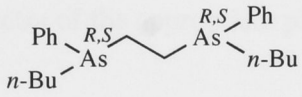
This compound was prepared by a published procedure.[58] Sodium cyanide (3.50 g, 71 mmol), (R^*_{As},R^*_{As})-(±)-[$PdCl_2$(**66**)] (6.46 g, 11.9 mmol). Colourless oil: 3.50 g (80%); bp 168–170 °C (0.2 mmHg) [Lit.[58] 156–158 °C (0.1 mmHg)]. ^{1}H NMR (300 MHz, $CDCl_3$): 1.16 (s, 6H, AsCH_3), 1.72 (dd, 2H, $^2J_{HH}$ = 6.9 Hz, $^3J_{HH}$ = 5.1 Hz, C*H*HC*H*H), 1.73 (dd, 2H $^2J_{HH}$ = 6.9 Hz, $^3J_{HH}$ = 5.1 Hz, CH*H*CH*H*) 7.26–7.44 (m, 10H, Ar*H*).

[*SP*-4-(S_P,S_P)(R_{As},R_{As})]-(+)-[1,2-*Bis*(methylphenylarsino)ethane][1,2-*bis*(methylphenylphosphino)benzene]platinum(II) triflate, [*SP*-4-(S_P,S_P)(R_{As},R_{As})]-69



A solution of (R^*_{As},R^*_{As})-(±)-**66** (0.48 g, 1.32 mmol) in dichloromethane was added to a solution of the complex (S_P,S_P)-**68** (1.03 g, 1.26 mmol) in the same solvent (10 mL). After 1 h, the volume of solution was reduced by half and diethyl ether (20 mL) was added. The mixture was stirred for 0.5 h and the colourless product was filtered off and recrystallised from methanol by the addition of diethyl ether. After two recrystallisations, configurationally pure (S_P,S_P)(R_{As},R_{As})-**69** was obtained as colourless needles: mp >350 °C; $[\alpha]_D^{25}$ +199 (*c* 1.0, CH_2Cl_2). Anal. Calcd. for $C_{38}H_{40}As_2F_6O_6P_2PtS_2$: C, 38.75; H, 3.42. Found: C, 38.75; H, 3.64. ^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2) δ 39.48 (s, $^1J_{PtP}$ = 2700 Hz). ^{1}H NMR (300 MHz, CD_2Cl_2): δ 1.52 (d, 6H, $^4J_{HP(trans)}$ = 1.8 Hz, $^3J_{HPt}$ = 16.2 Hz, AsCH_3), 1.89 (d, 6H, $^2J_{HP}$ = 11.1 Hz, $^3J_{HPt}$ = 33.9 Hz, 6 H, PCH_3), 2.22–2.35 (m, 2H, C*H*HC*H*H), 2.46–2.61 (m, 2H, CH*H*CH*H*), 7.41–7.71 (m, 24H, Ar*H*).

(R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-1,2-*Bis*(*n*-butylphenylarsino)ethane, (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-67



This compound was prepared by a modification of the literature method.[50] A solution of *n*-butyllithium (2.5 M in hexanes, 47.3 mL) was added to a solution of (R^*_{As},R^*_{As})-(±)/(R^*_{As},S^*_{As})-**62** (18.00 g, 45.0 mmol) in THF (400 mL) at 0 °C. The reaction mixture was stirred for 30 min and then the excess *n*-BuLi was quenched with water (50 mL). The solvent was evaporated from the mixture and replaced with dichloromethane (250 mL) and water (200 mL). The organic phase was separated and the aqueous phase was extracted with dichloromethane (2 × 50 mL). The combined organic fraction was dried ($MgSO_4$), filtered, and the solvent evaporated to leave the crude product that was purified by distillation to give a colourless oil: 17.54 g (87%); bp 178–181 °C (0.05 mmHg) [Lit.[50] 184–188 °C (0.06 mmHg)]. Anal. Calcd for $C_{22}H_{32}As_2$: C, 59.20; H, 7.23. Found: C, 59.26; H, 7.06. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.85 (t, 6H, $^3J_{HH}$ = 6.9 Hz, $As(CH_2)_3CH_3$), 1.27–1.44 (m, 8H, $AsCH_2(CH_2)_2$), 1.61–1.81 (m, 8H, $AsCH_2$), 7.29–7.43 (m, 10H, Ar*H*).

Asymmetric syntheses, general method

A solution of the appropriate alkyllithium reagent was added to a solution of (aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/(aR_P)(R_{As},S_{As})(aR_P)-**65** in CH_2Cl_2 (2 mL) at –95 °C. After stirring for ca. 5 min, the reaction mixture in each case was quenched with water (100 μL) and the cooling bath removed. When the reaction mixture had reached room temperature, it was dried ($MgSO_4$), filtered, and an excess of $Me_2S{\cdot}BH_3$ was added to boronate the displaced phosphine. After a further 10 min, the solution was evaporated to dryness and heated under vacuum to remove the excess $Me_2S{\cdot}BH_3$. The residue was dissolved in dichloromethane (2 mL) and a solution of (S_P,S_P)-**68** in the

same solvent (2 mL) was added. After 10 min, the solvent was removed from the solution and the stereoselectivities of the resulting diarsines were determined by recording the $^{31}P\{^{1}H\}$ NMR spectra of the appropriate platinum complexes, as described below.

Enantioselective synthesis of (R_{As},R_{As})-66

Methyllithium (1.6 M in diethyl ether, 20 μL), (aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/(aR_P)(R_{As},S_{As})(aR_P)-**65** (22.9 mg, 15.3 μmol), (S_P,S_P)-**68** (8.7 mg, 10.7 μmol). $^{31}P\{^{1}H\}$ NMR (CD_2Cl_2, 121 MHz): δ 38.58 (d, $^{3}J_{PP}$ = 11.05 Hz, 11%, (S_P,S_P)(R_{As},S_{As})-**69**), 38.91 (s, 74%, (S_P,S_P)(S_{As},S_{As})-**69**), 40.03 (s, 4%, (S_P,S_P)(R_{As},R_{As})-**69**), 40.32 (d, $^{3}J_{PP}$ = 11.05 Hz, 11%, (S_P,S_P)(R_{As},S_{As})-**69**), 43.83 (br s, (aR_P)-**45**·BH_3).

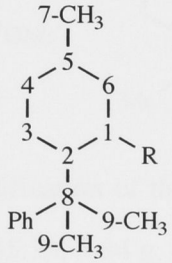
Enantioselective Synthesis of (R_{As},R_{As})-67

n-Butyllithium (1.5 M in hexanes, 20 μL), (aR_P)(R_{As},R_{As})(aR_P)/(aR_P)(S_{As},S_{As})(aR_P)/(aR_P)(R_{As},S_{As})(aR_P)-**65** (19.15 mg, 12.8 μmol), (S_P,S_P)-**68** (8.7 mg, 10.4 μmol). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 121 MHz): δ 37.86 (s, 72%, (S_P,S_P)(S_{As},S_{As})-**70**), 38.16 (d, $^{3}J_{PP}$ = 10.90 Hz, 11.5%, (S_P,S_P)(R_{As},S_{As})-**70**), 38.42 (d, $^{3}J_{PP}$ = 10.90 Hz, 11.5%, (S_P,S_P)(R_{As},S_{As})-**70**), 39.58 (s, 5%, (S_P,S_P)(R_{As},R_{As})-**70**), 42.70 (br s, (aR_P)-**45**·BH_3).

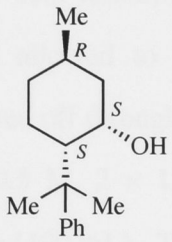
6.4 Experimental: Chapter 4

The compounds *trans,cis*-**72** (85:15),[113] ($1R_C,2S_C,5R_C$)-/($1S_C,2R_C,5R_C$)-**71** (85:15),[113] and ($1S_C,2S_C,5R_C$)-**73**[118] were prepared by the literature methods. [K(dioxane)$_2$]PPh$_2$ was synthesised by Paul Gugger of our group according to the literature procedure.[138] (R_C)-(+)-Pulegone, L-Selectride®, triethylamine, pyridine, and borane dimethyl sulfide were obtained from Aldrich Chemicals.

The following numbering is used in the ^{1}H NMR spectroscopic assignments:



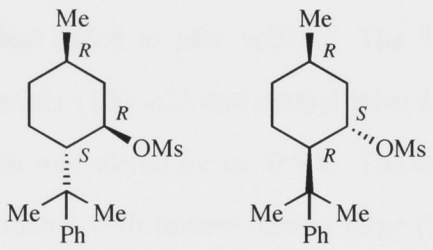
($1S_C,2S_C,5R_C$)-(+)-8-Phenyl*neo*menthol, ($1S_C,2S_C,5R_C$)-71



This compound was prepared by a modification of the literature method.[118] To a solution of L-Selectride® (1M in THF, 100 mL) at 0 °C was added dropwise, by syringe, a solution of *trans,cis*-**72** (85:15, 15.36 g, 66.7 mmol) in THF (60 mL). The reaction mixture was stirred at this temperature for 4 h prior to the addition of an aqueous solution of NaOH (3.0 M, 36 mL) followed by the dropwise addition of H_2O_2 (30%, 36 mL). The solution was then warmed to room temperature, and extracted with diethyl ether (5 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered and

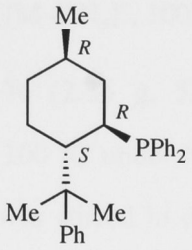
freed of solvent leaving a pale yellow oil that was distilled to give ($1S_C$,$2S_C$,$5R_C$)-**71** as a colourless oil: 12.06 g (84%); bp 120–122 °C (0.1 mmHg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.81 (d, $^3J_{HH}$ = 5.7 Hz, 3H, 7-CH_3) 0.83 –1.78 (m, 8H, aliphatic-*H*), 1.36 (s, 3H, 9-CH_3), 1.38 (s, 3H, 9-CH_3), 3.83 (br. apparent singlet, 1H, 1-C*H*), 7.16–7.38 (m, 5H, Ar*H*).

($1R_C$,$2S_C$,$5R_C$)-8-phenylmenthyl methanesulfonate/($1S_C$,$2R_C$,$5R_C$)-8-phenyl*iso*-menthyl methanesulfonate (85:15), ($1R_C$,$2S_C$,$5R_C$)/($1S_C$,$2R_C$,$5R_C$)-73 (85:15)



The mixture was prepared by a modification of the literature method.[118] To a solution of ($1R_C$,$2S_C$,$5R_C$)/($1S_C$,$2R_C$,$5R_C$)-**71** (85:15, 9.84 g, 42.3 mmol) and triethylamine (23.61 mL, 169.2 mmol) in diethyl ether (40 mL) at –10 °C was added dropwise methanesulfonyl chloride (4.92 mL, 63.5 mmol). The suspension was stirred at this temperature for 2 h before being allowed to warm to room temperature. The triethylammonium chloride was filtered off through a pad of $MgSO_4$ and the filtrate was washed with dilute HCl solution (0.5 M, 2 × 150 mL), water (100 mL), saturated Na_2CO_3 solution (100 mL), and brine (100 mL). The organic layer was dried ($MgSO_4$), filtered, and freed of solvent to give the product as a pale pink oil: 10.13 g (77%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86–2.42 (m, aliphatic-*H*, 8H), 0.95, 0.98 (overlapping doublets, $^3J_{HH}$ = 6.3 Hz (major), 3H, 7-CH_3), 1.28 (s, 3H, 9-CH_3), 1.47 (s, 3H, 9-CH_3), 2.53 (s, 3H, SCH_3) 4.78 (apparent dt, $^3J_{HH}$ = 10.5 Hz, $^3J_{HH}$ = 4.2 Hz, 0.9H, ($1R_C$,$2S_C$,$5R_C$)-1-C*H*), 4.83–4.87 (m, 0.1H, ($1S_C$,$2R_C$,$5R_C$)-1-C*H*), 7.15–7.39 (m, 5H, Ar*H*).

($1R_C$,$2S_C$,$5R_C$)-(–)-8-Phenylmenthyldiphenylphosphine, ($1R_C$,$2S_C$,$5R_C$)-74

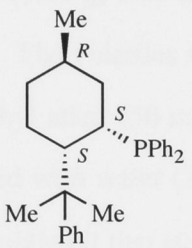


To a suspension of $[K(dioxane)_2]PPh_2$ (11.40 g, 28.47 mmol) in dry THF (100 mL) was added dropwise a solution of ($1S_C$,$2S_C$,$5R_C$)-**73** (8.89 g, 28.46 mmol) in the same solvent (50 mL). The mixture was stirred at room temperature for 48 h, until the deep orange colour of the phosphide had faded to pale yellow. The THF was then removed in vacuo, and deoxygenated water (100 mL) and diethyl ether (100 mL) were added. The resulting two-phase mixture was stirred for ca. 0.5 h. The organic layer was collected, the aqueous layer was extracted with further diethyl ether (3 × 40 mL); the combined organic fractions were dried ($MgSO_4$), filtered, and freed of solvent leaving a cloudy oil (10.10 g). The oil was transferred to a 25 mL distillation apparatus and the elimination by-products, diphenylphosphine and *trans*-**75**, were isolated as a single fraction: 5.96 g, bp 120–130 °C (0.35 mmHg). A solution of the residues (4.08 g) in THF (50 mL) was transferred to a 100 mL Schlenk flask and cooled to 0 °C; an excess of borane dimethyl sulfide (1.10 mL, 12.6 mmol) was then added dropwise and the solution was stirred for 2 h at this temperature before allowing to warm to room temperature. The solvent and unreacted borane dimethyl sulfide were removed in vacuo and then the flask was warmed under vacuum for ca. 1 h. The crude product was crystallised from dichloromethane by the addition of ethanol to give colourless plates of ($1R_C$,$2S_C$,$5R_C$)-**76**: 2.54 g (21%, from ($1S_C$,$2S_C$,$5R_C$)-**73**); mp 157–159 °C; $[\alpha]_D^{25}$ +101 (*c* 1.0, CH_2Cl_2). Anal. Calcd for $C_{28}H_{36}BP$: C, 81.16; H, 8.76. Found: C, 81.15; H, 8.78. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$) δ 24.93 (br. d, $^1J_{BP}$ = 59.3 Hz). $^{11}B\{^1H\}$ NMR (96 MHz, $CDCl_3$) δ –42.44 (br. s). ^1H NMR (300 MHz, $CDCl_3$) δ 0.52 (s, 3H, 9-CH_3), 0.78 (d, $^3J_{HH}$ = 6 Hz, 3H, 7-CH_3), 0.99–1.17 (m, 4H, aliphatic-*H*), 1.24 (s, 3H, 9-CH_3), 1.38–1.73 (m, 6H,

aliphatic-*H*, B*H*$_3$) 2.33–2.46 (m, 1H, 2-C*H*), 2.87–2.98 (m, 1H, 1-C*H*), 7.14–8.01 (m, 15H, Ar*H*). EI MS: *m/z* 400.2 amu ([M–BH$_3$]$^+$, 100).

The borane adduct (1R_C,2S_C,5R_C)-**76** (2.36 g, 5.69 mmol) was suspended in dry morpholine (35 mL) and heated to 100 °C under N_2 for 3 h. The volatiles were then removed in vacuo and the residue was stirred in deoxygenated diethyl ether (50 mL) and water (50 mL) for ca. 0.5 h. The organic layer was washed with further water (3 × 50 mL), dried ($MgSO_4$), filtered, and freed of solvent leaving an immobile oil that partially solidified: 1.54 g (68%); $[\alpha]_D^{25}$ –26 (*c* 0.98, CH_2Cl_2). Anal. Calcd for $C_{28}H_{33}P$: C, 83.96; H, 8.30. Found: C, 84.12; H, 8.24. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$) δ –1.20 (s). ^1H NMR (300 MHz, $CDCl_3$) δ 0.65 (d, $^3J_{HH}$ = 6.1 Hz, 3H, 7-CH_3), 0.72–0.87 (m, 2H, 3C*H*, 6C*H*), 1.09–1.23 (m, 2H, 4-C*H*, 5-C*H*), 1.27 (s, 3H, 9-CH_3), 1.54 (s, 3H, 9-CH_3), 1.69–1.74 (m, 3H, 3-C*H*, 4-C*H*, 6-C*H*), 1.82–1.91 (m, 1H, 2-C*H*), 2.00–2.08 (m, 1H, 1-C*H*), 6.98–7.31 (m, 15H, Ar*H*). EI MS: *m/z* 400.2 amu ([M]$^+$, 100).

(1S_C,2S_C,5R_C)-(+)-8-Phenyl*neo*menthyldiphenylphosphine, (1S_C,2S_C,5R_C)-74



A solution of (1R_C,2S_C,5R_C)/(1S_C,2R_C,5R_C)-**73** (85:15, 10.13 g, 32.60 mmol) in THF (50 mL) was added dropwise to a suspension of [K(dioxane)$_2$]PPh_2 (13.10 g, 32.70 mmol) in dry THF (100 mL). The mixture was stirred at room temperature for 7 days; the THF was then removed in vacuo, deoxygenated water (100 mL) and diethyl ether (100 mL) added, and the resulting two-phase mixture stirred for ca. 0.5 h. The organic layer was separated, the aqueous layer extracted with diethyl ether (3 × 40 mL); the combined organic fractions were dried ($MgSO_4$), filtered, and freed of solvent leaving a cloudy oil (12.87 g) that was transferred to a 25 mL distillation apparatus. The elimination by-

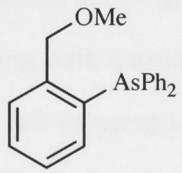
products, diphenylphosphine and *cis,trans*-**75**, were isolated as a single fraction: 10.76 g, bp 119–134 °C (0.35 mmHg). To a solution of the residues (2.09 g) in THF (50 mL) at 0 °C, was added dropwise an excess of borane dimethyl sulfide (0.80 mL, 9.15 mmol), the solution was stirred for 2 h at this temperature and overnight at room temperature. The solvent and unreacted borane dimethyl sulfide were removed in vacuo, and the flask was then warmed under vacuum for ca. 1 h. The crude product was crystallised from dichloromethane by the addition of ethanol to give colourless plates of ($1S_C$,$2S_C$,$5R_C$)-**76**: 1.27 g (9.4%, from ($1R_C$,$2S_C$,$5R_C$)/($1S_C$,$2R_C$,$5R_C$)-**73**); mp 156–158 °C; $[\alpha]_D^{25}$ +106 (*c* 1.0, CH_2Cl_2). Anal. Calcd for $C_{28}H_{36}BP$: C, 81.16; H, 8.76. Found: C, 81.19; H, 8.64. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$) δ 14.23 (br. s). $^{11}B\{^1H\}$ NMR (96 MHz, $CDCl_3$) δ –36.12 (br. s). ^1H NMR (300 MHz, $CDCl_3$) δ 0.58 (d, $^3J_{HH}$ = 6.1 Hz, 3H, 7-C*H*$_3$), 0.95–1.31 (m, 3H, aliphatic-*H*), 1.11 (s, 3H, 9-C*H*$_3$), 1.12 (s, 3H, 9-C*H*$_3$), 1.37 (br. s, 3H, B*H*$_3$), 1.64–1.70 (m, 2H, 4-C*H*, 6-C*H*), 2.00–2.04 (m, 1H, 3-C*H*), 2.14–2.27 (m, 1H, 5-C*H*), 2.44–2.57 (m, 1H, 2-C*H*), 3.15 (br. apparent doublet, $^2J_{PH}$ = 15 Hz, 1H, 1-C*H*), 6.94–7.77 (m, 15H, Ar*H*). EI MS: *m/z* 400.2 amu ([M–BH_3]$^+$, 100).

The borane adduct ($1S_C$,$2S_C$,$5R_C$)-**76** (1.60 g, 3.86 mmol) was heated in dry morpholine (30 mL) at 100 °C under N_2 for 3 h. The volatiles were then removed in vacuo and the residue stirred in deoxygenated diethyl ether (50 mL) and water (50 mL) for ca. 0.5 h. The organic layer was further washed with water (3 × 50 mL), dried ($MgSO_4$), filtered, and freed of solvent leaving an immobile oil that slowly crystallised on standing: 1.51 g (97%); mp 63–66 °C; $[\alpha]_D^{25}$ +118 (*c* 0.91, CH_2Cl_2). Anal. Calcd for $C_{28}H_{33}P$: C, 83.96; H, 8.30. Found: C, 83.98; H, 8.27. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$) δ –11.41 (s). ^1H NMR (300 MHz, $CDCl_3$) δ 0.32 (d, $^3J_{HH}$ = 6.0 Hz, 3H, 7-C*H*$_3$), 0.71–0.83 (m, 1H, 4-C*H*), 0.90 (apparent singlet, 1H, 5-C*H*), 1.07–1.19 (m, 1H, 6-C*H*), 1.23 (s, 3H, 9-C*H*$_3$), 1.31 (s, 3H, 9-C*H*$_3$), 1.54–1.63 (overlapping apparent singlets, 3H, 3-C*H*, 4-C*H*, 6-C*H*), 1.77–1.89 (m, 1H, 3-C*H*), 2.01–2.13 (m, 1H, 2-C*H*), 2.69 (apparent singlet, 1H, 1-C*H*), 6.71–7.95 (m, 15H, Ar*H*). EI MS: *m/z* 400.2 amu ([M]$^+$, 100).

6.5 Experimental: Chapter 5

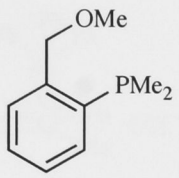
The compounds iododiphenylarsine,[139] 1-bromo-2-(methoxymethyl)benzene,[140] chloromethylphenylarsine,[141] dimethylphenylphosphine,[142] dimethylphenylarsine,[143] and [2-(methoxymethyl)phenyl]dimethylarsine[99] were prepared by the literature methods.

[2-(Methoxymethyl)phenyl]diphenylarsine, 88



Iododiphenylarsine (10.36 g, 29.1 mmol) in THF (30 mL) was added to a cooled solution of the Grignard reagent (0 °C) prepared from magnesium turnings (0.86 g, 35.2 mmol) and 1-bromo-2-(methoxymethyl)benzene (6.44 g, 32.0 mmol) in THF (20 mL). After the addition, the reaction mixture was heated under reflux for 1 h. The THF was removed in vacuo from the cooled solution and diethyl ether (50 mL) was added to the residue, followed by saturated aqueous ammonium chloride (25 mL). The two-phase mixture was left to warm to room temperature before the phases were separated. The aqueous phase was extracted with diethyl ether (2 x 50 mL) and the combined organic fraction was dried ($MgSO_4$), filtered, and the solvent removed from the filtrate to leave a pale yellow solid that crystallised from hot ethanol as colourless needles: 7.52 g (74%); mp 84–86 °C. Anal. Calcd for $C_{20}H_{19}AsO$: C, 68.58; H, 5.47. Found: C, 68.22; H, 5.18. ^{1}H NMR (300 MHz, $CDCl_3$) 3.23 (s, 3H, OC*H*$_3$), 4.60 (s, 2H, C*H*$_2$), 7.00–7.46 (m, 14H, Ar*H*). EI MS: *m/z* 350 ([M]$^+$), 241 amu ([M – MeOPh]$^+$).

[2-(Methoxymethyl)phenyl]dimethylphosphine, 90

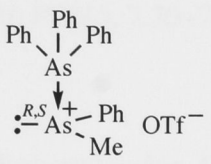


Dichloro[2-(methoxymethyl)phenyl]phosphine (3.06 g, 13.7 mmol) in diethyl ether (25 mL) was added to a solution (0 °C) of the Grignard reagent prepared from magnesium turnings (0.81 g, 33.2 mmol) and iodomethane (1.90 mL, 30.2 mmol). After the addition, the reaction mixture was heated under reflux for 0.5 h. The mixture was then cooled to 0 °C and treated with stirring with a saturated aqueous solution of ammonium chloride (25 mL). The mixture was left to warm to room temperature and then the two phases were separated. The aqueous phase was extracted with diethyl ether (2 x 50 mL); the combined organic fraction was dried ($MgSO_4$), filtered, and the solvent removed in vacuo to leave an oil that was distilled: 1.78 g (70%); bp 78 °C (0.7 mmHg). Anal. Calcd for $C_{10}H_{15}OP$: C, 65.92; H, 8.30. Found: C, 66.03; H, 8.38. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$) –58.04 (s). ^1H NMR (300 MHz, $CDCl_3$) 1.18 (d, $^2J_{HP}$ = 3.30 Hz, 6H, PCH_3), 3.32 (s, 3H, OCH_3), 4.60 (s, 2H, CH_2), 7.21–7.40 (m, 4H, Ar*H*). EI MS: *m/z* 183 amu ($[M]^+$).

General procedure for preparation of phosphine- and arsine-stabilised arsenium triflates.

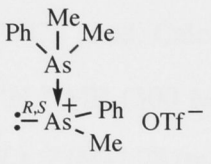
The tertiary phosphine or arsine (1.1 equiv.) was added to a solution of chloromethylphenylarsine (1.0 equiv.) containing Me_3SiOTf (1.1 equiv.). After ca. 0.5 h, the solvent and Me_3SiCl were removed in vacuo. The residues were redissolved in small quantities of dichloromethane and precipitated by the addition of diethyl ether to remove the small excesses of arsine or phosphine. The product in each case was dried and crystallised from dichloromethane–diethyl ether.

(±)-(Triphenylarsine-*As*)methylphenylarsenium Triflate, (±)-85



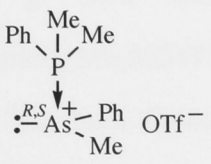
Chloromethylphenylarsine (1.36 g, 6.72 mmol), triphenylarsine (2.26 g, 7.39 mmol), Me_3SiOTf (1.34 mL, 7.39 mmol). Colourless prisms: 2.26 g (51%); mp 135–137 °C. Anal. Calcd for $C_{26}H_{23}As_2F_3O_3S$: C, 50.18; H, 3.72. Found: C, 50.18; H, 3.75. ^1H NMR (300 MHz, $CDCl_3$) 1.90 (s, 3H, As^+CH_3), 7.27–7.65 (m, 20H, Ar*H*).

(±)-(Dimethylphenylarsine-*As*)methylphenylarsenium Triflate, (±)-86



Chloromethylphenylarsine (1.10 g, 5.43 mmol), dimethylphenylarsine (1.12 g, 6.15 mmol), Me_3SiOTf (1.08 mL, 5.97 mmol). Colourless needles: 2.22 g (75%); mp 104–107 °C. Anal. Calcd for $C_{16}H_{19}As_2F_3O_3S$: C, 38.57; H, 3.84. Found: C, 38.25; H, 4.21. ^1H NMR (300 MHz, CD_2Cl_2) 1.79 (s, 3H, As^+CH_3), 2.04 (s, 6H, $AsCH_3$), 7.25–7.55 (m, 10H, Ar*H*).

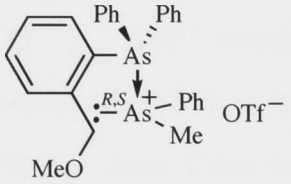
(±)-(Dimethylphenylphosphine-*P*)methylphenylarsenium Triflate, (±)-87



Chloromethylphenylarsine (1.20 g, 5.93 mmol), dimethylphenylphosphine (0.95 g, 6.88 mmol), Me_3SiOTf (1.18 mL, 6.52 mmol). Colourless prisms: 2.29 g (85%); mp 93–94 °C. Anal. Calcd for $C_{16}H_{19}AsF_3O_3PS$: C, 42.30; H, 4.22. Found: C, 42.42; H, 4.16.

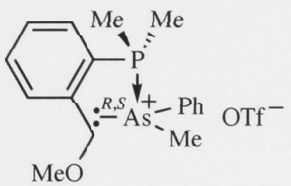
$^{31}P\{^{1}H\}$ NMR (121 MHz, $CDCl_3$) 8.89 (s). ^{1}H NMR (300 MHz, CD_2Cl_2) 1.68 (s, 3H, $As^{+}CH_3$), 2.13 (d, $^{2}J_{HP}$ = 13.2 Hz, 6H, PCH_3), 7.30–7.74 (m, 10H, Ar*H*).

(±)-[(2-{Methoxymethyl}phenyl)diphenylarsine-*As*]-methylphenylarsenium Triflate, (±)-91



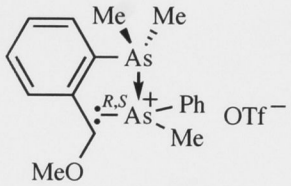
Chloromethylphenylarsine (1.14 g, 5.63 mmol), [2-(methoxymethyl)phenyl]-diphenylarsine (2.17 g, 6.19 mmol), Me_3SiOTf (1.13 mL, 6.19 mmol). Colourless prisms: 2.48 g (66%); mp 104–107 °C. Anal. Calcd for $C_{28}H_{27}As_2F_3O_4S$: C, 50.47; H, 4.08. Found: C, 50.40; H, 4.32. ^{1}H NMR (300 MHz, $CDCl_3$) 1.93 (s, 3H, $As^{+}CH_3$), 3.15 (s, 3H, OCH_3), 4.53 (s, 2H, CH_2), 7.09–7.78 (m, 19H, Ar*H*).

(±)-[(2-{Methoxymethyl}phenyl)dimethylphosphine-*P*]-methylphenylarsenium Triflate, (±)-92



Chloromethylphenylarsine (1.20 g, 5.93 mmol), [2-(methoxymethyl)phenyl]-dimethylphosphine (1.28 g, 7.03 mmol), Me_3SiOTf (1.28 mL, 7.03 mmol). Colourless plates: 2.13 g (72%); mp 107–108 °C. Anal. Calcd for $C_{18}H_{23}AsF_3O_3PS$: C, 43.38; H, 4.65. Found: C, 43.46; H, 4.70. $^{31}P\{^{1}H\}$ (121 MHz; CD_2Cl_2) 9.59 (s). ^{1}H NMR (300 MHz, CD_2Cl_2) 1.60 (d, $^{3}J_{HP}$ = 16.8 Hz, 3H, $As^{+}CH_3$), 1.97 (d, $^{2}J_{HP}$ = 13.2 Hz, 3H, PCH_3), 2.04 (d, $^{2}J_{HP}$ = 12.9 Hz, 3H, PCH_3), 3.51 (s, 3H, OCH_3), 4.57 (d, $^{2}J_{HH}$ = 12.6 Hz, 1H, CH_2), 4.63 (d, $^{2}J_{HH}$ = 12.6 Hz, 1H, CH_2), 7.31–7.86 (m, 9H, Ar*H*).

(±)-[(2-{Methoxymethyl}phenyl)dimethylarsine-*As*]-methylphenylarsenium Triflate, (±)-93



Chloromethylphenylarsine (1.33 g, 6.57 mmol), [2-(methoxymethyl)phenyl]-dimethylarsine (1.72 g, 6.71 mmol), Me_3SiOTf (1.31 mL, 7.23 mmol). Colourless prisms: 2.81 g (79%); mp 97–98 °C. Anal. Calcd for $C_{18}H_{23}As_2F_3O_4S$: C, 39.87; H, 4.28. Found: C, 39.46; H, 4.49. ^1H NMR (300 MHz, CD_2Cl_2) 1.75 (s, 3H, As^+CH_3), 1.84 (s, 6H, $AsCH_3$), 3.56 (s, 3H, OCH_3), 4.67 (s, 2H, CH_2), 7.28–7.59 (m, 9H, Ar*H*).

Appendices

Appendix 1

Table A1 The observed de ($^{31}P\{^1H\}$ NMR, CD_2Cl_2) of (aR_P,R_{As})/(aR_P,S_{As})-**58**

Temp. (°C)	Sample 1[a]	Sample 2	Sample 3	Mean	Std Dev.
0	66.18	65.56	67.18	66.307	0.667
–10	67.92	65.32	66.79	66.677	1.064
–20	68.83	69.77	69.21	69.270	0.386
–30	69.75	68.67	69.44	69.287	0.454
–40	71.49	72.67	71.65	71.937	0.523
–50	75.61	74.53	74.18	74.773	0.609
–60	80.05	76.94	78.26	78.417	1.274
–70	82.69	83.08	82.52	82.763	0.234
–80	85.97	87.11	86.89	86.657	0.494
–95	91.04	93.60	94.20	93.960	0.259

[a]Average of three integrals for each sample, at each temperature.

Table A2 The observed de (^1H NMR, $CDCl_3$) of (S_C,R_{As})/(S_C,S_{As})-**61**, corresponding to the ee of the arsine formed from the addition of *n*-BuLi to a CH_2Cl_2 solution of (aR_P,R_{As})/(aR_P,S_{As})-**58**

Temp. (°C)	Sample 1[a]	Sample 2	Sample 3	Mean	Std Dev.
–10	42.80	39.15	36.64	39.530	2.529
–20	42.91	40.61	41.87	41.800	0.940
–30	51.20	49.06	47.20	49.153	1.634
–40	55.12	56.00	57.24	56.120	0.870
–50	60.12	60.64	59.98	60.247	0.284
–60	60.47	62.78	61.41	61.553	0.948
–70	64.83	64.52	64.34	64.563	0.202
–80	67.46	69.87	68.61	68.647	0.984
–95	69.80	70.20	70.04	70.013	0.164
–103	70.70	68.64	70.10	69.813	0.866

[a]Average of three integrals for each sample, at each temperature.

Appendix 2

Figure A1 The aliphatic region of the COSY spectrum of (1R_C,2S_C,5R_C)-**74** ($CDCl_3$, 500MHz).

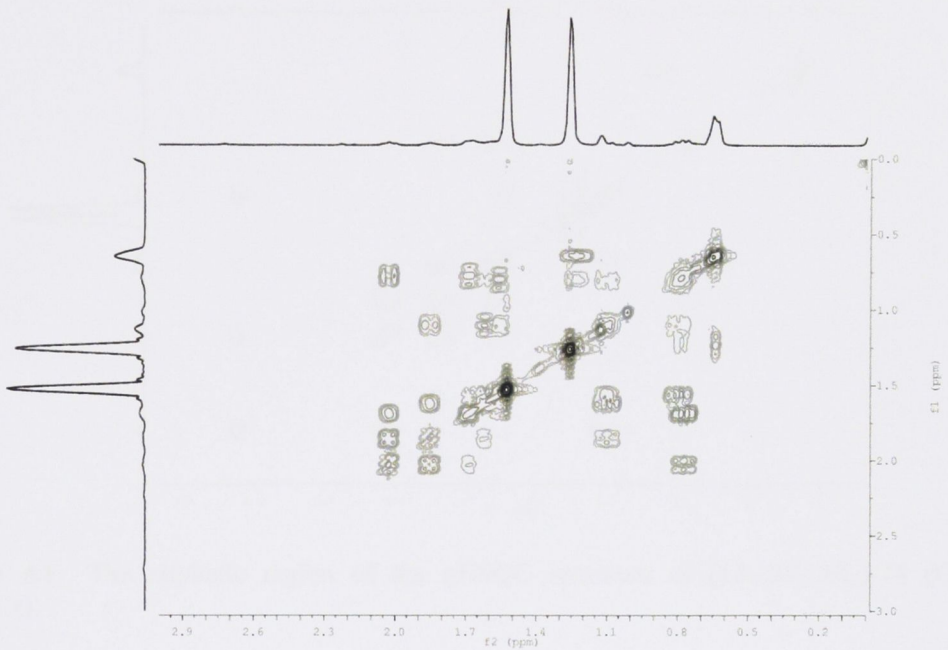


Figure A2 The aliphatic region of the gHSQC spectrum of (1R_C,2S_C,5R_C)-**74** ($CDCl_3$, 500MHz).

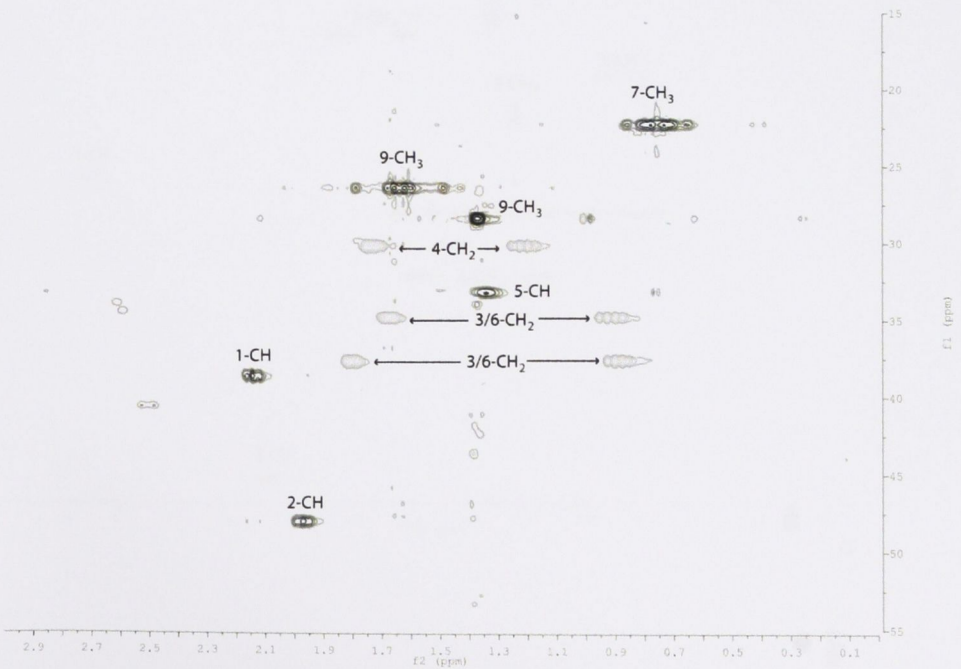


Figure A3 The aliphatic region of the COSY spectrum of ($1R_C$,$2S_C$,$5R_C$)-**74** ($CDCl_3$, 500MHz).

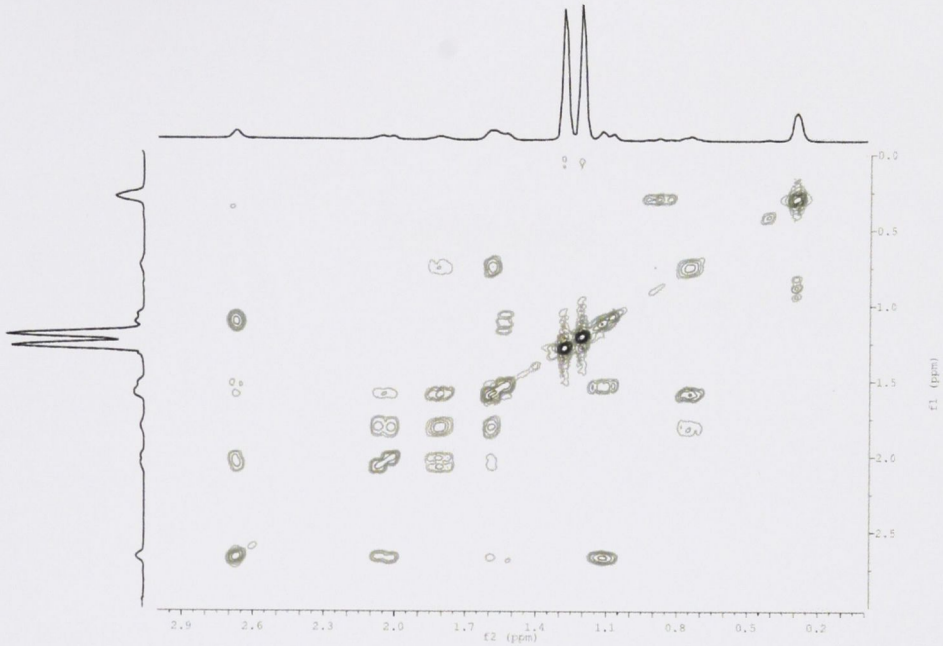
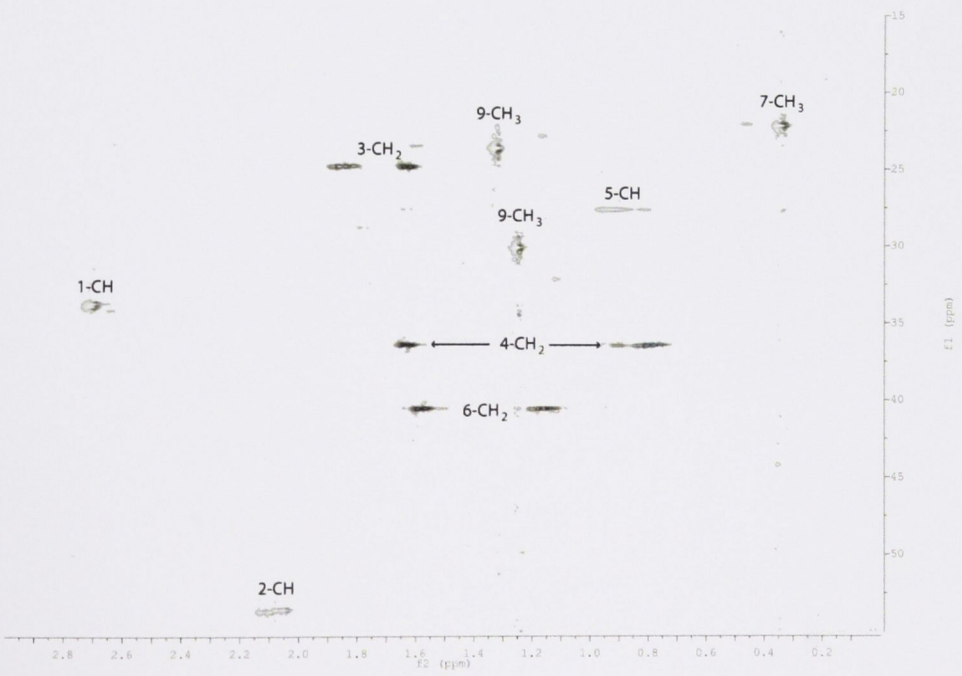


Figure A4 The aliphatic region of the gHSQC spectrum of ($1R_C$,$2S_C$,$5R_C$)-**74** ($CDCl_3$, 500MHz).



References

(1) Pope, W. J.; Peachy, S. J. *J. Chem. Soc.* **1899**, 1127–1131.

(2) Kumli, K. F.; McEwen, W. E.; Vander Werf, C. A. *J. Am. Chem. Soc.* **1958**, *81*, 248–249.

(3) Horner, L.; Mentrup, A. *Liebigs Ann. Chem.* **1961**, *81*, 248–249.

(4) Horner, L.; Fuchs, H.; Winkler, H.; Rapp, A. *Tetrahedron Lett.* **1963**, 965–967.

(5) Horner, L.; Fuchs, H. *Tetrahedron Lett.* **1962**, 203–204.

(6) Wild, S. B. In *The Chemistry of Organic Arsenic, Antimony and Bismuth Compounds*; Patai, S., Ed.; John Wiley and Sons, Inc.: Chichester, 1994; Vol. 1, pp 89–152.

(7) Eliel, E. H.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; John Wiley and Sons, Inc.: New York, 1994.

(8) Davis, F. A.; Jenkins, R. H., Jr. In *Asymmetric Synthesis*; Morrison, J. D., Scott, J. W., Eds.; Academic Press: Orlando, 1984; Vol. 4, pp 313–353.

(9) Baechler, R. D.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 3090–3093.

(10) Senkler, J., G. H; Mislow, K. *J. Am. Chem. Soc.* **1972**, *94*, 291.

(11) Horner, L.; Siegel, H.; Büthe, H. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 942.

(12) Knowles, W. S.; Sabacky, M. J. *J. Chem. Soc., Chem. Commun.* **1968**, 1445.

(13) Osborn, J. A.; Jardine, F. H.; Wilkinson, G. *J. Chem. Soc. (A)* **1966**, 1711–1732.

(14) Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D. *J. Chem. Soc., Chem. Commun.* **1972**, 10–11.

(15) Horner, L.; Schlotthauer, B. *Phosphorus Relat. Group V Elem.* **1978**, *4*, 155–165.

(16) Morrison, J. D.; Burnett, R. E.; Aguiar, A. M.; Morrow, C. J.; Phillips, C. *J. Am. Chem. Soc.* **1971**, *93*, 1301–1303.

(17) van Leeuwan, P. W. N. M.; Kramer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741–2769.

(18) Kagan, H. B.; Dang, T. P. *J. Am. Chem. Soc.* **1972**, *94*, 6492–6433.

(19) Fryzuk, M. D.; Bosnich, B. *J. Am. Chem. Soc.* **1977**, *99*, 6262–6267.

(20) Miyashita, M.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932–7934.

(21) Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8518–8519.

(22) Tongi, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062–4066.

(23) Grabulosa, A.; Grandell, J.; Muller, G. *Coord. Chem. Rev.* **2007**, *251*, 25–90.

(24) Crèpy, K. V. L.; Imamoto, T. In *New Aspects in Phosphorus Chemistry III*; Majoral, J.-P., Ed.; Springer: Heidelberg, 2003; Vol. 229, pp 1–40.

(25) Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946–5952.

(26) Gridnev, I. D.; Yamanoi, Y.; Higashi, N.; Tsuruta, H.; Yasutake, M.; Imamoto, T. *Adv. Synth. Catal.* **2001**, *343*, 118–136.

(27) Calhoun, A. D.; Kobos, W. J.; Nile, T. A.; Smith, C. A. *J. Organomet. Chem.* **1979**, *170*, 175–179.

(28) Kojima, A.; Boden, C. D. J.; Shibasaki, M. *Tetrahedron Lett.* **1997**, *38*, 3459–3460.

(29) Allen, D. G.; Wild, S. B.; Wood, D. L. *Organometallics* **1986**, *5*, 1009–1015.

(30) Mokhlesur Rahman, A. F. M. M.; Wild, S. B. *J. Mol. Catal.* **1987**, *39*, 155–160.

(31) Wild, S. B. *Coord. Chem. Rev.* **1997**, *166*, 291–311.

(32) Burrows, G. J.; Turner, E. E. *J. Chem. Soc.* **1921**, 426–437.

(33) Mann, F. G. *J. Chem. Soc.* **1945**, 65–73.

(34) Mills, W. H.; Raper, R. *J. Chem. Soc.* **1925**, 2479–2483.

(35) Lesslie, M. S.; Turner, E. E. *J. Chem. Soc.* **1934**, 1170–1174.

(36) Lesslie, M. S.; Turner, E. E. *J. Chem. Soc.* **1935**, 1051–1052.

(37) Mislow, K.; Zimmerman, A.; Melillo, J. T. *J. Am. Chem. Soc.* **1963**, *85*, 594–597.

(38) Gatilov, Y. F.; Kamai, K.; Ionov, L. B. *Zh. Obshch. Khim.* **1968**, *38*, 370–371.

(39) Gatilov, Y. F.; Ionov, L. B. *Zh. Obshch. Khim.* **1968**, *38*, 2561–2565.

(40) Gatilov, Y. F.; Ionov, L. B. *Zh. Obshch. Khim.* **1969**, *39*, 1064–1067.

(41) Gatilov, Y. F.; Ionov, L. B.; Molodtsov, S. S. *Zh. Obshch. Khim.* **1972**, *42*, 1535–1537.

(42) Gatilov, Y. F.; Yambushev, F. D. *Zh. Obshch. Khim.* **1973**, *43*, 1132–1135.

(43) Gatilov, Y. F.; Ionov, L. B.; Yambushev, F. D. *Zh. Obshch. Khim.* **1971**, *41*, 570–572.

(44) Gatilov, Y. F.; Yambushev, F. D.; Tenisheva, N. K. *Zh. Obshch. Khim.* **1973**, *43*, 2681–2683.

(45) Yambushev, F. D.; Gatilov, Y. F.; Tenisheva, N. K.; Savin, V. I. *Zh. Obshch. Khim.* **1974**, *44*, 1734–1737.

(46) Yambushev, F. D.; Gatilov, Y. F.; Tenisheva, N. K.; Savin, V. I. *Zh. Obshch. Khim.* **1974**, *44*, 2499–2502.

(47) Yambushev, F. D.; Gatilov, Y. F.; Tenisheva, N. K.; Savin, V. I. *Zh. Obshch. Khim.* **1975**, *45*, 2527–2529.

(48) Ionov, L. B.; Gatilov, Y. F.; Mukanov, I. P.; Kokorina, L. G. *Zh. Obshch. Khim.* **1974**, *44*, 1874–1877.

(49) Gatilov, Y. F.; Ionov, L. B.; Yambushev, F. D. *Zh. Obshch. Khim.* **1970**, *40*, 2250–2252.

(50) Chatt, J.; Mann, F. G. *J. Chem. Soc.* **1939**, 610–615.

(51) Holliman, F. G.; Mann, F. G. *J. Chem. Soc.* **1943**, 550–554.

(52) Horner, L.; Fuchs, H. *Tetrahedron Lett.* **1963**, *4*, 1573–1575.

(53) Horner, L.; Dickerhof, K. *Phosphorus and Sulfur* **1983**, *15*, 213–218.

(54) Horner, L.; Ernst, M. *Chem. Ber.* **1970**, *103*, 318–319.

(55) Horner, L. *Tetrahedron Lett.* **1966**, *28*, 3321–3322.

(56) Horner, L.; Samaan, S. *Phosphorus* **1973**, *3*, 153–158.

(57) Allen, D. G.; Wild, S. B. *Organometallics* **1983**, *2*, 394–399.

(58) Bosnich, B.; Wild, S. B. *J. Am. Chem. Soc.* **1970**, *92*, 459–464.

(59) Cope, A. C.; Ganellin, C. R.; Johnson, H. W., Jr.; Van Auken, T. V.; Winkler, H. J. S. *J. Am. Chem. Soc.* **1963**, *85*, 3276–3279.

(60) Cope, A. C.; Hecht, J. K.; Johnson, H. W., Jr.; Keller, H.; Winkler, H. J. S. *J. Am. Chem. Soc.* **1966**, *88*, 761–763.

(61) Cope, A. C.; Caress, E. A. *J. Am. Chem. Soc.* **1966**, *88*, 1711–1713.

(62) Chan, T. H. *J. Chem. Soc., Chem. Commun.* **1968**, 895–896.

(63) Otsuka, S.; Nakamura, A.; Kano, T.; Tani, K. *J. Am. Chem. Soc.* **1971**, *93*, 4301–4303.

(64) Tani, K.; Brown, L. D.; Ahmed, J.; Ibers, J. A.; Yokota, M.; Nakamura, A.; Otsuka, S. *J. Am. Chem. Soc.* **1977**, *99*, 7876–7886.

(65) Allen, D. G.; McLaughlin, G. M.; Robertson, G. B.; Steffen, W. L.; Salem, G.; Wild, S. B. *Inorg. Chem.* **1982**, 1007–1014.

(66) Cahn, E. L.; Ingold, C.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385–415.

(67) Roberts, N. K.; Wild, S. B. *J. Chem. Soc., Dalton Trans.* **1979**, 2015–2021.

(68) Roberts, N. K.; Wild, S. B. *J. Am. Chem. Soc.* **1979**, *101*, 6254–6260.

(69) Salem, G.; Wild, S. B. *J. Am. Chem. Soc.* **1983**, *22*, 4049–4054.

(70) Cook, V. C.; Willis, A. C.; Zank, J.; Wild, S. B. *Inorg. Chem.* **2002**, *41*, 1897–1906.

(71) Stackhouse, J.; Cook, R. J.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 953–955.

(72) Ionov, L. B.; Samitov, Y. Y.; Kokorina, L. G.; Korovyakoz, A. P.; Chernokal'skii, B. D. *Zh. Obshch. Khim.* **1977**, *47*, 1276–1282.

(73) Ionov, L. B.; Reshetnikov, S. M.; Marakova, L. L.; Flegontova, T. M. *Zh. Obshch. Khim.* **1985**, *55*, 862–867.

(74) Ionov, L. B.; Korovyakoz, A. P.; Chernokal'skii, B. D. *Zh. Obshch. Khim.* **1978**, *48*, 940–941.

(75) Ionov, L. B.; Korovyakoz, A. P.; Chernokal'skii, B. D. *Zh. Obshch. Khim.* **1979**, *49*, 184–188.

(76) Ionov, L. B.; Korovyakoz, A. P.; Chernokal'skii, B. D. *Zh. Obshch. Khim.* **1979**, *49*, 2514–2518.

(77) Ionov, L. B.; Reshetnikov, S. M.; Kornienko, I. G. *Zh. Obshch. Khim.* **1983**, *53*, 2712–2718.

(78) Salem, G.; Wild, S. B. *J. Organomet. Chem.* **1989**, *370*, 33–41.

(79) Gugger, P. A.; Willis, A. C.; Wild, S. B. *J. Chem. Soc., Chem. Commun.* **1990**, 1169–1170.

(80) Bernardo, M. H. *PhD Thesis*; The Australian National University, 2002.

(81) Porter, K. A.; Willis, A. C.; Zank, J.; Wild, S. B. *Inorg. Chem.* **2002**, *41*, 6380–6386.

(82) Anderson, R. H.; Cragg, R. H. *J. Chem. Soc., Chem. Commun.* **1971**, 1414.

(83) Henrick, K.; Mickiewicz, M.; Roberts, N.; Shewchuk, E.; Wild, S. B. *Aust. J. Chem.* **1975**, *28*, 1478–1488.

(84) Veith, M.; Bertsch, B.; Huch, V. *Z. Anorg. Allg. Chem* **1988**, *559*, 73–88.

(85) Burford, N.; Royan, B. W.; White, P. S. *J. Am. Chem. Soc* **1989**, *111*, 3746–3747.

(86) Burford, N.; Parks, T. M.; Royan, B. W.; Richardson, J. F.; White, P. S. *Can. J. Chem.* **1992**, *70*, 703–709.

(87) Payrastre, C.; Madaule, Y.; Wolf, J. G. *Tetrahedron Lett.* **1990**, *31*, 1145–1146.

(88) Payrastre, C.; Madaule, Y.; Wolf, J.-G. *Tetrahedron Lett.* **1992**, *33*, 1273–1276.

(89) Payrastre, C.; Madaule, Y.; Wolf, J. G.; Kim, T. C.; Mazières, M.-R.; Wolf, R.; Sanchez, M. *Heteroat. Chem.* **1992**, 157–162.

(90) Burford, N.; Parks, T. M.; Royan, B. W.; Borecka, B.; Cameron, T. S.; Richardson, J. F.; Gabe, E. J.; Hynes, R. *J. Am. Chem. Soc* **1992**, *114*, 8147–8153.

(91) Porter, K. A. *PhD Thesis*; The Australian National University, 2001.

(92) Coates, G. E.; Livingstone, J. G. *Chem. Ind.* **1958**, 1366.

(93) Braddock, J. M. F.; Coates, G. E. *J. Chem. Soc.* **1961**, 3208–3211.

(94) Burford, N.; Ragogna, P. J.; Sharp, K.; McDonald, R.; Ferguson, M. J. *Inorg. Chem.* **2005**, *44*, 9453–9460.

(95) Kilah, N. L.; Petrie, S.; Stranger, R.; Wielandt, J. W.; Willis, A. C.; Wild, S. B. *Organometallics* **2007**, *26*, 6106–6113.

(96) Krenske, E. H. *PhD Thesis*; The Australian National University, 2005.

(97) Coote, M. L.; Krenske, E. H.; Porter, K. A.; Weir, M. L.; Willis, A. C.; Zhou, S. B.; Wild, S. B. *Organometallics* **2008**, *27*, 5099–5107.

(98) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441–451.

(99) Kilah, N. L. *PhD Thesis*; The Australian National University, 2007.

(100) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; John Wiley and Sons, Inc.: New York, 1994.

(101) Watson, A. A.; Willis, A. C.; Wild, S. B. *J. Organomet. Chem.* **1993**, *445*, 78–78.

(102) Maigrot, N.; Mazaleyrat, J.-P. *Synthesis* **1985**, 317–320.

(103) Engelhart, L. M.; Leung, W. P.; Raston, C. L.; Salem, G.; Twiss, P.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1988**, 2403–2409.

(104) Xiao, D.; Zhang, Z.; Zhang, X. *Org. Lett.* **1999**, *1*, 1679–1681.

(105) Köbrich, G.; Merkle, H. R. *Chem. Ber.* **1966**, *99*, 1782–1792.

(106) Watson, A. A.; Willis, A. C.; Wild, S. B. *J. Organomet. Chem.* **1993**, *445*, 71–78.

(107) Kilah, N. L.; Weir, M. L.; Wild, S. B. *Dalton Trans.* **2008**, 2480–2486.

(108) Blom, R.; Haaland, A. *J. Mol. Struct.* **1985**, *128*, 21–27.

(109) Chatt, J.; Mann, F. G. *J. Chem. Soc.* **1939**, 1622–1634.

(110) Appelt, A.; Ariaratnem, V.; Willis, A. C.; Wild, S. B. *Tetrahedron: Asymmetry* **1990**, *1*, 9–12.

(111) Akitt, J. W.; Mann, B. E. *NMR and Chemistry*, 4th ed.; Stanley Thornes: Cheltenham, 2000.

(112) Corey, E. J.; Ensley, H. E. *J. Am. Chem. Soc.* **1975**, *97*, 6908–6909.

(113) Ort, O. *Org. Synth.* **1987**, *65*, 203–214.

(114) Fernández, F.; García-Mera, X.; López, C.; Rodríguez, G.; Rodríguez-Borges, J. E. *Tetrahedron: Asymmetry* **2000**, *11*, 4805–4815.

(115) Whitesell, J. K. *Chem. Rev.* **1992**, *92*, 953–964.

(116) Zhou, X.; Wild, S. B. *unpublished work*, 2005.

(117) Whitesell, J. K.; Liu, C.-L.; Buchanan, C. M.; Chen, H. H.; Minton, M. A. *J. Org. Chem.* **1986**, *51*, 551–553.

(118) Halterman, R. L.; Vollhardt, K. P. C. *Organometallics* **1988**, *7*, 883–892.

(119) Ito, K.; Tanizaki, A.; Fukuda, Y.; Matsushita, S.; Jpn. Kokai Tokkyo Koho, 2000; Vol. JP 2000128891.

(120) Schmidbaur, H. *J. Organomet. Chem.* **1980**, *200*, 287–306.

(121) Spangenberg, S. F.; Sisler, H. H. *Inorg. Chem.* **1969**, *8*, 1006–1010.

(122) Kopp, R. W.; Bond, A. C.; Parry, R. W. *Inorg. Chem.* **1976**, *15*, 3042–3046.

(123) Schultz, C. W.; Parry, R. W. *Inorg. Chem.* **1976**, *15*, 3046–3050.

(124) Burford, N.; Cameron, T. S.; Ragogna, P. J. *J. Am. Chem. Soc.* **2001**, *123*, 7947–7948.

(125) Burford, N.; Ragogna, P. J.; McDonald, R.; Ferguson, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 14404–14410.

(126) Burford, N.; Herbert, D. E.; Ragogna, P. J.; McDonald, R.; Ferguson, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 17067–17073.

(127) Weigand, J. J.; Riegel, C. D.; Burford, N.; Decken, A. *J. Am. Chem. Soc.* **2007**, *129*, 7969–7974.

(128) Althaus, H.; Breunig, H. J.; Lork, E. *Chem. Commun.* **1999**, 1971–1972.

(129) Wielandt, J. W.; Kilah, N. L.; Willis, A. C.; Wild, S. B. *Chem. Commun.* **2006**, 3679–3680.

(130) Conrad, E.; Burford, N.; McDonald, R.; Ferguson, M. J. *Inorg. Chem.* **2008**, *47*, 2952–2954.

(131) Conrad, E.; Burford, N.; McDonald, R.; Ferguson, M. J. *J. Am. Chem. Soc.* **2009**, *131*, 5066–5067.

(132) Conrad, E.; Burford, N.; McDonald, R.; Ferguson, M. J. *J. Am. Chem. Soc.* **2009**, *131*, 17000–17008.

(133) Kerr, P. G.; Leung, P. H.; Wild, S. B. *J. Am. Chem. Soc.* **1987**, *109*, 4321–4328.

(134) Armarego, W. F. L.; Chai, C. L. L. *Purification of Laboratory Chemicals*, 5th ed.; Butterworth-Heinemann: Amsterdam, 2003.

(135) Kamai, G. **1935**, *Ber. Dtsch. Chem. Ges.*, 1893–1898.

(136) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165–168.

(137) Bianco, V. D.; Doronzo, S. *Inorg. Synth.* **1976**, *16*, 155–163.

(138) Issleib, K.; Tzschach, A. *Chem. Ber.* **1959**, *92*, 1118–1126.

(139) Kokorev, G. I.; Yambushev, F. D.; Al'metkina, L. A. *Zh. Obshch. Khim.* **1988**, *58*, 330–333.

(140) Holliman, F. G.; Mann, F. G. *J. Chem. Soc.* **1947**, 1634–1642.

(141) Cragoe, E. J.; Andres, R. J.; Coles, R. F.; Elpern, B.; Morgan, J. F.; Hamilton, C. S. *J. Am. Chem. Soc.* **1947**, *69*, 925–926.

(142) Mann, F. G.; Chaplin, E. J. *J. Chem. Soc.* **1937**, 527–535.

(143) Burrows, G. J.; Turner, E. E. *J. Chem. Soc., Trans.* **1920**, *117*, 1373–1383.