The Development of Organolead Reagents in Organic Synthesis

A thesis submitted to the
Board of the Faculty of Physical Sciences
in partial fulfilment of the
requirements for the degree of

Doctor of Philosophy
of the
University of Oxford

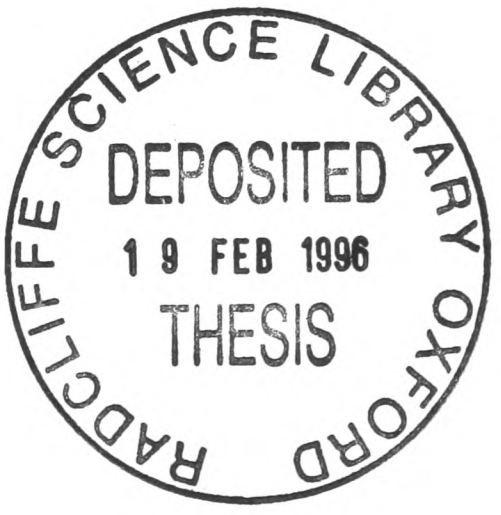
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ABSTRACT

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This thesis describes the synthesis of novel lead(IV) tetracarboxylates and the development of their use in carbon-carbon bond formation processes, with a particular emphasis on the construction of chiral, quaternary centres. Organolead(IV) tricarboxylates have been widely used in the functionalisation of a range of β-dicarbonyl compounds, and the available evidence suggests that these reactions occur by a ligand coupling mechanism. For this reason, by using chiral lead(IV) compounds, it may be possible to achieve a transfer of asymmetry in the bond formation reaction.

A variety of achiral and chiral dicarboxylic acid ligands were synthesised, either by reaction of phthalic or camphoric anhydride with a range of diols, or by elaboration of the camphoric acid skeleton directly. A range of novel lead(IV) compounds were constructed using these ligands, both as *bis*- complexes and as mixed ligand complexes. The complexes were characterised by a combination of IR and NMR techniques, including ^{207}Pb NMR spectroscopy, and elemental analysis. The reactivity of some of the complexes was demonstrated *via* reaction with allyltributyltin.

The lead(IV) complexes were used in the α-phenylation of a range of β-dicarbonyl substrates. Yields ranged from poor to excellent, but in all cases the enantiomeric excesses of the reactions were found to be no greater than 12%. Studies of these complexes by ^{207}Pb NMR spectroscopy revealed that each complex was present as more than one species in solution, which is thought to be the reason for the poor overall transfer of chirality in the phenylation reactions.

The arylation procedure uses catalytic mercury(II) acetate, which can in turn introduce further potential ligands to the exchanging system. It was found that alternative catalysts, such as mercury(II) chloride, could be used successfully in the α-phenylation reaction.

"Science begins with myths, and with the criticism of myths"

Sir Karl Popper

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APPENDICES

ABBREVIATIONS

The following abbreviations are used throughout this thesis:

Ac	acetyl
aq.	aqueous
Ar	aromatic
cat.	catalytic
CI	chemical ionisation
conc.	concentrated
COSY	correlation spectroscopy
δ	chemical shift
Δ	heat, reflux
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCCI	1,3-dicyclohexylcarbodiimide
DCI	desorption chemical ionisation
DCM	dichloromethane
DEPT	distortionless enhancement by polarisation transfer
DMAP	4-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	*N,N'*-dimethylformamide
DMSO	dimethylsulphoxide
DPE	1-diphenylethene
dppf	1,1'-*bis*(diphenylphosphino)-ferrocene
e.e.	enantiomeric excess
Et_3N	triethylamine
Et_2O	diethyl ether
EtOAc	ethyl acetate

eq.	equivalents
FT	fourier transform
GC	gas chromatography
GCMS	gas chromatography mass spectrometry
h	hours
HMBC	heteronuclear multiple bond correlation
Hz	hertz
IR	infra-red
lit.	literature value
LTA	lead(IV) tetraacetate
LTB	lead(IV) tetrabenzoate
min	minutes
m.p.	melting point
m/z	mass/charge ratio
NMR	nuclear magnetic resonance
p.p.m.	parts per million
py	pyridine
R_f	retention factor
r.t.	room temperature
sat.	saturated
TFA	trifluoroacetic acid
THF	tetrahydrofuran
t.l.c.	thin layer chromatography
UV	ultra violet

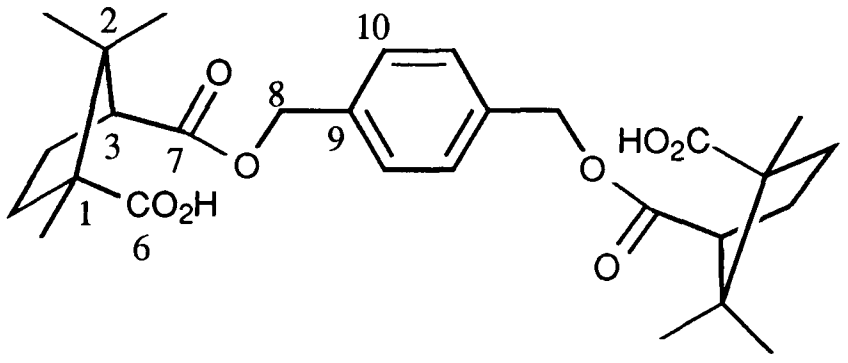
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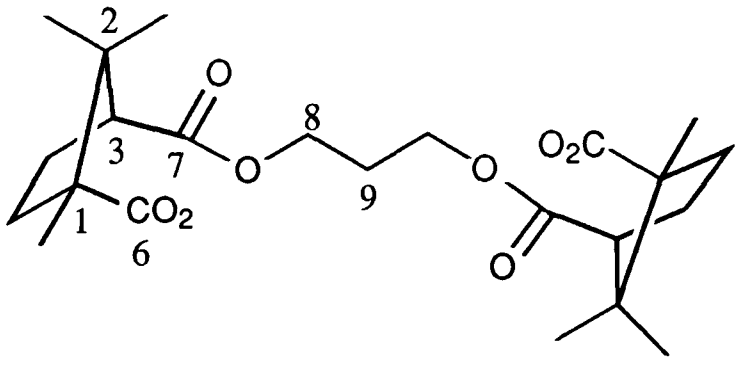
The nomenclature used to describe the compounds in this thesis is in accordance with the IUPAC conventions as detailed in "Nomenclature of Organic Chemistry", Sections A, B and C, Butterworths, London, 1969, with the following exceptions:

a) Trivial names are used when the S.I. name is cumbersome, or when the trivial name is more familiar than the S.I. name.

b) Known amino acids and derivatives thereof which do not increase the length of the main carbon chain are referred to as derivatives of the amino acid name, using standard amino acid nomenclature.

c) The five membered ring of derivatives of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid is numbered in a systematic way, with the carbon chains of esters of this compound being numbered as shown in the examples below.





STEREOCHEMISTRY

a) Absolute stereochemistry

Throughout this thesis, the Cahn-Ingold-Prelog (*R*, *S*) convention is used for all chiral centres. For compounds containing double bonds, the (*E*, *Z*) nomenclature is used.

b) Relative stereochemistry

A broken line is used to denote the α-configuration, where the substituent lies behind the general plane of the system, and a solid, wedged line denotes the β-configuration, where the substituent lies in front of the plane. If the stereochemistry at a centre is unknown, then a solid line has been used.

CHAPTER ONE

Introduction

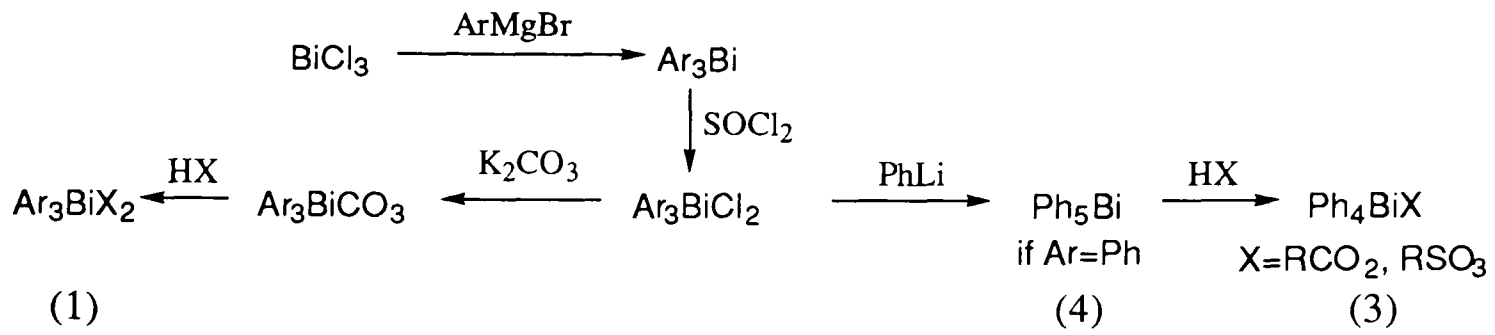
Over the last twenty years or so, there has been much interest in the development of synthetic methodology mediated by a variety of organometallic reagents. The arylation, vinylation and alkynylation of nucleophiles, especially soft carbon nucleophiles, using aryl-, vinyl- and alkynyl- organometallics have received particular attention. The metals (or metalloids) involved are principally derived from Groups 10 and 14, but other examples include bismuth(V) and iodine(III), and to a limited extent mercury(II) and thallium(III).

Significantly, and unlike many reactions involving transition metals (with the exception perhaps of palladium), the reactions mediated by heavy metals give easy access to aryl-, vinyl- and alkynyl- carbocation synthetic equivalents which are not easily prepared by alternative routes. The need for harsh reaction conditions and multiple steps is thus avoided.

Some of the reactions mediated by these metals and metalloids are outlined in the following discussion.

1.1 Bismuth[1]

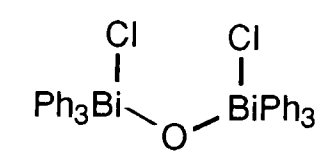
Organobismuth reagents have been known for some years,[2] and while there are many methods for their synthesis,[3] the most general method of preparation involves the reaction of a Grignard reagent with bismuth trichloride (Scheme 1.1).[4,5,6]



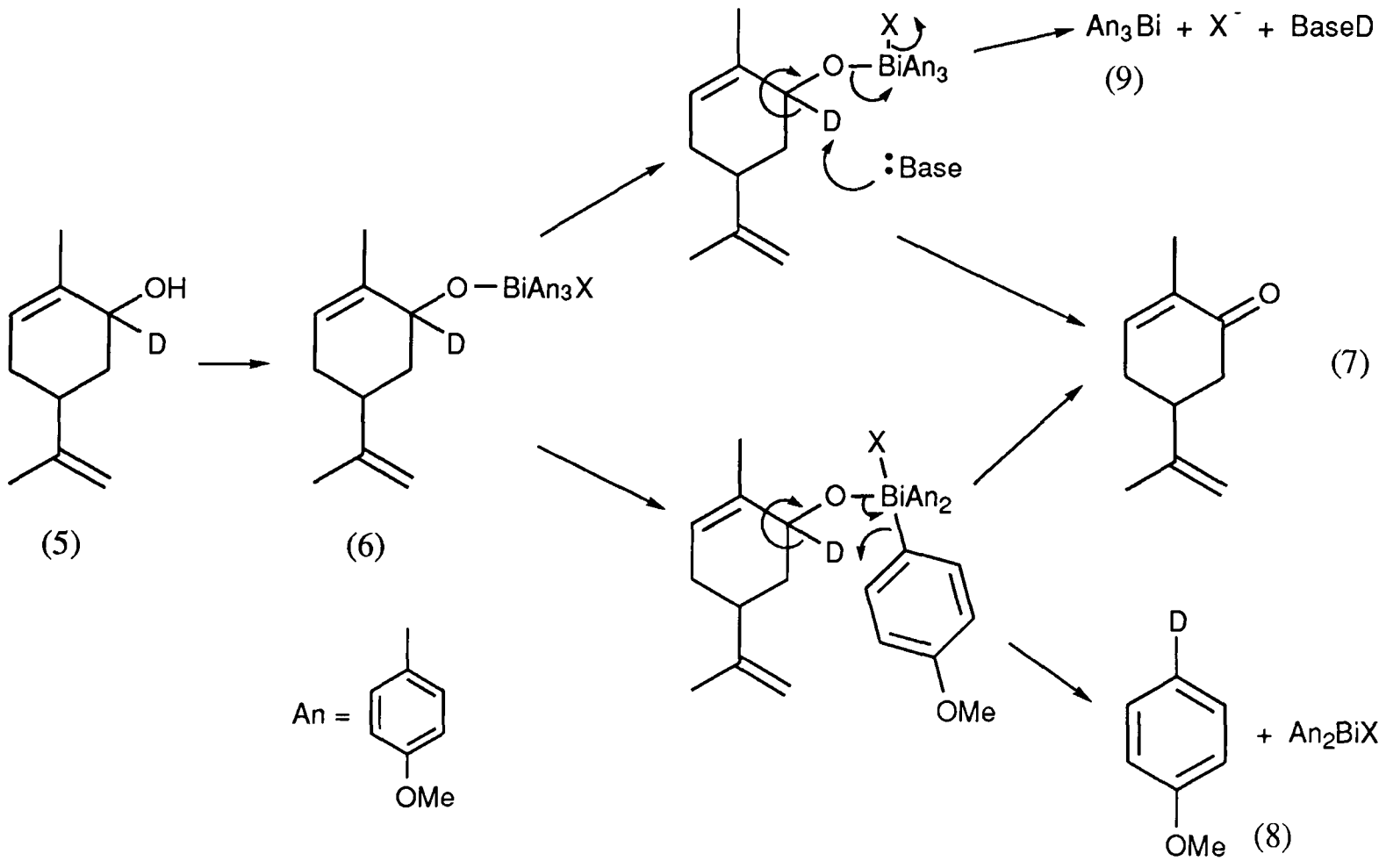
Scheme 1.1

1.1.1 Oxidation

Bismuth compounds (1), Ph_3BiX_2, are known to be mild and high yielding oxidising agents for primary, secondary, benzylic and especially allylic alcohols.[4,7,8,9] Two compounds of this type, μ-oxo*bis*(chlorotriphenylbismuth) (2) and triphenylbismuth carbonate are particularly selective for alcohols, even in the presence of sensitive functional groups such as indoles, pyrroles, thiols and selenides.[7,8] Under basic conditions, compounds such as (3), Ph_4BiX, will readily oxidise alcohols to the corresponding carbonyl derivatives,[10] as will Ph_5Bi (4).[11]



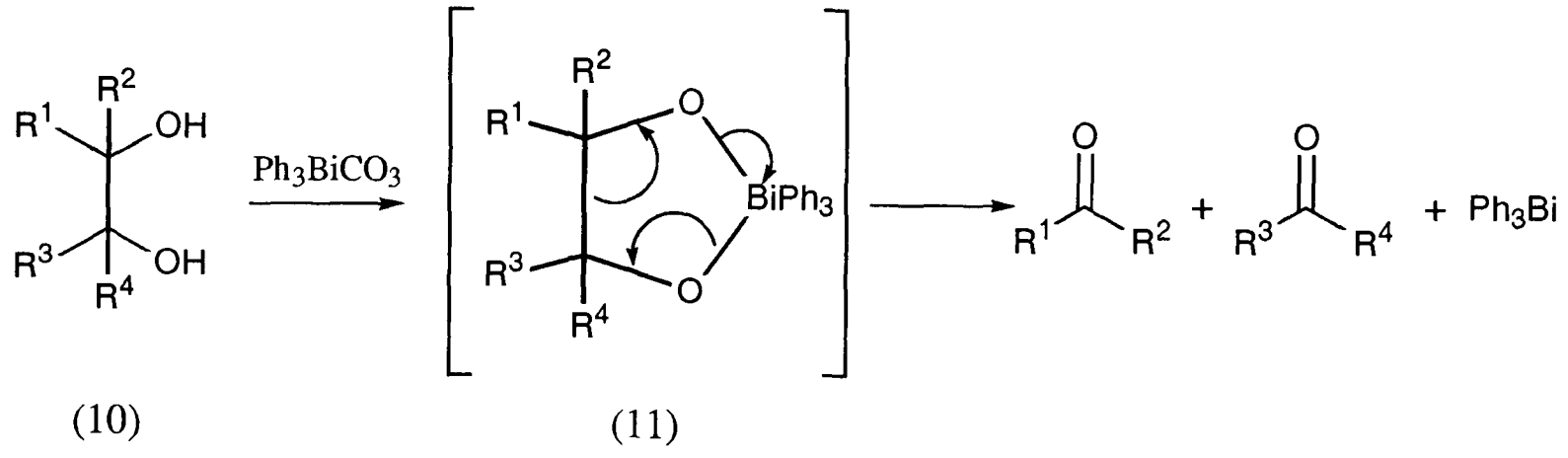
(2)



Scheme 1.2

All of these oxidation reactions are postulated to occur *via* a pentavalent bismuth(V) intermediate (such as (6) above) which is susceptible to reductive elimination. In the oxidation of (D)-deuteriocarvol (5) to carvone (7) two possible pathways have been detected. Both *p*-deutereoanisole (8) and tri-*p*-methoxyphenyl bismuth (9) were formed during the reductive elimination (Scheme 1.2).[4,12]

Triphenylbismuth carbonate (Ph_3BiCO_3) may be used stoichiometrically in the cleavage of 1,2-glycols (10) (Scheme 1.3).[4] The available evidence suggests that the reaction is likely to proceed *via* a cyclic bismuth intermediate (11).[4,13] Similarly, triphenylbismuth diacetate ($Ph_3Bi(OAc)_2$) may be used in the cleavage of 1,2-glycolstannylenes.[14] Both of these reactions may also be carried out using the bismuth reagents catalytically and using NBS as a reoxidant,[13] but in these cases a pentavalent bismuth derivative formed *in situ* does not act as the oxidant. The reaction in fact involves the formation of a glycol hypobromite which oxidises triphenylbismuth to a pentavalent species.



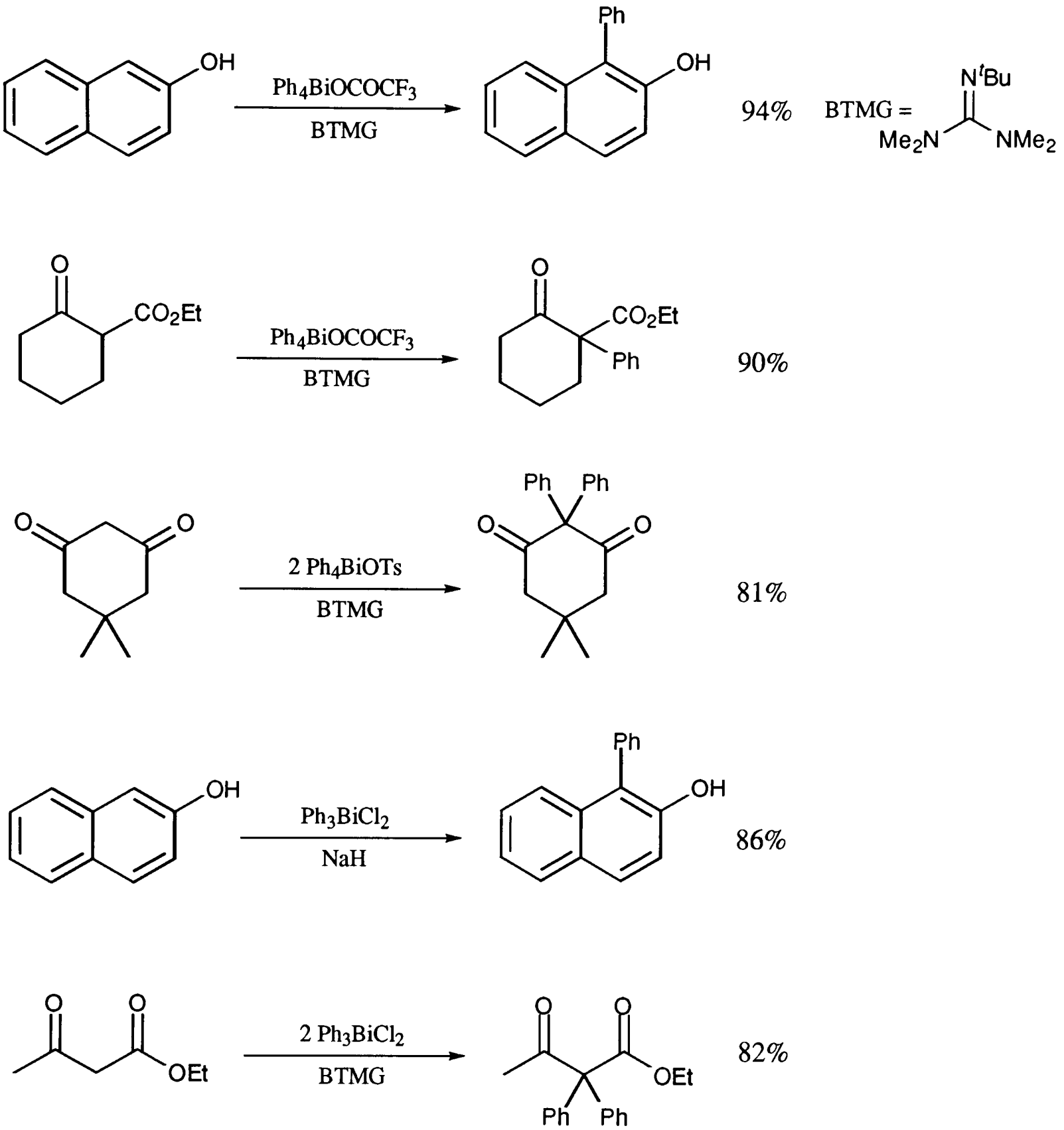
(10) (11)

Scheme 1.3

1.1.2 Phenylation

A variety of enolisable compounds may be smoothly α-phenylated by triphenylbismuth carbonate (Ph_3BiCO_3).[5,11,15,16,17] Tetraphenylbismuth esters (when under basic conditions) are excellent and selective reagents for the α-*C*-phenylation of phenols, enols, ketones and β-diketones.[15,16,17] Triphenylbismuth dichloride (Ph_3BiCl_2), in the presence of a suitable base, is also an efficient reagent for phenylation (Scheme 1.4).[5,16] In reactions of triphenylbismuth dichloride with phenols, the nature of the substituents on the aromatic ring of

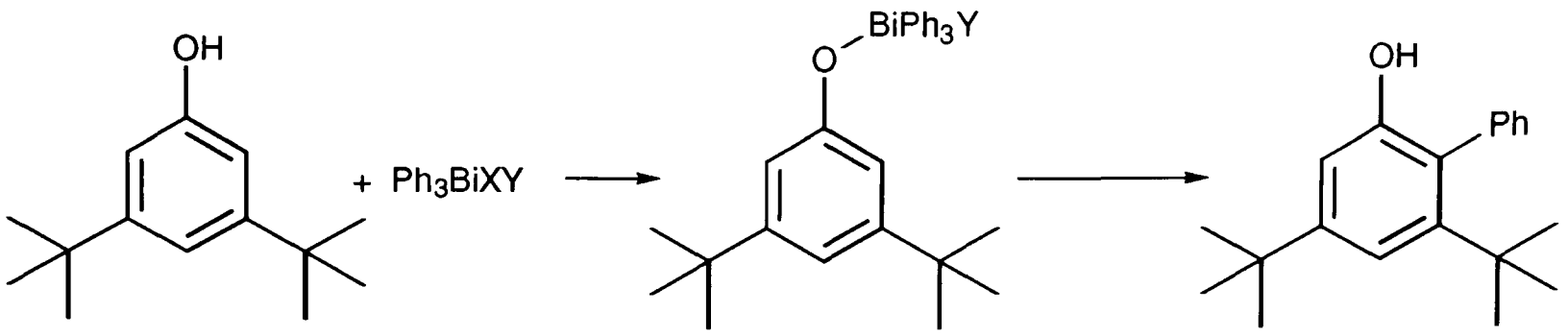
the phenol affects the regioselectivity of the reaction. In the case of phenols bearing electron-withdrawing groups, the major product is that of *O*-phenylation. When, however, the phenol is substituted with an electron-donating group, the phenol is predominantly α-*C*-phenylated.[18]



Scheme 1.4

In the *C*-phenylation process, a covalently bonded bismuth(V) intermediate has been detected. Proton NMR studies of the reaction of 3,5-di-*t*-butylphenol (12) with Ph_3BiCl_2 or $Ph_3Bi(OCOCF_3)_2$ under basic conditions or with Ph_5Bi have indicated the formation of intermediate (13) (Scheme 1.5)[5] which under controlled thermal degradation is converted to

the phenylated adduct (14) in 82% yield.



(12) (13) (14)

Scheme 1.5

Migratory aptitude studies have shown that the *C*-phenylation reaction is not ionic, and ESR and chemical trapping experiments[19] indicate that the reductive elimination reaction is unlikely to proceed *via* a free-radical pathway. It is more likely that the phenylation occurs by a non-synchronous concerted mechanism (Figure 1.1).[20] This type of mechanism is analogous to the reductive elimination pathways which feature so predominantly in transition metal chemistry, and are especially synthetically important for palladium species.

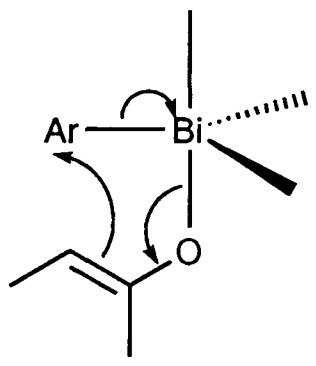
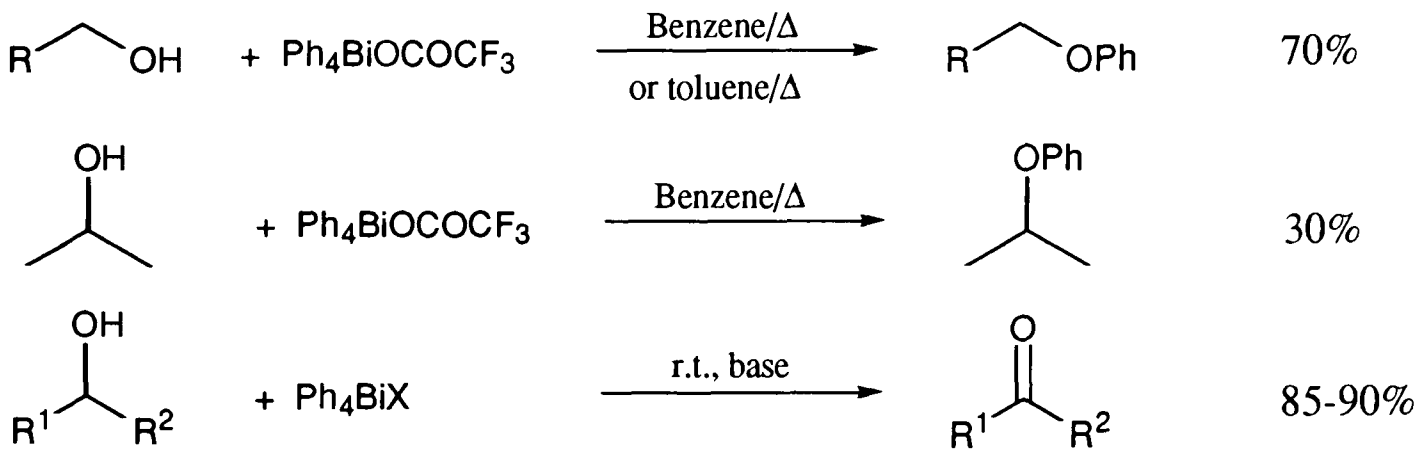


Figure 1.1

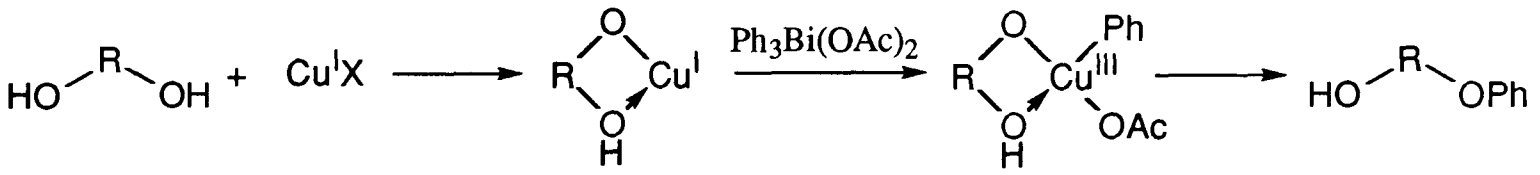
1.1.3 Phenylation of alcohols and amines

Tetraphenylbismuth trifluoroacetate shows a marked pH dependence in its reactions with alcohols. Under basic conditions, primary and secondary alcohols are oxidised by $Ph_4BiOCOCF_3$ *via* a covalent Bi-O intermediate. However, under neutral conditions $Ph_4BiOCOCF_3$ reacts with both primary and secondary alcohols to give *O*-phenyl ethers *via* an aromatic S_N2-type displacement (Scheme 1.6).[10]



Scheme 1.6

In 1981, David and Thieffry[14] established that it was possible to selectively mono-*O*-phenylate diols by reaction with $Ph_3Bi(OAc)_2$. Around the same time, Dodonov *et al.*[21] found that aliphatic alcohols could be slowly *O*-phenylated using $Ph_3Bi(OAc)_2$ and copper salts in the absence of solvent. It was found that in both the glycol and other *O*-phenylation reactions copper(II) acetate catalysis increased the reaction rate significantly.[22] It is likely that the reaction is catalysed by oxidative addition of a phenyl group and an acetate group to a copper(I) species, followed by transfer of a phenyl group to the hydroxy function (Scheme 1.7). Under the same conditions, aromatic primary and secondary amines are phenylated to give mono- or di-*N*-phenyl amines in good yield.[23]



Scheme 1.7

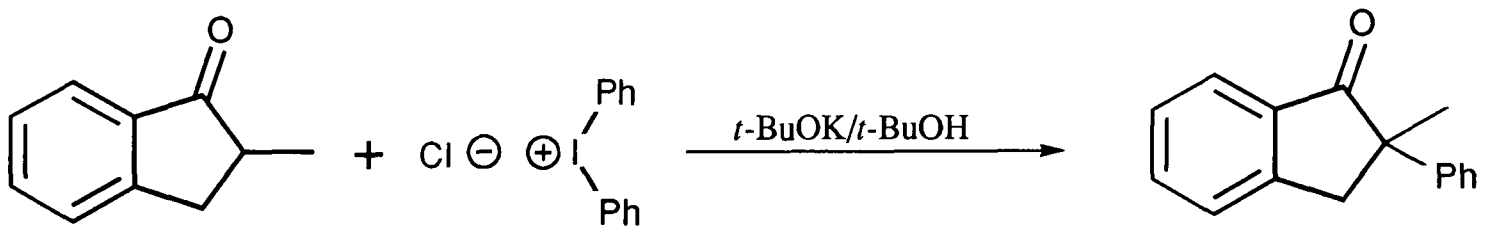
1.1.4 Summary

Organobismuth compounds are convenient and versatile reagents for a wide variety of reactions, including arylation. Control of selectivity is possible by careful choice of reagent and reaction conditions.

1.2 Iodine

Hypervalent iodine species are known to mediate carbon-carbon bond formation

processes in an analogous fashion to organometallic species.[24] The iodine acts as a centre around which potential reacting partners can be assembled, with the high-valent iodine atom providing an electron sink. A typical example of a reaction using hypervalent iodine is shown in Scheme 1.8.[25] It is likely that the reaction proceeds by addition of the enolate anion of carbonyl compound (15) to the positively charged iodine centre of (16) to give a tricoordinate intermediate. Carbon-carbon bond formation to give the product (17) then occurs either by concerted ligand coupling or by a radical process.

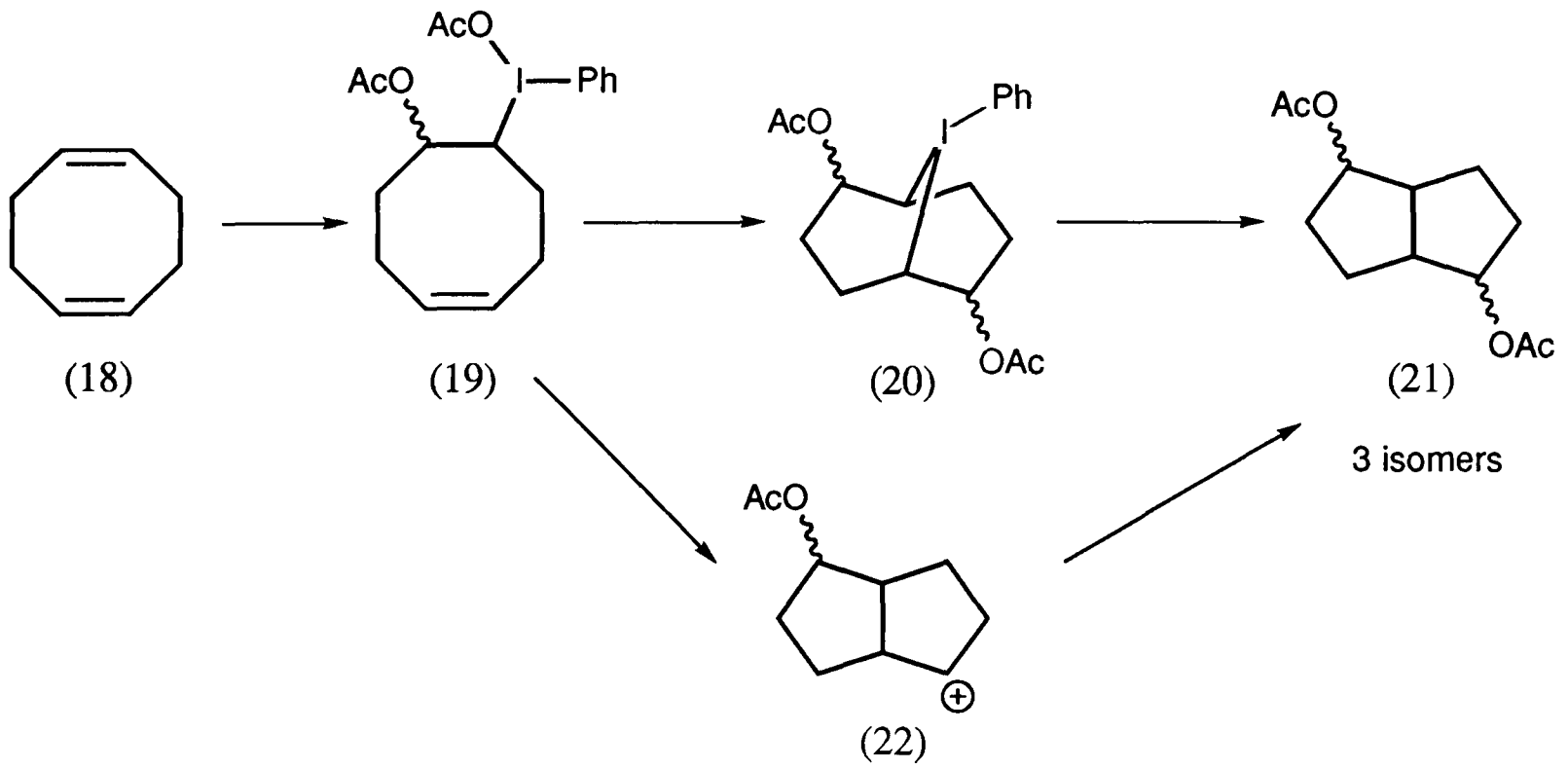


(15) (16) (17)

Scheme 1.8

1.2.1 Uses of hypervalent iodine species in synthesis

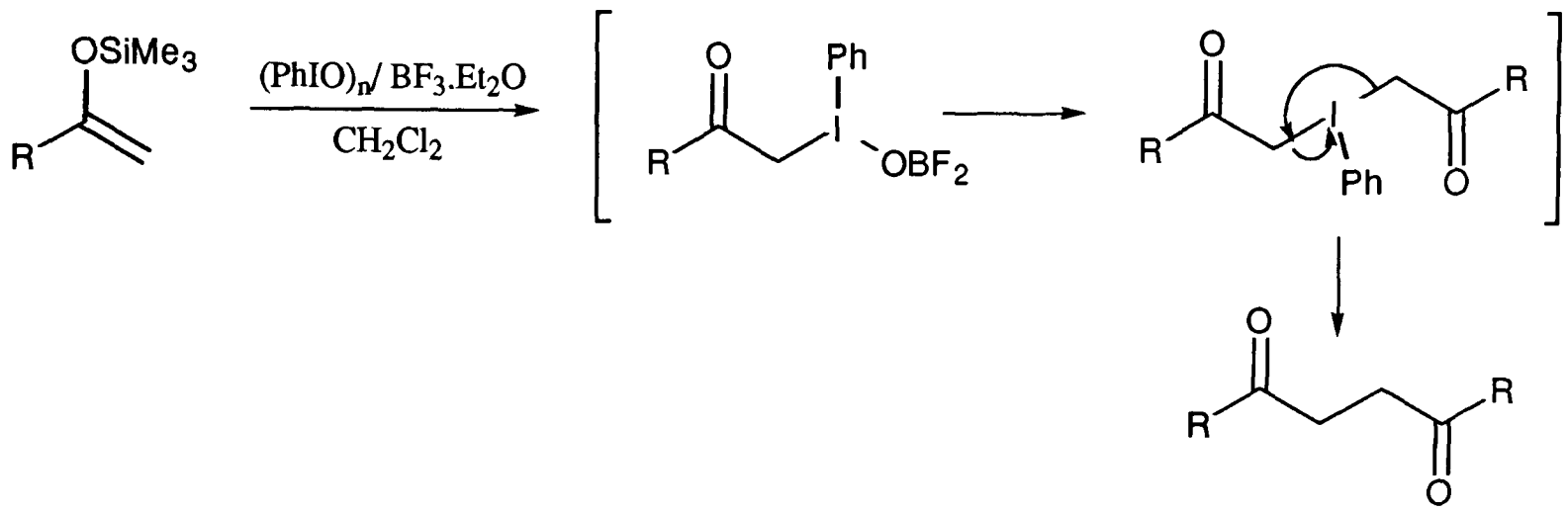
Hypervalent iodine compounds have found use in intramolecular carbocyclisation reactions, for example the reaction of *cis-cis*-cyclooctadiene (18) with (diacetoxyiodo)benzene which is shown in Scheme 1.9.[26]



(18) (19) (20) (21) (22)

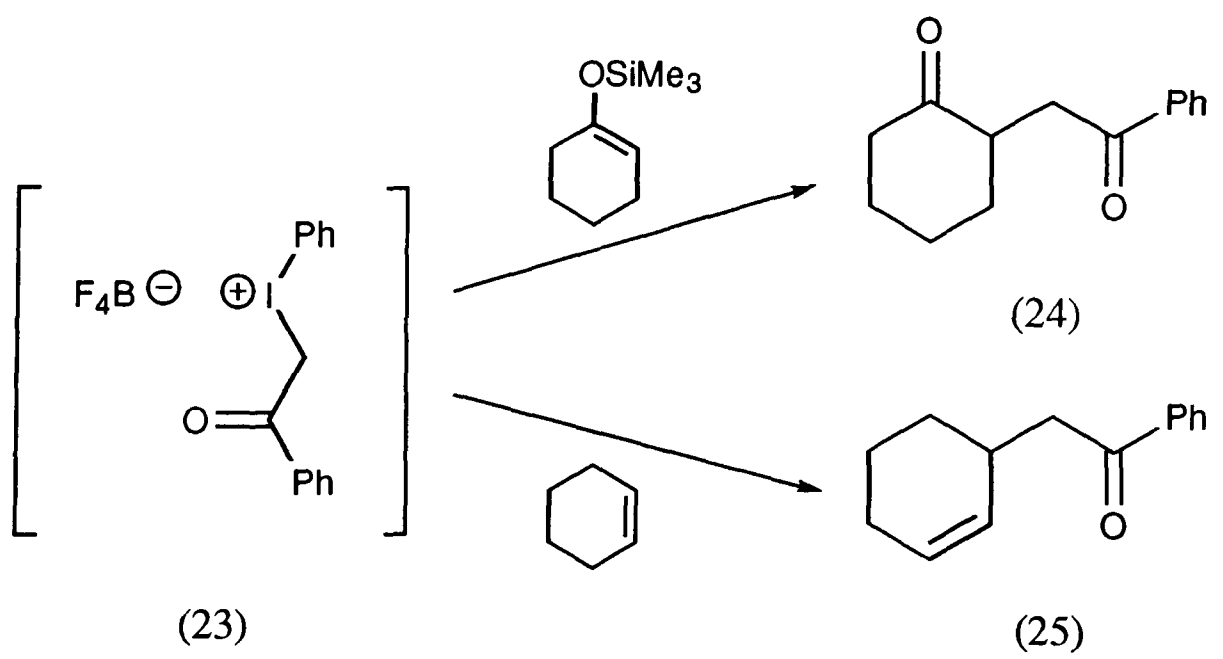
Scheme 1.9

The proposed[1] first step of this reaction involves the addition of one double bond to an (acetoxy)iodobenzene cation followed by attack of acetate to give (19). Transannular attack of another acetate gives (20) which then undergoes ligand coupling to give (21). Alternatively, in a second proposed route, carbon-iodine bond cleavage may occur, followed by carbon-carbon bond formation giving cation (22), which is then trapped by an acetate molecule to give the product (21).



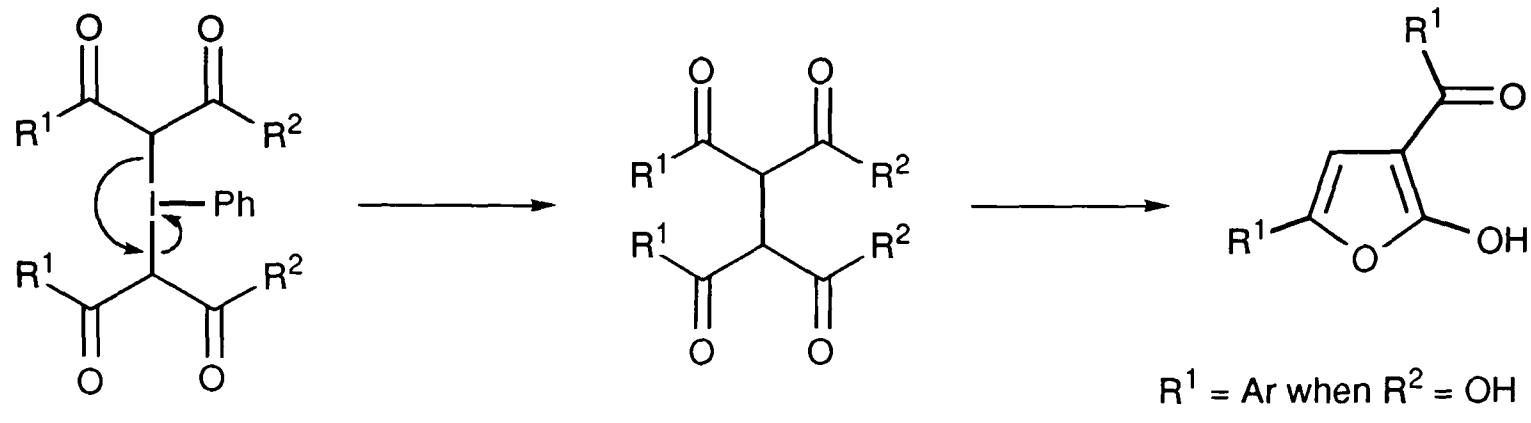
Scheme 1.10

Symmetrical 1,4-diketones may be synthesised in good yield from trimethylsilyl enol ethers as shown in Scheme 1.10.[27,28] Unsymmetrical diketones may be synthesised from the highly reactive phenacyl(phenyl)iodonium tetrafluoroborate (23), which is itself formed by reaction of the silyl enol ether of acetophenone with $PhI.HBF_4$. Thus, compound (23) reacts with silyl enol ethers and alkenes to give unsymmetrical 1,4-difunctionalised products such as (24) and (25) (Scheme 1.11).[29]



Scheme 1.11

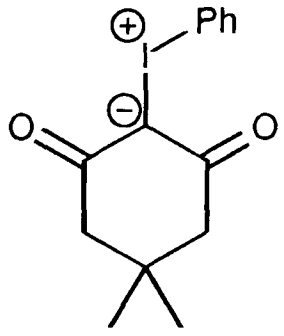
Coupling of β-dicarbonyl compounds may be achieved using iodosobenzene and boron trifluoride etherate *via* intermediates such as (26).[30] Therefore, 4-aryl-2,4-dioxobutanoic acids may be coupled to give products (27), R^1=Ar, R^2=OH, which spontaneously cyclise to give 3-aroyl-5-aryl-2-hydroxyfurans (28) (Scheme 1.12).[31]



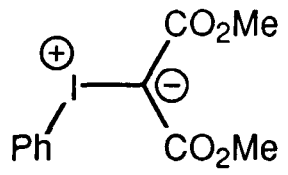
(26) (27) (28)

Scheme 1.12

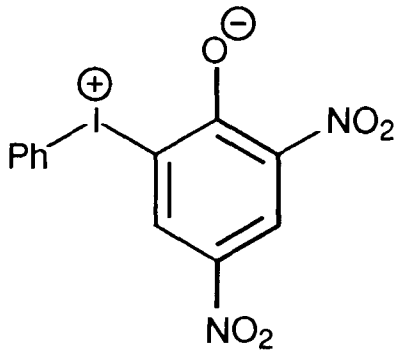
1.2.2 Iodonium ylides



(29)

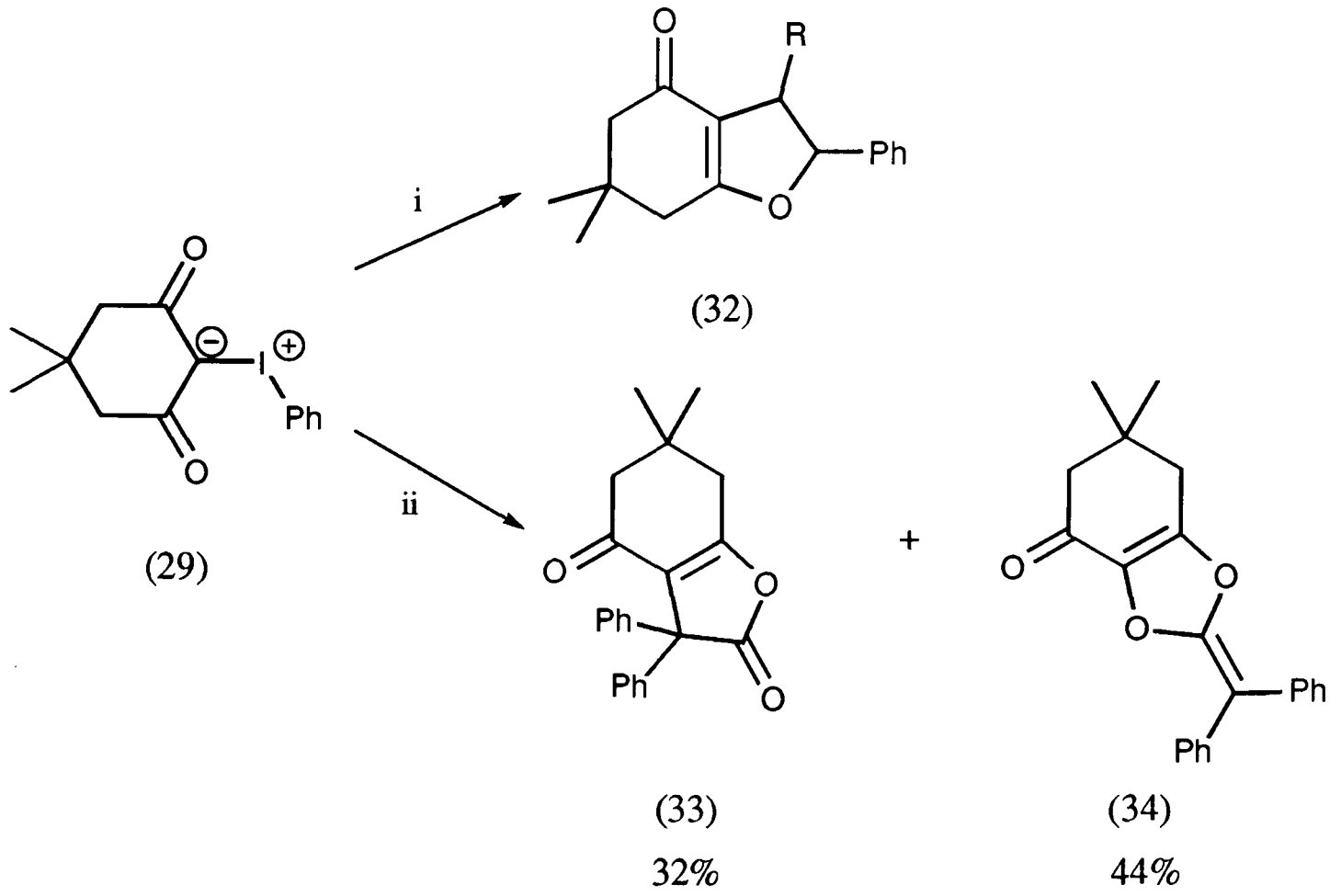


(30)



(31)

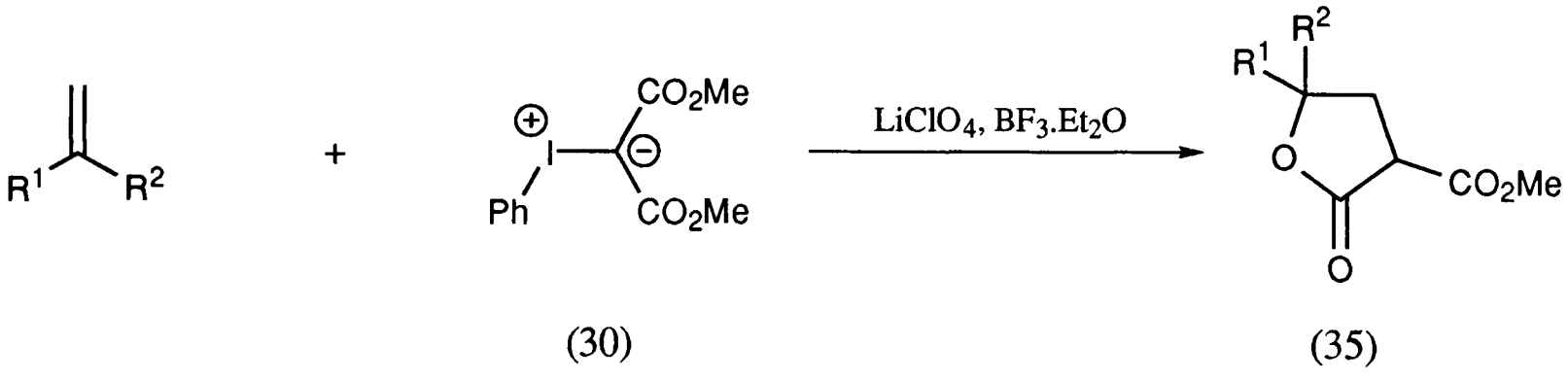
Some examples of iodonium ylides which find use in synthesis are shown above. Phenyliodonium dimedonate (29) may be synthesised from dimedone by reaction with (difluoroiodo)benzene. Iodonium ylides derived from β-dicarbonyl compounds (for example ylide (30)) are generally synthesised by reaction of the β-dicarbonyl compound with (diacetoxyiodo)benzene in alcoholic base.[32] 4,6-Dinitro-2-(phenyliodonio)phenolate (31) is made by reaction of the corresponding phenol with [*bis*(trifluoroacetoxy)iodo]benzene.[33]



i) PhCH=CHR, MeCN, hν
ii) $Ph_2C=C=O$, DCM, r.t.

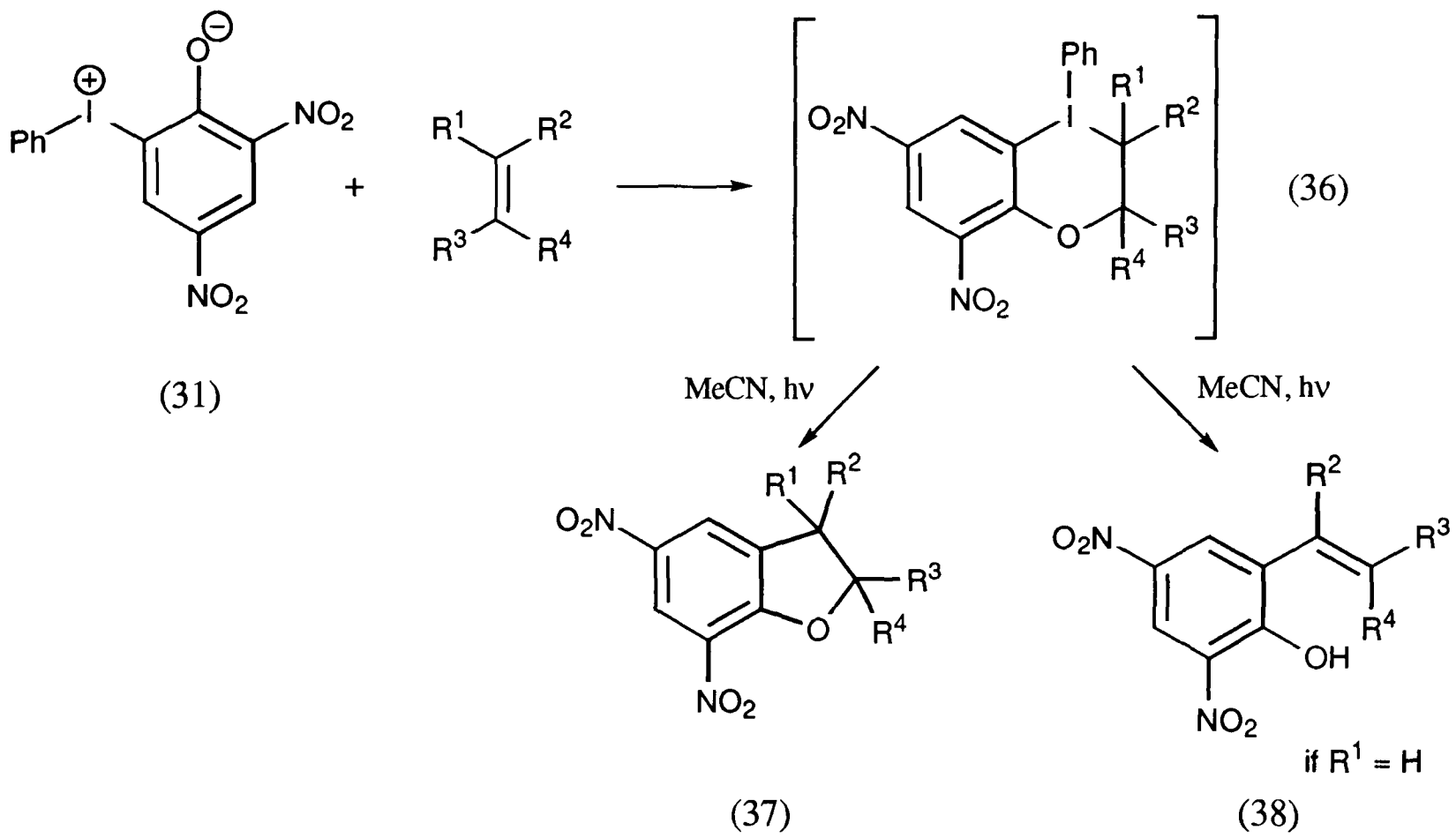
Scheme 1.13

Irradiation of phenyliodonium dimedonate (29) in the presence of an olefin in acetonitrile results in the formation of a substituted hexahydrobenzofuran such as (32).[34] Reaction of (29) with diphenylketene in DCM at room temperature leads to the formation of lactone (33) and ketene acetal (34) as shown in Scheme 1.13.[35] Phenyliodonium dimethoxycarbonylmethanide (30) reacts with olefins in the presence of Lewis acids to form 5,5-disubstituted γ-lactones (35) (Scheme 1.14).[36]



Scheme 1.14

Irradiation of 4,6-dinitro-2-(phenyliodonio)phenolate (31) in the presence of an olefin leads to the formation of a 2,3-dihydrobenzofuran (37) or a 6-alkenyl-2,4-dinitrophenol (38) (when R^1=H).[37] The reaction proceeds *via* an intermediate such as (36) shown in Scheme 1.15.

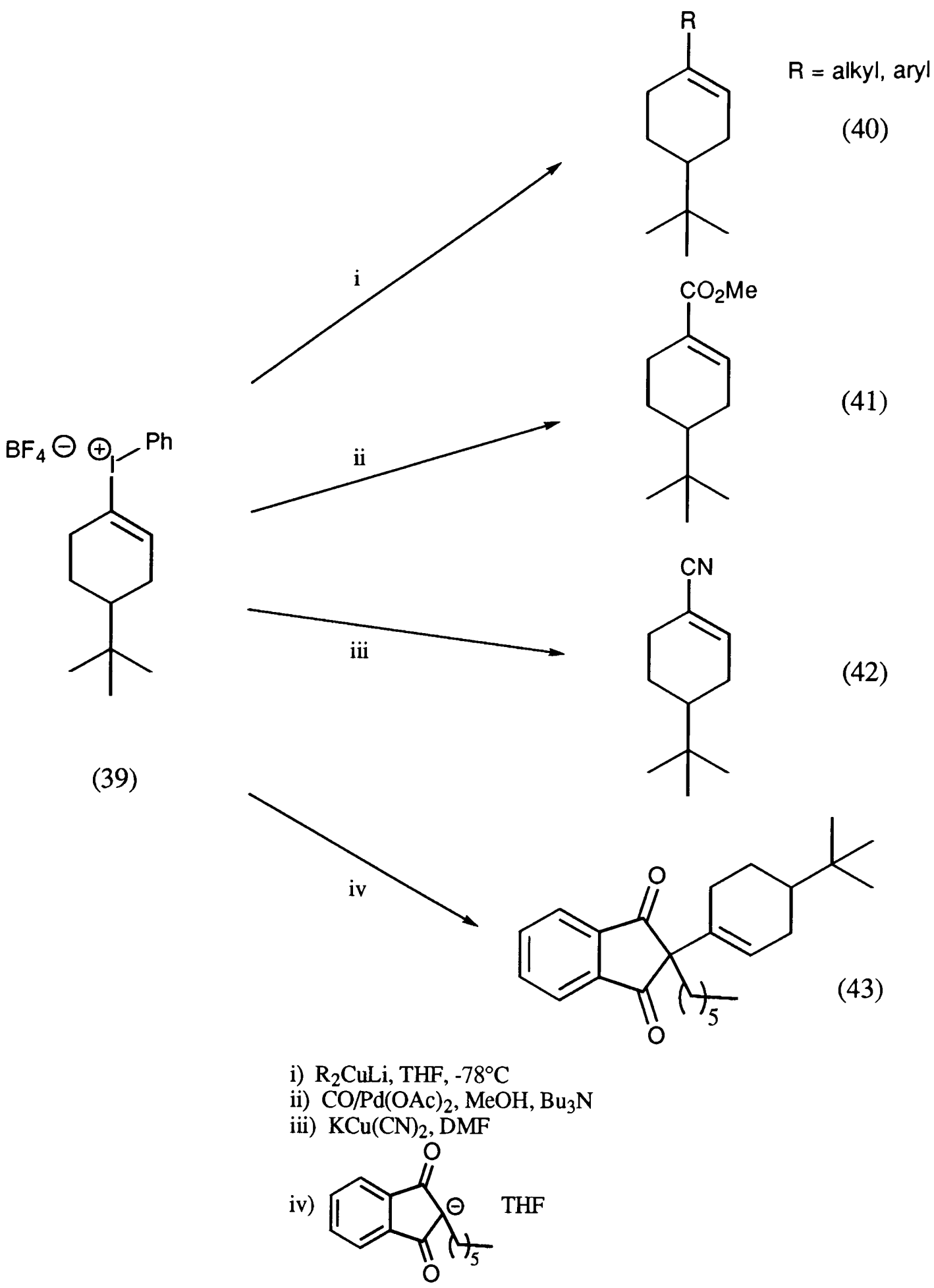


Scheme 1.15

1.2.3 Iodonium salts

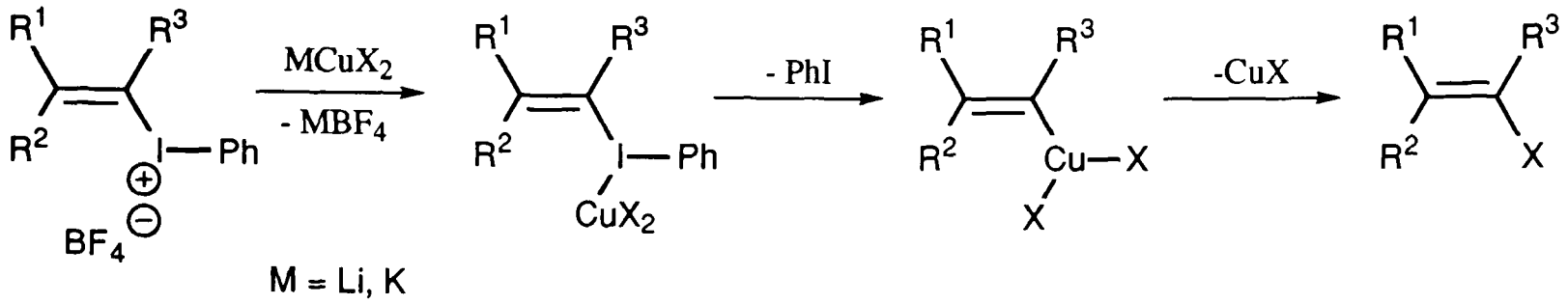
These important compounds have received considerable attention in recent years.[38] While they may be used in many reactions, this discussion will be restricted to the alkenyl-, alkynyl- and aryl- iodonium salts.

Scheme 1.16 shows some of the reactions of alkenyliodonium salts.[39,40] Reaction of iodonium salt (39) with an organocuprate reagent leads to the formation of a substituted cyclohexene (40). Alkoxycarbonylation to give (41) may be achieved by reaction of (39) with carbon monoxide in the presence of palladium(II) acetate and methanol. Reaction of (39) with potassium dicyanocuprate in DMF yields nitrile (42). Stable carbanions of 1,3-dicarbonyl compounds form substitution products such as (43) on reaction with alkenyliodonium salts.



Scheme 1.16

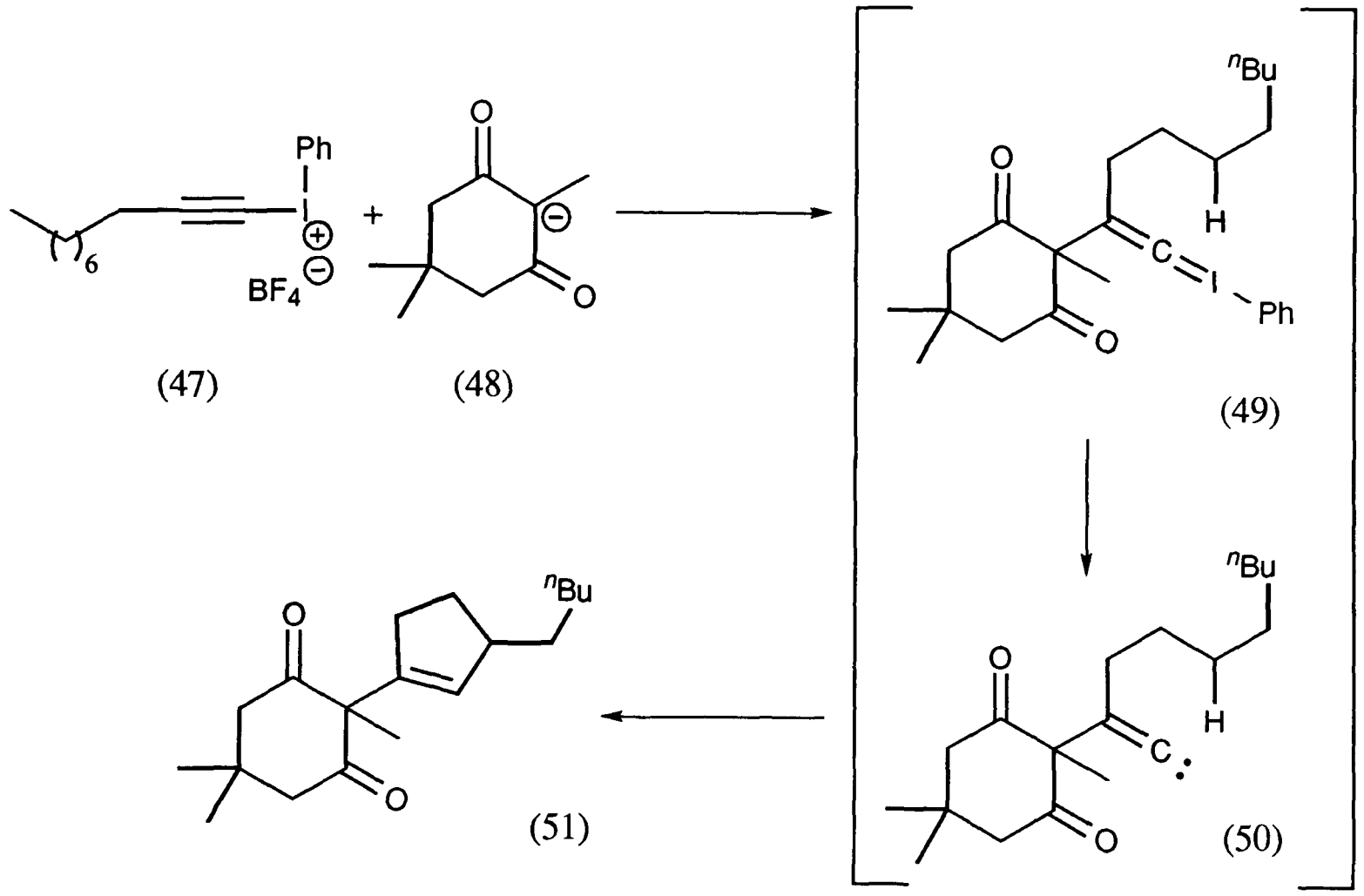
A possible mechanism for the reactions of alkenyliodonium salts with cuprates is shown in Scheme 1.17. The first step involves the oxidative addition of the cuprate to give (44) followed by ligand coupling on the iodine atom to give a vinyl copper(III) species (45). A second ligand coupling reaction then occurs to give the product (46).[40]



(44) (45) (46)

Scheme 1.17

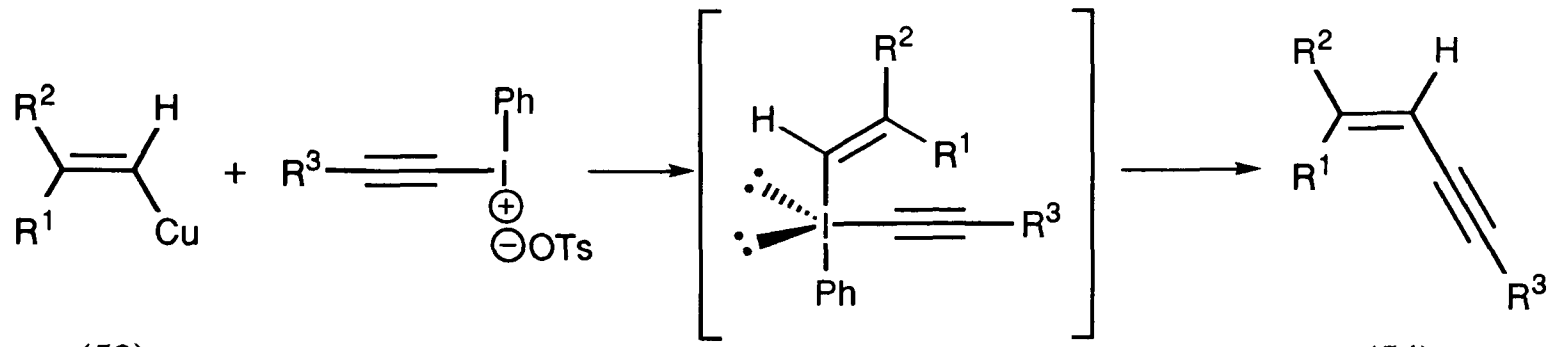
The reaction of 1-alkynyl(phenyl)iodonium tetrafluoroborate (47) with a stable enolate leads to the formation of a substituted cyclopentene (51) in good yield, as shown in the example below (Scheme 1.18).[41] The reaction proceeds by Michael addition of the enolate (48) to the iodonium salt to give an unstable ylide which can also be drawn as the "iodoallene" (49). This intermediate undergoes reductive elimination to give the alkylidene carbene (50) which in turn carries out a regioslective 1,5-CH insertion to give the substituted cyclopentene (51) in 50% yield.



(47) (48) (49) (50) (51)

Scheme 1.18

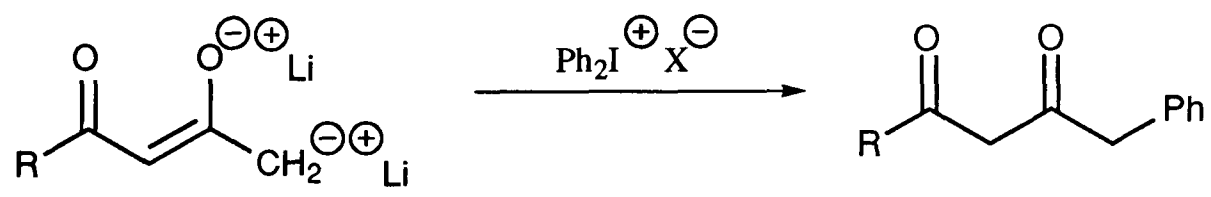
Alkynyliodonium tosylates (53) may be used in the synthesis of conjugated enynes (54) as shown in Scheme 1.19.[42] The reaction proceeds with retention of stereochemistry in the alkenyl copper reagent (52), and effects the same transformation as the Stille coupling of acetylenic tin and vinyl halides which will be discussed in the Section 1.3.1.



(52) (53) (54)

Scheme 1.19

Diaryliodonium salts are important reagents for the *C*-arylation of a range of nucleophilic substrates. Reactions are usually carried out with the carbanion generated *in situ*, but in some cases stable alkali salts may be used.[43] It should be noted that β-diketones give the products of both *C*-arylation and *O*-arylation.[44] Treatment of the dianion of diketones such as (55) with diaryliodonium salts has resulted in γ-arylation (Scheme 1.20).[45]



(55)

Scheme 1.20

1.2.4 Summary

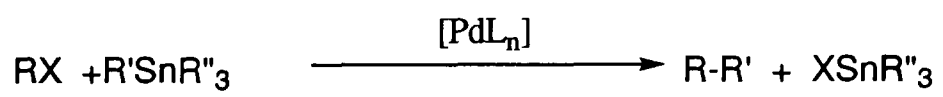
Hypervalent iodine species currently play, and will increase to play, a significant role in carbon-carbon bond formation reactions. Many of these are analogous to the more widely known and utilised reactions of palladium(0), palladium(I), platinum(0) and platinum(III).

1.3 Palladium

The use of palladium complexes in carbon-carbon bond formation reactions is well documented,[46] and therefore the discussion here will be confined to the Stille, Suzuki and Heck reactions. The most important property of palladium metal in these bond forming reactions is the ability of the metal to initiate ligand coupling by reductive elimination.

1.3.1 The Stille coupling[47]

The palladium catalysed coupling of organotin compounds with organic halides is known as the Stille coupling. The reaction is shown in general form in Scheme 1.21. Under the correct conditions, tin compounds can be successfully coupled to acid chlorides, benzyl halides, allyl halides and acetates, vinyl halides and triflates, and aryl halides. The palladium catalyst most commonly used in the Stille coupling is benzyl(chloro)*bis*(triphenylphosphine) palladium(II).

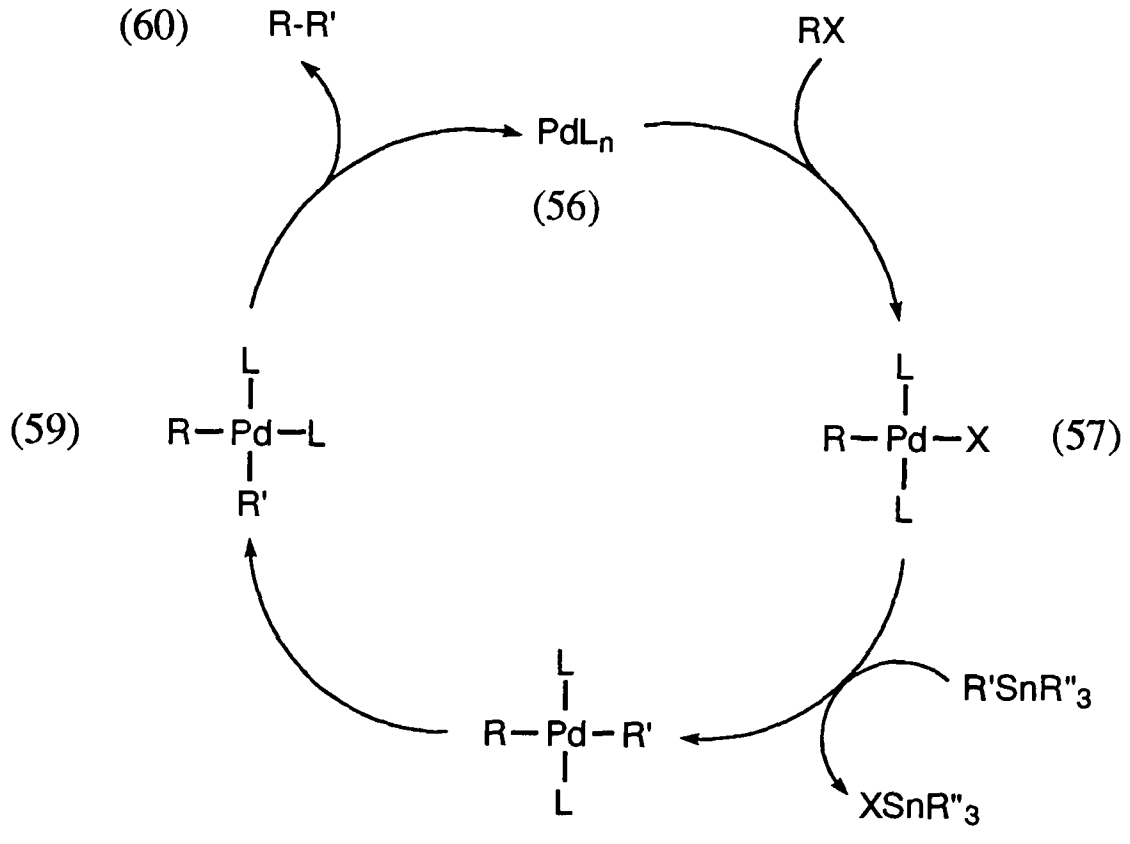


Scheme 1.21

The reaction proceeds in high yields and under mild conditions, and other functional groups (for example, CO_2R, CN, OH and CHO) are well tolerated. The Stille coupling proceeds in an *ipso* sense for coupling reactions of allyl halides and allyl tin compounds, and occurs stereospecifically with inversion of configuration at sp^3 centres bound to tin and/or the halogen. Retention of configuration at double bonds is usually observed, regardless of which reactant the double bond is in.

A representation of the catalytic cycle in the Stille coupling reaction is shown in Scheme 1.22. The first step is the oxidative addition of the organic electrophile RX to the palladium species (56) to give intermediate (57). The group R' is then transferred from tin to palladium to give the disubstituted species (58). Following rearrangement to place the two reacting partners in adjacent positions (59), ligand coupling induced by reductive elimination

occurs to give the product (60). The reaction cannot be carried out using electrophiles (*i.e.* the RX component) bearing a hydrogen on an sp^3 β-carbon as β-elimination from species (57) is faster than transmetallation to give species (58). The tin component, however, can carry a β–hydrogen as the catalytic steps following transmetallation are faster than β-elimination.

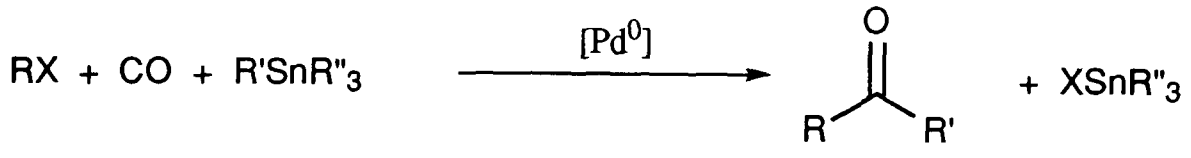


(58)

Scheme 1.22

1.3.2 The Stille carbonylative coupling[47]

The palladium catalysed coupling of organic halides and tin compounds in the presence of carbon monoxide is known as the Stille carbonylative coupling (Scheme 1.23), as opposed to the direct coupling reaction discussed in Section 1.3.1. The reaction can be carried out using benzyl halides, allyl chlorides, vinyl halides and vinyl triflates.



Scheme 1.23

The reaction is particularly useful if an acid chloride is not available to carry out the direct coupling reaction, as in this case the organic halide with one less carbon atom can be

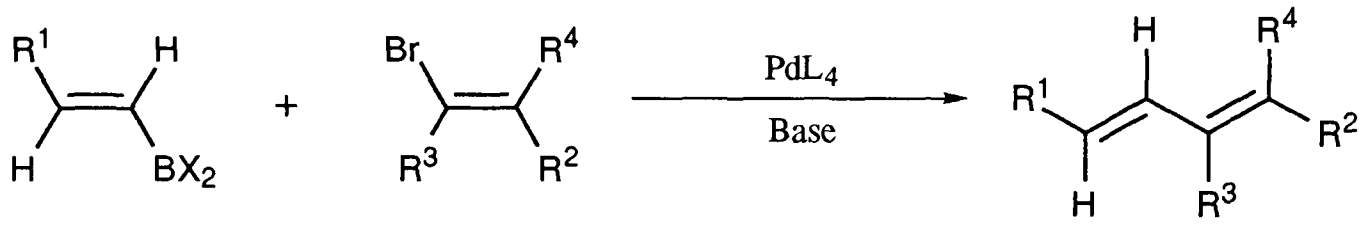
used. This leads to the same acylpalladium intermediate and hence the required product. Furthermore, the use of organic halides rather than acid chlorides means that functional groups such as OH and NH_2 can be present in the reacting partners.

The Stille carbonylative coupling reaction may also be used to synthesise aldehydes from organic halides using tributyltin hydride and a palladium catalyst in the presence of carbon monoxide. Under these mild conditions, other functional groups are unaffected.

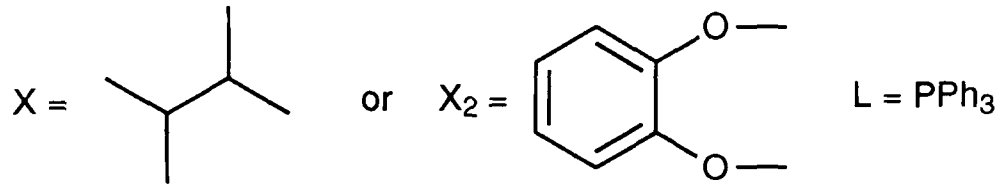
The catalytic cycle may be represented in a similar manner to the direct coupling reaction, with carbon monoxide insertion occurring after the formation of species (57), but before transmetallation.

1.3.3 The Suzuki coupling

In 1979, Suzuki *et al.*[48] reported a novel cross coupling reaction between 1-*E*-alkenyl boranes (61) and 1-*E*-alkenyl halides (62) to give substituted alkenyl alkenes (63) catalysed by tetrakis(triphenylphosphine) palladium in the presence of base (Scheme 1.24).



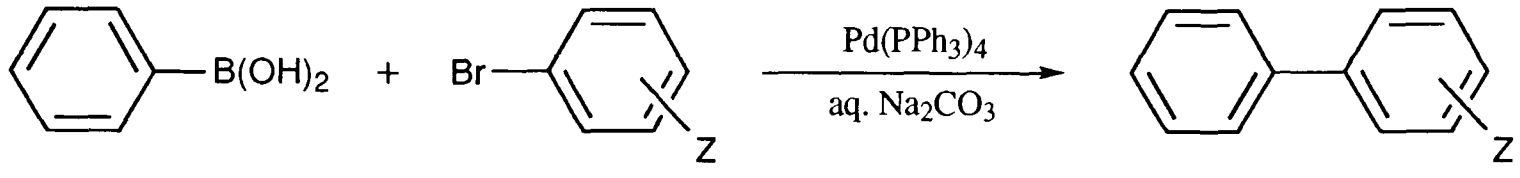
(61) (62) (63)



Scheme 1.24

This methodology has now been extended to the coupling of alkynyl halides,[48] aryl halides,[49] allylic bromides and benzylic bromides[50] with alkyl-, alkenyl- and aryl- boranes or boronic esters; the most commonly used catalysts for the Suzuki coupling are $Pd(PPh_3)_4$ and

$PdCl_2(dppf)$. The reaction is stereospecific and proceeds with retention of configuration. As in the Stille coupling, substituents on either partner are well tolerated. The catalytic cycle may be represented in a similar manner to that of the Stille coupling, with transmetallation occurring from boron rather than from tin. In recent years, the Suzuki coupling has been used in the synthesis of unsymmetrical biaryls as shown in Scheme 1.25.[51]

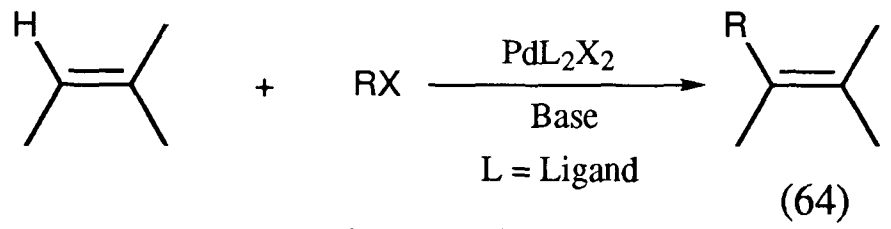


Scheme 1.25

Although the Stille and Suzuki coupling reactions may be used to carry out many of the same transformations, the Suzuki coupling has the great advantage of avoiding the use of highly toxic organostannanes.

1.3.4 The Heck reaction[52]

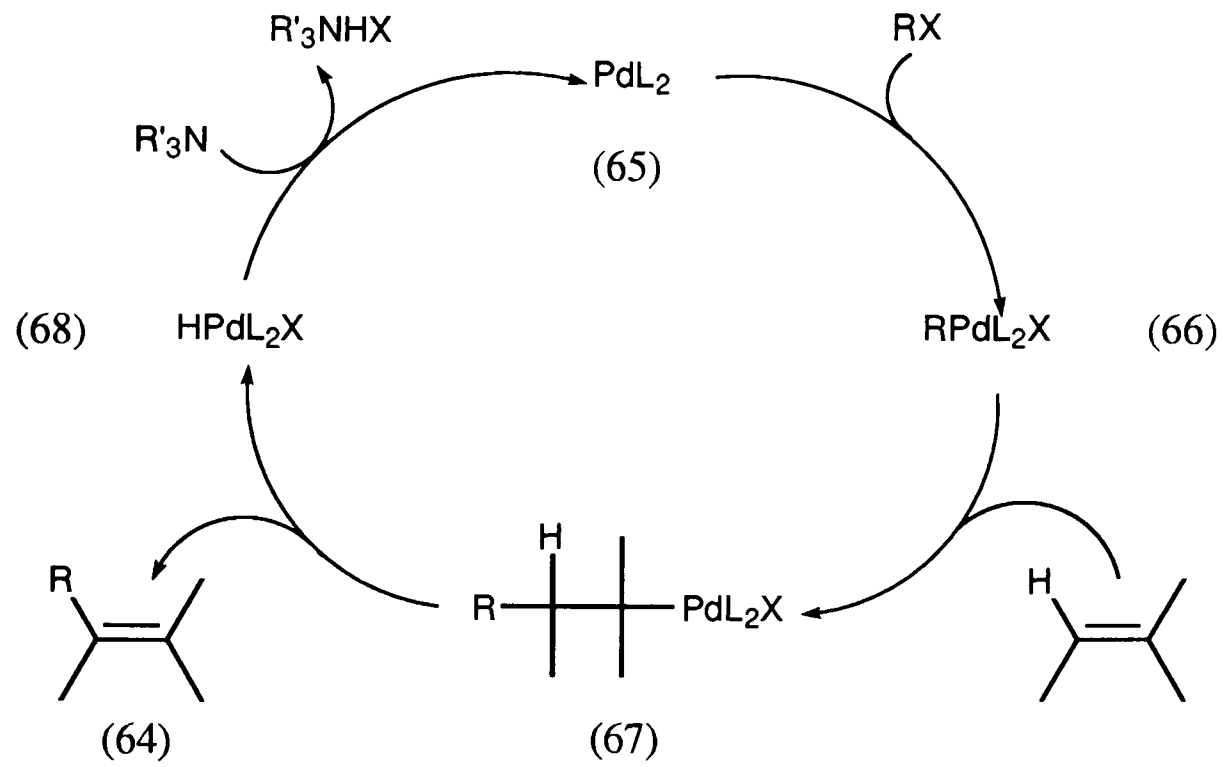
The palladium catalysed vinylation of organic halides is known as the Heck reaction. This important reaction results in carbon-carbon bond formation at an unsubstituted vinylic position as shown in Scheme 1.26.



(64)

Scheme 1.26

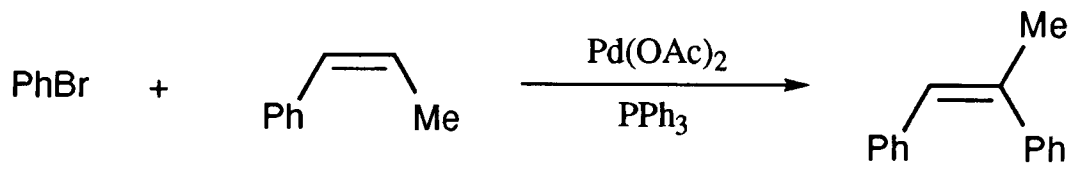
The mechanism may be represented in a similar way to the Stille coupling, as shown in Scheme 1.27. The first step involves the oxidative addition of the organic electrophile RX to the palladium species PdL_2 (65) to give the species $RPdL_2X$ (66). This then adds to the alkene double bond to give the alkyl palladium species (67) which undergoes *cis*-β-elimination to give the product (64) and the palladium species $HPdL_2X$ (68). The palladium(0) catalyst (65) is regenerated by elimination of HX from species (68).



Scheme 1.27

This reaction is general for aryl-, benzylic-, vinylic- and heterocyclic halides. The halide is normally bromine or iodine. As in the Stille coupling, halides with a hydrogen at the β-position cannot be used as β-elimination occurs rapidly from species (66). Terminal, internal, 1,1-disubstituted and some trisubstituted olefins will react according to Scheme 1.26, but it is generally the case that reaction rates decrease with increasing substitution.

The Heck reaction is very selective and almost any functional group on either reacting partner will be unaffected by the reaction conditions. For steric reasons, addition occurs at the least substituted end of the double bond. Scheme 1.28 shows the stereoselectivity of the Heck reaction which is best explained in terms of *syn*-addition of an active palladium intermediate followed by *syn*-elimination to give the product.



Scheme 1.28

1.3.5 Summary

While only four reaction types have been discussed in a general sense, it can be seen that there are many instances where carbon-carbon bond formation may be mediated by palladium species. These processes rely on the ability of palladium to coordinate π-functionality and to readily participate in oxidative addition and reductive elimination reactions leading to ligand coupling.

1.4 Lead

Lead(IV) reagents find wide use in oxidation reactions in organic chemistry[53] as a consequence of the thermodynamically favourable reduction of lead(IV) to lead(II) (Figure 1.2).[54] This reduction is considerably more facile than many other common oxidation couples, for example palladium(II) to palladium(0) and tin(IV) to tin(II). As a result of this, lead tetraacetate (LTA) is commonly used as an oxidising agent for a variety of functional groups in synthesis, for example in the cleavage of 1,2-diols to aldehydes.[53]

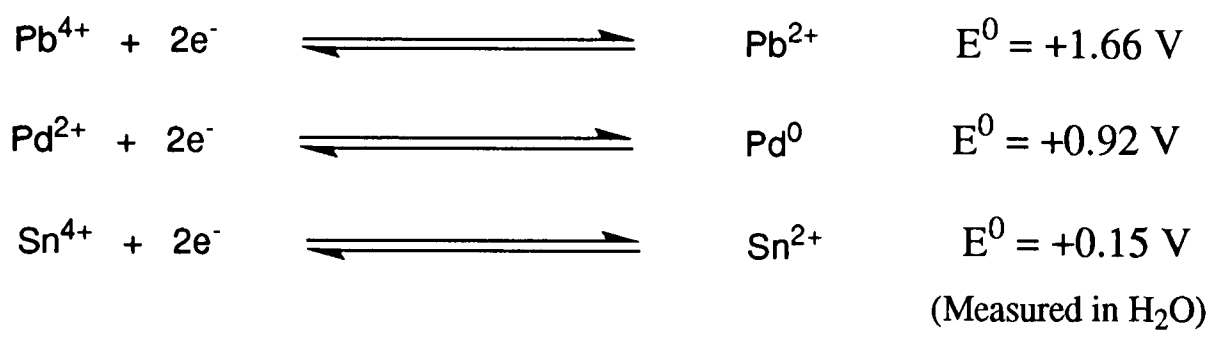
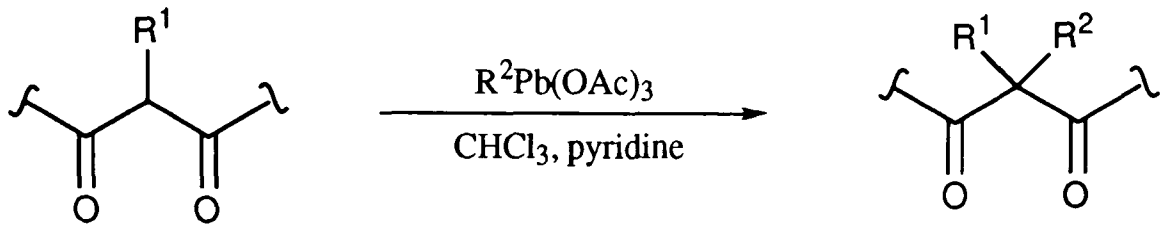


Figure 1.2

As in the cases of bismuth, iodine and palladium, lead(IV) may also be used as a centre around which potential reacting partners can be assembled. Carbon-carbon bond formation again occurs by a reductive elimination-type mechanism.

1.4.1 Reactions of organolead tricarboxylates

In the early 1970's, Pinhey began a study of aryllead tricarboxylates and found that these and their vinyllead and alk-1-ynllead counterparts could be used in the functionlisation of a wide range of soft carbon nucleophiles (Scheme 1.29).[55]



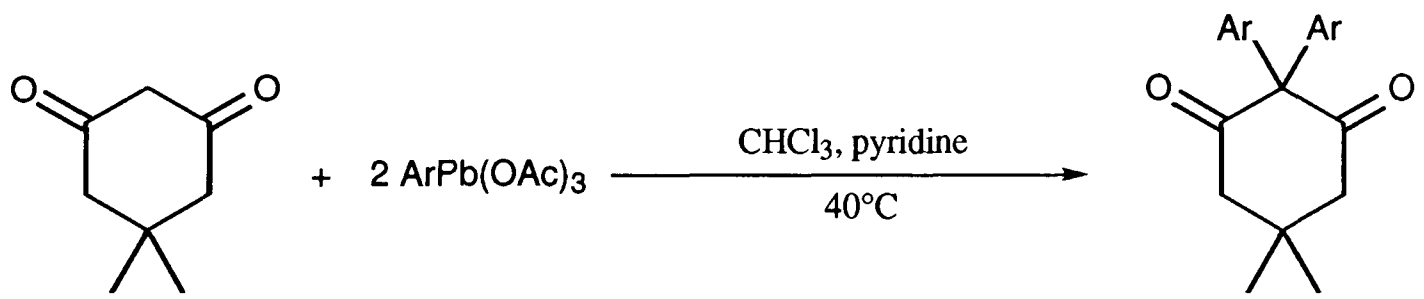
R^2 = aryl, vinyl, alk-1-ynyl

Scheme 1.29

These reactions are generally faster and higher yielding when the β–diketone is functionalised at the α-position, and are therefore a mild and efficient way of generating quaternary carbon centres.

1.4.1.1 Aryllead triacetates

Aryllead triacetates act as aryl cation synthetic equivalents. These compounds react readily with nucleophiles forming, for example, substituted phenols, aryl iodides, aryl azides, aryl fluorides and *N*-aryl amines.[55] The facile *C*-arylation of certain phenols led to questions as to whether aryllead triacetates would react similarly with enols. As a consequence, dimedone (69) was successfully diarylated[56] to give the diaryl compounds (70) as shown in Scheme 1.30.



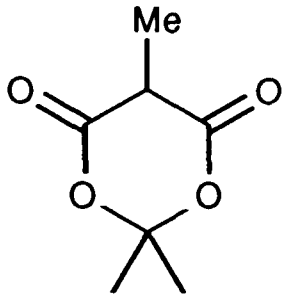
Ar = *p*-MeO-C_6H_4, *p*-Me-C_6H_4

(69) (70)

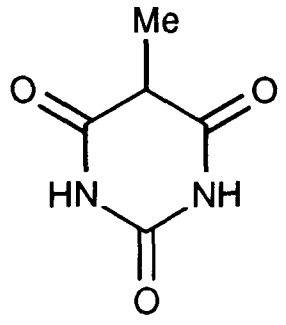
Scheme 1.30

This led to a wide ranging examination of the arylation reactions of other substrates including β–diketones, β-ketoesters, enolate salts of ketones and silyl enol ethers.[55] Generally, the highest yielding reactions were those in which the substrate possessed only one acidic

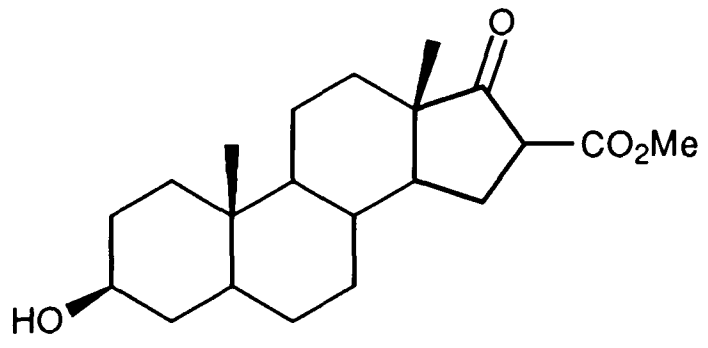
proton (but in some cases, steric and electronic factors may have an influence) and those in which the substrates were more acidic, such as 1,2,2-trimethyl-1,3-dioxane-4,6-dione (71) and barbituric acid (72).[57]



(71)

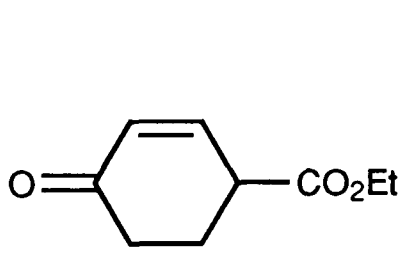


(72)

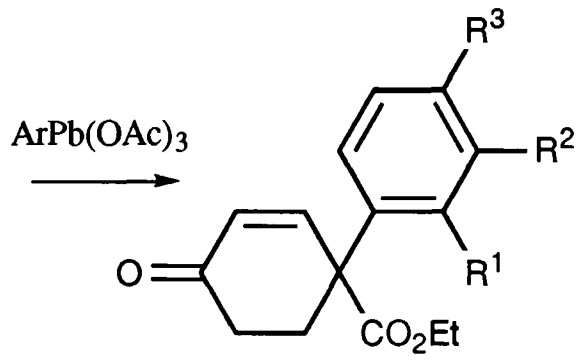


(73)

In the case of the steroidal β-ketoester (73), α-arylation was achieved in good yield leaving the secondary hydroxyl group untouched.[56] The α-aryl esters (75), (76) and (77) formed from compound (74), as shown in Scheme 1.31,[58] have successfully been used in syntheses of (±)-*o*-methyljoubertiamine (78),[59] (±)-mesembrine (79)[59] and (±)-lycoramine (80).[60]

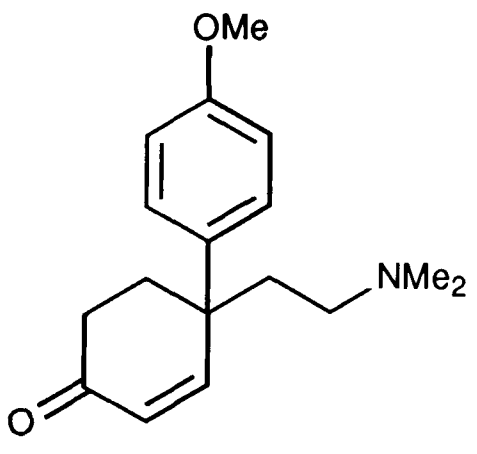


(74)

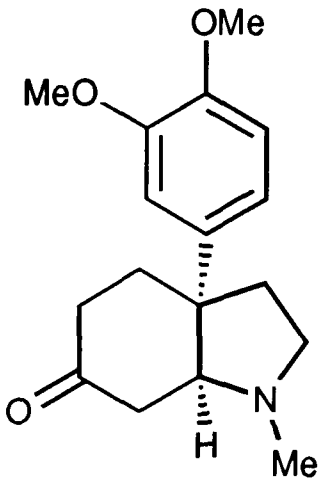


	R^1	R^2	R^3
(75)	H	H	OMe
(76)	H	OMe	OMe
(77)	OMe	OMe	H

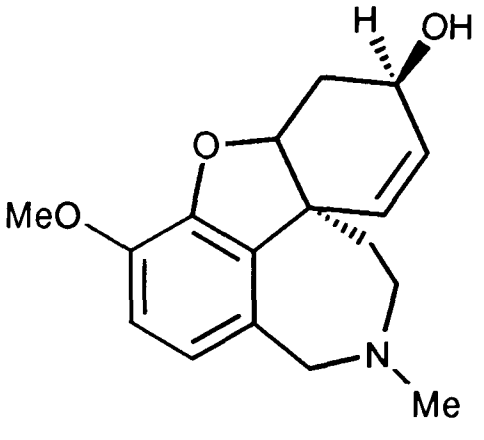
Scheme 1.31



(78)



(79)

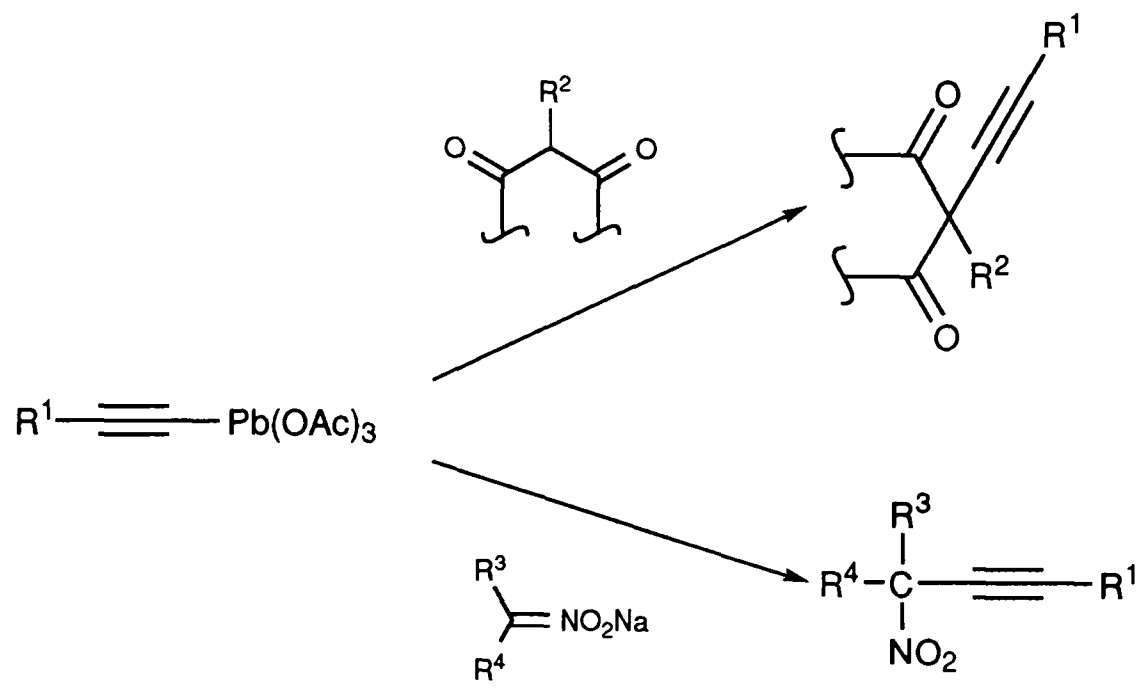


(80)

1.4.1.2 Vinyllead triacetates and alk-1-ynyllead triacetates

Vinyllead triacetates and the analogous alk-1-ynyllead compounds have been examined in much less detail than their aryllead counterparts. Vinyllead triacetates react with a range of β-dicarbonyl compounds, nitronate salts and phenols, behaving in these reactions as electrophilic vinylating agents.[55] As they are relatively unstable, rapid reaction with the nucleophile is a prerequisite for successful vinylation.

Alk-1-ynyllead triacetates demonstrate similar instability and similar reactivity. They may be used in the functionalisation of β-dicarbonyl compounds and nitronate salts as shown in Scheme 1.32.[61,62]

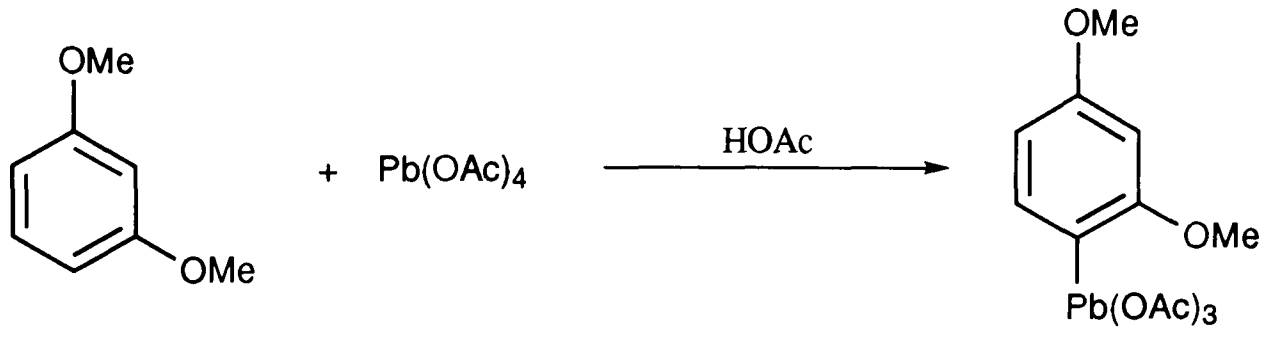


Scheme 1.32

1.4.2 Synthesis of organolead triacetates

1.4.2.1 Aryllead triacetates

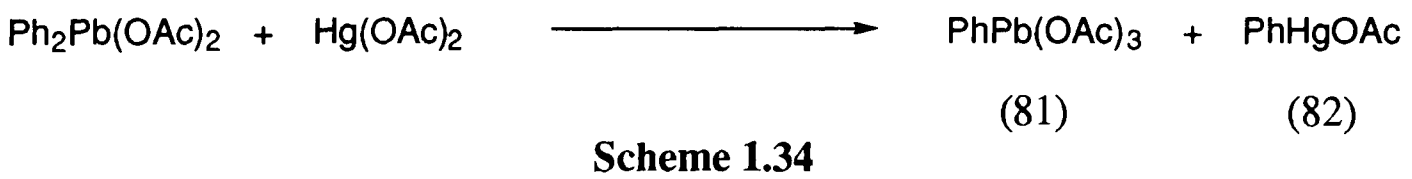
Aryllead triacetates may be prepared by two methods. The first, direct plumbation (Scheme 1.33), is rather restrictive and is unsuccessful for aromatic compounds less electron-rich than halobenzenes. The second method of preparation of aryllead triacetates, metal-metal exchange,[63,64] is a much more general procedure.



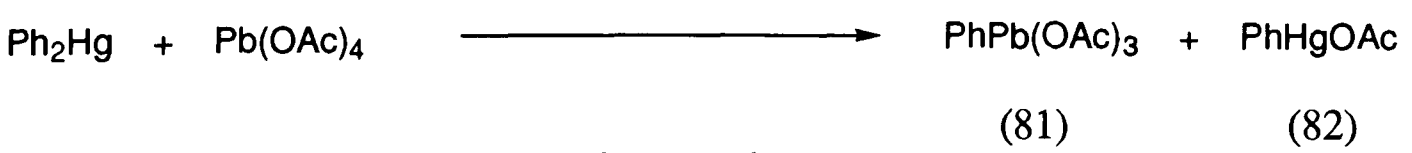
Scheme 1.33

In 1952, Panov and Kocheshkov[65] used metal-metal exchange in the first reported synthesis of an aryllead triacetate. Reaction of diphenyllead diacetate with mercury(II) acetate led to the formation of phenyllead triacetate (81) as shown in Scheme 1.34. Criegee[66] later reported a more general procedure (Scheme 1.35) which involved the rapid generation of the phenyllead intermediate which could then be used without isolation in the functionalisation of nucleophiles. In both these cases, isolation of the required product (81) from phenylmercury acetate (82) was found to be problematic.

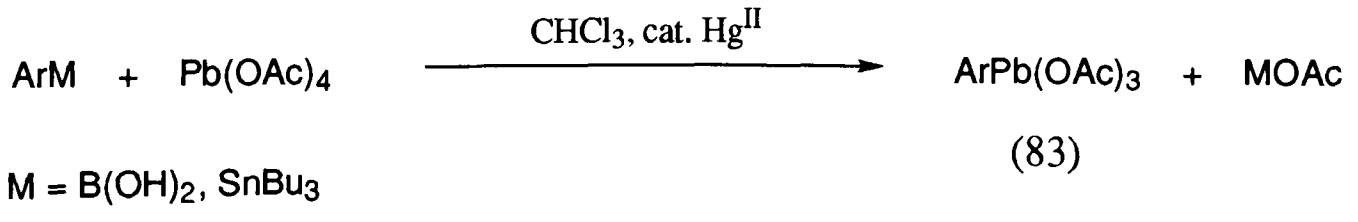
In recent years, trialkyl(aryl)stannanes[67] and arylboronic acids or esters[68] have been shown to undergo rapid metal-metal exchange in the presence of mercury(II) catalysts (Scheme 1.36). In the case of tin-lead exchange, the aryllead triacetate (83) can be readily isolated by precipitation.



Scheme 1.34



Scheme 1.35



Scheme 1.36

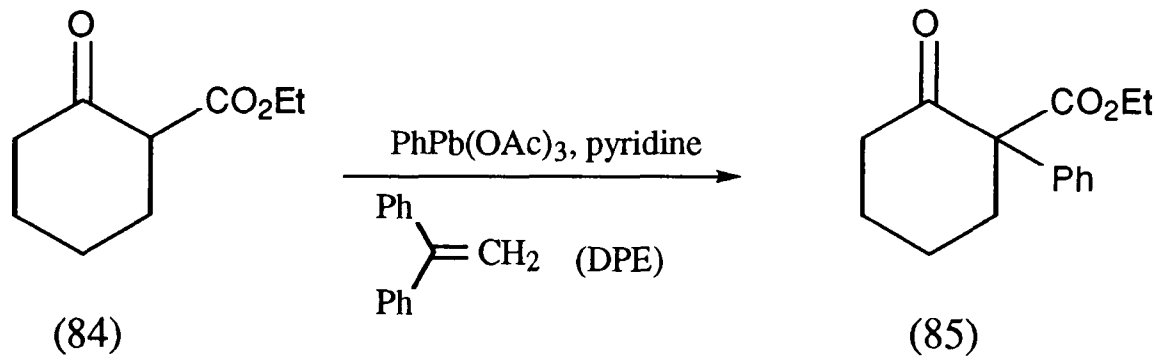
1.4.2.2 Vinyllead triacetates and alk-1-ynyllead triacetates

Metal-metal exchange may also be used to synthesise vinyllead triacetates and alk-1-ynyllead triacetates. Therefore, reaction of trialkyl(vinyl)stannanes or divinylmercury compounds with LTA may be used to generate vinyllead triacetates.[69,70] Similarly, *bis*(alk-1-ynyl)mercury and trialkyl(alk-1-ynyl)stannanes can be used to produce alk-1-ynyllead triacetates.[61] In 1990, Ikegami[62] developed a new method for the synthesis of alk-1-ynyllead triacetates involving the addition of a lithium acetylide in THF to a solution of LTA in dichloromethane at low temperature. Pinhey[55] has modified this procedure by moderating the reactivity of the acetylide by its conversion to a zinc reagent prior to addition of LTA.

1.4.3 Mechanism of arylation

1.4.3.1 Exclusion of a radical pathway

The ready arylation of iodide and azide ions and the salts of nitroalkanes, but not of other non-carbon nucleophiles in the absence of a copper catalyst, has led to questions as to whether arylation reactions using aryllead triacetates proceed *via* a single electron transfer mechanism. However, work by Barton in 1987[19] clearly established that arylation does not occur by a radical mechanism. The arylation of β-ketoester (84) was carried out in the presence and the absence of the radical trap 1,1-diphenylethene (DPE). Product (85) was obtained in approximately the same yield in both cases (Scheme 1.37 and Table 1.1).



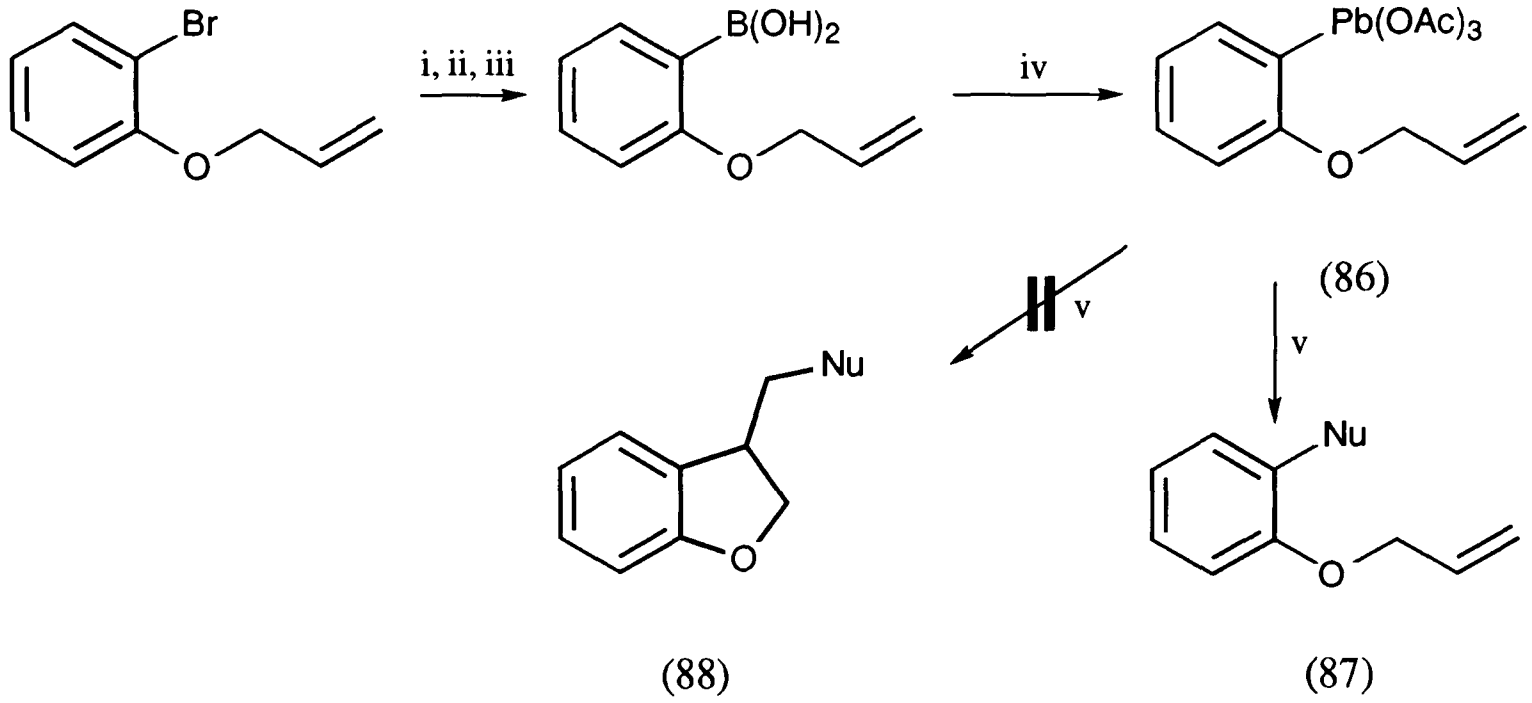
(84) (85)

Scheme 1.37

(84) (eq.)	$PhPb(OAc)_3$ (eq.)	Pyridine (eq.)	DPE (eq.)	Time (h)	(85) (%)
1	1.1	1.1	0	15	78
1	1.1	1.1	2	15	76

Table 1.1

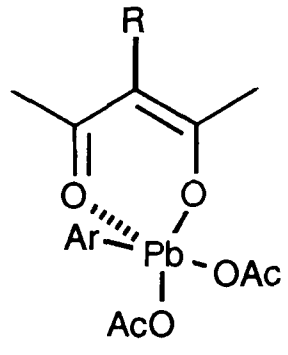
Pinhey has also recently carried out work similar to Beckwith's intramolecular trapping experiments to further confirm the non-radical nature of the arylation mechanism. *o*-Allyloxyphenyllead triacetate (86) was synthesised as shown in Scheme 1.38. Reaction of (86) with sodium iodide, sodium azide or β-ketoesters gave exclusively the substitution products (87) and not benzofurans (88), the formation of which would be expected if a radical pathway were in operation.[71]



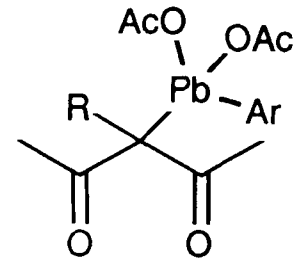
i) BuLi, -78°C
ii) $B(OCHMe_2)_3$, -78°C
iii) H_3O^+
iv) $Pb(OAc)_4$, 10% $Hg(OAc)_2$, $CHCl_3$
v) $Nu^{\ominus}$

Scheme 1.38

The arylation reaction probably proceeds by ligand exchange which places both reacting partners on lead(IV), followed by ligand coupling to give the arylated product. However, unlike similar reactions of bismuth where Bi-O bonded intermediates have been observed, no analogous lead species have been isolated. Possible structures for intermediates in the reactions of aryllead species are (89) and (90).

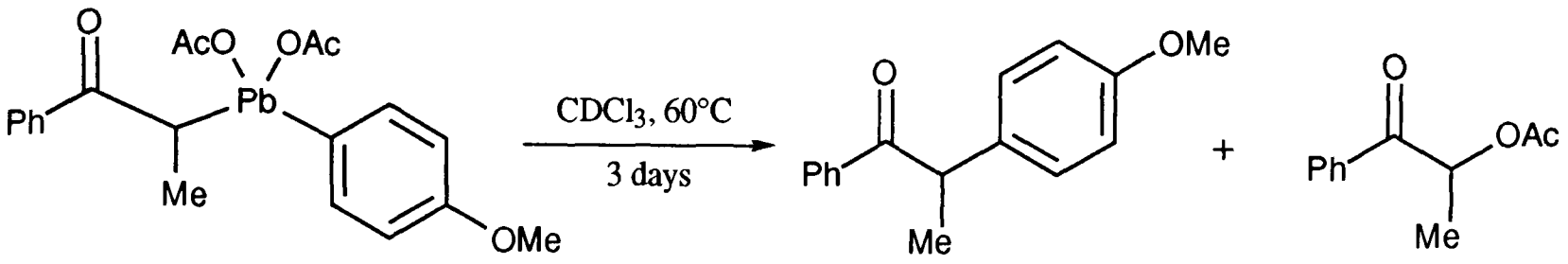


(89)



(90)

In further work by Pinhey,[72] compounds such as (91) were synthesised from silyl enol ethers and *p*-methoxyphenyllead triacetate. When this compound was heated to 60°C in chloroform, aryl ketone (92) and $Pb(OAc)_2$ were formed in modest yields, providing evidence for the occurrence of a ligand coupling reaction (Scheme 1.39). The only other product isolated was that of α-acetoxylation (93); it is significant that no symmetrical products, which would arise by intermolecular coupling, were observed.



37% 10%

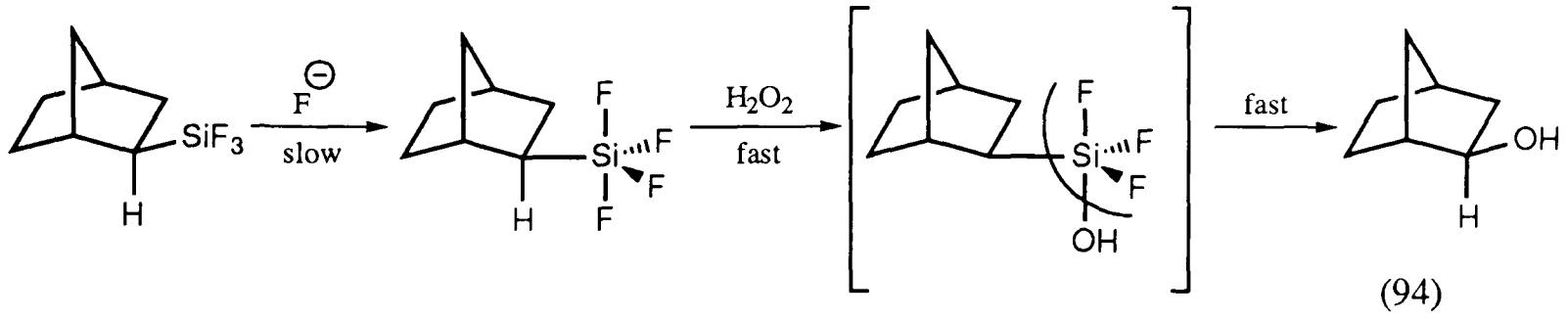
(91) (92) (93)

Scheme 1.39

A single crystal X-ray structure of (91) has been obtained.[72] This shows the complex to be dimeric with each lead centre having pentagonal bipyramidal geometry. The *p*-methoxyphenyl and α-methylphenacyl groups are axial and the lead atom is unsymmetrically bonded to both oxygens of the two acetate units. One oxygen atom in each monomer is bonded to both lead atoms. The diaxial arrangement of the coupling partners means that direct collapse to the product is not favoured. For the orbital overlap required for ligand coupling to occur, there must be a thermal rearrangement to take one of the groups to an equatorial position. This is in fact the proposed pathway for ligand coupling of hypervalent species.

1.4.3.2 Ligand coupling

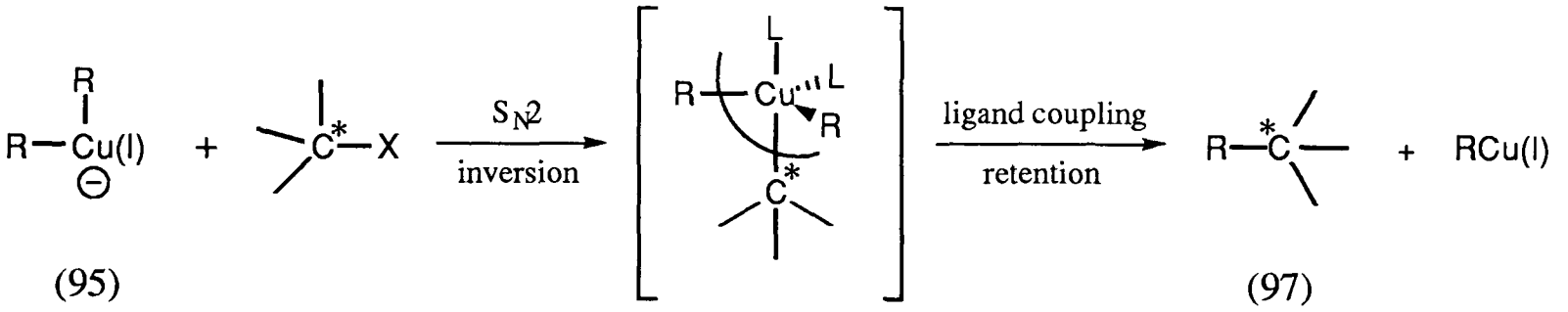
Ligand coupling is a concept reported by both Trost[73] and Oae.[74] The coupling reactions are concerted and occur *via* orbital interaction between an axial and an equatorial ligand on a suitable core atom, for example sulphur, silicon, iodine or lead. An important consequence of this orbital interaction is that ligand coupling reactions proceed with retention of configuration in both ligands.



(94)

Scheme 1.40

In the example shown in Scheme 1.40, interaction between the OH group and the norbornane ring leads to concerted expulsion of the ligand coupling product (94). Many similar reactions are known for pentavalent phosphorus and sulphur. There are also a number of reactions of hypervalent species which appear to proceed by a ligand coupling mechanism. Such couplings are well known for copper species, for example those involving the Gilman reagent (Scheme 1.41).[75] Oxidative addition to cuprate (95) generates a copper(III) intermediate (96) which undergoes ligand coupling to give the product (97) with retention of configuration.



(95)

L = solvent or ligand

(96)

(97)

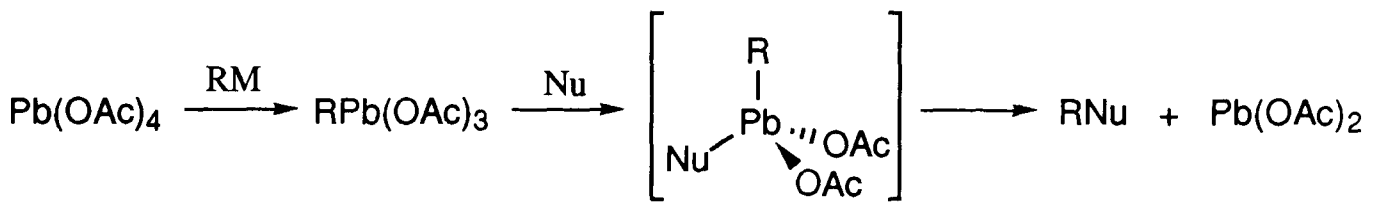
Scheme 1.41

Ligand coupling appears to occur in reactions of other metals, including lead(IV). In recent years, Barton has invoked a ligand coupling mechanism in the lead(IV) mediated syntheses of hindered phenols[76] and 3-aryl-4-hydroxy-1-benzopyran-2-ones.[77]

1.5 Development of lead(IV) chemistry

1.5.1 Introduction

All of the previous discussion has highlighted that lead(IV) mediates a wide range of synthetically useful reactions. These reactions include functional group interconversions (particularly oxidations) and, more importantly, carbon-carbon bond formation. In the latter reactions, lead(IV) species (98) act as synthetic equivalents for vinyl-, aryl- and alk-1-ynyl-cations and therefore offer easy access to carbocations which are otherwise difficult to generate. It has also been demonstrated that ligand exchange on lead(IV) to give alkyllead(IV) species (98) may be easily carried out by metal-metal exchange reactions using tin, mercury and boron compounds. Further reaction with soft carbon nucleophiles (Nu) presumably leads to intermediates such as (99), which, by lead(IV) mediated carbon-carbon bond formation give products (100) (Scheme 1.42).



(98) (99) (100)

Scheme 1.42

The available evidence indicates that this carbon-carbon bond formation occurs *via* a ligand coupling mechanism. Therefore, it may be possible to achieve a transfer of asymmetry in the bond formation reaction, which would not be expected if a radical process was in operation. There is ample precedent for this type of behaviour in the case of other metals, particularly palladium.

The work in this thesis outlines efforts to develop the utility of lead(IV) reagents in synthesis with a particular emphasis on chirality transfer. An initial aim was to examine chiral dicarboxylic acids as ligands, as lead(IV) carboxylates are well reported in the literature (see Section 1.5.3). Carboxylic acids provide the electron donating power required of a ligand, but

are not readily oxidised, in contrast with other heteroatom functional groups.

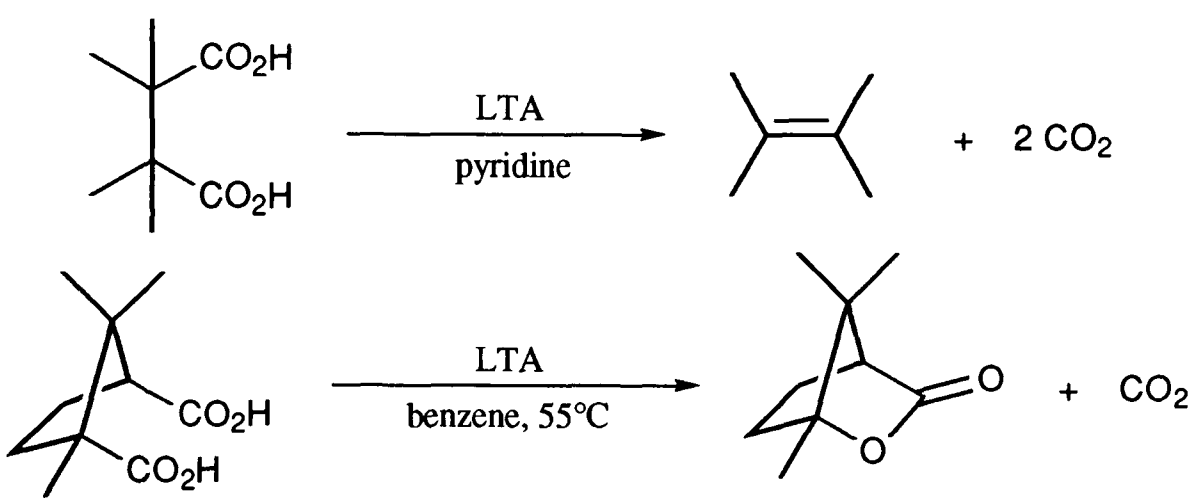
1.5.2 Designing ligands for lead(IV)

The use of organolead(IV) tricarboxylates in carbon-carbon bond formation has already been discussed. The aim of this work was to develop a chiral lead(IV) complex which was suitable for carrying out these same transformations enantioselectively. In this type of reaction, the complex must be able to both activate the substrates and control the selectivity. The ligands must, therefore, consist of a unique combination of donor atoms in a defined chiral environment with the asymmetric centre as close to the reacting components as possible.

In a recent review, Sharpless[78] has described some of the effects of introducing ligands to existing catalysed systems. In these cases, the addition of a specific ligand may lead to a faster, "ligand-accelerated" reaction. Examples of "ligand-accelerated" reactions include the titanium catalysed asymmetric epoxidation of allylic alcohols, and the osmium tetroxide catalysed asymmetric dihydroxylation of olefins. It is also possible that the binding of a suitably chosen chiral ligand can increase the rate of the catalysed reaction, resulting in the domination of the stereoselective pathway. Thus, even for systems where there are multiple species in solution, asymmetric catalysis can be achieved.

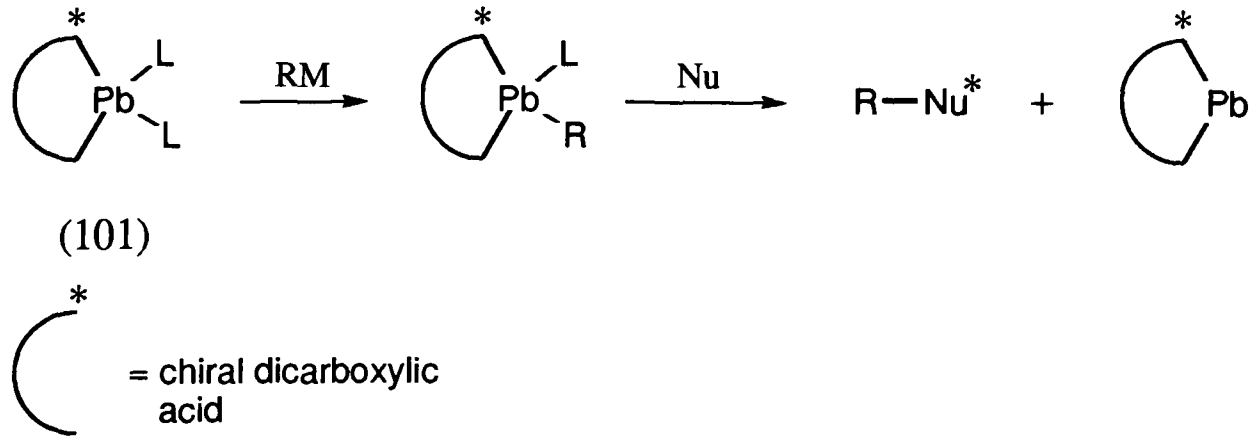
For any significant selectivity to be observed in carbon-carbon bond formation, the reaction must occur *via* a highly organised transition state. A single reactive species is desirable since this avoids the participation of other species with different reactivity and selectivity.[79] In work to develop chiral hydroxamate catalysts for asymmetric epoxidation,[80,81] it was found that the catalyst was deactivated by binding of a chiral ligand and that the system was in dynamic ligand exchange. Both these facts meant that the development of a useful catalyst was impossible. In contrast, in asymmetric epoxidation reactions catalysed by a titanium-tartrate system, the major species in solution was found to be the most reactive and the most selective.[78] Achieving the correct metal and ligand combination and stoichiometry in such systems is notoriously difficult.

In the design of ligands for lead(IV), some more specific points must be taken into consideration. As has been mentioned before, lead(IV) is a highly oxidising metal, and therefore the potential application of heteroatom ligands (for example oxygen, nitrogen and sulphur) is limited since facile oxidation of such ligands would be expected. It is for this reason that carboxylic acids are by far the most common ligands for lead(IV). However, in the preparation of lead(IV) tetracarboxylates, care must be taken, as under forcing conditions, decarboxylation of acids occurs readily as shown in Scheme 1.43.[82,83] Unfortunately, when using carboxylic acids as chiral ligands, the chiral centre is by necessity remote in relation to the lead centre.



Scheme 1.43

However, this work will concentrate on the development of a lead(IV) tetracarboxylate such as (101) as this would provide a reagent of great versatility (Scheme 1.44). An understanding of the chemistry of lead(IV) tetracarboxylates is therefore vital for this work.



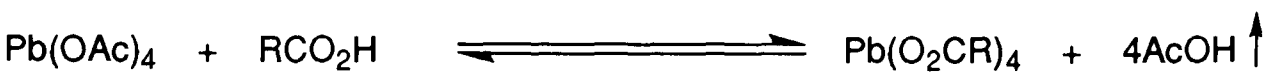
(101)

Scheme 1.44

1.5.3 Lead(IV) tetracarboxylates

1.5.3.1 Synthesis of lead(IV) tetracarboxylates

The most common method for the preparation of lead(IV) tetracarboxylates is shown in Scheme 1.45. The acetate ligands from lead(IV) tetraacetate (LTA) are metathesised with other carboxylates, the reaction being driven to completion by removal of acetic acid liberated during transligation.

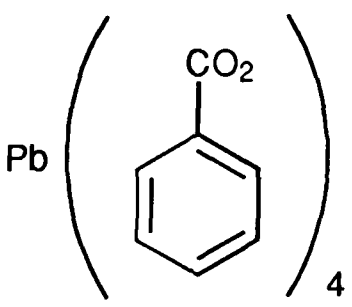


Scheme 1.45

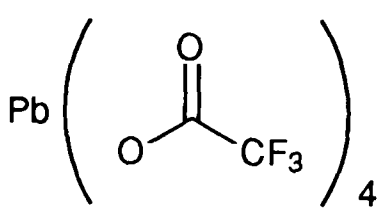
Removal of acetic acid is normally achieved in one of two ways. Bachmann and Wittman used high boiling solvents to remove acetic acid under reduced pressure reflux.[84] This method is however cumbersome, and is restricted to complexes which can withstand the high temperatures required to remove the solvent following transligation. Heusler *et al.*[85] used a simpler procedure whereby benzene was used to azeotropically remove acetic acid. A modification of this procedure using toluene rather than benzene[86] has been used extensively both in this and other work to prepare a wide range of lead(IV) tetracarboxylates.

1.5.3.2 Known lead(IV) tetracarboxylates

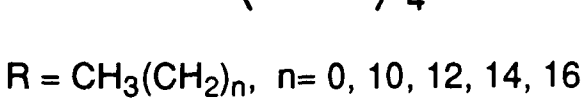
Lead(IV) tetrabenzoate (LTB)[87] (102) and lead(IV) tetrakistrifluoroacetate[88] (103) are fairly common lead complexes which have found some use, principally as oxidants, in organic synthesis. Yakawa and Sakai[89] have prepared lead(IV) tetracarboxylates (104) and (105) using monodentate and bidentate ligands respectively.



(102)

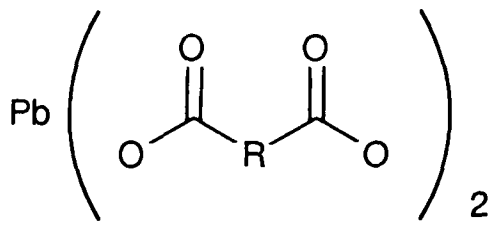


(103)



R = $CH_3(CH_2)_n$, n= 0, 10, 12, 14, 16
R = Ph, $PhCH_2$, Ph_2CH, Ph_2CHCH_2

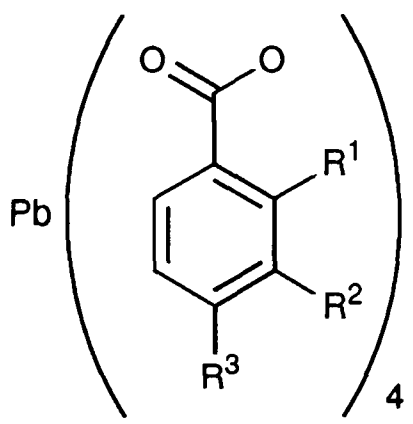
(104)



R = $-(CH_2)_n-$, n = 7,8

(105)

More recently, work in this group has demonstrated that it is possible to prepare a wide range of monodentate lead(IV) complexes *via* the transligation method described above using toluene as the azeotroping solvent.[86]



R^1=R^2=R^3=H
R^1= OMe, R^2=R^3=H
R^1= R^3= H, R^2=OMe
R^1= R^2= H, R^3=OMe
R^1= Cl, R^2=R^3=H
R^1= R^2= H, R^3=Cl

$(RCO_2)_4$ Pb

R = 1-naphthyl-
R = 2-naphthyl-
R = adamantyl-
R = C_6H_{11}-
R = trans-PhCH=CH-
R = trans- MeCH=CH-
R = Me_2C=CH-
R = PhC≡C-
R = $PhCH_2$-
R = *p*-$NO_2C_6H_4CH_2$-

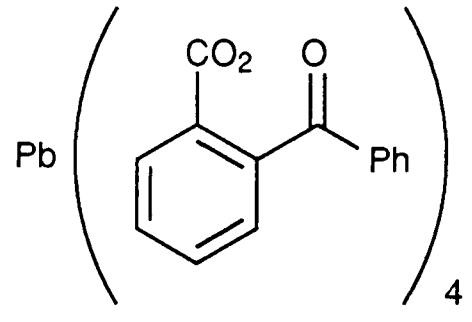
Figure 1.3

1.5.3.3 Structures of lead(IV) tetracarboxylates

Very little is known about the geometry and coordination of lead(IV) tetracarboxylates. Kamenar[90] has published a crystal structure of LTA, which showed the structure to consist of two symmetrical and independent sets of molecules with no bridging atoms between the lead centres. The coordination polyhedron appears as a flattened trigonal dodecahedron. Unfortunately, atomic coordinates for this structure have not been published. Partch and Monthony[91] have investigated the IR spectra of LTA in solvents of differing coordinating power. They observed that the carboxylate band diminished in favour of a carbonyl band as the apparent coordinating power of the solvent increased. This was explained in terms of

bidentate ligands being displaced to monodentate ligands as the solvent complexed to lead(IV).

An X-ray crystal structure of lead(IV) tetrabenzoylbenzoate (106)[92] has recently been obtained. This shows that each molecule has S_4 symmetry and that the benzoyl oxygen is situated well away from the lead(IV) centre. Each coordinating carboxylate has two Pb-O bonds of different lengths (2.24 Å and 2.31 Å). Each ligand is bidentate and thus the lead(IV) centre is eight-coordinate, with the oxygens in a dodecahedral environment (Figure 1.4).



(106)

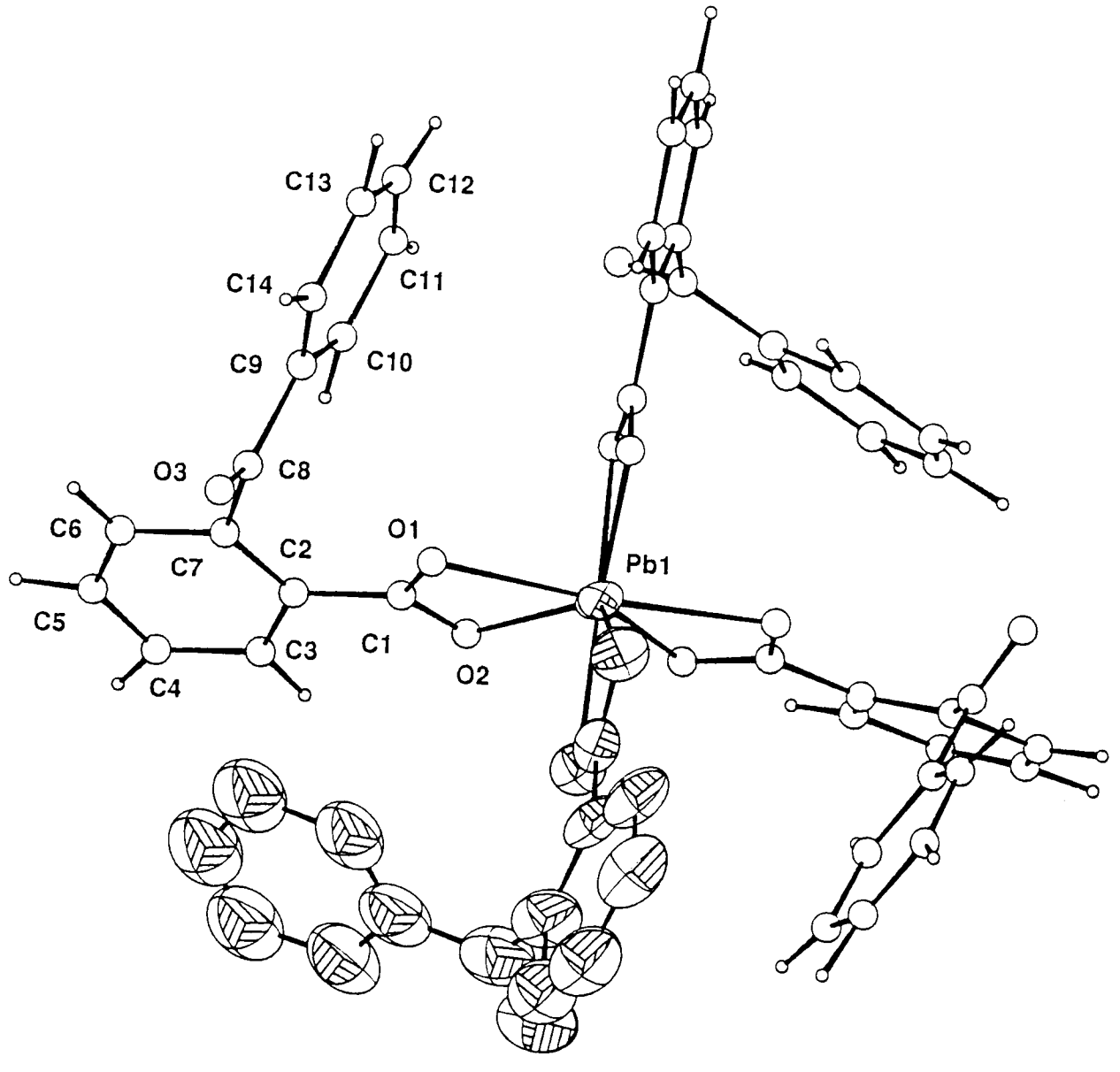


Figure 1.4

1.6 Aims of the present work

- The design and construction of novel ligands for lead(IV) which may be used to form complexes which are both stable and reactive.

- Using these reagents, to develop carbon-carbon and carbon-heteroatom bond formation methodologies with a particular emphasis on the construction of chiral, quaternary centres.

CHAPTER TWO

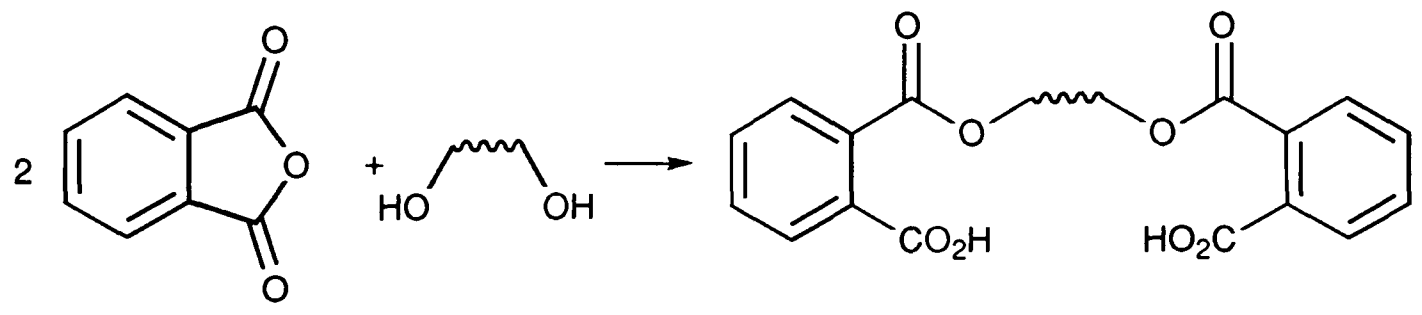
Synthesis of Novel Dicarboxylic Acid Ligands

This thesis outlines work to develop novel lead(IV) reagents suitable for enantioselective carbon-carbon bond formation. Lead(IV) tetracarboxylates are well reported in the literature[86,87,88,89] and contain ligands which are stable with respect to oxidation by lead(IV). Thus, this Chapter describes the synthesis of novel dicarboxylic acids, both chiral and achiral, which would be suitable for complexation to lead(IV).

2.1 Synthesis of achiral dicarboxylic acid ligands

2.1.1 Phthalic anhydride precursor

Initial attempts to synthesise achiral ligands centred upon the use of phthalic anhydride (107) as a carboxylic acid group precursor. Opening of phthalic anhydride with suitable diols (108) was expected to give easy access to a range of dicarboxylic acid ligands (109) of different lengths (Scheme 2.1).



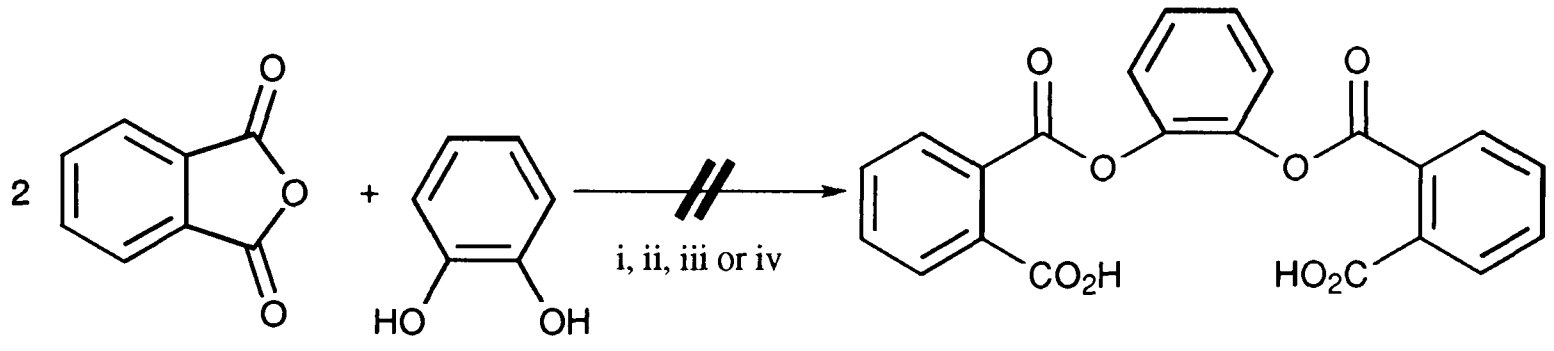
(107) (108) (109)

Scheme 2.1

The first diol linking unit studied was catechol (110). Heating two equivalents of phthalic anhydride with one equivalent of catechol in toluene failed to yield the required dicarboxylic acid (111), as did reaction in chloroform with *p*-toluenesulphonic acid catalysis.[93] Reaction of phthalic anhydride with catechol in chloroform in the presence of catalytic DMAP

resulted in recovery of unreacted starting materials (Scheme 2.2).

In 1955, Prajer[94] reported that heating a mixture of one equivalent of *trans*-2,3-dihydroxy-1,2,3,4-naphthalene and two equivalents of phthalic anhydride in pyridine resulted in the formation of the corresponding phthalate ester. However, reaction of catechol and phthalic anhydride under these conditions failed to yield dicarboxylic acid (111) (Scheme 2.2).



(107) (110) (111)

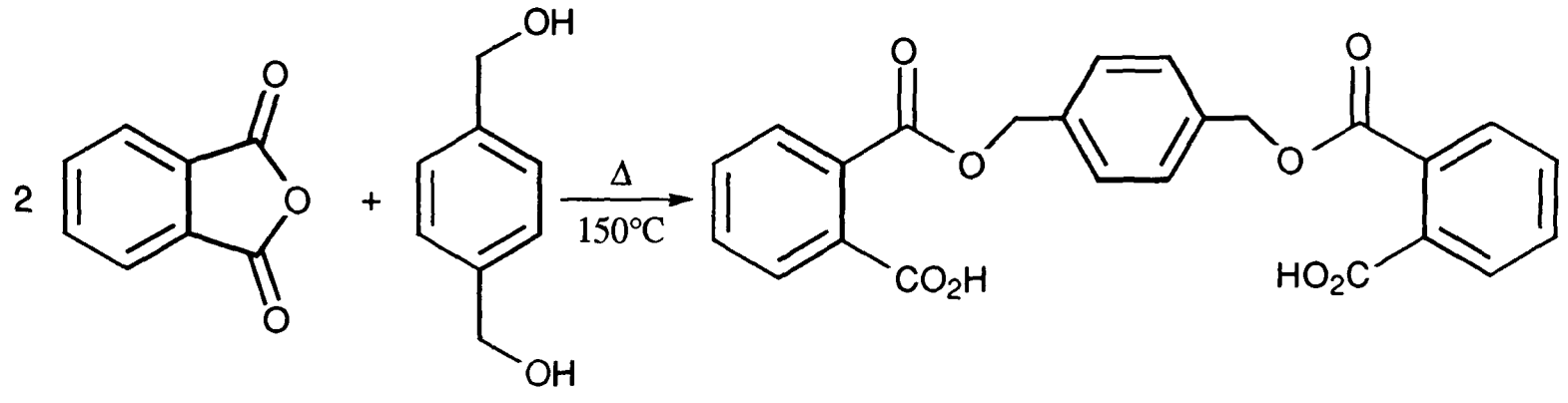
i) Toluene, Δ
ii) $CHCl_3$, 0.5 eq. *p*-toluenesulphonic acid, Δ
iii) $CHCl_3$, 0.2 eq. DMAP, Δ
iv) Pyridine, Δ

Scheme 2.2

The failure to effect opening of phthalic anhydride could be attributed either to low reactivity of the hydroxyl groups of catechol, or to possible steric hindrance in the product dicarboxylic acid (111). Both of these possible problems could be overcome by using benzene-1,4-dimethanol as a linking unit.

After an initial unsuccessful attempt to prepare 1,1'-(benzene-1,4-dimethyl)diphthalate (113) by combining phthalic anhydride with benzene-1,4-dimethanol (112) and catalytic *p*-toluenesulphonic acid in chloroform at reflux, a literature search revealed an alternative method for the formation of half-acid half-ester compounds from phthalic anhydride.[95] In a procedure to resolve 2-octanol, phthalic anhydride was opened to give 2-octyl hydrogen phthalate by heating the anhydride with 2-octanol at 110-115°C for twelve to fifteen hours. Therefore, benzene-1,4-dimethanol (m.p. 117-119°C) was combined with phthalic anhydride (m.p. 131-134°C) and heated at 150°C for around six hours. After this time, the homogeneous

melt solidified to a white solid. This was recrystallised from ethyl acetate to give 1,1'-(benzene-1,4-dimethyl)diphthalate (113) in 31% yield (Scheme 2.3). Although the yield of the product was rather low, the ease of preparation nevertheless allowed the synthesis of ligand (113) on gram scale.

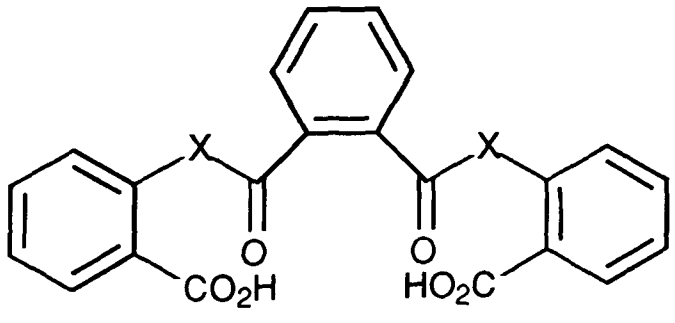


(107) (112) (113)

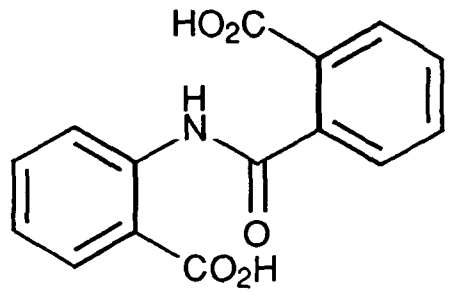
Scheme 2.3

A further attempt to synthesise ligand (111) using this methodology was made by heating catechol (m.p. 104-106°C) and phthalic anhydride (m.p. 131-134°C) together at 130°C for one hour. Recrystallisation of the white solid so obtained failed to give any of the required product.

It was hoped that the solid fusion methodology could be extended to allow the preparation of ligands such as (114) and (115) by reaction of phthalic anhydride with benzoic acid derivatives. However, heating of phthalic anhydride with 2-hydroxybenzoic acid or 2-aminobenzoic acid failed to give the required products (114) and (115) respectively. This is despite a report in the literature of the successful ring opening of phthalic anhydride with 2-aminobenzoic acid to give *N*-(2-carboxyphenyl)phthalamide (116).[96]



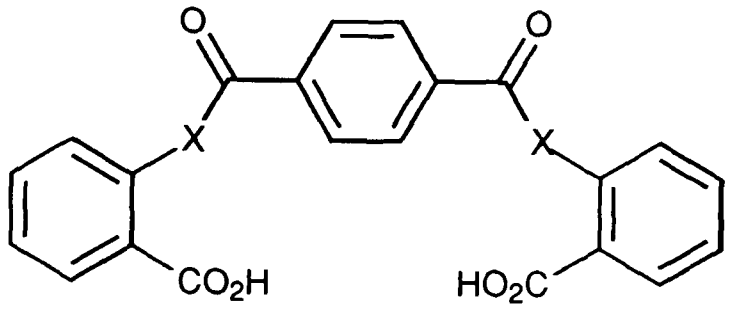
X = O (114)
X = NH (115)



(116)

2.1.2 Terephthaloyl-linked ligands

In recent years, Japanese patents[97] have reported the synthesis of *N,N'-bis*(2-carboxyphenyl)terephthalamide (117). As well as being a dicarboxylic acid, this compound also contains two nitrogen atoms, the lone pairs of which could act to complete the coordinative saturation of any complex formed using (117) as a ligand.



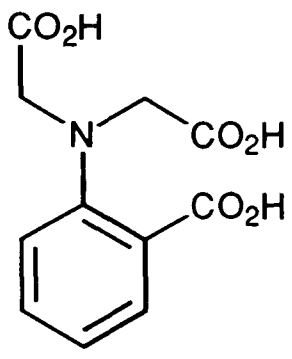
X = NH (117)
X = O (118)

However, reaction of terephthaloyl chloride with 2-aminobenzoic acid in basic aqueous acetone at room temperature according to the literature protocol failed to yield *N,N'-bis*(2-carboxyphenyl)terephthalamide (117).

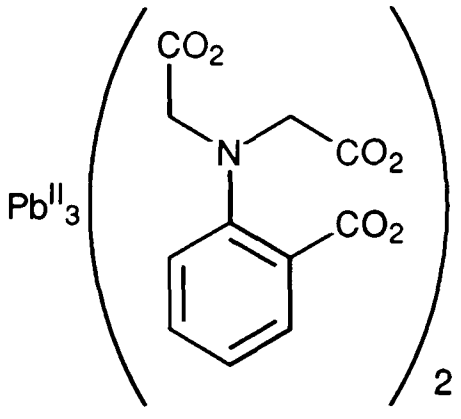
An attempt to synthesise the analogous oxygen-linked ligand (118) by heating 2-hydroxybenzoic acid, terephthaloyl chloride and triethylamine at reflux in chloroform also failed to give the required product (118).

2.1.3 Elaboration of 2-aminobenzoic acid

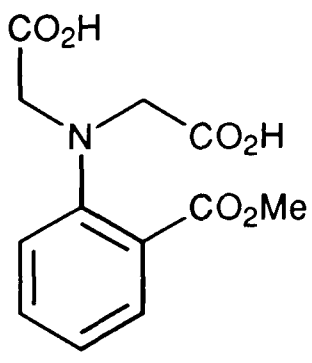
Early in this work, attempts were made to synthesise lead(IV) complexes of the 2-aminobenzoic acid derivative (119) (Chapter 3). Transligation of LTA with two equivalents of (2-carboxyphenylimino)diacetic acid (119) resulted in the formation of the trimeric lead(II) complex (120). It was thought that if methyl 2-aminobenzoate could be elaborated to give the diacid (121), this could be transligated to form monomeric lead(IV) complexes.



(119)



(120)

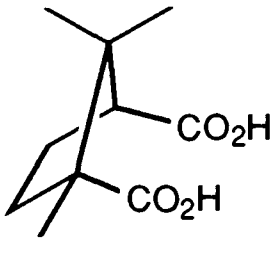


(121)

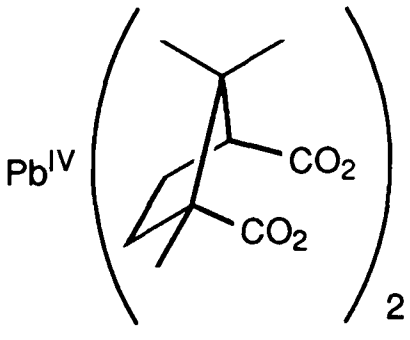
Heating of methyl 2-aminobenzoate with two equivalents of chloroacetic acid in aqueous basic solution at 70°C for seven hours[98] did result in the formation of a small quantity of the required diacid (121). A repeat of the procedure, but heating the reactants at reflux, did not result in formation of any of the required product. At this point, the construction of achiral ligands in this manner was abandoned as it seemed that 2-aminobenzoates would not make useful templates for ligand synthesis due to their poor nucleophilicity.

2.2 Synthesis of chiral ligands - 1

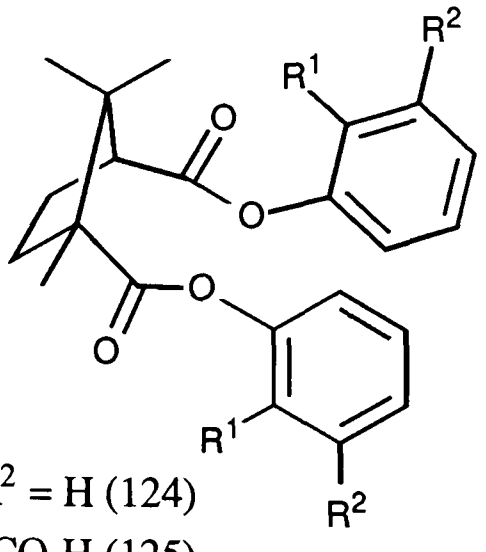
(1*R*, 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid (camphoric acid) (122) is a cheap, commercially available dicarboxylic acid, and at the start of this work, a lead(IV) complex (123) of this diacid was synthesised (Chapter 3). This complex, however, was only soluble in DMSO. It was hoped that by using camphoric acid as a chiral template, bidentate ligands such as (124) and (125) could be prepared which, when coordinated to lead(IV), would give asymmetric complexes which were more soluble in organic solvents than complex (123).



(122)



(123)

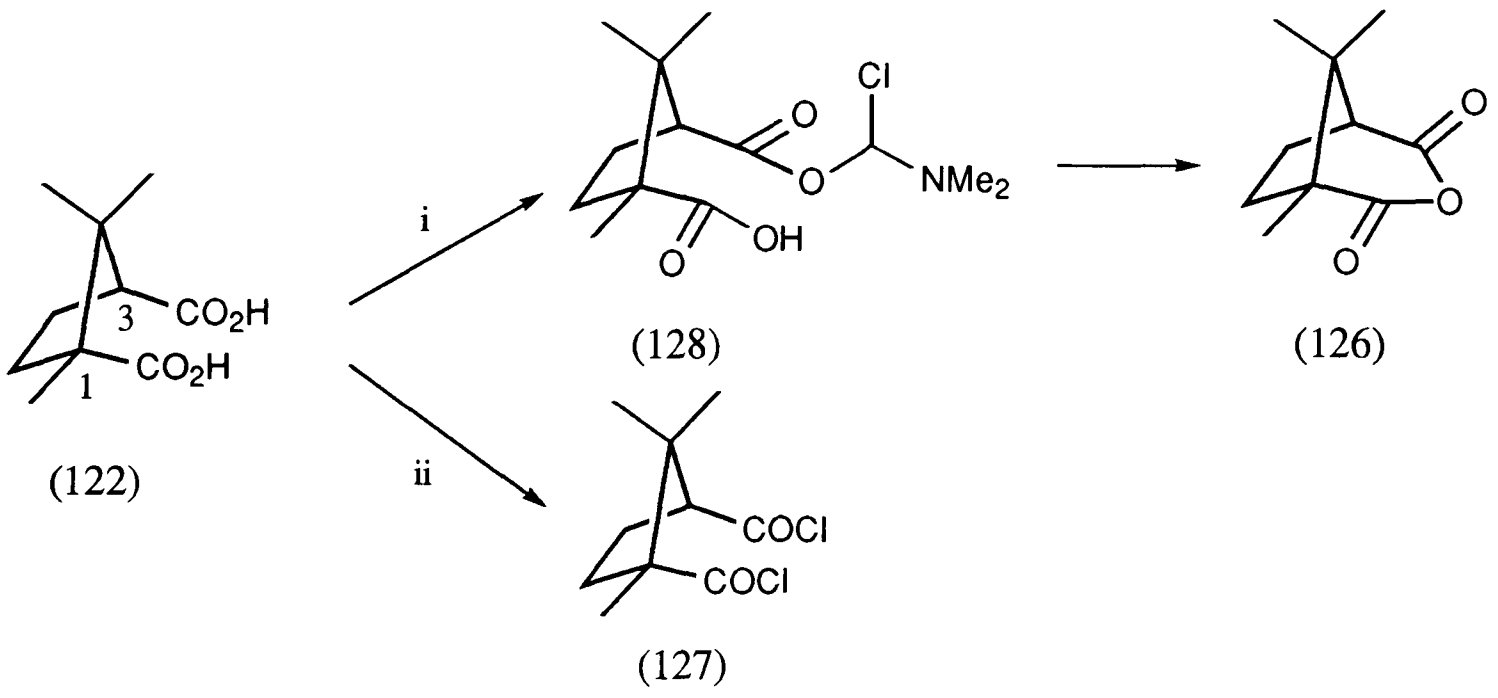


$R^1 = CO_2H$, $R^2 = H$ (124)
$R^1 = H$, $R^2 = CO_2H$ (125)

2.2.1 Synthesis of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarbonyl chloride (127)

The first planned step in the synthesis of ligands (124) and (125) was the conversion of camphoric acid to (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarbonyl chloride (127) (camphoric acid chloride); coupling of this derivative with suitable carboxylic acids would then provide the desired ligands (124) and (125). In an initial attempt to synthesise camphoric acid chloride, camphoric acid and thionyl chloride were heated at reflux in carbon tetrachloride and DMF according to a literature procedure.[99] Contrary to the earlier report, however, removal of the solvent *in vacuo* yielded a solid which, after recrystallisation from ethanol, was found to be (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic anhydride (126) (camphoric anhydride). The reaction has since been repeated many times, in all cases leading to the formation of anhydride (126) in 60-70% yield.

Following the failure of this method to give the correct product, acid chloride (127) was successfully synthesised by stirring a suspension of camphoric acid (122) and phosphorus pentachloride in pentane, initially at 0°C and then at room temperature overnight.[100] After filtration to remove unreacted PCl_5 and removal of the solvent *in vacuo*, pure camphoric acid chloride (127) could be isolated in 87% yield by short path distillation (Scheme 2.4).



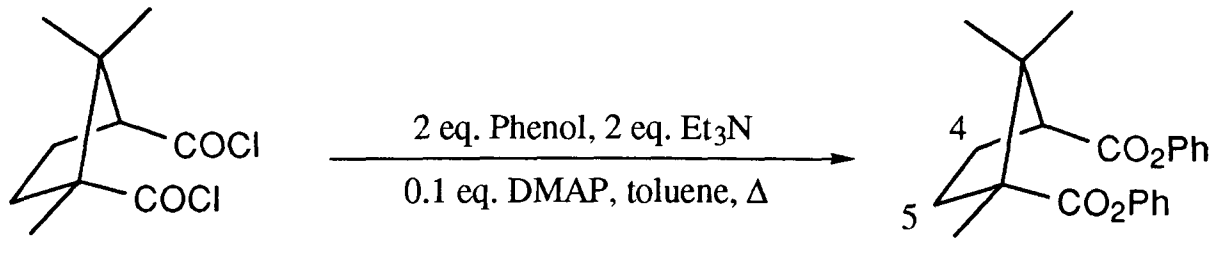
i) $SOCl_2$, cat. DMF, CCl_4, Δ
ii) PCl_5, pentane, 0°C to r.t.

Scheme 2.4

In retrospect, these results are not surprising as it has been reported[101] that dibasic acids which readily give anhydrides do not give acid chlorides on treatment with thionyl chloride, rather they form the anhydrides directly. In 1904, Bone *et al.*[102] reported work on the partial hydrolysis of neutral diesters, in which it was found that hydrolysis of the least substituted ester proceeds at a faster rate. By analogy, it might be expected that reaction with thionyl chloride/DMF at C(3) will occur preferentially to give an intermediate such as (128), which could then be attacked by the C(1) acid group, rather than chloride ion, to give anhydride (126) (Scheme 2.4). It would seem, at least for this reaction, that PCl_5 is more reactive than the thionyl chloride/DMF system and shows less discrimination between the C(3) and C(1) acid groups. Therefore, intermediates analogous to (128) are not formed and formation of the acid chloride is possible.

2.2.2 Establishment of coupling conditions

In order to establish appropriate reaction conditions for the preparation of the more elaborate systems (124) and (125), the reaction of phenol with camphoric acid chloride was studied. In this model system, camphoric acid chloride, phenol, triethylamine and DMAP were combined in toluene and heated at reflux for three hours. Removal of the solvent *in vacuo* yielded the crude product which was dissolved in chloroform, washed with acid (2M HCl) and base (saturated $NaHCO_3$) and purified by silica chromatography to give diphenyl ester (129) in 66% yield (Scheme 2.5).



(127) (129)

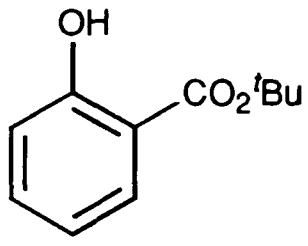
Scheme 2.5

Proton NMR COSY studies of the product (129) allowed assignment of the protons at C(4) and C(5). The protons at δ 2.01-2.09 and δ 2.37-2.44 gave crosspeaks to protons at

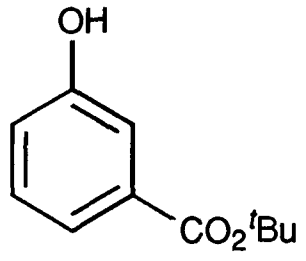
δ 1.72-1.77 and δ 2.76-2.83 and to the proton at δ 3.17 which was known to be C(3)H. These could therefore be assigned as being C(4)H. The protons at δ 1.72-1.77 and δ 2.76-2.83 which gave crosspeaks to δ 2.01-2.09 and δ 2.37-2.44 only could be assigned as being C(5)H. Peaks in the ^{13}C NMR spectrum were readily assigned by DEPT analysis. This ester therefore provided a useful reference compound, allowing proton and carbon atoms in all later compounds based on the (1*R*, 3*S*)-1,2,2-trimethylcyclopentane skeleton to be assigned by comparison.

2.2.3 Synthesis of ligands (124) and (125) as free acids

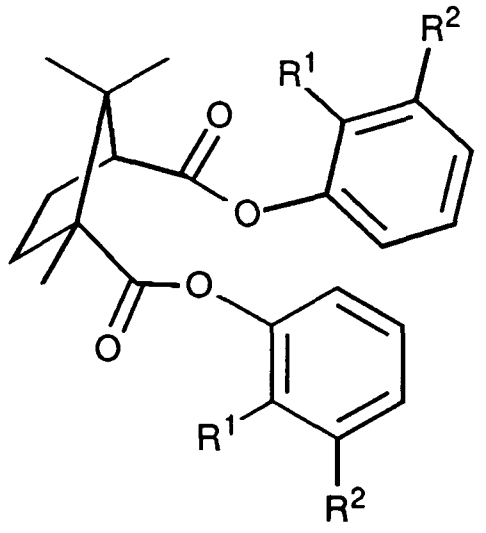
Following establishment of the appropriate conditions for the coupling of camphoric acid chloride with phenol, reaction of 2-hydroxybenzoic acid and 3-hydroxybenzoic acid with camphoric acid chloride was attempted under these conditions. However, it was not possible in either case to identify the required products in the crude reaction mixtures. The ligands (125) and (125) may indeed have been present, but as they are diacids, their isolation from any unreacted benzoic acid present would not have been straightforward.



(130)



(131)



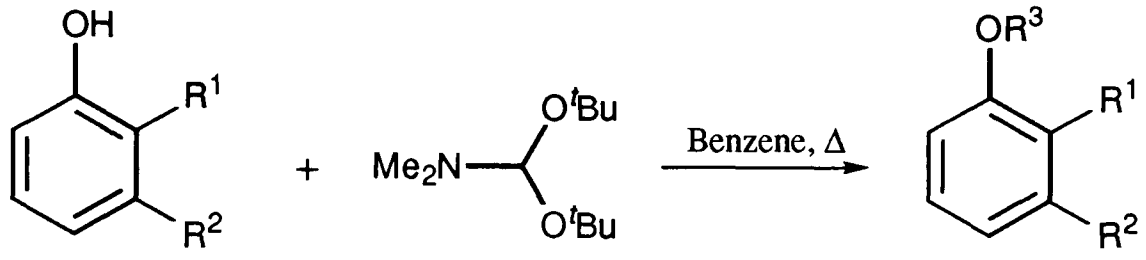
$R^1 = CO_2{}^tBu$, $R^2 = H$ (132)
$R^1 = H$, $R^2 = CO_2{}^tBu$ (133)

A more practical synthesis of the ligands (124) and (125) would involve the preparation of their *t*-butyl esters (132) and (133), the identification and purification of which would be expected to be trivial; deprotection with TFA would then give the required ligands as their free acids. Thus, the first step was the synthesis of the *t*-butyl esters of 2-hydroxybenzoic acid and 3-hydroxybenzoic acid.

2.2.4 Synthesis of *t*-butyl esters (130) and (131)

Heating of 2-hydroxybenzoic acid with four equivalents of *N,N'*-dimethylformamide di-*t*-butyl acetal at reflux in dry benzene for half an hour gave a crude product which was purified by silica chromatography to give *t*-butyl 2-hydroxybenzoate (130) as a colourless oil in 61% yield (Scheme 2.6).[103,104]

Reaction of 3-hydroxybenzoic acid under the same conditions led to the formation of a mixture of ester (131) and ether (134) in a ratio of approximately 3:1. These compounds could be readily separated by silica chromatography to give *t*-butyl 3-hydroxybenzoate (131) in 56% yield. The reaction to form *t*-butyl 3-hydroxybenzoate was later adapted due to the high cost (£1.15/mmol) of the *N,N'*-dimethylformamide di-*t*-butyl acetal starting material. It was found that by using two equivalents of *N,N'*-dimethylformamide di-*t*-butyl acetal instead of the original four, the product could be isolated in 50% yield (Scheme 2.6).



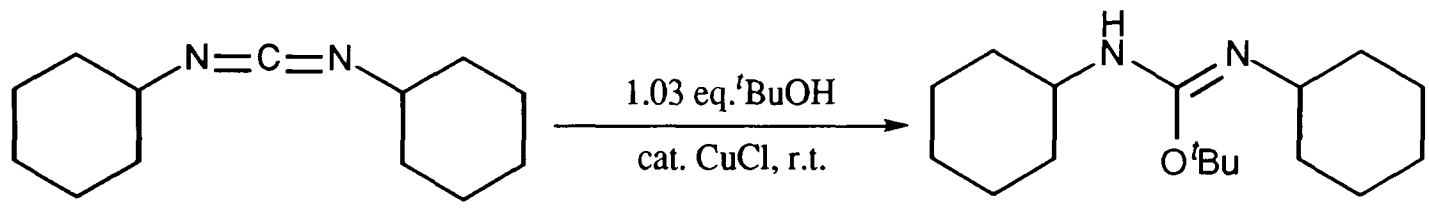
$R^1 = CO_2H$, $R^2 = H$
$R^1 = H$, $R^2 = CO_2H$

$R^1 = CO_2{}^tBu$, $R^2 = H$, $R^3 = H$ (130)
$R^1 = H$, $R^2 = CO_2{}^tBu$, $R^3 = H$ (131)
$R^1 = H$, $R^2 = CO_2{}^tBu$, $R^3 = {}^tBu$ (134)

Scheme 2.6

However, the high cost of the esterification reagent created the need to examine other methodology. In work to prepare 1- and 2-*t*-butyl 5-substituted tetrazoles, Henry[105] used *O-t*-butyl-*N,N'*-dicyclohexyl isourea (135) as a butylating agent. The reagent was prepared by stirring a mixture of DCCI, *t*-BuOH and copper(I) chloride under a calcium chloride drying tube for five days (Scheme 2.7). The solution was then diluted with dichloromethane, cooled to 5°C and treated with a dried 5-substituted tetrazole over thirty minutes. After stirring for twenty hours, the solution was filtered and purification of the organic layer gave the required

t-butyl tetrazole. However, no yields were quoted for these reactions.

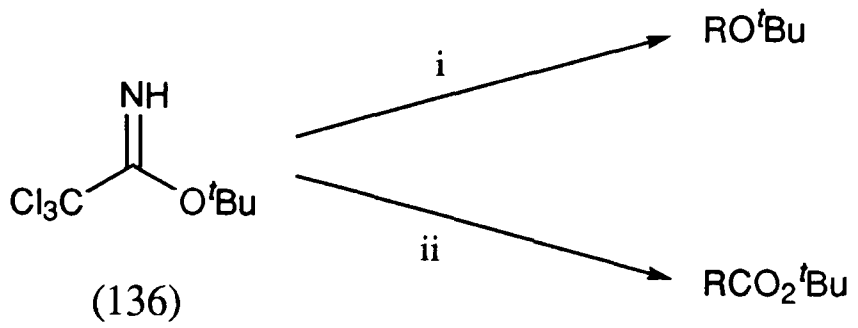


(135)

Scheme 2.7

In an attempt to prepare *t*-butyl 3-hydroxybenzoate in a similar fashion, DCCI, *t*-BuOH and copper(I) chloride were stirred at room temperature overnight in a flask fitted with a calcium chloride drying tube. The resulting cloudy solution was filtered through Celite® and the solid washed with dichloromethane. 3-Hydroxybenzoic acid was added to the resulting solution and the mixture stirred for fifteen hours, after which time t.l.c. showed none of the required benzoate ester to be present.

In 1988, Jackson *et al.*[106] reported a mild and effective method for the conversion of carboxylic acids and alcohols to their corresponding *t*-butyl esters and ethers using commercially available *t*-butyl trichloroacetimidate (136) in the presence of boron trifluoride etherate (Scheme 2.8). This method avoids the use of the strong acids which are required to effect *t*-butylation with isobutylene and is more convenient than Henry's described above, which generally gives only moderate yields of *t*-butyl esters. In addition, the *t*-butyl trichloroacetimidate reagent is somewhat cheaper (£0.61/mmol) than *N,N'*-dimethylformamide di-*t*-butyl acetal used earlier in this work.



(136)

i) ROH, $BF_3.Et_2O$
ii) RCO_2H, $BF_3.Et_2O$

Scheme 2.8

The reaction is generally carried out by stirring the reactants in cyclohexane at room temperature. As most carboxylic acids are insoluble in cyclohexane, 3-hydroxybenzoic acid was first dissolved in dichloromethane (1ml/mmol) then a solution of *t*-butyl trichloroacetimidate in cyclohexane (2ml/mmol) added followed by boron trifluoride etherate (2μl/mmol). The mixture was stirred at room temperature for twelve hours, after which solid sodium bicarbonate was added and the mixture filtered through a silica plug to remove excess *t*-butyl trichloroacetimidate. The solvent was removed *in vacuo*, but none of the required product (131) was found to be present.

The failure of this reaction seemed be due to the rather low solubility of 3-hydroxybenzoic acid in dichloromethane. The use of more polar solvents to circumvent this problem was not however the most obvious solution, since Jackson had found that using more polar solvents gave rather poor results, presumably due to rapid decomposition of *t*-butyl trichloroacetimidate in solvents where ionisation is favoured. It was hoped that by using ethyl acetate as a co-solvent but in higher dilution, significant decomposition of *t*-butyl trichloroacetimidate could be avoided and product formation enhanced.

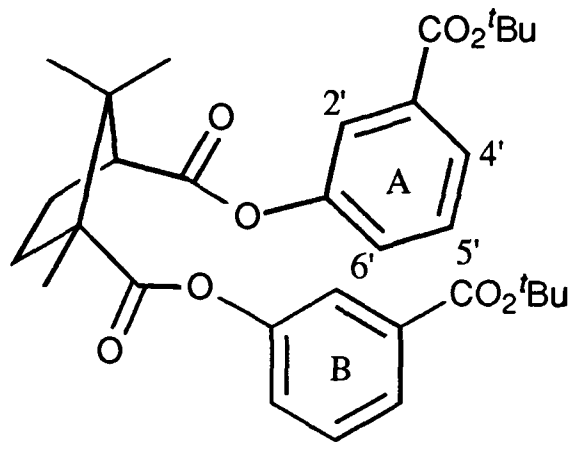
Therefore, 3-hydroxybenzoic acid was dissolved in ethyl acetate (7ml/mmol) and cyclohexane (14ml/mmol). To this was added *t*-butyl trichloroacetimidate in cyclohexane (7ml/mmol) and boron trifluoride etherate (2μl/mmol) and the solution stirred for sixteen hours at room temperature in a flask fitted with a calcium chloride drying tube. The work-up was carried out as before, and t.l.c. analysis of the crude product showed that some of the ester (131) was present. The crude product was purified by silica chromatography to give ester (131) in a rather disappointing yield of 5%.

It was therefore decided that although formation of (130) and (131) using *N,N'*-dimethylformamide di-*t*-butyl acetal was a rather expensive procedure, it did appear to be the most efficient method for the synthesis of the ligand precursor.

2.2.5 Synthesis of ligands (124) and (125)

The next step in the synthesis of ligands (124) and (125) was the coupling of *t*-butyl esters (132) and (133) with camphoric acid chloride (127), the conditions for which had already been established (Section 2.2.2). However, attempted coupling of *t*-butyl 2-hydroxybenzoate (130) with acid chloride (127) in a solution of triethylamine and DMAP in toluene at reflux failed to yield the protected ligand (132). This may have been due to the sterically demanding *t*-butyl ester groups being in the *ortho*- position on each aromatic ring, thus placing them very close to the (1*R*, 3*S*)-1,2,2-trimethylcyclopentane skeleton in the desired product.

Coupling of *t*-butyl 3-hydroxybenzoate (131) with the acid chloride (127) was attempted under the same conditions as before. T.l.c. analysis after six hours showed the appearance of a product, and reaction was therefore continued for a further twenty nine hours. After this time, the solvent was removed *in vacuo* and the crude material obtained dissolved in ethyl acetate which was washed with 2M HCl and 2M NaOH, dried and the solvent removed *in vacuo* to give the di-*t*-butyl ester (133) in 39% yield.



(133)

On careful examination of the ^{1}H NMR spectrum of this compound, it appeared that the protons in the aromatic region showed some unusual coupling patterns. On first inspection, the C(6') protons appeared as a multiplet overlapping with the solvent peak, the C(5') protons appeared as a triplet, the C(2') protons as a doublet of triplets and the C(4') protons as a doublet of quartets. The system was studied further by selective proton decoupling

experiments (Appendix 1).

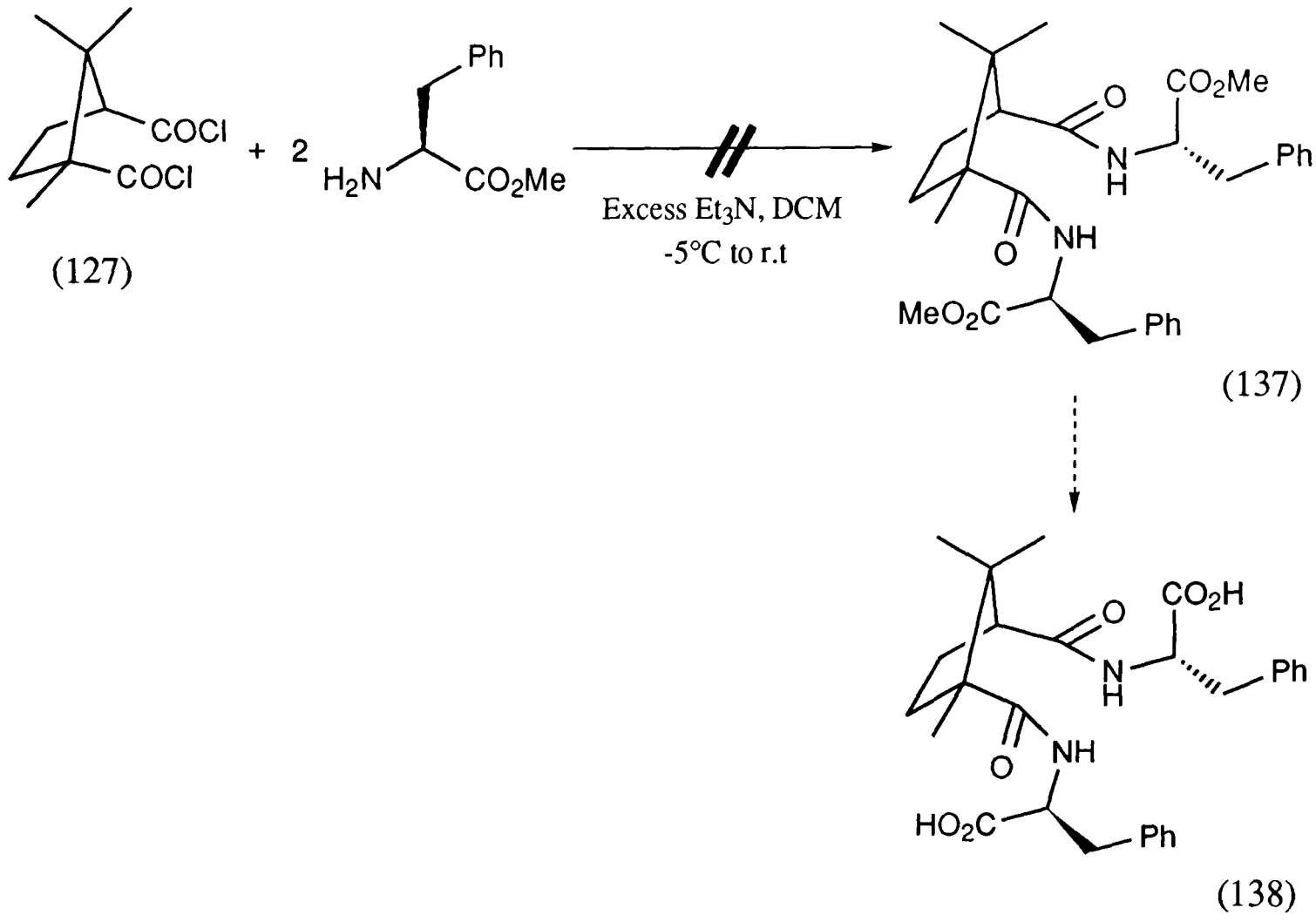
Irradiation of the protons at C(6') resulted in a collapse in coupling at C(5') (to one multiplet), C(2') (to two doublets) and C(4') (to two triplets). Irradiation of the protons at C(5') resulted in a collapse in coupling at C(4') (to one multiplet). Irradiation of the protons at C(2') resulted in a collapse in coupling at C(6') (to two simpler multiplets) and C(4') (to two multiplets). Irradiation of the protons at C(4') resulted in a collapse in coupling at C(6') (to two simpler multiplets), C(5') (to one multiplet) and C(2') (to two doublets).

Analysis of this data, and also of coupling constants, shows that both C(5') protons occur as a triplet (due to coupling to C(4')H and C(6')H), and that both C(4') protons occur as a doublet of quartets (due to coupling to C(5')H, C(2')H and C(6')H). The C(6') peaks are in fact two multiplets, as the C(6') protons on the two rings A and B are not equivalent. Each C(6') proton is coupled to C(5')H, C(2')H and C(4')H. Similarly, the C(2') protons are not equivalent in rings A and B and appear as two triplets, due to coupling to C(4')H and C(6')H.

Deprotection of the di-*t*-butyl ester (133) was easily effected by stirring the ester in a solution of 50% TFA in chloroform at room temperature overnight, or until t.l.c. no longer showed the presence of the protected ligand. Ligand (125) was obtained as a methanol-soluble white solid in quantitative yield.

2.2.6 Synthesis of a ligand derived from L-phenylalanine

Following the success of the above procedure, it was anticipated that amino acid derived ligands could be synthesised in a similar manner. Thus, reaction of camphoric acid chloride (127) with L-phenylalanine methyl ester would give ester (137), which on deprotection (for example with NaOH) would give the ligand (138), which has chirality closer to the carboxylic acid functionality than ligand (125) (Scheme 2.9).



(127)

(137)

(138)

Scheme 2.9

L-Phenylalanine methyl ester and an excess of triethylamine were stirred in dichloromethane at -5°C. Camphoric acid chloride (127) in DCM was slowly added to this solution, keeping the temperature below 0°C throughout.[107] The solution was warmed to room temperature; removal of the solvent *in vacuo* failed to give the required product (137). This route to substituted (1*R*, 3*S*)-1,2,2-trimethylcyclopentane ligands was consequently abandoned.

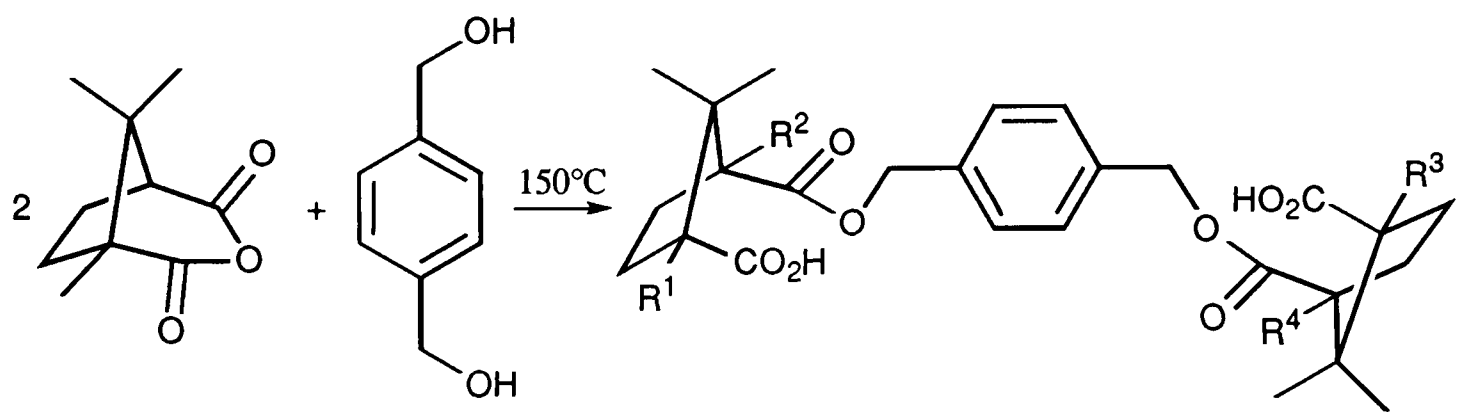
2.3 Synthesis of chiral ligands - 2

As described in Section 2.2.1, attempts were made to synthesise camphoric acid chloride (127) from the corresponding acid using thionyl chloride. However, in common with other dibasic acids, this reaction resulted in the formation of camphoric anhydride (126) in 60-70% yield. That this compound had been formed was confirmed by comparison of its melting point (224-225°C) with a literature value (222-223°C).[108] As earlier in this work, it was

hoped that this anhydride could be used as a precursor for dicarboxylic acid ligands.

2.3.1 Opening with benzene-1,4-dimethanol (112)

This Chapter has described the use of a fusion reaction, whereby phthalic anhydride (107) was opened using benzene-1,4-dimethanol (112) by heating the two solids together in the absence of a solvent. Following the synthesis of anhydride (126), albeit accidentally, it was hoped that the same procedure could be adopted to allow the synthesis of an analogous chiral ligand (139), (140) or (141) (Scheme 2.10).



(126) (112)

R^1 = Me, R^2 = H, R^3 = Me, R^4 = H (139)
R^1 = H, R^2 = Me, R^3 = H, R^4 = Me (140)
R^1 = Me, R^2 = H, R^3 = H, R^4 = Me (141)

Scheme 2.10

Scheme 2.10 shows that on opening camphoric anhydride with a diol, there are three possible diastereomeric products (139), (140) and (141). C_2-Symmetrical diacids (139) and (140) result either from opening of the anhydride at the least hindered side (*i.e.* at C(3)) at both ends of the molecule, or from opening of the anhydride at the most hindered side (*i.e.* at C(1)) at both ends of the molecule. Diacid (141) would result from opening at C(3) by one end of the diol and opening at C(1) by the other.

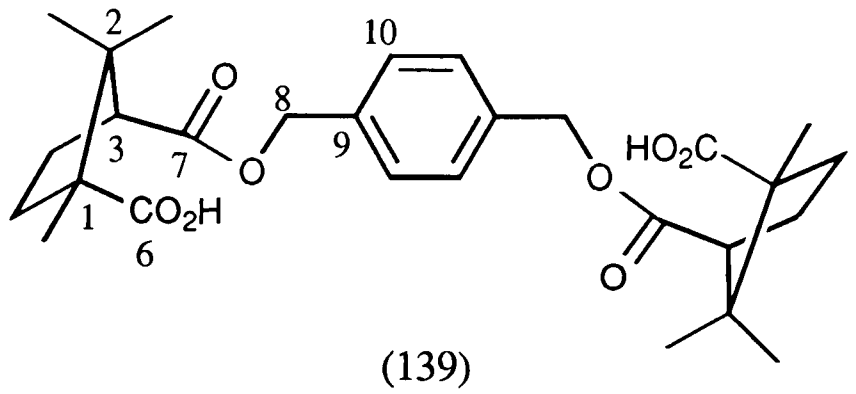
It is known that in the case of unsymmetrical anhydrides, opening of the anhydride ring occurs at the least hindered side of that ring, despite a possibly crowded angle of approach.[101] For example, when unsymmetrical anhydrides are opened with sodium alkoxides, esterification occurs at the least hindered side. As described earlier (Section 2.2.1), Bone[102]

found that in the case of methyl substituted succinic acids, partial hydrolysis of the neutral esters always gave hydrolysis of the least substituted ester. Thus, for the opening of camphoric anhydride, it would be expected that opening of the ring at C(3) to give diacid (139) would predominate over the more unfavourable ring openings to give diacids (140) and (141).

Heating of three equivalents of camphoric anhydride (126) (m.p. 224-225°C) with benzene-1,4-dimethanol (112) (m.p. 117-119°C) at 150°C for twenty four hours led to the formation of a solid, from which the product could be obtained by dissolving the residue in ethyl acetate and washing the organic layer with base. The aqueous layer was acidified and re-extracted into dichloromethane to give diacid (139) in 60-70% yield as a white hygroscopic foam which was highly soluble in organic solvents. Three equivalents of anhydride were used in order to achieve maximum conversion of benzene-1,4-dimethanol to product, as this is otherwise difficult to remove.

By proton NMR spectroscopy, the product appeared to be a single diastereomer, but the carbon NMR spectrum indicated that two diastereomers were present, one in approximately 95% abundance (estimated from peak heights), the second accounting for the other 5% of material. In the carbonyl region, the major isomer gave shifts at δ 181.99 (acid carbonyl) and δ 173.60 (ester carbonyl). In addition, there were minor peaks at δ 180.00 and δ 175.23 due presumably to the minor diastereomer. It should be noted, however, that the ratio of these inseparable products was variable, and that in at least one case, a single diastereomer was obtained. Additionally, it was found that when the reaction time was halved, an increased 10% of the minor isomer was found to be present.

It was assumed that the major product of this reaction was diastereomer (139) in accordance with the results described for analogous systems and this was confirmed by HMBC spectroscopy. Using pulse techniques, correlations between certain known proton and carbon resonances were used to determine the connectivity of the molecule (Appendix 2).



(139)

It was known that the C(8) protons occurred as two doublets at δ 5.10 and δ 5.16. Irradiation of these protons at δ 5.2 showed correlations to the known aromatic carbon atoms C(9) and C(10) and to the known ester carbon C(7). It was further known that C(3)H occurred at δ 2.86, and irradiation of this proton at δ 2.9 showed correlations to C(2), two C(2) methyl groups and, importantly, to C(7). This established that C(7) was attached to the carbon atom bearing a proton, *i.e.* the ester group was on the C(3) side of the cyclopentane ring.

The protons at C(4) and C(5) were assigned by comparison with (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid diphenyl ester (129) studied earlier. Thus, irradiation of the C(5) protons at δ 2.5 showed correlations to C(4), C(1), the C(1) methyl group and C(6). Irradiation of the C(4) protons at δ 2.2 showed correlations to C(5), C(3), C(7) and C(1). Irradiation of the C(4) protons at δ 1.9 showed correlations to C(5), C(3) and C(2). Irradiation of the C(5) protons at δ 1.6 showed correlations to C(1), the C(1) methyl group, C(4), C(3) and C(2).

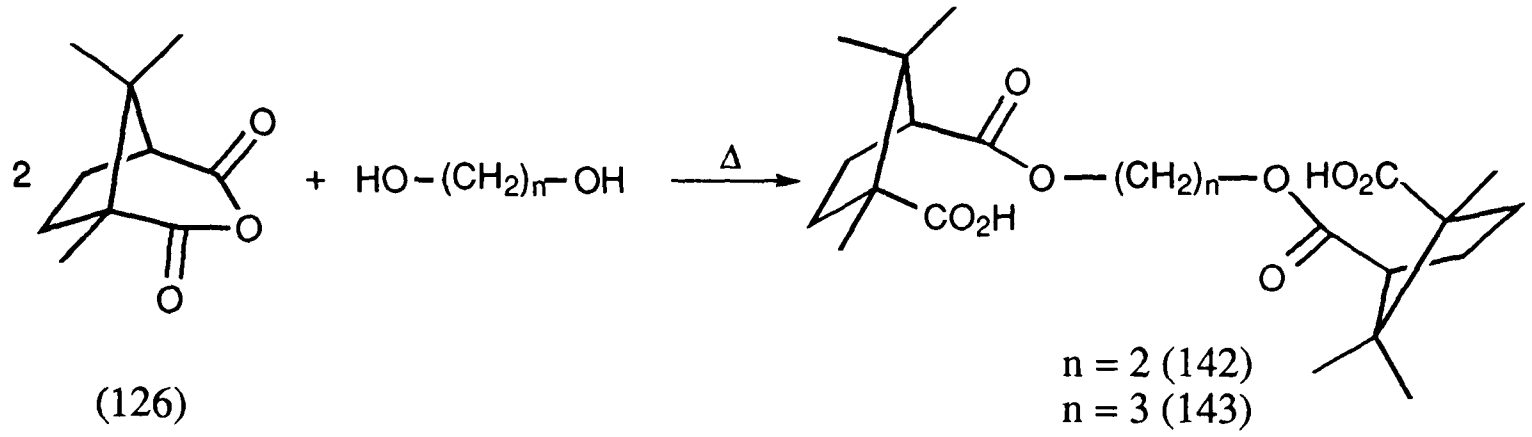
Irradiation of the C(1) methyl group and one of the C(2) methyl groups together at δ 1.3 showed correlations to the other C(2) methyl group, C(5) (from $C(1)CH_3$), C(2), C(3), C(1) and C(6) (from $C(1)CH_3$). Finally, irradiation of the second C(2) methyl group at δ 0.8 showed correlations to C(2), the other C(2) methyl group, C(3) and C(1).

This series of experiments confirmed that the acid carbonyl C(6) was connected to a carbon bearing a methyl group, C(1), which itself was connected to C(5). They also proved that the ester carbonyl group, C(7), was connected to the carbon bearing a proton, C(3), which

was itself connected to C(4). Thus, the structure of the major product was as shown above. The minor diastereomer was almost certainly the unsymmetrical product (141).

2.3.2 Opening with straight chain diols

Using this same procedure, it was hoped that chiral ligands could be synthesised with alkyl chain linking units. This would give ligands which were more flexible and, in some cases, shorter than ligand (139). Thus, opening of camphoric anhydride (126) with ethane-1,2-diol, propane-1,3-diol and butane-1,4-diol would be expected to lead to the formation of ligands (142), (143) and (144) (Scheme 2.11).

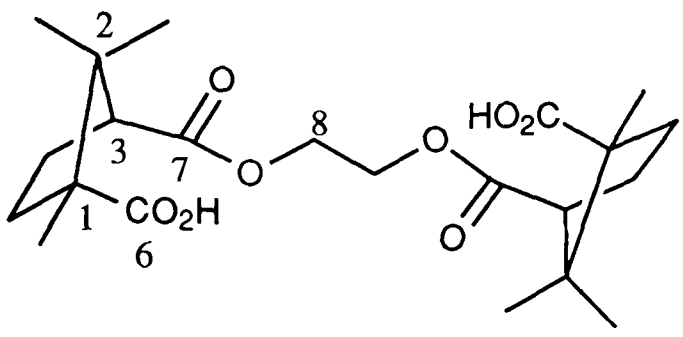


(126)

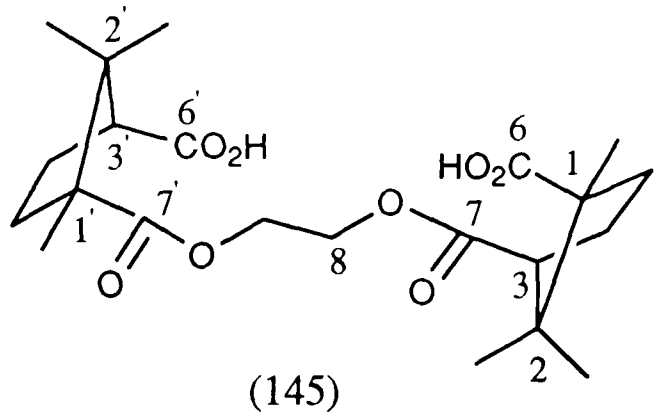
n = 2 (142)
n = 3 (143)
n = 4 (144)

Scheme 2.11

Anhydride (126) was heated with ethane-1,2-diol at 180°C for twenty four hours. A brown solid was formed which was dissolved in ethyl acetate and extracted with base. The aqueous layer was acidified and washed with dichloromethane. Removal of the solvent gave a brown oil which could be purified by silica chromatography to give diacid (142) in 15% yield as a hygroscopic white foam. Both proton and carbon NMR spectroscopy indicated the presence of a second diastereomer which could not be separated from the major product (142) by silica chromatography. By carbon NMR spectroscopy, it was estimated that the product obtained was a 3:1 mixture of the required ligand (142) and the unsymmetrical diacid (145).



(142)



(145)

As in the case of 3,3'(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139), the carbon NMR spectrum of ligand (142) showed peaks in the carbonyl region at δ 174.05 and δ 182.64 due to C(7) and C(6) respectively, but peaks were also observed at δ 175.70 and δ 180.65 due to C(7') and C(6'). In addition, peaks were observed at δ 53.67 (due to C(1')) and δ 54.21 (due to C(3')).

Heating of camphoric anhydride and propane-1,3-diol at 175°C for twenty four hours resulted in the formation of a brown solid. This was dissolved in ethyl acetate and extracted into base which was acidified and re-extracted into dichloromethane. This gave a brown oil which was purified by silica chromatography to give the ligand (143) in 20% yield as a white hygroscopic foam. By carbon NMR spectroscopy, there appeared to be around 10% of the minor diastereomer present.

In a similar fashion, camphoric anhydride (126) and butane-1,4-diol were heated together at 170°C for ten hours. The resulting brown solid was dissolved in ethyl acetate and extracted into base. Following acidification and re-extraction, a brown oil was obtained which was purified by silica chromatography to give the ligand (144) in 40% yield as a hygroscopic white foam. By carbon NMR spectroscopy, it appeared that this ligand was formed almost exclusively as one diastereomer.

2.4 Summary

This Chapter has described syntheses of a variety of novel dicarboxylic acids. Thus, reaction of anhydrides (either phthalic anhydride or camphoric anhydride) with a range of diols or elaboration of the camphoric acid skeleton allowed easy access to both achiral and chiral dicarboxylic acids which, in general, possessed good solubility properties. The application of these ligands for lead(IV) complexation is discussed in Chapter Three.

CHAPTER THREE

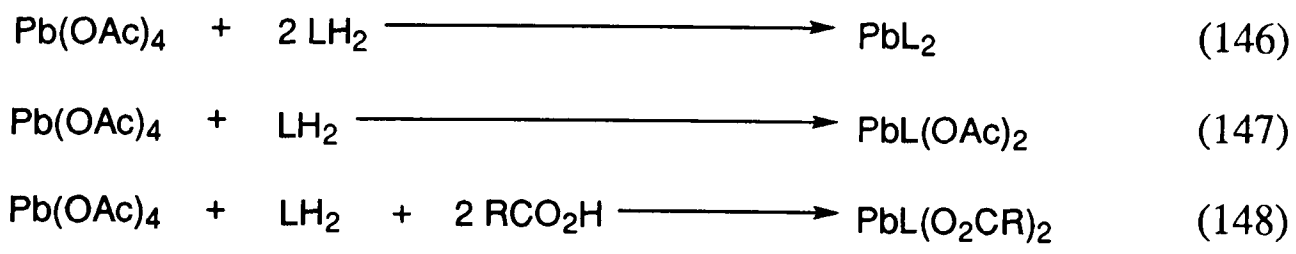
Synthesis of Novel Lead(IV) Complexes

Chapter Two of this thesis discussed the synthesis of a range of novel dicarboxylic acids. This Chapter will discuss the synthesis of novel lead(IV) complexes using these ligands, their characterisation and initial studies of their reactivity.

3.1 General procedures

As discussed in Chapter One of this thesis, there are a number of methods available for the synthesis of lead(IV) tetracarboxylates;[84,85] most of the lead(IV) compounds synthesised during the course of this work were prepared by a method developed within this group.[86] Some complexes, as described in the text, were prepared using more forcing conditions.[84,109]

For each dicarboxylic acid ligand, it was possible to prepare both *bis*- complexes (146) and mixed ligand complexes (147) and (148) (Scheme 3.1).



Scheme 3.1

3.1.1 Synthesis of *bis*- complexes (146)

The *bis*- complexes described in this work were all prepared by the same method. In each case, two equivalents of a dicarboxylic acid ligand were dissolved in dry toluene along with one equivalent of LTA (which was not dried prior to use), acetic acid (*ca.* 1ml) being added to aid dissolution if necessary. The solvent was removed *in vacuo* at 35°C using a pressure of 70mmHg to 20mmHg. The residue obtained was dissolved or suspended in dry

toluene (no further acetic acid was added at this point) and the solvent removed *in vacuo* at 35°C. From examination of the proton NMR spectrum of a complex, it could be determined whether complete complexation had occurred by the absence of a singlet at δ 2.2 due to an acetate group. In some cases, this occurred after two additions of toluene; other complexes required further additions of toluene for complete complexation to be achieved. In general, the *bis*- complexes were found to be rather less soluble in organic solvents than the mixed ligand complexes.

3.1.2 Synthesis of mixed ligand complexes (147) and (148)

Lead(IV) dicarboxylate diacetate complexes (147) were readily prepared by reaction of one equivalent of LTA with one equivalent of a dicarboxylic acid ligand in the manner described above (Section 3.1.1). In this case, complete complexation had occurred when the integral of the acetate peak corresponded to there being one dicarboxylate ligand and two acetate ligands present. The diacetate complexes were, however, found to be rather unstable and decomposed within hours both in the solid state and in solution.

Using the same method, lead(IV) dicarboxylate dibenzoate and lead(IV) dicarboxylate di-*p*-toluate complexes (148) were also easily prepared. These complexes generally have good organic solubility and are more stable than the analogous diacetate complexes.

The mixed ligand complexes (147) and (148) are ideal for use in the mediation of carbon-carbon bond formation reactions as they consist of one bidentate, chelating ligand, and two labile ligands which could easily be replaced by reactants R and Nu, as described in Chapter One, Scheme 1.44. Ligand coupling, under the influence of the fixed chiral ligand, could then occur to give the product R-Nu enantioselectively (Figure 3.1). These complexes are analogous to molybdenum complexes[110] (149) used in the asymmetric epoxidation of allylic alcohols by Yamada, and to Seebach's titanium taddolates (150),[111] containing labile monodentate alkoxide ligands, which are used in the addition of diethyl zinc to aldehydes.

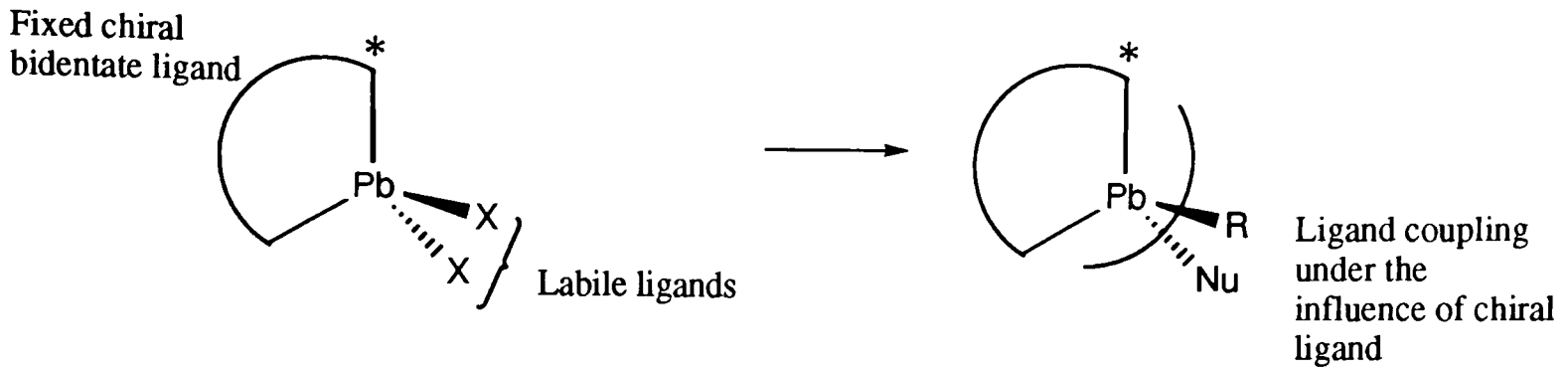
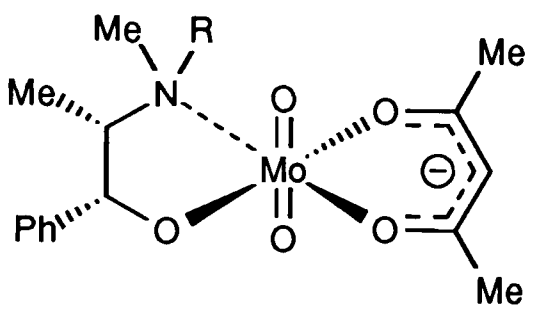
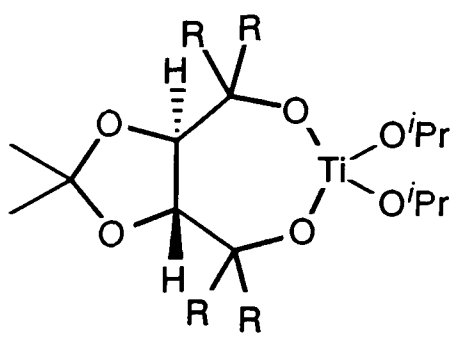


Figure 3.1



R = Me, Et

(149)



R = β-naphthol

(150)

3.1.3 Characterisation of lead(IV) complexes

The lead complexes described in this work were characterised by a combination of IR and NMR techniques (^{1}H, ^{13}C and ^{207}Pb); the use of proton NMR spectroscopy has been described above. Elemental analysis was obtained where possible to confirm the proposed constitution of complexes. It was unfortunately not possible to obtain crystals of any of the novel lead(IV) complexes which were studied.

At the start of the work in this group regarding the complexation of carboxylic acids to lead(IV), it was hoped that IR spectroscopy would prove to be a useful tool for examining the coordination modes of the carboxylate groups. However, this did not prove to be possible,[86] and for the work described in this thesis, IR spectra were only used to indicate that complexation had taken place by observing the shifts of carboxylic acid stretches out of the carbonyl region.

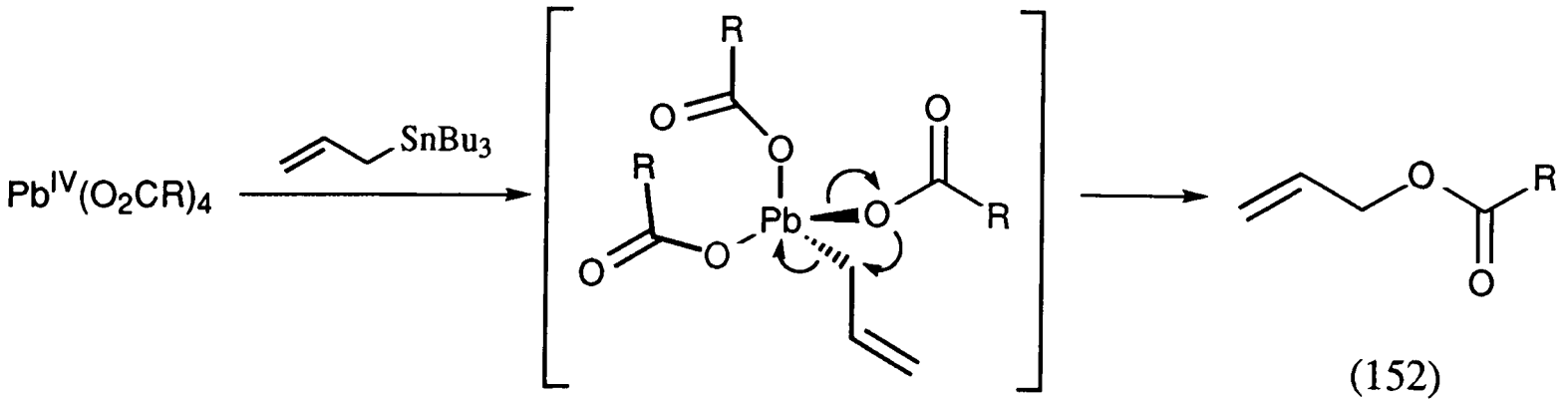
Carbon NMR spectroscopy was used as a diagnostic tool with particular reference to the carbonyl region. It was observed that in many cases where a ligand contained both an acid group and an ester group, the ester carbonyl remained unchanged on complexation, whereas

the peak due to the acid carbonyl group was reduced in intensity and became broader. The broadness of these peaks was probably due to the fact that each complex consisted of more than one species in solution,[112] and thus each coordinated carbonyl group was present in more than one environment. In some cases, similar changes were observed for carbon atoms adjacent to the coordinated carbonyl group.

Lead NMR spectroscopy was used extensively in this work to establish that complexes were indeed lead(IV) compounds as these occur within a characteristic spectral range (-1870±25ppm).[113] It was also used to establish the composition of the complexes in solution, as earlier lead NMR studies of simpler mixed ligand systems (for example lead(IV) diacetate dibenzoate) had shown that these existed as up to five exchanging lead(IV) species in solution.[113] Spectra were carried out at low temperature (223K or 253K) and in many cases, overnight acquisition was found to be necessary.

3.1.4 Reactivity probe using allyltributyltin

In earlier work, it was shown that vinyl- and alkynyl-[61,69,114] stannanes react with LTA to give the corresponding organolead(IV) tricarboxylates which act as carbocation synthetic equivalents. On reaction with nucleophiles, these species undergo carbon-carbon bond formation processes. Recent work within this group[86] has shown that a wide range of lead(IV) tetracarboxylates will react with allyltributyltin to form the corresponding allyl esters (152) presumably *via* intermediate allyllead(IV) tricarboxylates (151) (Scheme 3.2).



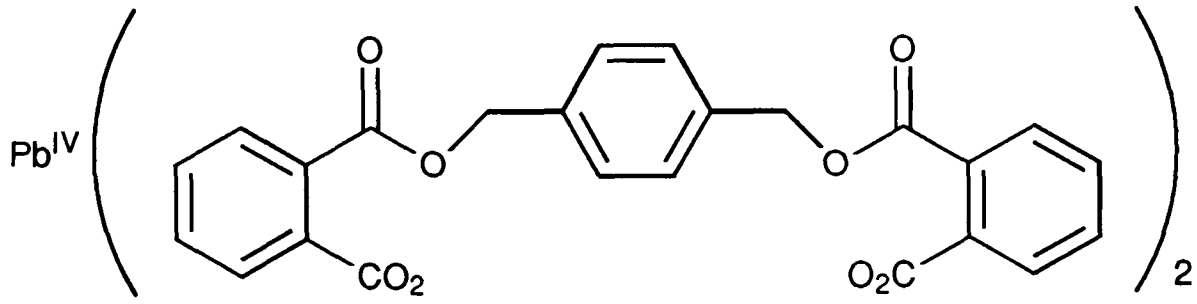
Scheme 3.2

Therefore, this reaction can be used as a simple probe of the reactivity of any new

lead(IV) complex. The reactants were generally combined in chloroform at room temperature; for those reactions of simple lead(IV) carboxylates with allyltributyltin, reaction was generally complete within five minutes (as observed by proton NMR spectroscopy).

3.2 Synthesis of lead(IV) complexes of 1,1'-(benzene-1,4-dimethyl)diphthalate (113)

3.2.1 Synthesis of *bis*- complex (153)

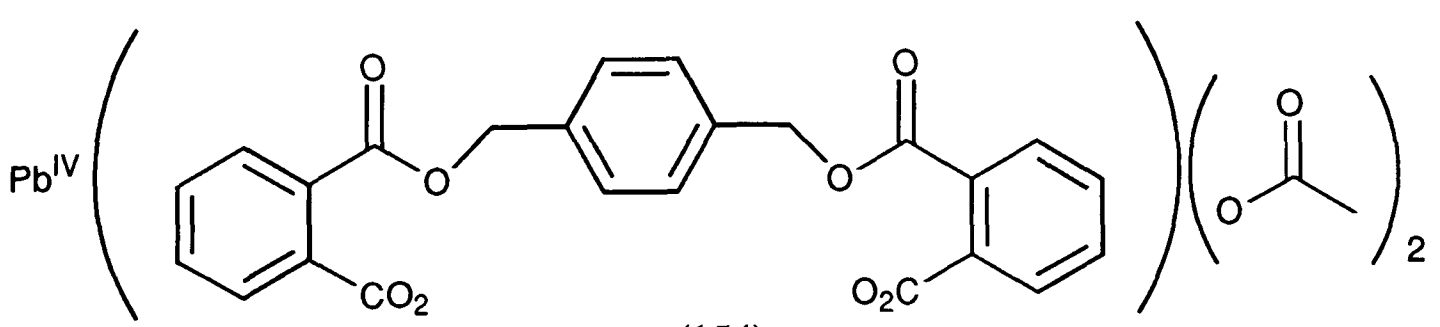


(153)

Lead(IV) *bis*[1,1'-(benzene-1,4-dimethyl)diphthalate] (153) was successfully synthesised by reaction of the diphthalate ligand (113) with LTA under standard conditions for *bis*- complex formation. The complex was formed as a pale yellow, partially chloroform-soluble solid. The IR spectrum of the complex indicated that the acid group had indeed complexed, as there was only one stretch in the carbonyl region due to the ester carbonyl. The proton NMR spectrum of the product also indicated that no acetate groups were present.

The reactivity of the complex was studied by treatment with allyltributyltin. However, after twelve hours, the proton NMR spectrum of the reaction mixture did not show any signs of allyl ester formation.

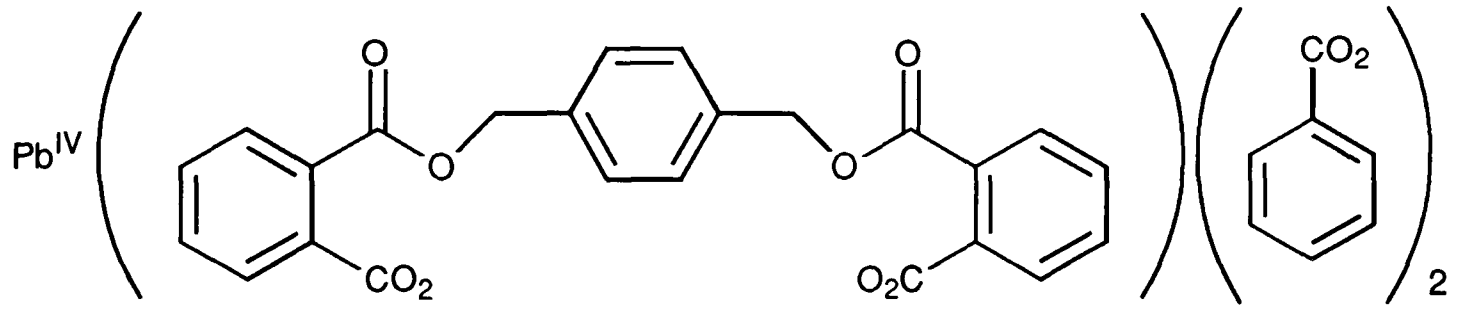
3.2.2 Synthesis of diacetate complex (154)



(154)

Reaction of one equivalent of 1,1'-(benzene-1,4-dimethyl)diphthalate (113) with one equivalent of LTA under standard conditions for mixed ligand complex formation resulted in the formation of a chloroform-soluble, pale brown solid which proton NMR spectroscopy indicated was indeed diacetate complex (154). However, this complex decomposed rapidly (*ca.* one hour) in the solid state and more rapidly in solution, and thus further characterisation was not carried out.

3.2.3 Synthesis of dibenzoate complex (155)



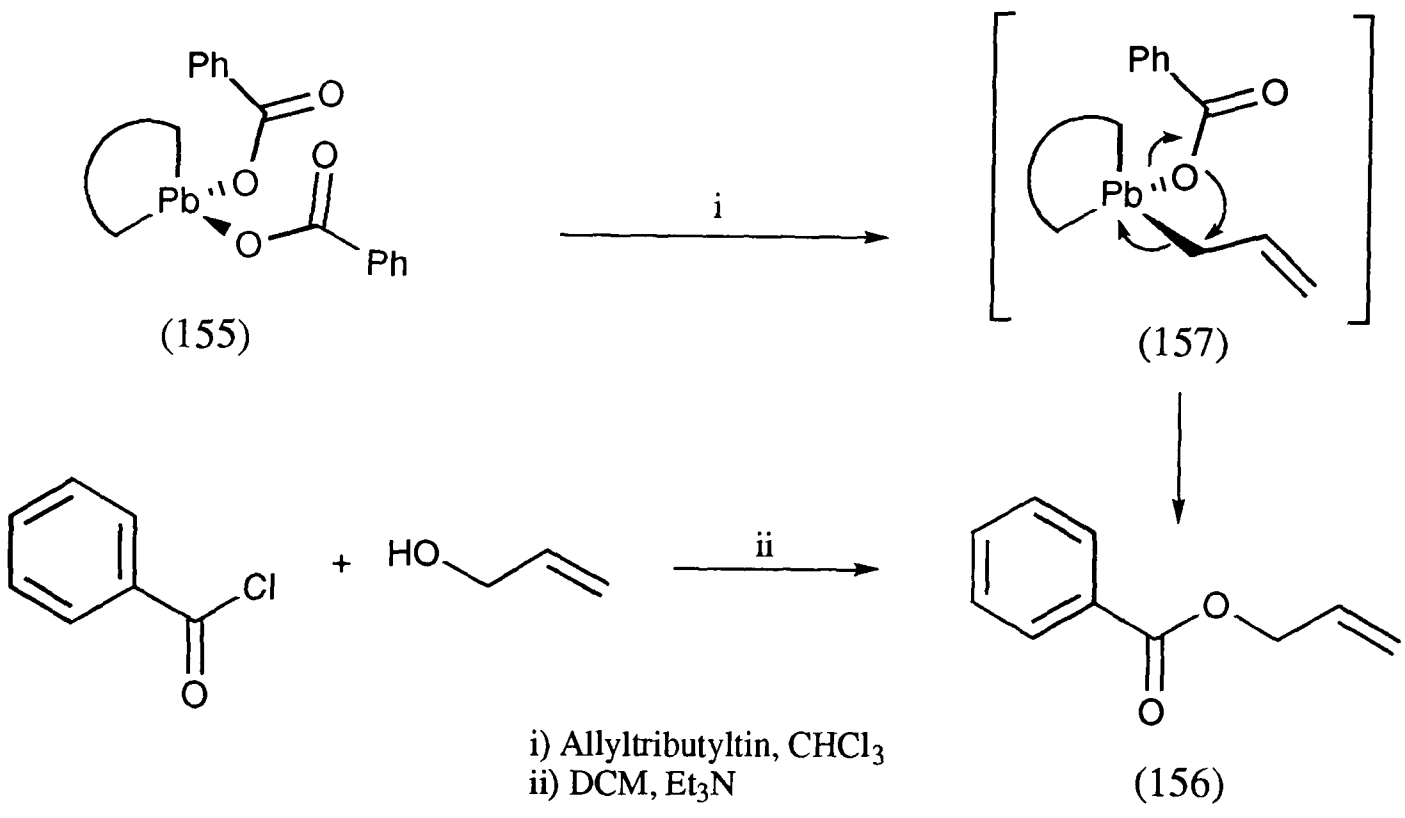
(155)

Following the successful synthesis of the soluble, but unstable, complex (154), it was hoped that dibenzoate complex (155) would have the solubility properties of the analogous diacetate (154) but would be more stable to decomposition (lead tetrabenzoate is stable in air at room temperature for days, while LTA begins to decompose under the same conditions within half an hour).

Reaction of 1,1'-(benzene-1,4-dimethyl)diphthalate (113), benzoic acid and LTA under the standard conditions for mixed ligand complex formation resulted in the formation of a yellow solid which was very soluble in chloroform and more stable than diacetate (154). The proton NMR spectrum showed complete complexation had occurred by the absence of any acetate peaks. The IR spectrum of the product showed only one stretch in the carbonyl region due to the ester group of the ligand, thus indicating that the acid group was complexed to the lead(IV) centre.

The lead NMR spectrum of complex (155) at 253K gave two peaks in the characteristic region for lead(IV), one of which may have been due to the presence of lead tetrabenzoate (LTB) (Appendix 3). This indicates that complex (155) exists in solution as at least two species in dynamic equilibrium as has been observed in simpler mixed ligand systems.[113]

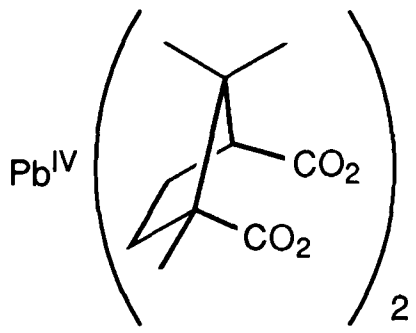
Reaction of this complex with allyltributyltin in chloroform resulted in the formation of a crude product containing allyl benzoate (156) which was purified by silica chromatography to give the allyl ester in 14% yield. The allyl benzoate was presumably formed *via* an intermediate (157). That the product was indeed allyl benzoate was confirmed by synthesis of an authentic sample by reaction of benzoyl chloride with allyl alcohol in dichloromethane and triethylamine (Scheme 3.3);[115] comparison of the two samples by proton NMR spectroscopy and t.l.c. indicated that they were identical.



Scheme 3.3

3.3 Synthesis of lead(IV) complexes of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid (122)

3.3.1 Synthesis of *bis*- complex (123)

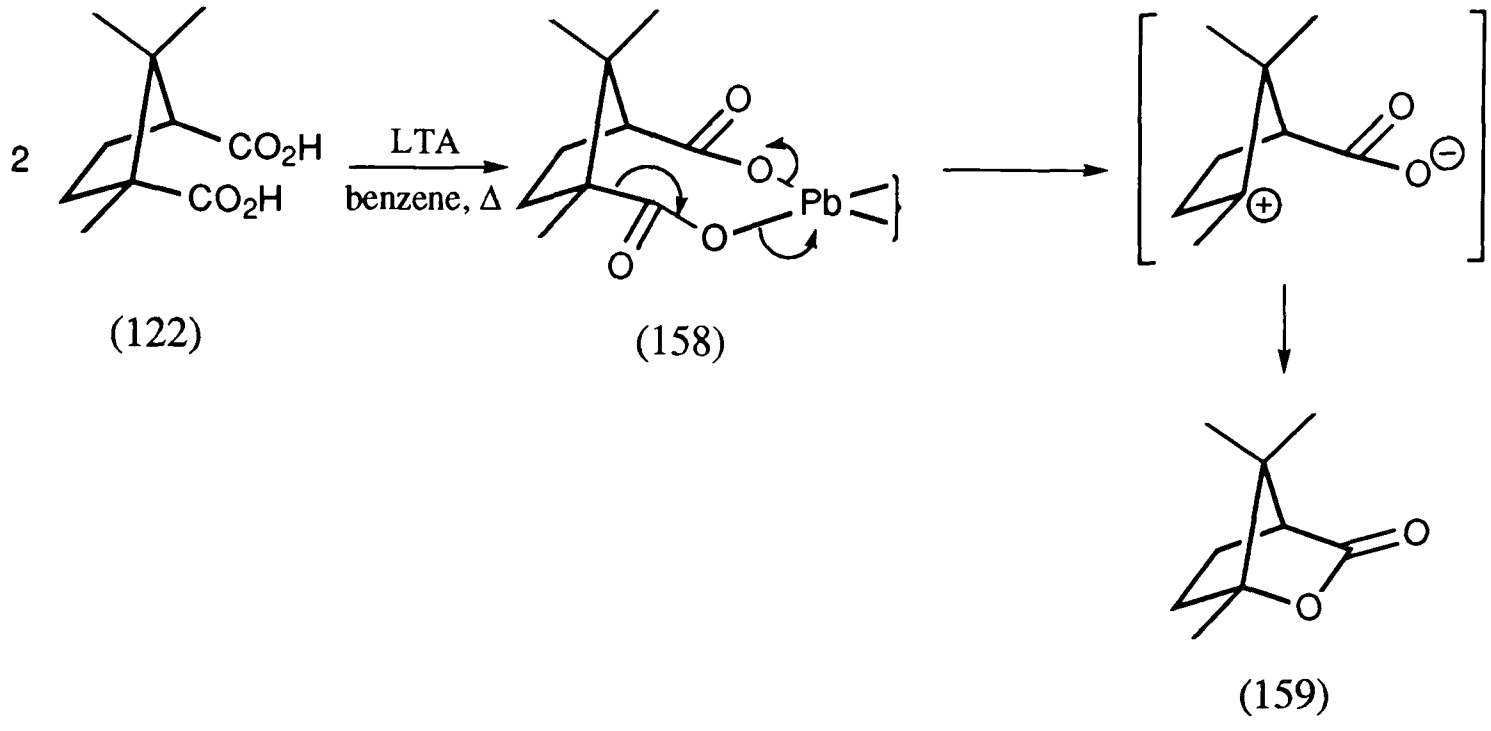


(123)

(1*R*, 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid (camphoric acid) (122) is a commercially available, chiral, dicarboxylic acid, and as such was studied as a potential ligand for lead(IV) in this work. Combining two equivalents of the diacid with one equivalent of LTA in toluene, removing the solvent and then repeating the procedure resulted in the formation of a white solid. This was washed with ether to give a white powder which was only soluble in DMSO. The IR spectrum of this product indicated that complexation had occurred to give (123) due to the absence of any stretches in the carbonyl region.

The proton NMR spectrum of complex (123) at room temperature consisted of a series of broad peaks. However, a 500MHz ^{1}H NMR spectrum recorded at 373K was better defined and showed that acetate groups were no longer present. Attempts were made to crystallise the complex by layer diffusion from DMSO/methanol and DMSO/ether, but neither was successful.

The synthesis of this complex is surprising in the light of work by McCoy[82] in which it was reported that on treatment of camphoric acid with LTA in benzene at reflux, oxidative decarboxylation of the diacid readily occurred to give lactone (159) in 70% yield (Scheme 3.4). However, under the milder conditions employed in this work, it was possible to form complex (123); there was no evidence of decomposition of the complex to lactone (159).



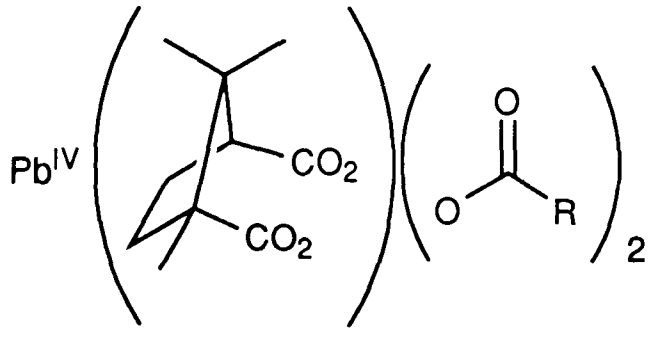
(122) (158) (159)

Scheme 3.4

The reactivity of complex (123) was studied by reaction with allyltributyltin. However, stirring a suspension of complex (123) in chloroform with allyltributyltin for four hours failed to yield any allylated product.

3.3.2 Attempted syntheses of mixed ligand complexes

As the *bis*- complex of camphoric acid was so insoluble in organic solvents, it was hoped that mixed ligand complexes of the same diacid would be more soluble in, for example, chloroform. However, attempts to synthesise lead(IV) [(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] di(*p*-methoxybenzoate) (160) and lead(IV) [(1*R*, 3*S*)-1,2,2-trimethyl cyclopentane-1,3-dicarboxylate] di(*m*-methoxybenzoate) (161) failed as it was found that complete complexation could not be achieved in either case. An attempt to synthesise lead(IV) [(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] diacetate (162) resulted in the formation of an unstable brown solid which was not soluble in chloroform. Reaction of one equivalent of LTA with one equivalent of camphoric acid and two equivalents of benzoic acid also resulted in the formation of a complex which was not soluble in organic solvents. Attempted formation of lead(IV) [(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] di-*p*-*t*-butyl benzoate (163) resulted in the formation of what appeared to be lead(IV) tetra-*p*-*t*-butyl benzoate.

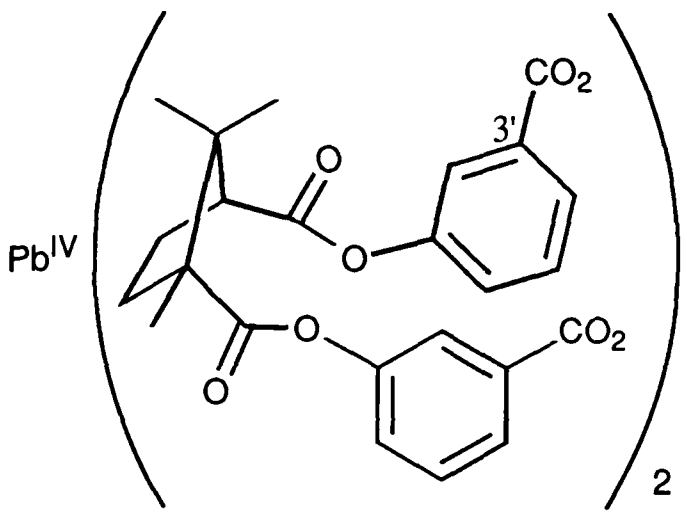


R = *p*-$MeOC_6H_4$- (160) *m*-$MeOC_6H_4$- (161) Me- (162) *p*-$^tBuC_6H_4$- (163)

3.4 Synthesis of lead(IV) complexes of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester (125)

Due to the failure to synthesise a lead(IV) complex of camphoric acid which was soluble in organic solvents, the diacid skeleton was elaborated to give ligand (125) as described in Chapter Two. It was hoped that complex formation using this ligand would result in the formation of lead(IV) compounds based on the chiral camphoric acid functionality which were soluble in chloroform.

3.4.1 Synthesis of *bis*- complex (164)



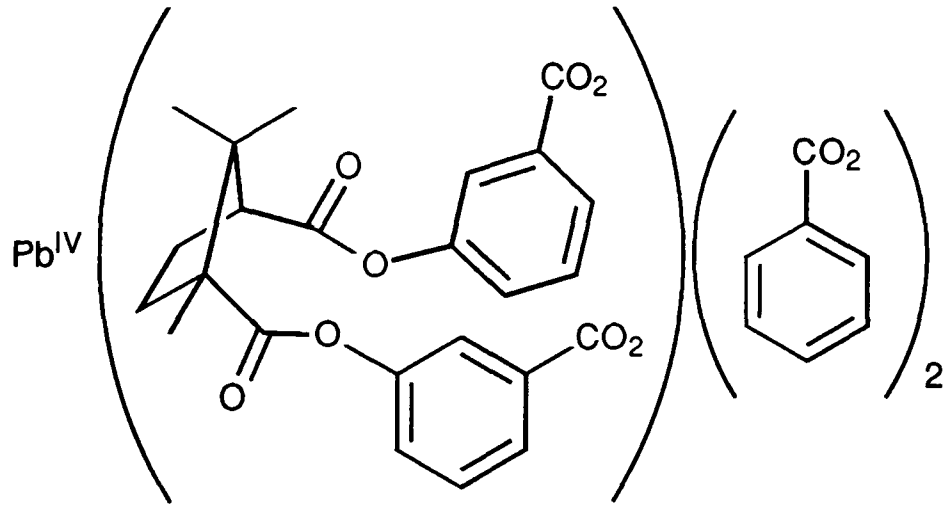
(164)

Reaction of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester (125) with LTA under the standard conditions for *bis*- complex formation resulted in the formation of a DMSO-soluble yellow solid. The IR spectrum of this product indicated that complexation had taken place as only one carboxylate stretch was

observed at 1752cm^{-1} due to the ester carbonyl. The carbon NMR of the product also gave strong evidence for the formation of complex (164): the two carboxylate groups coordinated to lead appeared as broad peaks of low intensity at δ 169.28 and δ 175.00, rather than as sharp peaks as in the case of the free ligand. The peak due to C(3') was also observed to be broad and of low intensity in the spectrum of the product.

In order to test the reactivity of the complex, a small quantity was suspended in chloroform and allyltributyltin added. After stirring the mixture at room temperature for twenty three hours, proton NMR spectroscopy indicated that around half of the allyltributyltin had been consumed and that an allyl ester had indeed been formed (appearance of a doublet at δ 4.88 and a multiplet at δ 5.25-5.45). However, it proved impossible to isolate this product.

3.4.2 Synthesis of dibenzoate complex (165)



(165)

Reaction of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester (125) and benzoic acid with LTA under standard conditions for mixed ligand complex formation resulted in the formation of a chloroform-soluble yellow solid. First evidence for the fact that this was indeed complex (165) came from the IR spectrum, which again showed a single stretch in the carbonyl region due to the ester carbonyls, and from the proton NMR spectrum which showed no acetate groups to be present. In the carbon NMR spectrum, peaks due to the carbon atoms of coordinated carboxylates were not observed, but nor were peaks due to uncoordinated carboxylic acid groups; the ester

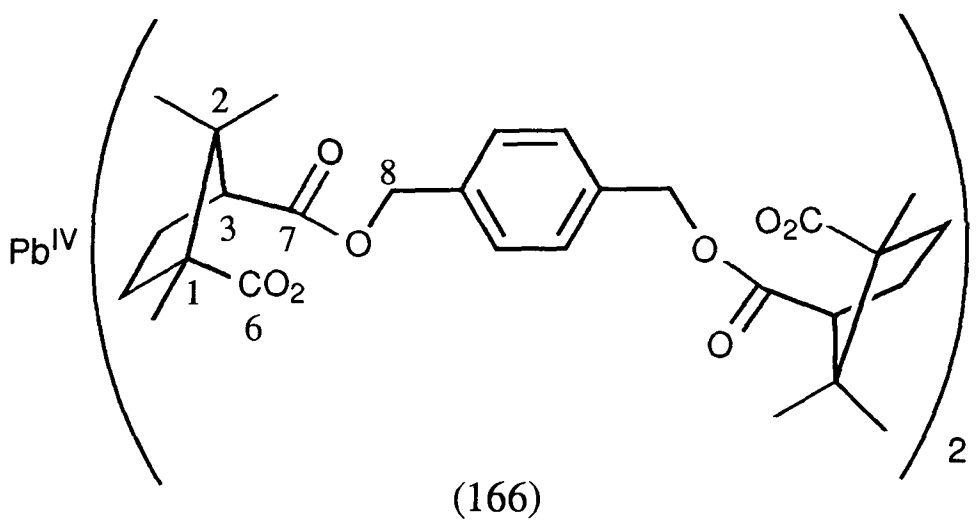
carbonyl groups were, however, clearly present.

The lead NMR spectrum of this complex at 223K was also studied (Appendix 3). This showed five peaks in the characteristic region, confirming that the ligands were bound to a lead(IV) centre. As before, one of the peaks could be tentatively assigned as being due to the presence of LTB. The fact that a number of peaks were observed again indicates that, in solution, complex (165) exists as a number of lead(IV) species in dynamic equilibrium.

The reactivity of complex (165) was investigated by combining it with allyltributyltin in chloroform and stirring the solution at room temperature overnight. After this time, the solvent was removed to yield a crude product which contained allyl benzoate (156), although this product was not isolated.

3.5 Synthesis of lead(IV) complexes of 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139)

3.5.1 Synthesis of *bis*- complex (166)



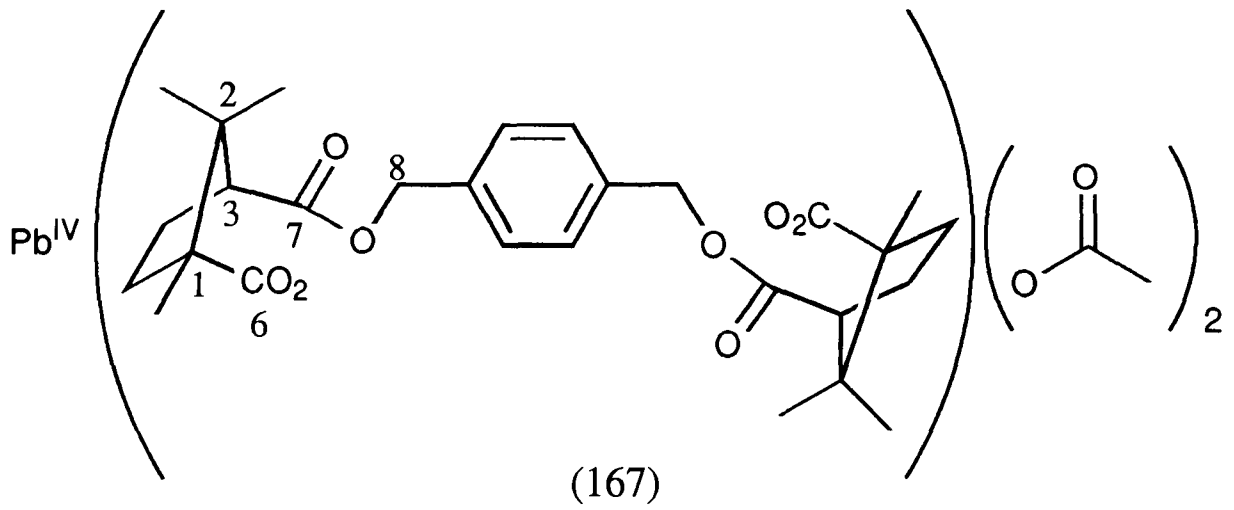
(166)

Complex (166) was synthesised as a highly soluble, yellow crystalline solid by combining two equivalents of the chiral ligand (139) and one equivalent of LTA under standard conditions. As for the other lead(IV) complexes discussed in this Chapter, the IR spectrum of the complex provided an initial indication of complexation as only the ester stretch was observed in the carbonyl region. The lead NMR spectrum of this complex was

recorded later in the work, and this confirmed that the ligand was coordinated to a lead(IV) centre; this will be discussed in more detail in Chapter Four.

In contrast with other lead(IV) complexes, this complex showed significant differences in the proton NMR spectrum when compared with the free ligand (Appendix 4). Beginning with the methyl groups, in the free ligand these occurred at δ 0.82, δ 1.24 and δ 1.25. In the complexed ligand, one methyl group was shifted upfield by around 0.5ppm to δ 0.35 and the splitting of the other two methyl groups increased from 0.01ppm to 0.2ppm (giving peaks which occurred at δ 0.95 and δ 1.15). A more significant shift was observed for the C(8) protons which provided an easy method for determining that the ligand was fully complexed. In both the free and complexed ligand, the C(8) protons (C(8)H and C(8)H') were coupled to each other and occurred as two doublets with a typical geminal coupling constant of around 12Hz. In the free ligand, C(8)H and C(8)H' were in almost identical chemical environments and occurred as close doublets separated by 0.06ppm. For the complexed ligand, the separation between the doublets increased to 1.21ppm, indicating that C(8)H and C(8)H' were no longer in similar chemical environments.

3.5.2 Synthesis of diacetate complex (167)

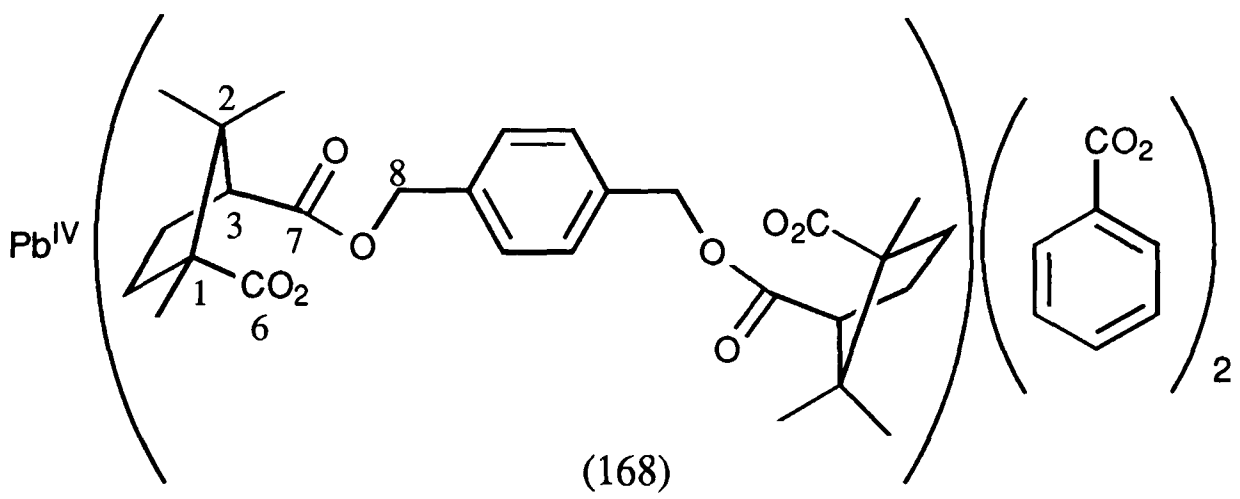


(167)

Complex (167) was synthesised by reaction of one equivalent of 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139) with one equivalent of LTA under standard conditions. As was observed for its achiral analogue (154), the complex was found to be rather unstable, decomposing from a yellow solid to a brown solid

over about an hour. However, the complex was studied by proton NMR spectroscopy which showed that complete complexation had taken place as there was no sign of residual acetate. As in the case of the *bis*- complex (166), the methyl groups had shifted slightly, and the C(8) protons had split out to appear as two multiplets at δ 4.56-4.68 and δ 5.74-5.83.

3.5.3 Synthesis of dibenzoate complex (168)



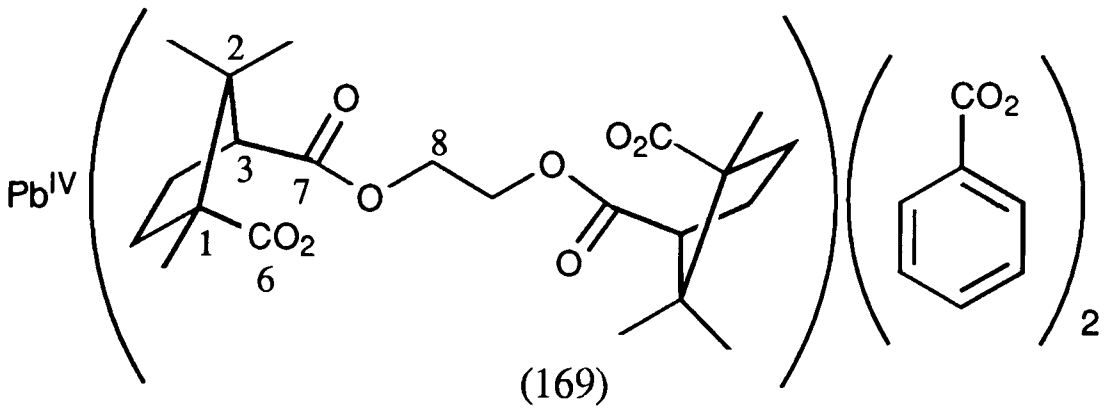
(168)

Complex (168) was synthesised by reaction of LTA with chiral ligand (139) and benzoic acid under standard conditions. The complex was formed as an orange-yellow crystalline solid which was very soluble in organic solvents. As for the *bis*- complex (166) and the diacetate complex (167), the methyl groups were observed to have shifted in the proton NMR spectrum when compared with the uncomplexed ligand, although in this case they appeared as multiplets rather than singlets. Similarly, the C(8) protons were observed as two sets of multiplets at δ 4.59-4.72 and δ 5.11-5.82 rather than as a close pair of doublets. The lead NMR spectrum of the complex showed that the ligands were complexed to a lead(IV) centre; this spectrum will be discussed further in Chapter Four.

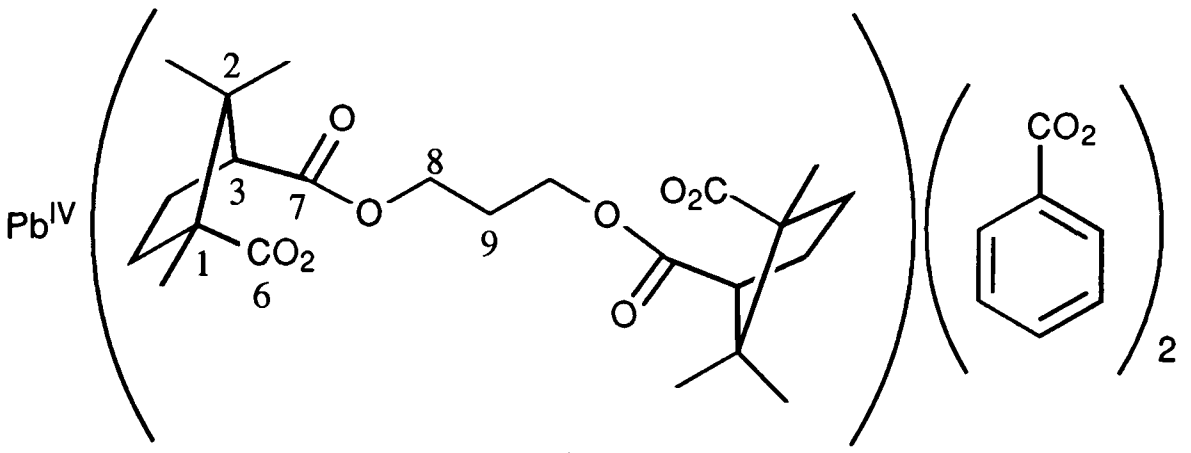
As before, the reactivity of complex (168) was investigated by studying its reaction with allyltributyltin. The complex was combined with the stannane in chloroform and stirred at room temperature overnight. Analysis of the resulting product by proton NMR spectroscopy indicated that formation of allyl benzoate (156) had occurred, and therefore that complex (168) was reactive in this type of carbon-carbon bond formation reaction.

3.6 Synthesis of complexes (169) and (170)

Ligands (142) (3,3'-(ethylene-1,2-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]) and (143) (3,3'-(propylene-1,3-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]) were complexed only as their dibenzoates (169) and (170) respectively, as this type of mixed ligand complex had been found to be generally the most stable and soluble in the earlier work.



(169)



(170)

3.6.1 Synthesis of dibenzoate complex (169)

Complex (169) was synthesised by reaction of LTA with the chiral ligand (142) (as a mixture of diastereomers) and benzoic acid under standard conditions and was formed as a foamy, yellow, hygroscopic solid. As before, the IR spectrum showed only a single stretch in the carbonyl region due to the ester group of the complexed ligand. The proton NMR spectrum appeared as a series of broad peaks and no significant shifts from the free ligand were observed.

In the carbon NMR spectrum, the peaks in the carbonyl region were of particular interest. For the uncomplexed ligand, the ester carbonyl peak appeared at δ 174.05 and the

acid carbonyl at δ 182.64. In complex (169), a broad, low intensity peak was evident at δ 182.29 (indicating that the carboxylate group was now coordinated), but the ester carbonyl peak was essentially unchanged, and occurred as a sharp peak at δ 173.81. A second broad, low intensity peak was observed at δ 175.14, and this was probably due to the coordinated benzoate carbonyl group.

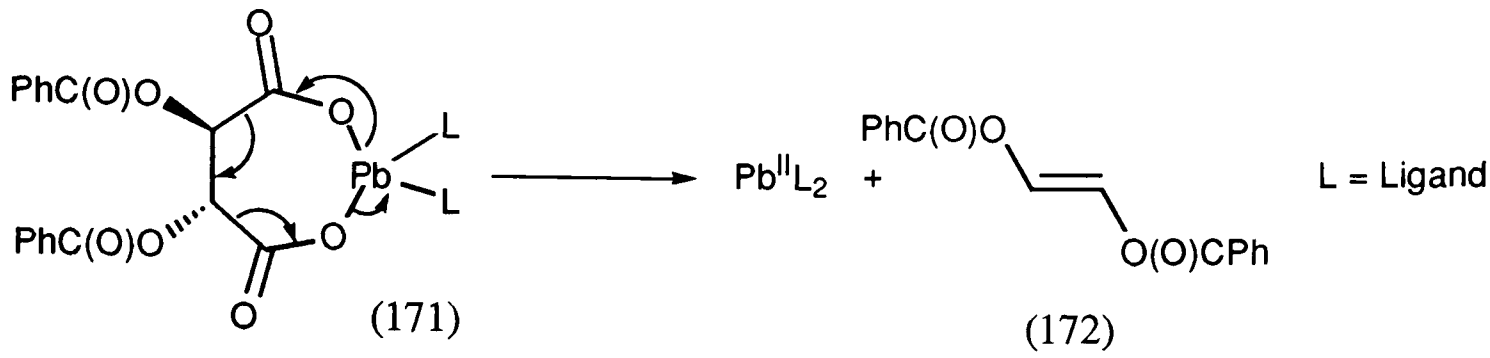
The lead NMR spectrum of this complex was recorded at 223K, and showed five peaks in the characteristic region indicating that, in solution, complex (169) existed as five lead(IV) species in dynamic equilibrium (Appendix 3). Comparison of the spectrum with that of LTB again indicated the presence of this complex in the equilibrium.

3.6.2 Synthesis of dibenzoate complex (170)

Reaction of LTA with 3,3'-(propylene-1,3-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethyl cyclopentane-1,3-dicarboxylate] (143) and benzoic acid under standard conditions resulted in the formation of complex (170) as orange plates. In the IR spectrum of the complex, a single stretch was observed in the carbonyl region, indicating, as before, that the acid group was now complexed to the lead centre. Again, the proton NMR spectrum was rather broad and did not show any significant shifts when compared with the spectrum of the free ligand. In the carbon NMR spectrum, no peaks due to complexed carboxylates could be observed, although the ester group at C(7) was observed. The fact that C(6) did not give an observable peak and C(7) did was a good indication that complexation at C(6) had occurred.

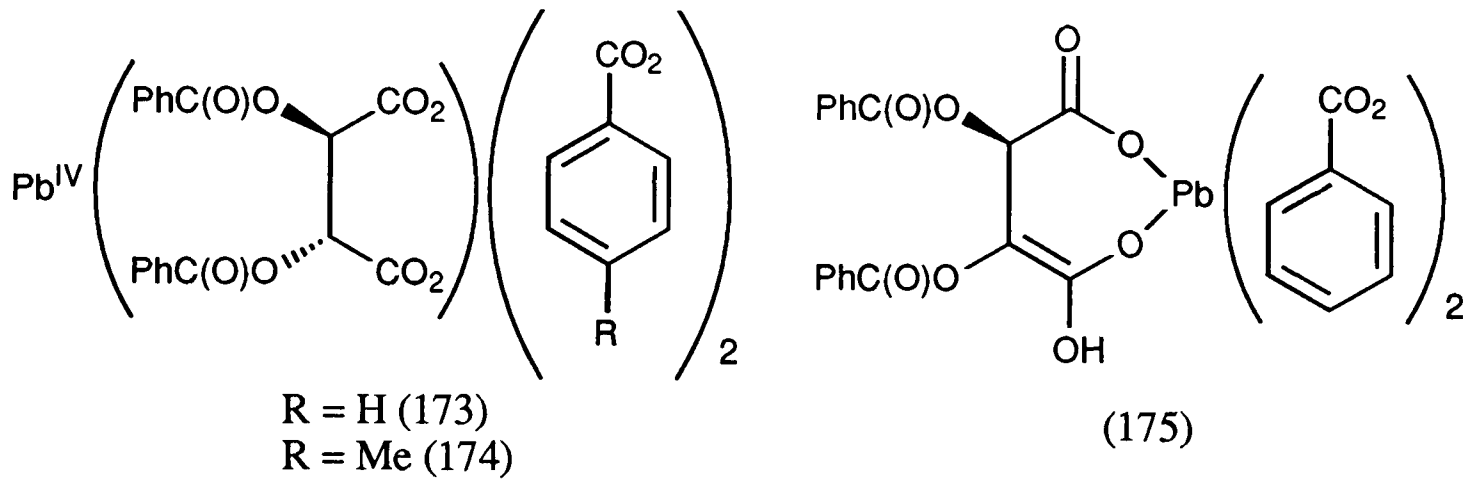
3.7 Synthesis of complexes of dibenzoyl-L-tartaric acid

Dibenzoyl-L-tartaric acid is a commercially available dicarboxylic acid and, like camphoric acid, had potential as a bidentate ligand for lead(IV). However, complexation of this diacid was not attempted until late in this work as it had been felt that complexes (171) formed using this ligand would readily decarboxylate in an analogous manner to literature precedent[83,116] to give substituted alkene (172) as shown in Scheme 3.5.



Scheme 3.5

However, reaction of one equivalent of LTA with one equivalent of dibenzoyl-L-tartaric acid and two equivalents of either benzoic acid or *p*-toluic acid resulted in the formation of complexes (173) and (174) as chloroform-soluble yellow solids. As before, examination of the IR spectra of these complexes showed the presence of a single carbonyl stretch due to the ester group.



The proton NMR spectrum of complex (173) showed the presence of a hydroxyl group, and also that the CH protons had only a relative integral of one. The IR spectrum of the complex also indicated the presence of a hydroxyl group. This would appear to suggest that the structure of the complex was actually of the form (175) shown above.

The carbon NMR spectrum of dibenzoate complex (173) showed, in the carbonyl region, a broad peak at δ 175.36, which was presumably due to the complexed carbonyl of the tartrate ligand, and a sharp peak at δ 164.72, which was due to the ester carbonyl group. The signal due to the carbon of the CH groups was also broad when compared with the uncomplexed case. Similar changes in peak characteristics and intensities from the free ligand were observed in the carbon NMR spectrum of the di-*p*-toluate complex (174).

Both complexes showed peaks in the characteristic lead(IV) region in their lead NMR spectra recorded at 223K (Appendix 3). Complex (173) appeared to exist as two exchanging species in solution; complex (174) appeared to exist as three exchanging species in solution.

3.8 Other ligands for lead(IV)

3.8.1 β- Keto esters

Early in this work an attempt was made to synthesise a lead(IV) complex of dibenzoylmethane (176). A mixture of LTA and dibenzoylmethane was heated at reflux in 1,2-dichlorobenzene under high vacuum.[109] Removal of the solvent resulted in the formation of a yellow solid, some of which dissolved in chloroform. It was found that the remaining yellow solid dissolved in, and could be slowly recrystallised from, DMSO. The crystals obtained were shown by single crystal X-ray analysis[117] to be lead(II) di(dibenzoylmethane) (177) (Figure 3.2, Appendix 5). The structure clearly showed that the dibenzoylmethane units were coordinated to the lead centre in a bidentate fashion as shown, the two Pb-O bonds being different lengths (2.29 Å and 2.40 Å). The ligands were arranged at roughly 120° to each other.

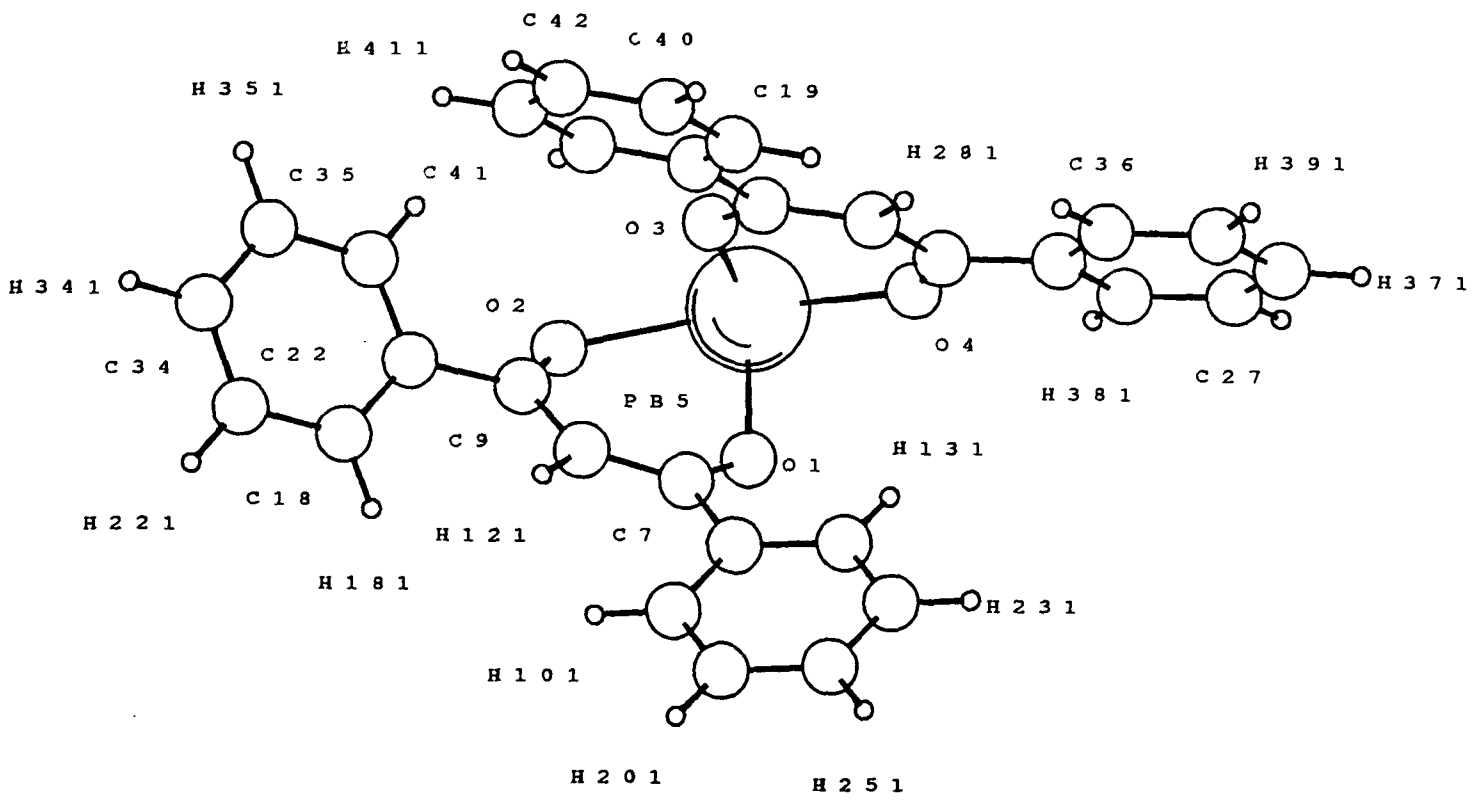
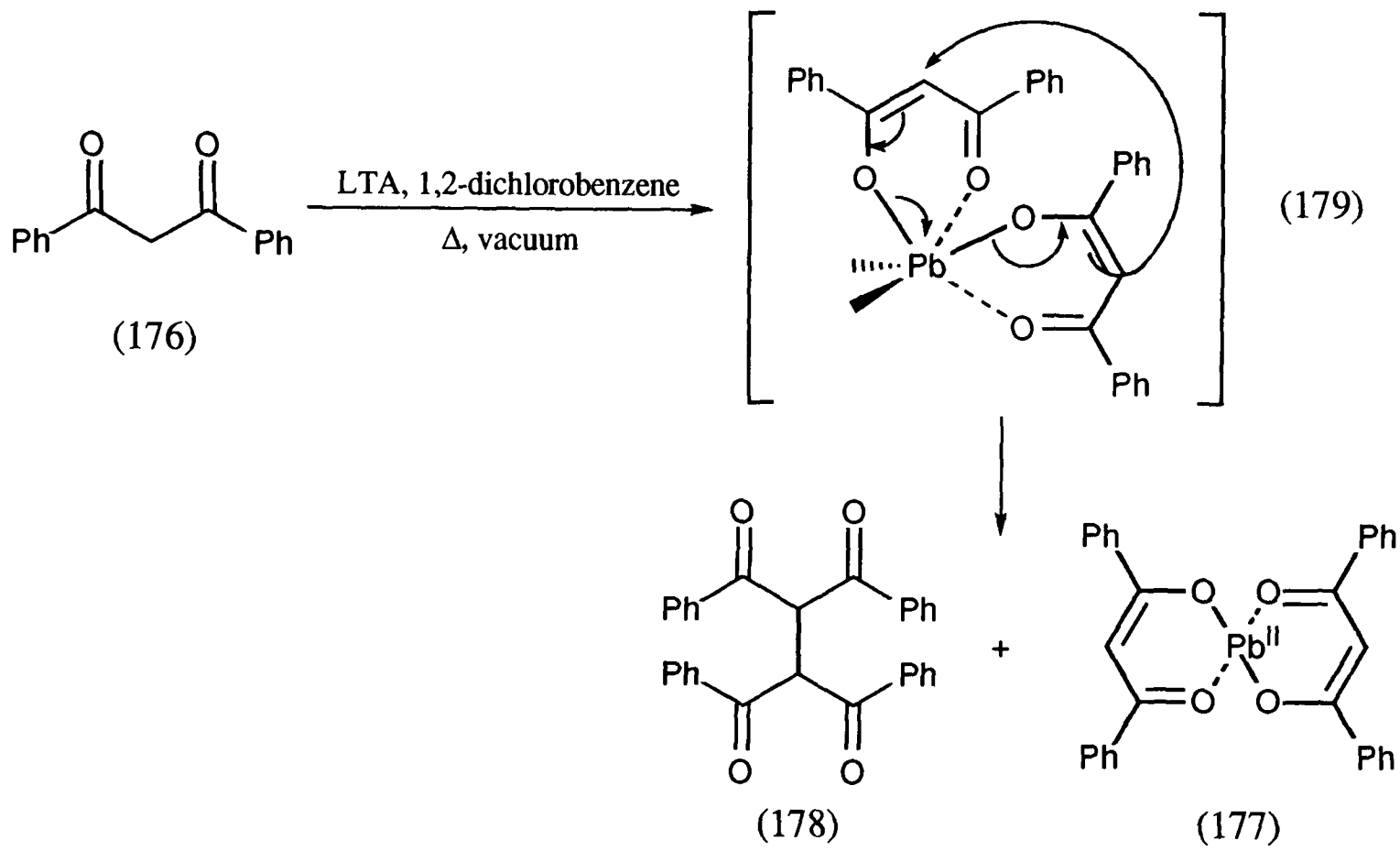


Figure 3.2

The available evidence suggested that the organic soluble product may be the dimer (178) (as evidenced by the observation of an MH^+ peak for dimer (178) in the mass spectrum), although it did not prove possible to unequivocally assign this to be the structure. Coordination of dibenzoylmethane to lead(IV), followed by lead-mediated dimerisation *via* a species such as (179) would result in the formation of the observed lead(II) compound (177) (Scheme 3.6). The same products resulted when complexation of dibenzoylmethane was attempted under the milder conditions of dissolution in toluene and solvent removal.



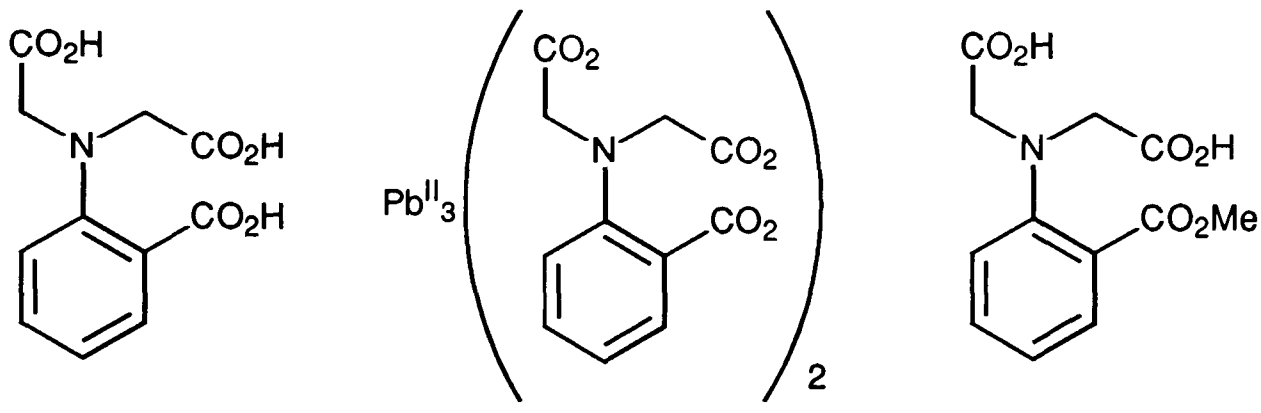
Scheme 3.6

3.8.2 Derivatives of 2-aminobenzoic acid

In addition to the main work of this project involving the use of dicarboxylic acids as ligands, the use of tricarboxylate ligands was also explored. It was hoped to synthesise lead(IV) complexes of the commercially available 2-aminobenzoic acid derivative, (2-carboxyphenylimino)diacetic acid (119). An initial attempt to form the monoacetate complex of this ligand by dissolving ligand (119) and LTA in 1,2-dichlorobenzene and heating the mixture at reflux under vacuum resulted in the formation of a brown solid which appeared to contain one (2-carboxyphenylimino)diacetic acid ligand and three acetate ligands ($PbL(OAc)_3$). Attempted preparation of a complex containing two equivalents of ligand (119)

resulted in the formation of what appeared to be $PbL_2(OAc)_2$. A repeat of this attempted complexation under milder conditions (dissolving the ligand and LTA in toluene, and then removing the solvent) resulted in the formation of a pale brown DMSO-soluble powder.

The IR spectrum of this product showed that, when compared with the free ligand, there were no OH groups present, and that the carbonyl stretch was no longer present. The proton NMR spectrum of this product at room temperature was rather broad, but at 373K sharp peaks could be observed, and the spectrum showed there to be no acetate groups remaining. Elemental analysis of this complex showed that it was in fact the trimeric lead(II) complex (120). Studies were then directed towards the synthesis of a methyl-substituted version of this ligand (121) as described in Chapter Two. Unfortunately, these routes were unsuccessful, and no further lead(IV) complexes of this type were prepared.



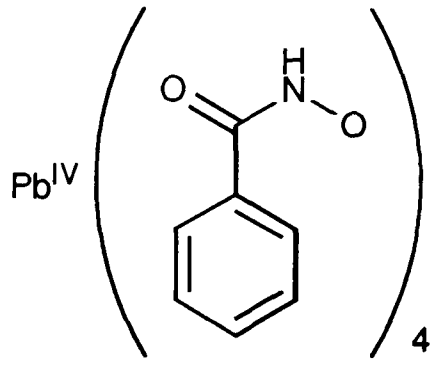
(119) (120) (121)

3.8.3 Hydroxamic acids

As part of this work, the use of hydroxamic acids as ligands was studied, as it was hoped that these would bind more tightly to the lead(IV) centre and allow the formation of non-exchanging lead species. There is considerable literature precedent for the use of hydroxamate compounds as ligands: in early work on asymmetric epoxidation, Sharpless *et al.* used chiral hydroxamates as ligands for vanadium.[81] More recently, hydroxamate compounds have found use as ligands for the actinides[118] and for iron(III).[119]

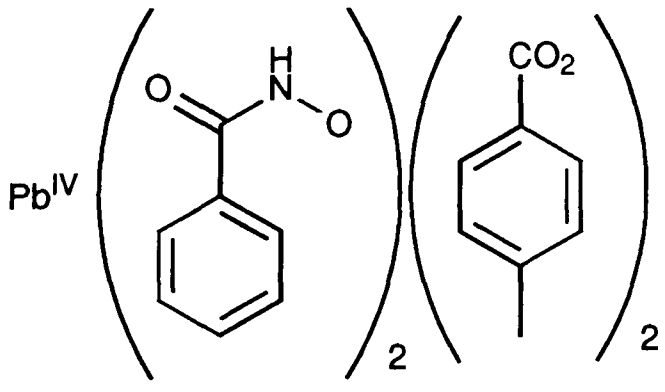
An early attempt to form lead(IV) tetrabenzohydroxamate (180) by the standard procedure resulted in the formation of a product which was not highly soluble in chloroform

and gave a very complicated proton NMR spectrum. This showed there to be acetate groups still present, even after azeotroping ten times with toluene. An attempt to form lead(IV) dibenzohydroxamate dibenzoate also failed to yield the correct product.

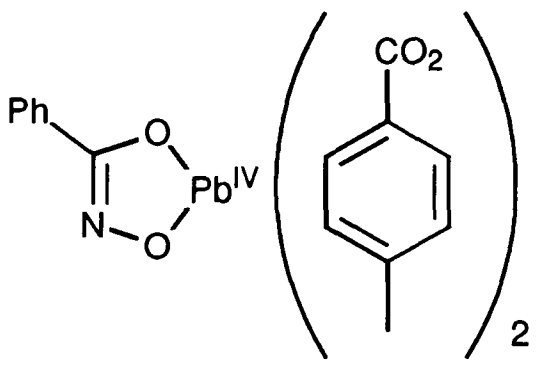


(180)

It was felt that more forcing conditions may be required to successfully form lead(IV) complexes with hydroxamic acids. Synthesis of lead(IV) dibenzohydroxamate di-*p*-toluate (181) was first attempted as it was hoped that this complex would be readily formed as a chloroform-soluble solid. Deduction of the stoichiometry of the complex from its proton NMR spectrum would also be straightforward. Thus, the appropriate quantities of ligands and LTA were combined in toluene and heated at reflux for one hour. The solvent was then removed to give a pale brown solid which was partially soluble in chloroform. By proton NMR spectroscopy this appeared to contain the correct complex, but also some impurities. Trituration of the solid with ether resulted in the formation of an off-white solid which was very soluble in chloroform.



(181)



(182)

The IR spectrum of this compound showed no evidence of NH or OH groups, thus indicating that complexation had occurred. However, examination of the integrals in the

proton NMR spectrum indicated that the product could not be the expected complex (181), rather that the structure may in fact be (182). The IR spectrum also showed a strong peak at 1676cm^{-1} which may be due to a C=N bond. However, it proved impossible to confirm that the structure of the complex was as represented by (182), as a satisfactory nitrogen analysis could not be obtained for this compound. In addition, no lead NMR spectrum of the product could be obtained.

3.9 Summary

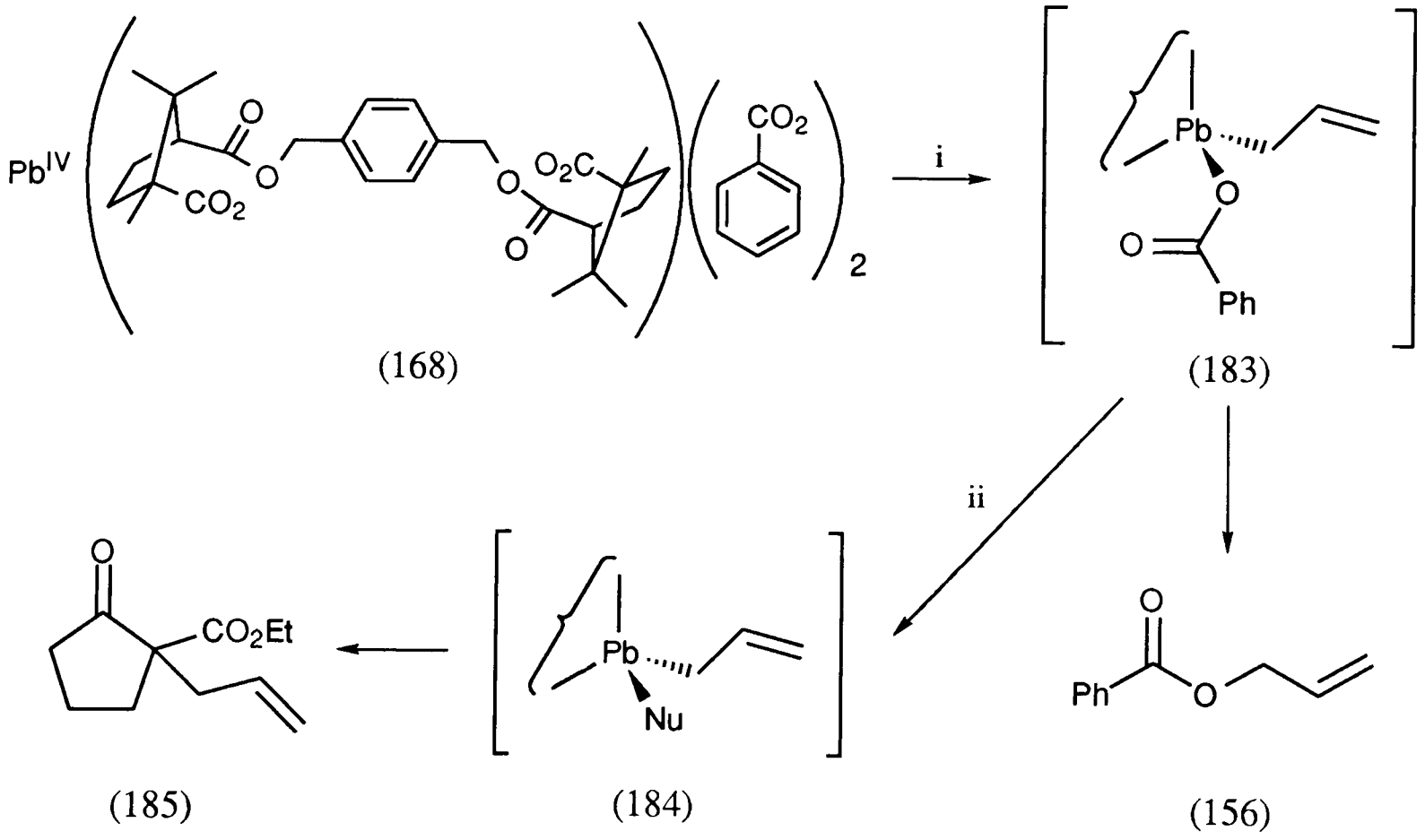
This Chapter has described the preparation of a range of novel achiral and chiral lead(IV) compounds, both as their *bis*- complexes and as their mixed ligand complexes. Characterisation was carried out by a combination of IR and NMR spectroscopy, including lead NMR techniques, and elemental analysis. The reactivity of some of these complexes was demonstrated by reaction with allyltributyltin, although this technique was not so suitable for the *bis*- complexes. In these cases, the products of reaction with allyltributyltin were difficult to identify and isolate. Further use of the complexes described in this Chapter in bond formation reactions will be discussed in Chapter Four.

CHAPTER FOUR

Carbon-Carbon Bond Formation Reactions

This Chapter describes the use of novel lead(IV) complexes in the mediation of carbon-carbon bond formation reactions. Following the successful synthesis of allyl esters *via* transmetallation of allyltributyltin species with lead(IV), initial studies focused on the extension of this reaction to the allylation[120] of carbon nucleophiles. Later work concentrated on the use of phenyllead(IV) compounds as phenyl cation synthetic equivalents in a range of α-phenylation processes.

4.1 Attempted allylation reactions



(168) (183) (185) (184) (156)

i) Allyltributyltin
ii) Nu = ethyl 2-oxocyclopentane carboxylate (186)

Scheme 4.1

It was demonstrated in Chapter Three (Section 3.5.3) that complex (168) underwent transmetallation with allyltributyltin, and that in the absence of external nucleophiles, this

resulted in the formation of allyl benzoate. It was hoped that the scope of this reaction could be extended by trapping the reactive allyllead(IV) intermediate (183) with a nucleophile such as ethyl 2-oxocyclopentanecarboxylate (186) (Scheme 4.1).

Complex (168) was combined in chloroform with allyltributyltin, and, after stirring for fifteen minutes, ethyl 2-oxocyclopentanecarboxylate (186) was added.[61] The solution was stirred for a further four hours to give a crude product, which t.l.c. and proton NMR spectroscopy showed to be a complex mixture containing allyl benzoate (156) and unreacted ethyl 2-oxocyclopentanecarboxylate (186). The presence of allyl benzoate indicated that coupling of the allyl group and the original benzoate ligand had occurred before the nucleophile had coordinated to lead(IV). Thus, a reaction was attempted whereby complex (168) was initially combined with the nucleophile and the stannane added after half an hour. In this case, the proton NMR spectrum of the crude material indicated that although it did not contain allyl benzoate, none of the required allylated product had been formed.

The same reaction was carried out using dibenzoylmethane and diethyl malonate as nucleophiles, adding these to the lead(IV) complex prior to the addition of stannane as before. In both cases, the crude product proved to contain unreacted β-dicarbonyl compound (186) and a trace of allyl benzoate. The reaction with dibenzoylmethane was repeated at reflux, but as before, the starting material (186) was recovered. In all these reactions, it appeared that coordination of the β-diketone to lead(IV) was not being achieved under the conditions employed. Therefore, an attempt was made to allylate dibenzoylmethane by pre-complexing the nucleophile to lead(IV), and then treating this compound with allyltributyltin. As before, however, proton NMR spectroscopy indicated that no reaction had occurred.

In 1979, Ono *et al.*[121] reported the alkylation and acylation of active methylene compounds with alkyl and acyl halides in the presence of DBU. As this type of reaction is analogous to the functionalisation of β-diketones such as (186) using organolead tricarboxylates, an attempt was made to allylate ethyl 2-oxocyclopentanecarboxylate by

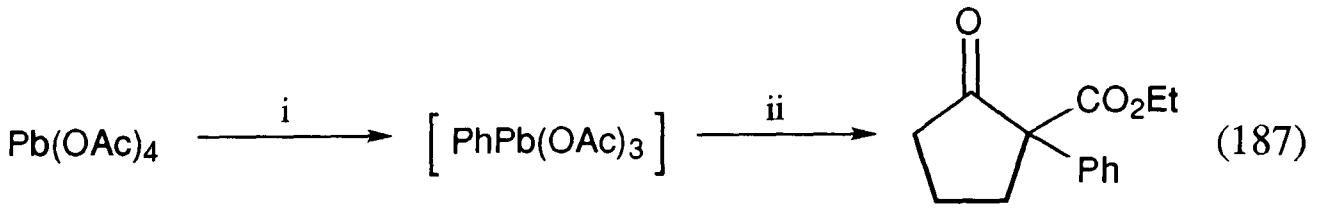
dissolving complex (168) and allyltributyltin in toluene and adding the nucleophile in DBU and toluene to the mixture. Purification of the crude product yielded only unreacted ethyl 2-oxocyclopentanecarboxylate and allyl benzoate.

The failure of these lead-mediated allylations, and also of other similar work carried out concurrently within this group,[122] was probably due to the high stability of the allyl cation. Thus, although allyllead(IV) tricarboxylates could be formed, their decomposition to form allyl benzoate or other more complex products was very rapid, and took place before coordination of the nucleophilic β-dicarbonyl compound had taken place.

4.2 Lead(IV)-mediated phenylation reactions - 1

4.2.1 Experimental procedures

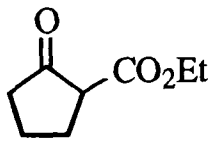
Chapter One of this thesis has described the formation of phenyllead(IV) tricarboxylates and their use as phenyl cation synthetic equivalents. The phenyllead triacetate (81) was formed, for example, *via* a boron-lead transmetallation reaction carried out in the presence of mercury(II) acetate. Following the generation of this species, a nucleophile (for example (186)) could be introduced to the system, giving the α-phenylated product (187) (Scheme 4.2).[68]



(187)

(81)

i) 1 eq. $PhB(OH)_2$, 0.1 eq. $Hg(OAc)_2$, $CHCl_3$, 1 h 40°C, r.t. overnight

ii) 0.91 eq. 

(186), 3.03 eq. pyridine, $CHCl_3$, 1 h 40°C, r.t. overnight

Scheme 4.2

All phenylation reactions described in this Chapter were carried out according to a modification of a procedure described by Morgan and Pinhey.[68] The phenyllead

tricarboxylate was generated *in situ* by stirring phenylboric acid with LTA (or another lead(IV) tetracarboxylate) and mercury(II) acetate in chloroform at 40°C for one hour and then at room temperature overnight. According to the literature, transmetallation is generally complete after one hour of heating, but further stirring overnight ensures that the reaction has gone to completion.[68] The catalytic mercury(II) present in the reaction mixture acts as a species which transfers a phenyl group from boron to lead (as direct boron-lead transfer is very slow).

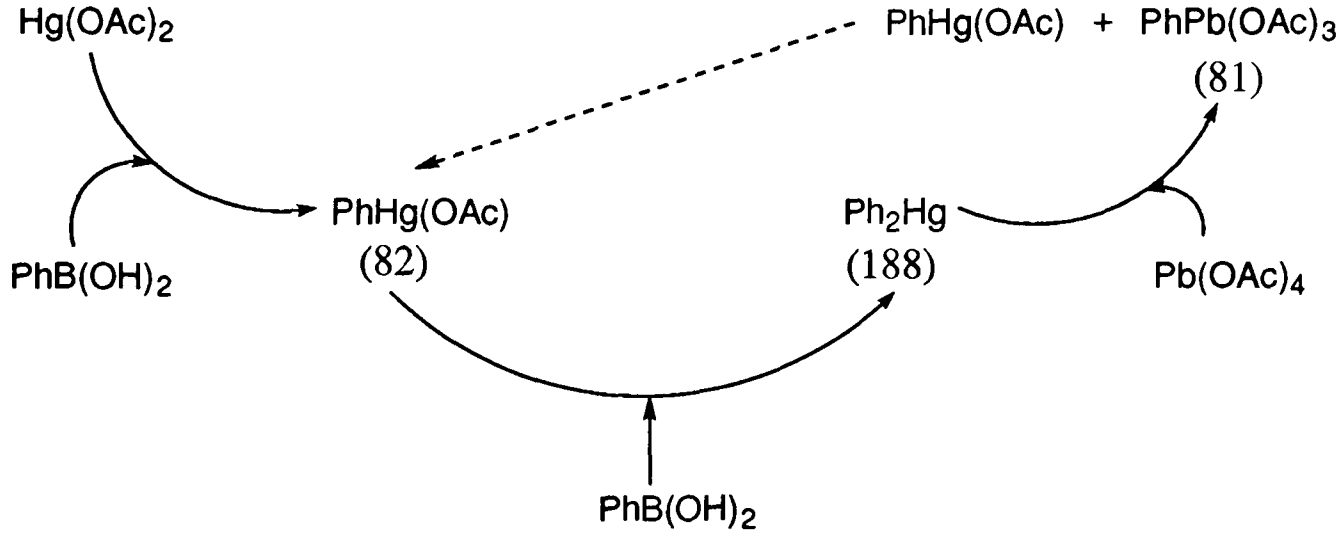


Figure 4.1

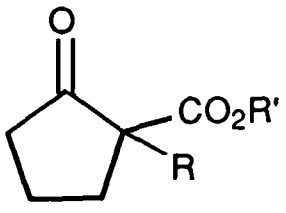
Figure 4.1 shows the role of mercury(II) in the reaction of phenylboric acid with LTA. The initial step in the reaction is the transfer of one phenyl group from boron to mercury, giving phenylmercury acetate (82). Transfer of a second phenyl group to this species leads to the formation of diphenyl mercury (188), which, on reaction with LTA, forms phenyllead triacetate (81) and phenylmercury acetate which re-enters the catalytic cycle.

Following the generation of intermediate (81), a suitable nucleophile was added as a solution in pyridine and chloroform, and the resulting solution heated at 40°C for one hour, and then stirred at room temperature overnight as before. Work-up was carried out by filtering the reaction mixture through Celite® to remove lead(II) and boron residues, and washing with acid to remove pyridine. It was not found necessary to wash the organic layer with 3M sodium hydroxide as described in the literature procedure. In some reactions, however, the proton NMR spectrum of the crude product showed that free acid ligands were present, and in these cases the crude product was washed with saturated sodium bicarbonate solution.

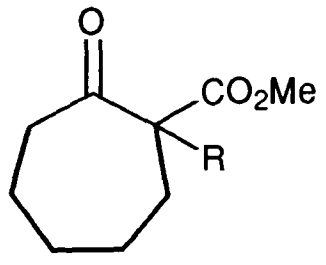
These reactions have generally only been carried out using lead tetraacetate, although recent work in this group has established that other lead(IV) tetracarboxylates (for example, lead(IV) tetra-*p*-toluate and lead(IV) tetra(benzoyl benzoate)) can be used to effect the same transformations.[122] Thus it was hoped to extend this methodology to the α-phenylation of similar substrates using the novel lead(IV) complexes described in Chapter Three.

4.2.2 Preparation of authentic racemic samples using LTA

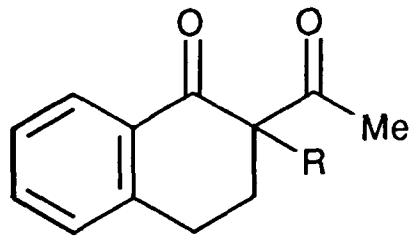
Before phenylation reactions were attempted using the novel lead(IV) complexes already described in this thesis, it was first necessary to prepare authentic racemic samples of all phenylated substrates. This would allow comparisons of yields obtained, and would also allow conditions for the separation of enantiomers of the products by chiral shift NMR spectroscopy and chiral GC to be established. The substrates chosen for study in this work are shown below. Ethyl ester (186) had been used extensively by Pinhey in his arylation studies, but for the work described in this thesis, the methyl ester (190) was generally used in preference, as this facilitated estimation of enantiomeric excesses by chiral shift NMR spectroscopy. The analogous seven membered ring compound (192) was used as it was a slightly bulkier substrate, as was 2-acetyl tetralone (194). 2,2,5-Trimethyl-1,3-dioxane-4,6-dione (71) (methyl Meldrum's acid) was used as this substrate had generally given high yields of arylated products in studies reported in the literature.[57]



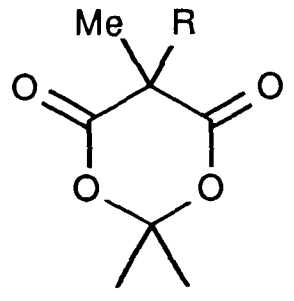
R' = Et, R = H (186)
R' = Et , R = Ph (187)
R' = Me, R = H (190)
R' = Me, R = Ph (191)



R = H (192)
R = Ph (193)



R = H (194)
R = H (195)



R = H (71)
R = Ph (196)

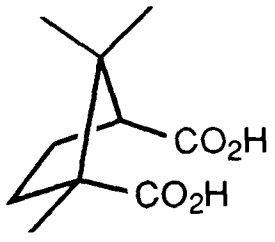
Reactions were carried out according to the literature procedure described above, and the results are shown in Table 4.1. In all cases, the α-phenylated products were obtained in yields ranging from reasonable to good.

Substrate	Conditions	Yield
(186)	LTA, 1 h 40°C, r.t. overnight	67%
(190)	LTA, 1 h 40°C, r.t. overnight	70%
(192)	LTA, 1 h 40°C, r.t. overnight	77%
(194)	LTA, 1 h 40°C, r.t. overnight	50%
(71)	LTA, 1 h 40°C, r.t. overnight	71%

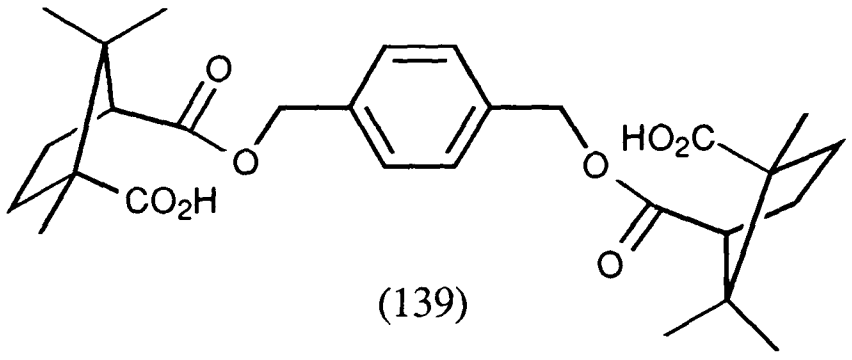
Table 4.1

Having synthesised these authentic products, it was then necessary to establish conditions for the separation of the enantiomers of (191), (193) and (195) by use of chiral shift reagents and chiral gas chromatography. Conditions for the separation of enantiomers of methyl 1-phenyl-2-oxocyclopentanecarboxylate (191) and methyl 1-phenyl-2-oxocyclo-heptanecarboxylate (193) by both chiral shift NMR spectroscopy and chiral GC are described in Chapter Six and Appendix 6. It did not, however, prove possible to establish appropriate conditions for the separation of enantiomers of α-phenyl-α-acetyl-1-tetralone (195).

4.2.3 Phenylations using LTA with added free chiral ligands



(122)



(139)

Initially, work was carried out to investigate the possibility of achieving chiral induction in the carbon-carbon bond formation reactions of phenyllead tricarboxylates with nucleophiles simply by the addition of free chiral dicarboxylic acids (122) and (139) to the

reaction mixtures. The results of these experiments are shown in Table 4.2.

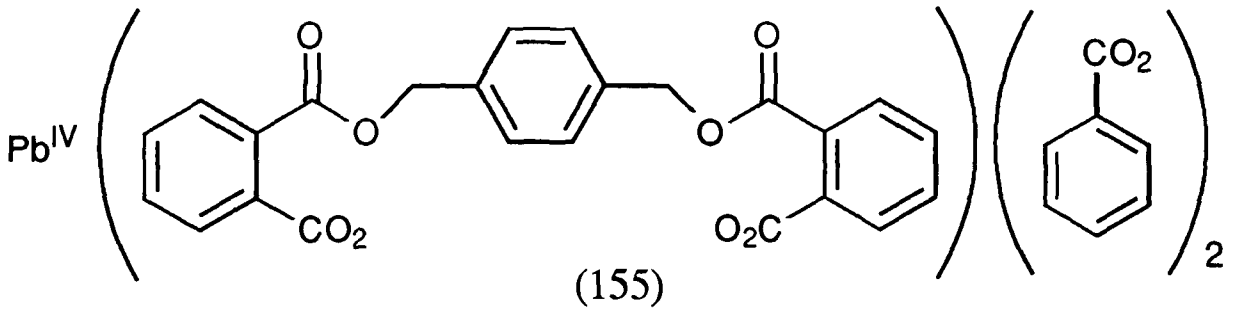
Substrate	Conditions	Yield	e.e. (%)
(190)	LTA, 1 eq. (122) 1 h 40°C, r.t. overnight	61%	0§
(190)	LTA, 2 eq. (122) 1 h 40°C, r.t. overnight	57%	0§
(190)	LTA, 1 eq. (139) 1 h 40°C, r.t. overnight	28%	0§
(190)	LTA, 2 eq. (139) 1 h 40°C, r.t. overnight	34%	0§

§ By chiral shift NMR spectroscopy

Table 4.2

When one or two equivalents of camphoric acid (122) were added to the reaction mixture, the phenylated product (191) was obtained in around 60% yield, in both cases contaminated with camphoric anhydride (126). For both reactions, chiral shift NMR spectroscopy indicated that the products were racemic. The addition of one or two equivalents of 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139) resulted in the formation of the α-phenyl product (191) in 28% and 34% yield respectively. The products were again contaminated with camphoric anhydride (126), and chiral shift NMR spectroscopy indicated that they were racemic.

4.2.4 Phenylation using complex (155)

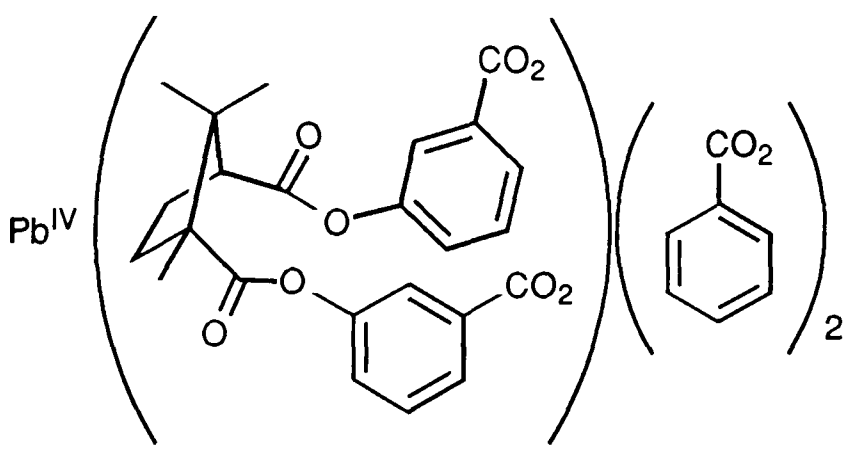


(155)

Phenylation of methyl Meldrum's acid (71) using complex (155) was achieved in 52%

yield. This was an encouraging result, as the product was isolated in a yield which was comparable with that obtained when the reaction was mediated by LTA (71%). It could be concluded from this result that the reactivity of the lead(IV) centre had not been altered significantly by the complexation of the novel dicarboxylic acid ligand.

4.2.5 Phenylations using complex (165)



(165)

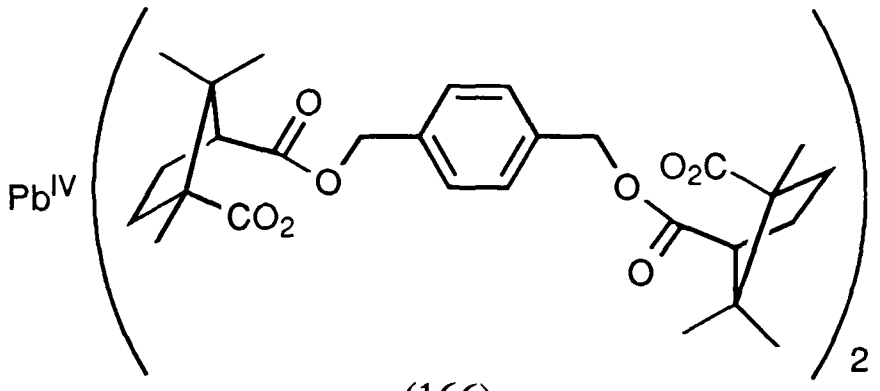
Encouraged by the success of the phenylation reaction using complex (155) above, studies into the use of chiral complexes were initiated. The results of early reactions using complex (165) are shown in Table 4.3. Phenylation of methyl 2-oxocyclopentanecarboxylate (190) was achieved in 44% yield, and methyl Meldrum's acid (71) was phenylated in 62% yield. As before, both these results were encouraging as they showed that the novel lead(IV) complex (165) was almost as effective as LTA in carbon-carbon bond formation reactions. Unfortunately, in the case of reaction with methyl 2-oxocyclopentanecarboxylate, chiral shift NMR spectroscopy showed that the product was in fact racemic. This is probably a consequence of the distance of the chiral centre from the reacting species in this particular complex.

Substrate	Conditions	Yield	e.e. (%)
(190)	(165), 1 h 40°C, r.t. overnight	44%	0§
(71)	(165), 1 h 40°C, r.t. overnight	62%	-

§ By chiral shift NMR spectroscopy

Table 4.3

4.2.6 Phenylations using complex (166)



(166)

Despite the failure of a reaction of complex (166) with allyltributyltin (Chapter Three), a series of phenylation reactions were attempted using this complex. The results of these are shown in Table 4.4.

Substrate	Conditions	Yield	e.e. (%)
(186)	(166), 1 h 40°C, r.t. overnight	18%	-
(190)	(166), 1 h 40°C, r.t. overnight	Contaminated	-
(190)	(166), 2 h 40°C, r.t. 48 h	10%	12§, 4†
(192)	(166), 1 h 40°C, r.t. overnight	8% (crude)	-
(71)	(166), 1 h 40°C, r.t. overnight	0%	-

§ By chiral shift NMR spectroscopy, † By chiral GC

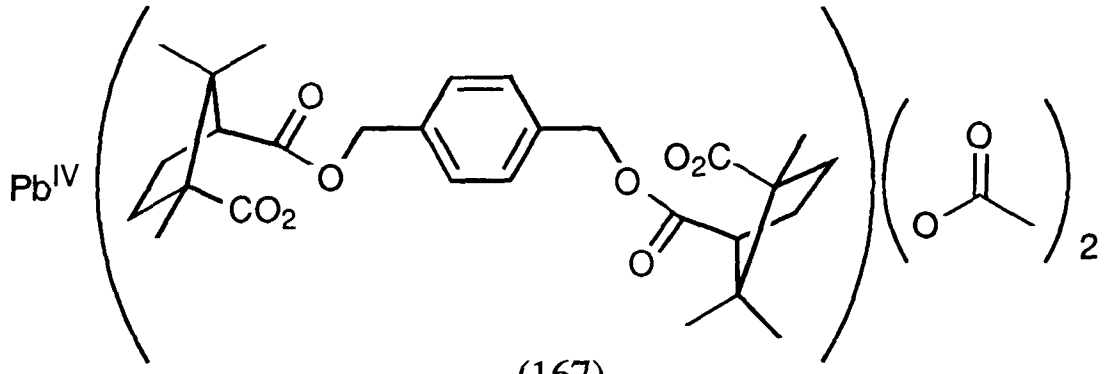
Table 4.4

Ethyl 1-phenyl-2-oxocyclopentanecarboxylate (187) was obtained in 18% yield; an initial reaction of methyl 2-oxocyclopentanecarboxylate (190) with complex (166) under the standard conditions gave a crude product which, after silica chromatography, proved to contain a small quantity of the required product (191), but contaminated with around 90% camphoric anhydride (126). This reaction was repeated under slightly altered conditions, heating the reaction mixture for two hours at 40°C and stirring at room temperature for forty eight hours at each stage, and in this case the product (191) was obtained in 10% yield. The enantiomeric

excess was found to be 12% by chiral shift NMR spectroscopy and 4% by chiral GC. In the case of methyl 2-oxocycloheptanecarboxylate (192), the crude product was obtained in 8% yield (as estimated from the proton NMR spectrum), but unfortunately this could not be further purified by silica chromatography. When phenylation of methyl Meldrum's acid (71) was attempted, the proton NMR spectrum indicated that less than 5% of the product was present, and this could not be isolated by silica chromatography.

Thus, for this complex, yields of phenylated products were rather low, and for phenylation of methyl 2-oxocyclopentanecarboxylate, where it had been hoped to observe chiral induction in the carbon-carbon bond formation reaction, no significant enantiomeric excess was observed.

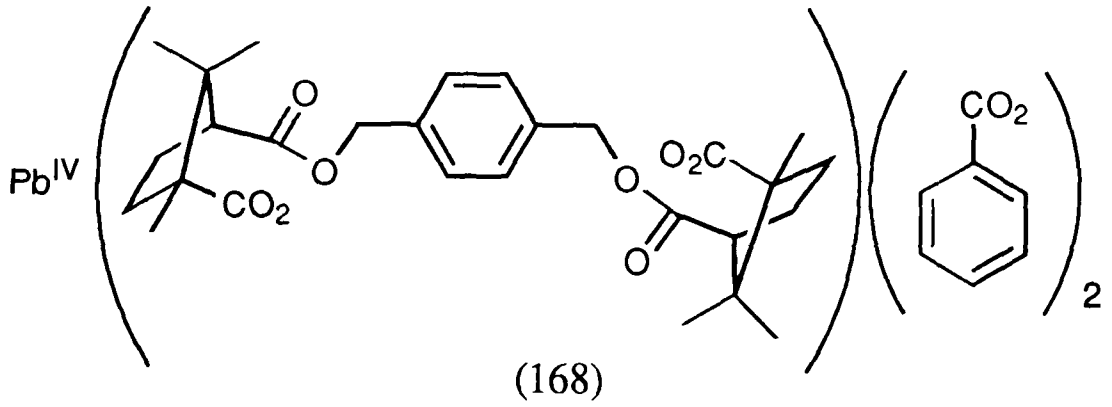
4.2.7 Phenylation using complex (167)



(167)

Diacetate complex (167) was found to be unstable with respect to decomposition, both in the solid state and in solution, as described in Chapter Three. However, it was found that if the complex was prepared and used immediately, phenylation of methyl 2-oxocyclopentane-carboxylate (190) was possible, the product being obtained in an encouraging 37% yield. In this case, the reaction time was extended to three hours at 40°C, as this had been found to give slightly increased yields of products for the analogous dibenzoate complex (168) (*vide infra*). The enantiomeric excess of the reaction was found to be 8% by chiral shift NMR spectroscopy and 1% by chiral GC.

4.2.8 Phenylations using complex (168)



(168)

A series of phenylation reactions were performed using chiral dibenzoate complex (168) and the results of these are shown in Table 4.5 below. The first reaction, with ethyl 2-oxocyclopentanecarboxylate (186), was carried out to explore the possibility of forming carbon-carbon bonds using complex (168) under the conditions employed. Although the product was not isolated, analysis of the crude product by GCMS showed that phenylation of the substrate had indeed occurred.

Substrate	Conditions	Yield	e.e. (%)
(186)	(168), 1 h 40°C, r.t. overnight	GCMS	-
(190)	(168), 1 h 40°C, r.t. overnight	20%	-
(190)	(168), 2 h 40°C, r.t. 48 h	21%	8§, 4†
(190)	(168), 3 h 40°C, r.t. overnight	33%	5§
(192)	(168), 1 h 40°C, r.t. overnight	17%	6§, 4†
(194)	(168), 1 h 40°C, r.t. overnight	8%	-
(71)	(168), 1 h 40°C, r.t. overnight	52%	-

§ By chiral shift NMR spectroscopy, † By chiral GC

Table 4.5

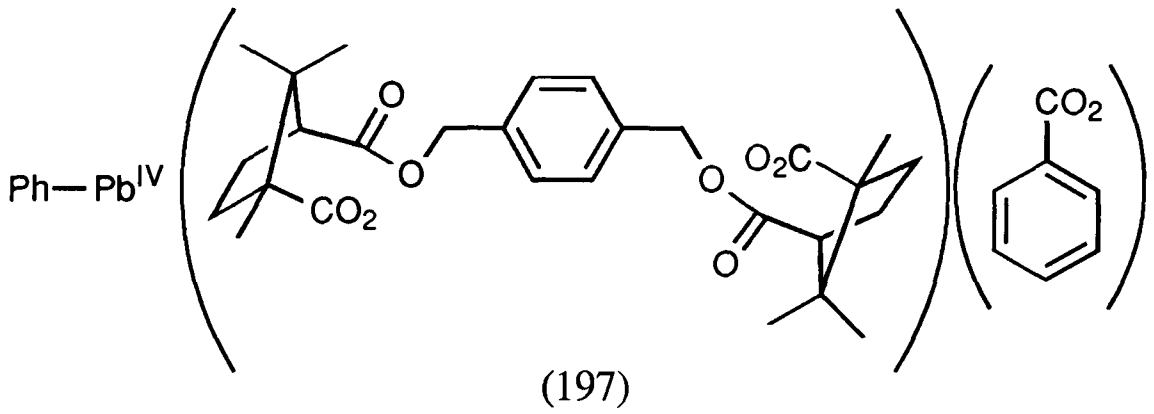
As before, studies quickly moved to the use of methyl 2-oxocyclopentanecarboxylate (190) as a phenylation substrate, as determination of the enantiomeric excess in reactions using this substrate by chiral shift NMR spectroscopy was straightforward. In an initial reaction carried out according to the general procedure, the product (191) was isolated cleanly after simple work-up and did not require further purification by silica chromatography. However, the yield of the reaction was found to be a rather low 20% (the remaining material being unreacted methyl 2-oxocyclopentanecarboxylate). In an attempt to optimise this yield, reaction times were doubled at each stage of the reaction. In this case, the product was isolated in essentially the same yield (21%) after silica chromatography. In a third reaction, the mixture was heated at 40°C for three hours (rather than one) and then at room temperature overnight at each stage. In this reaction, the product was obtained in 33% yield. Further work to optimise the yield of this reaction was not carried out. In those cases where the enantiomeric excess of this reaction was determined, it was found to be between 4% and 8% by both NMR spectroscopy and GC.

In the case of methyl 2-oxocycloheptanecarboxylate (192), reaction with complex (168) and phenylboric acid in the presence of catalytic mercury(II) acetate resulted in the formation of a crude product containing both phenylated ester (193) and unreacted starting material (192). An attempt was made to separate these by silica chromatography, but this was not successful. It was hoped that the unreacted starting material (192) could be removed by washing the crude product with a 0.5M solution of copper(II) sulphate in a 0.5M solution of sodium bicarbonate, as it was thought that copper(II) ions would coordinate to the unreacted β-dicarbonyl, transferring this into the water layer. This was successful, and resulted in the isolation of methyl 1-phenyl-2-oxocycloheptanecarboxylate (193) in 17% yield. The enantiomeric excess of the reaction was again low, being measured at 6% by NMR spectroscopy and 4% by GC.

2-Acetyl tetralone (194) was phenylated in 8% yield using complex (168), but in this case it did not prove possible to determine the enantiomeric excess of the reaction. For the

achiral substrate (71), the phenylated product (196) was obtained in 52% yield. As before, this was a good indication that complex (168) was reactive, and that the lead(IV) centre had not been over-stabilised by the coordination of new ligands.

For complex (168), then, it was shown that phenylation of a range of β-dicarbonyl compounds could be achieved in poor to reasonable yields; in all cases, the mass balance of the reaction was made up of unreacted starting materials. For substrates (186), (190) and (192) the low yields obtained were, to some extent, due to difficulties in the separation of products from starting materials. For the more acidic methyl Meldrum's acid (71), the yield of phenylated product was considerably improved, showing that complex (168) was almost as reactive as LTA under the same conditions.



(197)

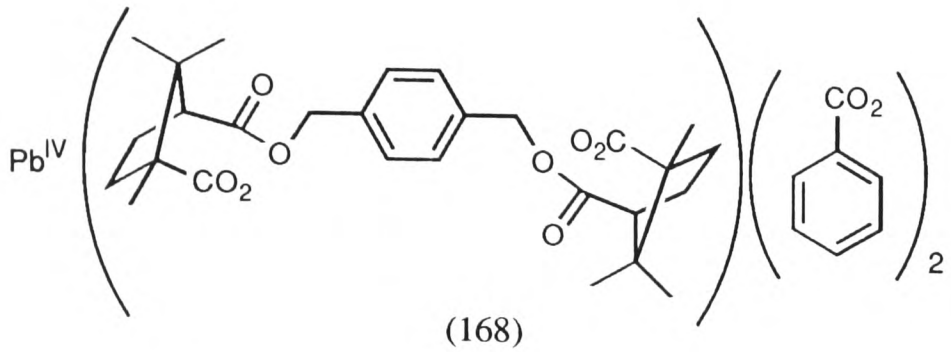
An attempt was made to isolate the phenyllead tricarboxylate (197) synthesised from dibenzoate complex (168). Therefore, complex (168) was combined with mercury(II) acetate in chloroform, and phenylboric acid in chloroform was added slowly to this solution. After stirring at 40°C for one hour and at room temperature overnight, the solution was filtered through Celite®, and the organic layer washed and concentrated. Petrol was added to the remaining solution and the mixture stored at 0°C overnight,[68] after which time a white precipitate was formed. Although proton NMR spectroscopy did not allow this compound to be unambiguously identified as the phenyllead compound (197), it was dissolved in chloroform and a solution of methyl 2-oxocyclopentanecarboxylate in pyridine added. The mixture was heated and stirred as normal, and on work-up a product was isolated which contained a small amount (*ca.* 3mg, 70% yield) of the phenylated material. This translated to around 10% yield of the product over two steps.

4.2.9 Lead NMR studies of complex (168)

Following the failure to achieve any significant enantioselectivity in carbon-carbon bond formation reactions using complex (168), this complex was studied by ^{207}Pb NMR spectroscopy. At room temperature, the spectrum of complex (168) appeared as a series of broad peaks, which, as the temperature was lowered became more defined (Spectra 4.1, 4.2 and 4.3). At 223K, the spectrum showed that, in solution, this complex consisted of a number of exchanging lead(IV) species (Spectrum 4.3).

A spectrum of complex (166) was also recorded, and this appeared to exist largely as one species, with minor species present being due to exchange with residual acetate (Spectrum 4.4). By direct comparison of Spectrum 4.3 with Spectrum 4.4, it could be seen that one of the species present in the solution equilibrium of complex (168) was the *bis*- complex (166). Further species in the solution equilibrium of complex (168) could be identified by comparison with the spectrum of the LTA/LTB system. When these two spectra were overlaid (Spectrum 4.5), it could be seen that LTA and LTB were certainly present in the solution of (168), as well as some of the other intermediate species.

This may go some way to explaining the lack of selectivity observed in the phenylation reactions described earlier. If, for example, LTB was the most reactive lead(IV) species present in significant quantity, then it would be expected that this would react in preference to any less reactive, chiral species present, giving a racemic product. Thus, it seemed that for the complex systems investigated thus far, ligand exchange was too rapid, leading to the presence of multiple species in solution; the problems of obtaining good selectivity in such systems has previously been discussed (Chapter One). Therefore, if ligands were chosen which would bind more tightly to lead, this type of ligand exchange could be avoided, and defined species containing chiral ligands could undergo carbon-carbon bond formation reactions.



(168)

Spectrum 4.3

225K

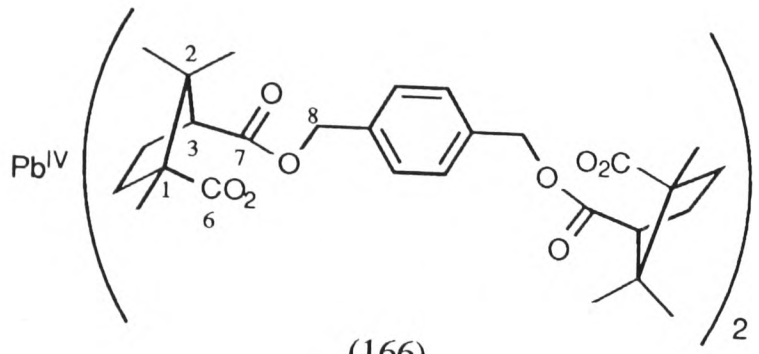
Spectrum 4.2

255K

Spectrum 4.1

295K

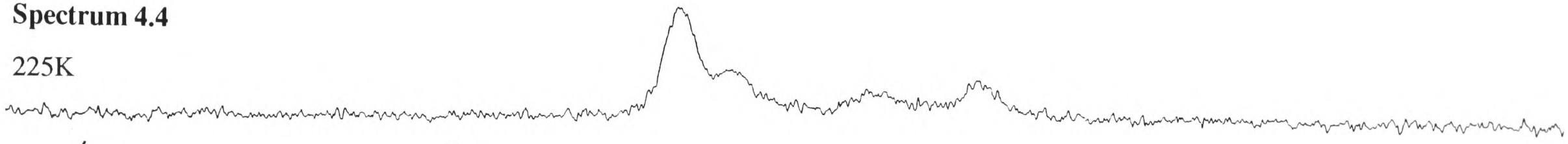
-1870 -1880 -1890

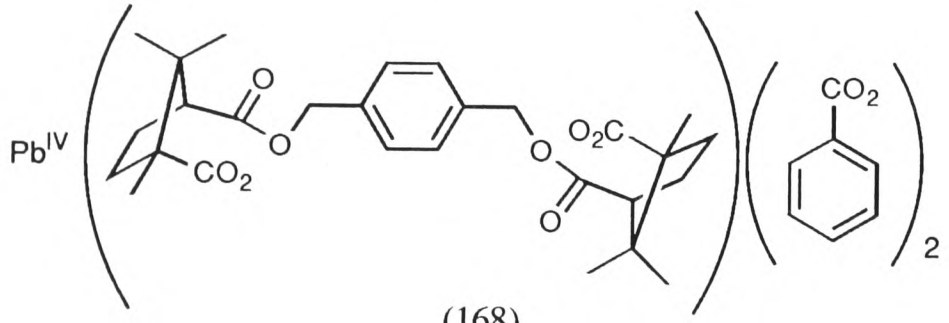


(166)

Spectrum 4.4

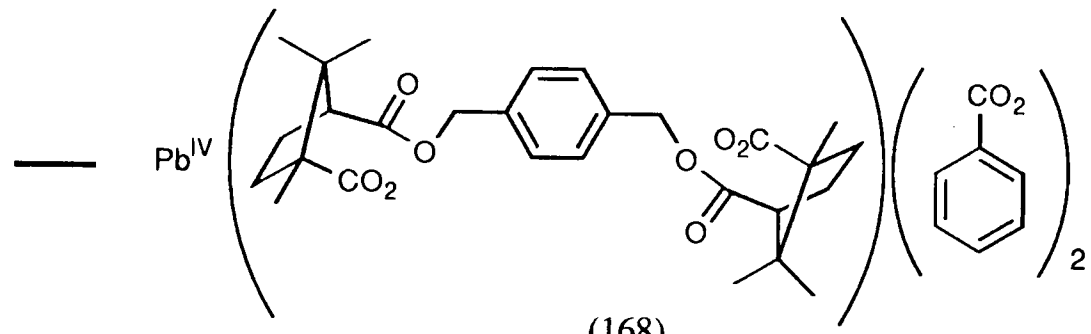
225K



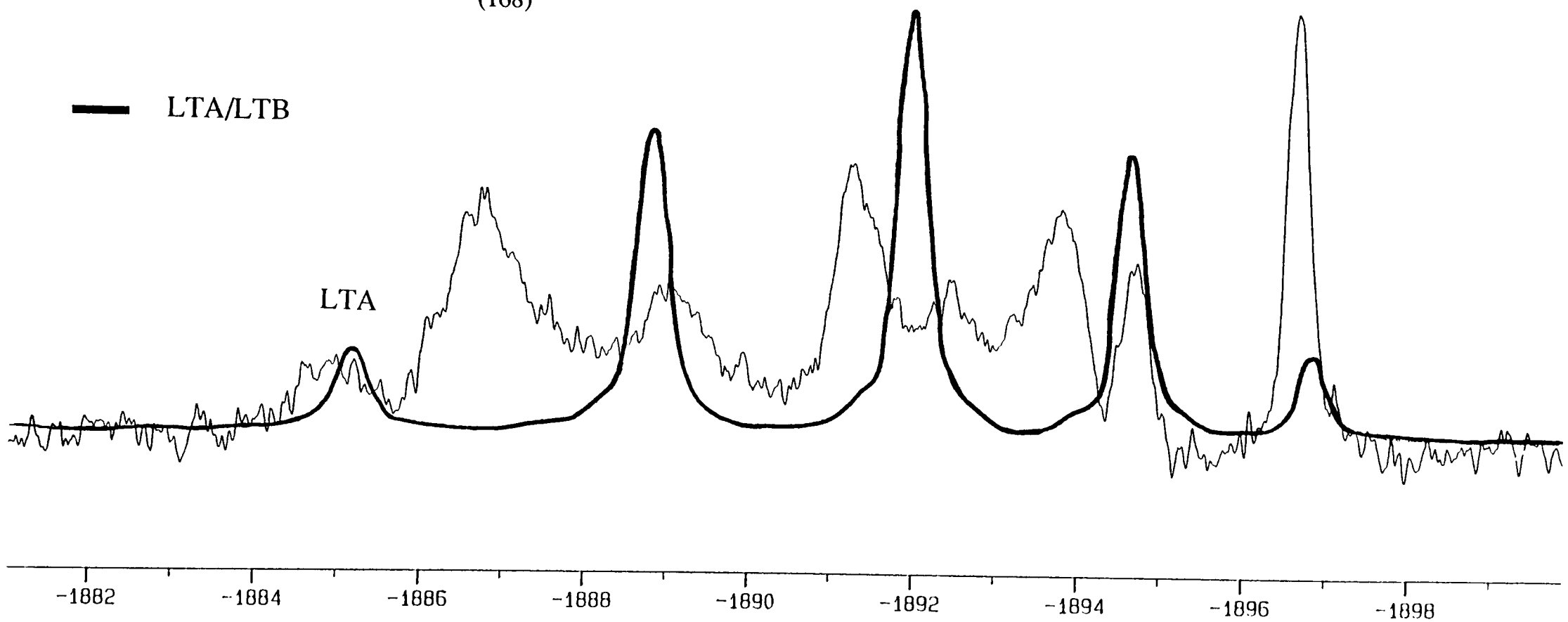


(168)

Spectrum 4.3



(168)

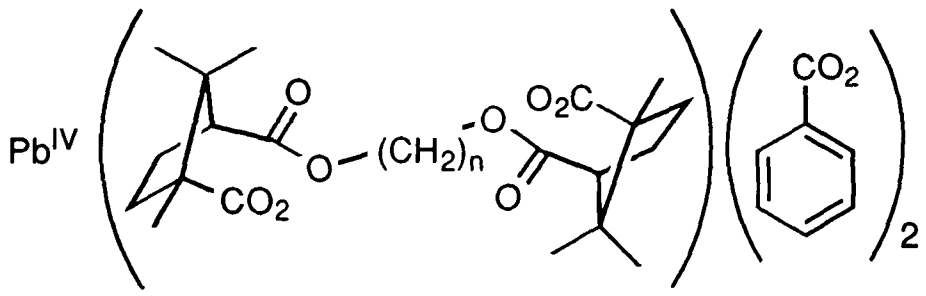


Spectrum 4.5

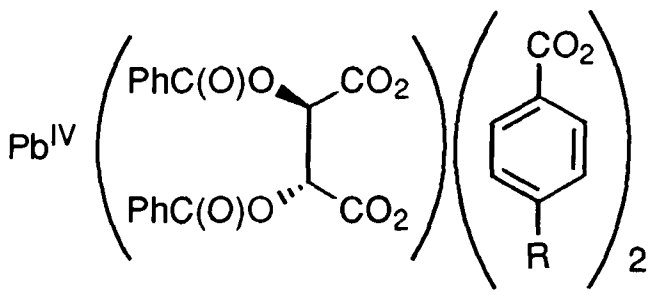
4.3 Lead(IV)-mediated phenylation reactions - 2

4.3.1 Use of shorter ligands

As discussed above, it was thought that the lack of enantioselectivity observed in phenylation reactions, for example those of complex (168), was due to the presence of a large number of species (both chiral and achiral) in the reaction mixture. By using tighter binding ligands, this type of exchange could be minimised or even eliminated allowing bond formation reactions to be mediated by one defined, chiral species. It was thought that shorter ligands could fulfil this role, and thus complexes (169) and (170), which are analogues of dibenzoate complex (168), and the tartrate complexes (173) and (174) were synthesised as described in Chapter Two and Chapter Three.



n = 2 (169)
n = 3 (170)



R = H (173)
R = Me (174)

The lead NMR spectra of all these complexes indicated that each was present as more than one species in solution, but the number of species present was certainly less than observed for complex (168). The results of a series of phenylation reactions with methyl 2-oxocyclopentanecarboxylate (190) using these complexes is shown in Table 4.6. Phenylation reactions using complex (170) are discussed in Chapter Five.

All three complexes gave good yields of phenylated products, which were comparable to the yield obtained when the phenylation of this substrate was mediated by LTA. However, as before, enantiomeric excesses were very low (4-10%). Thus, it appeared that ligand exchange was still too rapid, and that the chiral species were not reacting in preference to any others.

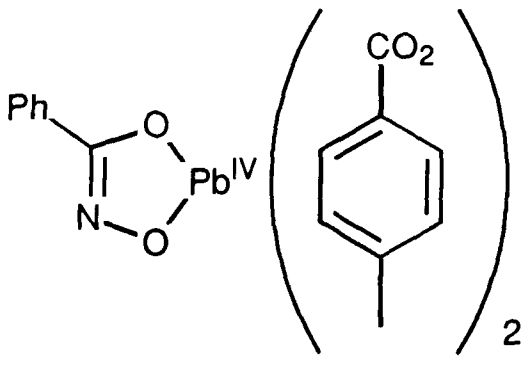
Substrate	Conditions	Yield	e.e. (%)
(190)	LTA, 1 h 40°C, r.t. overnight	70%	-
(190)	(169), 1 h 40°C, r.t. overnight	69%	10§, 6†
(190)	(173), 1 h 40°C, r.t. overnight	71%	4§, 4†
(190)	(174), 1 h 40°C, r.t. overnight	58%	4§, 4†

§ By chiral shift NMR spectroscopy, † By chiral GC

Table 4.6

4.3.2 Use of ligands other than carboxylates

The rapid exchange of lead(IV) carboxylate species when in solution was proving to be problematic in this work, and thus the use of ligands other than carboxylates was investigated. As described in Chapter Three, attempts were made to synthesise lead(IV) dibenzohydroxamate di-*p*-toluate (181), resulting in the formation of what appeared to be complex (182). Although it had not proved possible to confirm the structure and oxidation state of this compound, phenylation of methyl Meldrum's acid (71) using complex (182) was attempted. However, all attempts to effect this transformation failed.



(182)

4.4 Summary

This Chapter has demonstrated the use of novel lead(IV) complexes in the α-phenylation of a range of substrates. Yields ranged from poor to excellent, and in some cases the products were obtained in yields comparable to reactions mediated by LTA. Enantiomeric excesses of these reactions were found to be no greater than 12%. This was thought to be due to rapid ligand exchange of lead(IV) carboxylates in solution leading to the presence of achiral species which were potentially more reactive than the more elaborate chiral species. The use of shorter ligands was explored, as it was hoped that these would bind more tightly to lead(IV) and reduce the number of exchanging species present in the solution equilibrium. In these cases, however, enantiomeric excesses were still no greater than 10%.

A further problem inherent in the phenylation procedure is the use of mercury(II) acetate as a catalyst. This can introduce further potential ligands to already complex, exchanging mixtures of lead(IV) species. The use of other catalysts in the phenylation reaction is discussed in Chapter Five.

CHAPTER FIVE

Catalyst Studies

As described at the conclusion of Chapter Four, the use of mercury(II) acetate as a catalyst in phenylation reactions had inherent problems, as this introduced further potential ligands for lead(IV) into already exchanging systems. This Chapter describes studies directed towards the use of alternative catalysts and sources of aryl- groups in the phenylation reaction.

5.1 Investigation of catalysts

A series of reactions using alternative catalysts were carried out according to the standard procedure using LTA. The results of these reactions are shown below (Table 5.1) and discussed in Sections 5.1.1 and 5.1.2.

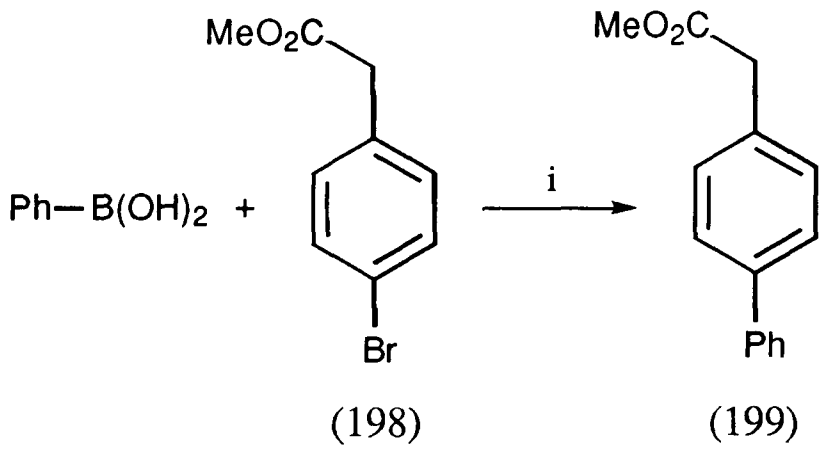
Substrate	Catalyst	Quantity of catalyst	Yield
(190)	$Hg(OAc)_2$	0.1 equivalents	70%
(190)	None	-	Complex mixture
(190)	CsF	1 equivalent	5% (crude)
(190)	CsF	3 equivalents	4% (crude)
(190)	KF	1 equivalent	0%
(190)	$HgCl_2$	1 equivalent	53%
(190)	$HgCl_2$	0.1 equivalents	58%

Table 5.1

Initially, phenylation of methyl 2-oxocyclopentanecarboxylate (190) was attempted in the absence of any catalyst. However, a proton NMR spectrum of the crude material indicated that although the product was present (*ca.* 20%) as well as unreacted starting material (*ca.* 18%), three other species containing methyl groups had also been formed.

5.1.1 Fluoride ion catalysis

As described in Chapter One of this thesis, the palladium catalysed coupling of boronic acids with aryl- and vinyl- bromides, iodides and triflates is a powerful method for the formation of carbon-carbon bonds.[48,49,50,51] In all of these reactions bases are used, the function of which is thought to be the formation of a boronate anion which is capable of effecting boron to palladium transmetallation.[123] Recent work in the literature has described the use of fluoride ions in place of bases in this type of coupling reaction.[124]



(198) (199)

M^+	Yield (%)
Et_4N	86
Bu_4N	80
Cs	95
K	91
Na	0

i) 2 eq. MF, DME/MeOH, 3 mol% $Pd(PPh_3)_4$, Δ, 8 h

Scheme 5.1

A representative reaction is shown in Scheme 5.1 above. When phenylboric acid and methyl 4-bromophenylacetate (198) were subjected to a palladium catalysed coupling reaction in the presence of sodium bicarbonate or sodium carbonate, only the saponified 4-phenylphenylacetic acid was isolated. When triethylamine was used as the base, no biaryl products were isolated. However, for those reactions carried out in the presence of fluoride ions, the ester (199) was obtained in good yield, apart from when reaction was carried out in the presence of sodium fluoride which was insoluble in the reaction mixture. Reactions were generally found to proceed more rapidly in aprotic solvents, and in these solvents

potassium fluoride was found to be less effective than cesium fluoride.

Lead(IV)-mediated phenylation reactions using phenylboric acid were therefore attempted using cesium fluoride and potassium fluoride as catalysts as shown in Table 5.1 (*vide supra*). When one equivalent of cesium fluoride was added to the usual reaction mixture, the yield of the required product calculated from the proton NMR spectrum of the crude material was only around 5%. An attempt was made to increase the yield of this reaction by using three equivalents of cesium fluoride catalyst, but in this case, the yield of product was calculated to be only 4%. As was found in the work described above, potassium fluoride was observed to be a less efficient catalyst as none of the required product was formed.

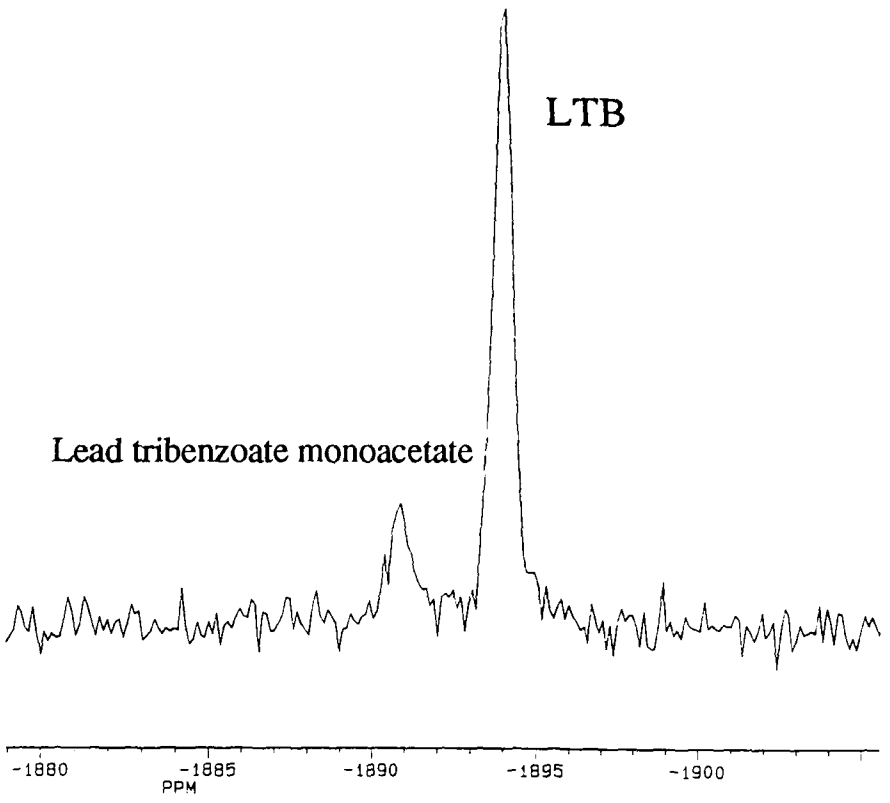
5.1.2 Mercury(II) chloride catalysis

Following the failure to effect α-phenylation in good yields using fluoride ion catalysis, the use of mercury(II) salts other than mercury(II) acetate was explored. Mercury(II) chloride was chosen as a potential catalyst for the arylation process as it was expected that phenyl transfer from boron to lead could occur as before, without affecting the composition of the lead complex in solution. As shown in Table 5.1, phenylation was initially carried out using one equivalent of mercury(II) chloride, and in this case the product was obtained in 53% yield (the mercury(II) acetate catalysed reaction gave the product in 70% yield). When mercury(II) chloride was used catalytically (0.1 equivalents) the product was obtained in 58% yield. Mercury(II) chloride was thus shown to be almost as efficient a catalyst as mercury(II) acetate.

5.1.3 Lead NMR studies of catalytic systems

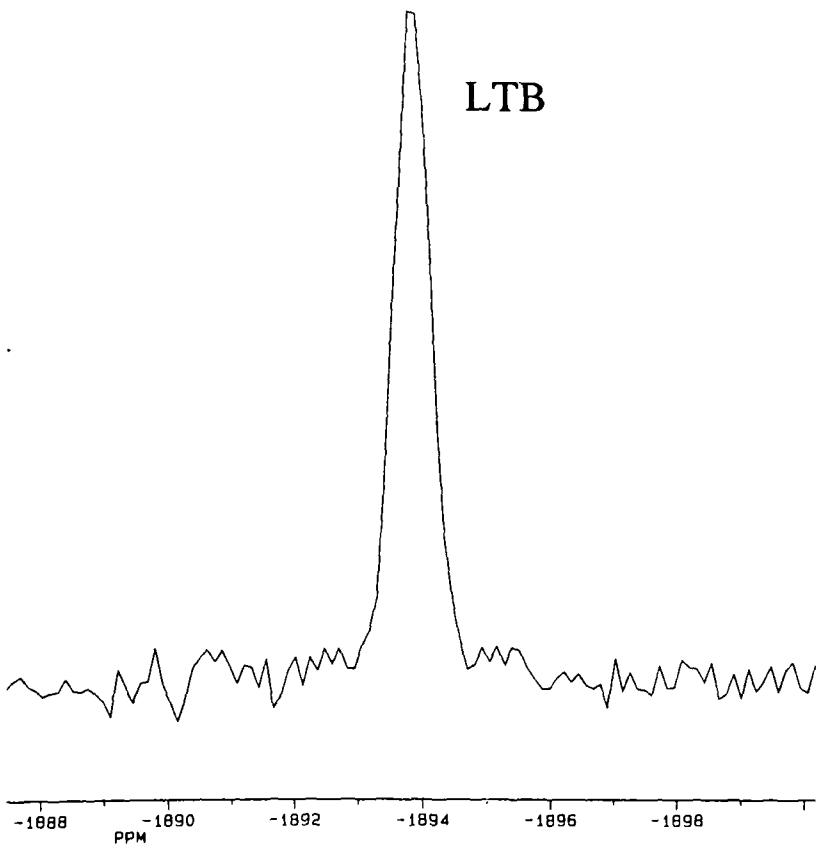
In order to demonstrate the effect of the two mercury(II) catalysts on lead complexes in solution, lead NMR studies were carried out as shown below. Spectra of lead tetrabenzoate (LTB) were recorded at 253K with quantities of each catalyst added. Spectrum 5.1 shows the effect of adding 0.1 equivalents of mercury(II) acetate to LTB: it can be seen that the presence of additional acetate groups in the system resulted in exchange with the benzoate ligands of LTB giving additional species, as evidenced by the presence of the second peak as marked.

This was probably due to the presence of lead(IV) tribenzoate monoacetate. Spectrum 5.2, in contrast, shows that no additional species resulted when one equivalent of mercury(II) chloride was added to LTB in solution.



1 eq. LTB + 0.1 eq. $Hg(OAc)_2$

Spectrum 5.1

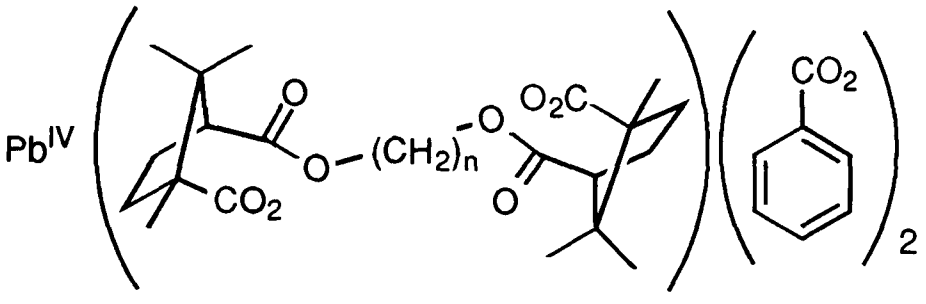


1 eq. LTB + 1 eq. $HgCl_2$

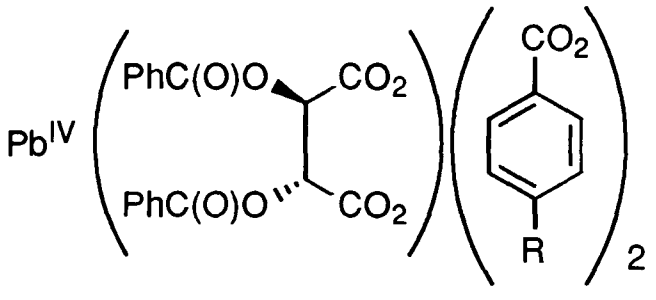
Spectrum 5.2

5.1.4 Reactions of novel lead(IV) complexes catalysed by mercury(II) chloride

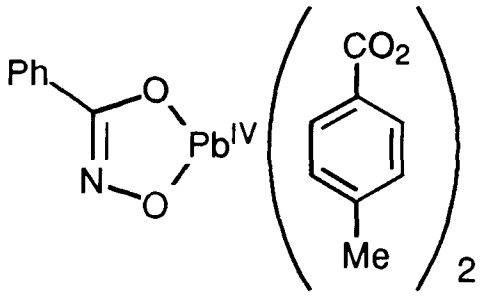
Following the success of the phenylation reaction with LTA catalysed by mercury(II) chloride, a series of phenylation reactions using the novel complexes shown below and catalysed by mercury(II) chloride were carried out using methyl 2-oxocyclopentane-carboxylate (190); the results of these reactions are shown below (Table 5.2).



n = 2 (169)
n = 3 (170)



R = H (173)
R = Me (174)



(182)

Complex	Catalyst	Yield [$Hg(OAc)_2$ catalysed]	e.e. (%)
(169)	$HgCl_2$ (0.1 eq.)	16% [69%]	6†
(170)	$HgCl_2$ (0.1 eq.)	57%	6†
(173)	$HgCl_2$ (1 eq.)	65% [71%]	6§, 3†
(174)	$HgCl_2$ (1 eq.)	54% [58%]	8§, 5†
(182)	$HgCl_2$ (0.1 eq.)	0%	-

§ By chiral shift NMR spectroscopy, † By chiral GC

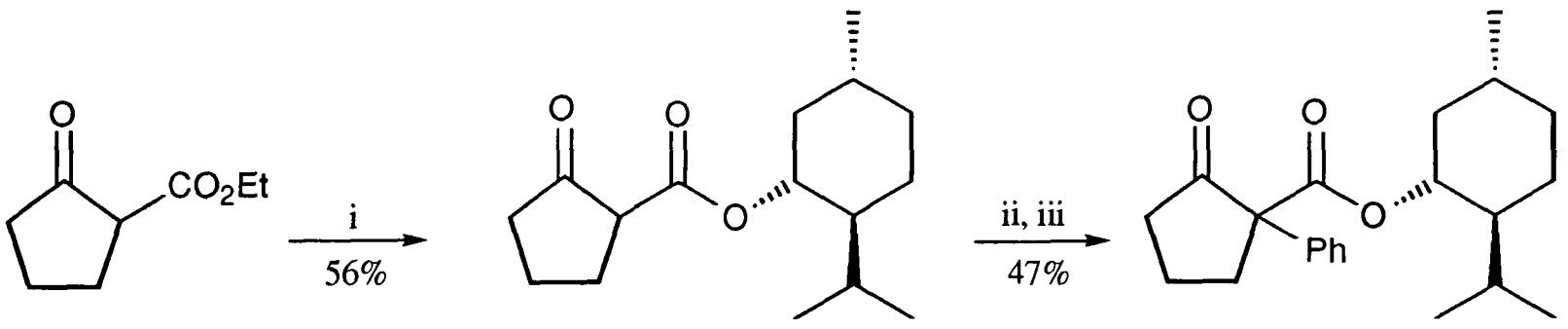
Table 5.2

As observed for mercury(II) acetate catalysed reactions, the dibenzoyl-L-tartrate complexes (173) and (174) gave good yields of phenylated products. These yields were comparable to the mercury(II) acetate catalysed reactions of the same species and also to

the mercury(II) acetate catalysed reactions using LTA. Complexes (169) and (170) also gave the required phenylated products, although in the case of complex (169), the yield was rather low. This could be due to the reaction being carried out on a very small scale (using only 0.09mmol of complex (169)). As was observed for the mercury(II) acetate catalysed case, no product formation was observed when hydroxamate complex (182) was used.

In those cases where it had been hoped to observe chiral induction in the formation of the product, enantiomeric excesses were again found to be no greater than 8%, despite the use of an alternative catalyst which would not be expected to cause exchange of lead(IV) ligands. Thus, it appeared that the failure to observe enantioselectivity in this type of reaction was due to the inherent lability of the carboxylate ligands, leading to the presence of multiple species in solution, as demonstrated by lead NMR spectroscopy.

In a final attempt to observe selectivity in carbon-carbon bond formation reactions using the novel, chiral lead(IV) complexes synthesised in this work, it was decided to attempt phenylation of a bulky substrate, for example (1*R*, 2*S*, 5*R*)-(-)-menthyl 2-oxocyclopentane-carboxylate (200).



(186) (200) (201)

i) 3 eq. (1*R*, 2*S*, 5*R*)-(-)-Menthol, 0.1 eq. DMAP, toluene, Δ
ii) 1 eq. LTA, 1 eq. $PhB(OH)_2$, 0.1 eq. $HgCl_2$, $CHCl_3$
iii) 0.91 eq. (200), 3.03 eq. pyridine, $CHCl_3$

Scheme 5.2

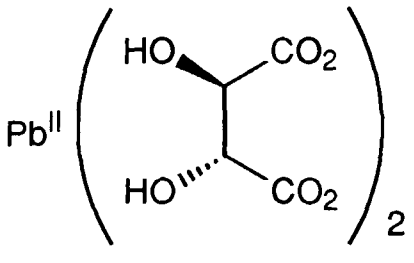
Ester (200) was synthesised in 56% yield from ethyl 2-oxocyclopentanecarboxylate (186) *via* transesterification with (1*R*, 2*S*, 5*R*)-(-)-menthol by heating a solution of the two in toluene at reflux in the presence of the nucleophilic catalyst DMAP.[125] The carbon NMR

spectrum of the product showed that ester (200) had been formed as a single diastereomer, as observed by Decicco and Buckle.[126] Phenylation of this substrate using LTA, catalysed by mercury(II) chloride, was achieved in 47% yield, giving the product (201) as two diastereomers in a ratio of approximately 1:1, as estimated from the carbon NMR spectrum.

Phenylation of (200) was also attempted using chiral lead(IV) dibenzoyl-L-tartrate di-*p*-toluate (174), and again catalysed by mercury(II) chloride. In this case, the product (201) was obtained in 32% yield, and was again observed to be a roughly 1:1 mixture of two diastereomers.

5.1.5 Lead(II) acetate catalysis

If the arylation process could be catalysed by lead(II), then the reaction would be autocatalytic. In addition, it is possible that lead(II) analogues of the chiral lead(IV) species already described in this work could be synthesised and used as catalysts, eliminating problems caused by ligand exchange from the catalyst. Thus, phenylation of methyl Meldrum's acid (71) was attempted using LTA and one equivalent of lead(II) diacetate, and the α-phenylated product was obtained in 39% yield. While this yield did not compare well with the mercury(II) acetate and mercury(II) chloride catalysed processes, it was by no means an optimised yield. Lead(II) acetate is supplied as its trihydrate, and as such may have caused some decomposition of LTA. In addition, this lead(II) salt was observed to be rather insoluble in the reaction solvent which may have again reduced the product yield. This particular area is one which is worthy of further study, as chiral lead(II) complexes which may be more soluble in organic solvents than lead(II) acetate, such as lead(II) tartrate (202), are commercially available.



(202)

5.1.6 "Ligand-accelerated" reactions

Chapter One of this thesis introduced the concept of "ligand-accelerated" catalysis as reported by Sharpless *et al.*.[78] In early work regarding the asymmetric epoxidation of allylic alcohols, it was found that on binding of a chiral hydroxamate ligand to vanadium, the optimised reaction time increased from less than one day to four days.[81] Successive replacement of the alkoxide ligands by the chiral, bidentate hydroxamate ligand reduces, and then destroys the activity of the complex. Replacement of more than one alkoxide group results in the formation of inactive complexes because the mechanism of the reaction requires the presence of two labile groups in adjacent positions (Figure 5.1).[127]

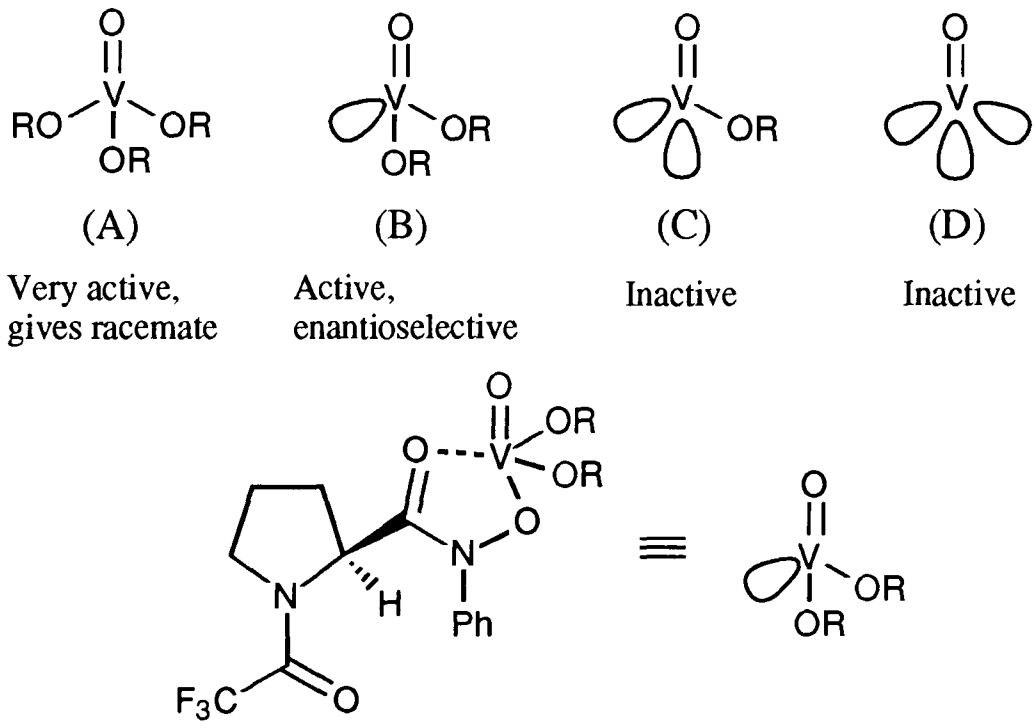


Figure 5.1

If species (B) represents the major species in solution, this will still be in equilibrium with (A) and (C); species (C) is inactive, but species (A) is more active than (B). To avoid the contribution of (A) to reaction, all of the vanadium must be maintained as species (C) and (D) and depend upon occasional disproportion of (C) into (B) (the required enantioselective catalyst) and (D). In order to achieve this, it is necessary to have an excess of hydroxamic acid present in the reaction mixture. If all of the vanadium is bound within inactive complexes, the enantiomeric excess is found to be up to 80%, but this is achieved at the expense of reaction rate.

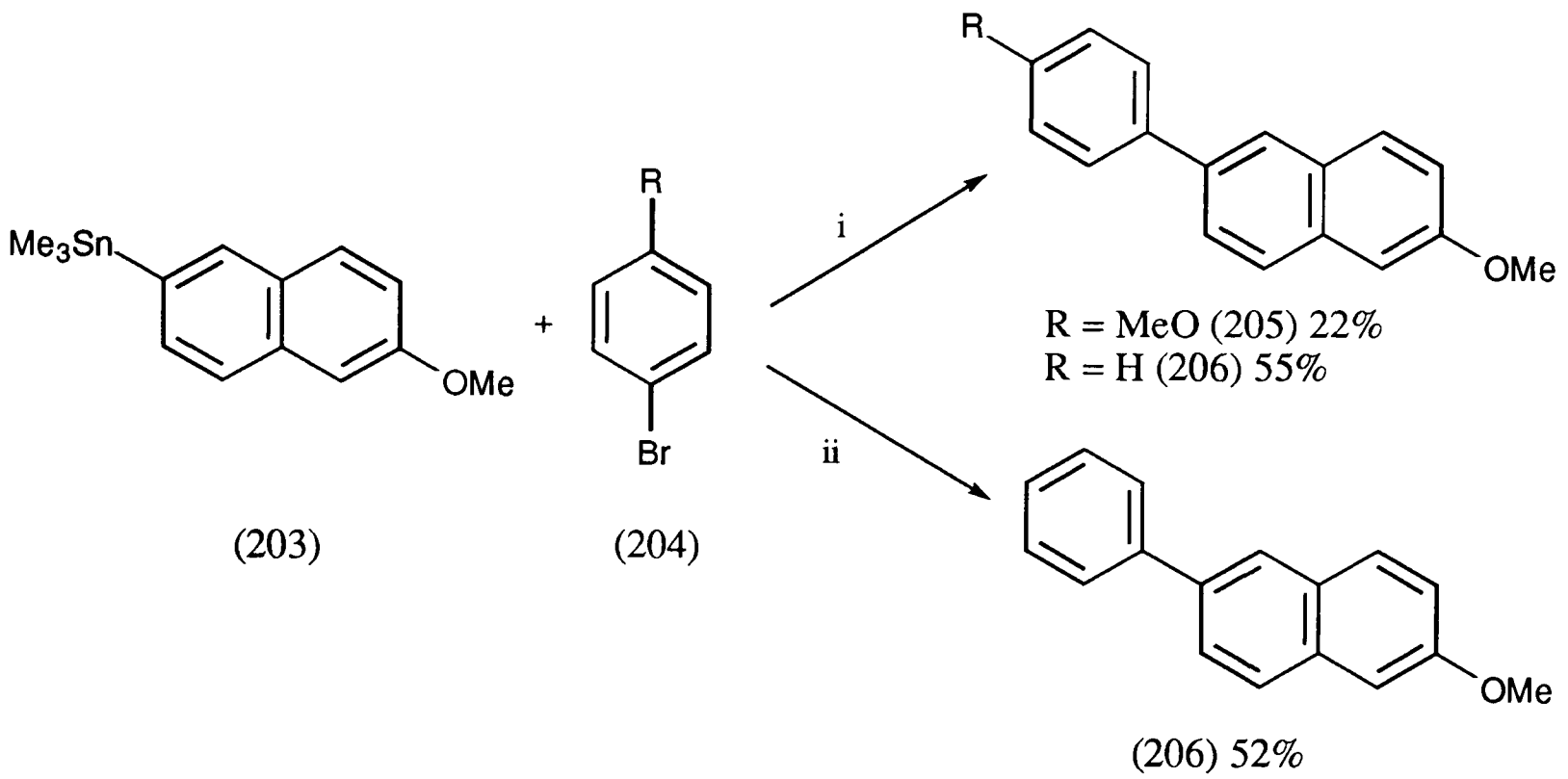
As the ligand systems used in this work show similarities to the vanadium system described above, it was hoped that the equilibrium of exchanging species could be forced towards those containing chiral ligands (*i.e.* the equivalent species to (B), (C) and (D) above) by the addition of a free chiral ligand to the reaction mixture. Thus, lead(IV) dibenzoyl-L-tartrate dibenzoate (173) was combined with dibenzoyl-L-tartaric acid, mercury(II) chloride and phenylboric acid, and, after initial reaction to form the phenyllead(IV) species, methyl 2-oxocyclopentanecarboxylate was added. However, the only product isolated from the crude reaction mixture proved to be unreacted methyl 2-oxocyclopentanecarboxylate. It is however possible that, as in the case of the vanadium complexes, the reaction rate had been slowed significantly, to the extent that product formation was not observed.

5.2 Sources of phenyl groups

Throughout this work phenylboric acid was used as a source of the phenyl group which was transferred from boron to lead(IV) *via* mercury(II). As part of studies towards the use of a catalyst other than mercury(II) acetate in the arylation process, the use of tetraphenylphosphonium bromide (Ph_4PBr) as a source of the phenyl group was explored as it was felt that this reagent might be used without the addition of any catalyst.

In a recent publication,[128] Segelstein and co-workers reported that in Stille coupling reactions of 6-methoxy-2-(trimethylstannyl)naphthalene (203) with a series of aryl halides catalysed by tetrakis(triphenylphosphine)palladium(0), the products isolated were the expected methoxy-substituted biaryl (205) and also phenyl adduct (206), with (206) generally being the major product (Scheme 5.3). The fact that phenyl product (206) was observed suggested that exchange was occurring between the phenyl groups of the phosphine ligand and the oxidative addition product of the aryl halide and the palladium catalyst. In the Heck reaction, it has also been observed that there is a competing side reaction, whereby a tetraphenylphosphonium salt is formed, with the precipitation of a palladium(0) species as the solubilising phosphine ligands are consumed.[129] It was therefore suspected that tetraarylphosphonium ions may

undergo oxidative addition and enter the catalytic cycle of the Stille reaction. Therefore, stannane (203) was treated with tetraphenylphosphonium bromide using *bis*(acetonitrile)palladium(II) chloride as the catalyst. In this case, phenyl substituted product (206) was formed in 52% yield.



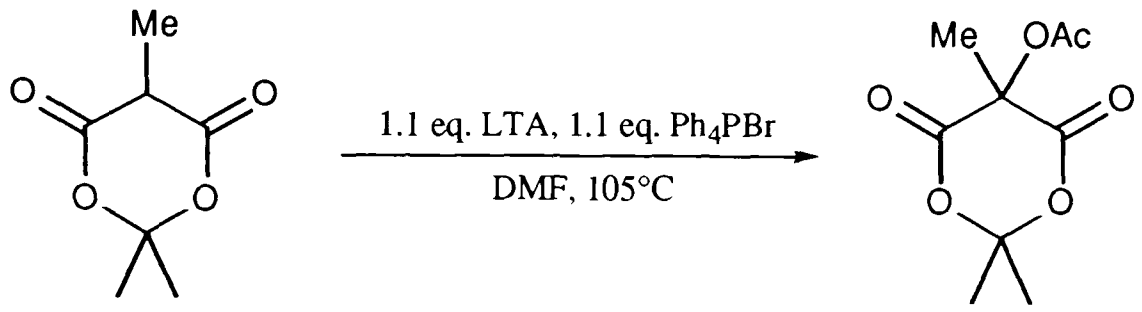
(203) (204) (206) 52%

i) DMF, $(Ph_3P)_4Pd$ 5mol%, 105°C

ii) DMF, Ph_4PBr, $(MeCN)_2PdCl_2$, 105°C

Scheme 5.3

In view of this work, it was decided to attempt lead(IV)-mediated phenylation reactions using tetraphenylphosphonium bromide. Using the method described by Segelstein *et al.*, LTA, tetraphenylphosphonium bromide and methyl Meldrum's acid (71) were combined in DMF giving a yellow solution. This was warmed to 105°C, and heated for twenty four hours after which time the reaction mixture was partitioned between water and ether. After removal of the solvent *in vacuo*, the only product isolated was 1-acetyl-1,2,2-trimethyl-1,3-dioxane-4,6-dione (207) in 42% yield (Scheme 5.4). It therefore seemed that coordination of the nucleophile to lead(IV) followed by reductive acetoxylation had occurred before phenyl transfer from the phosphine species to lead could occur. This type of acetoxylation reaction is well known as a method for the synthesis of α-hydroxy compounds.[130]



(71) (207)

Scheme 5.4

As it appeared that the lead(IV) complex was undergoing reductive elimination prior to coordination of a phenyl group, a second experiment was attempted whereby LTA and tetraphenylphosphonium bromide were first combined in DMF, giving a deep red solution which became clear as the solution was warmed, and nucleophile (71) was added after thirty minutes. After stirring the reaction mixture at 105°C overnight, however, no phenylated or acetoxylated products were observed in the proton NMR spectrum of the crude material. The deep red colour of the initial solution may indicate oxidation of bromide to bromine by LTA.

A reaction was also carried out under the same conditions as employed for phenylation reactions using phenylboric acid. However, attempted reaction of methyl Meldrum's acid (71) with tetraphenylphosphonium bromide and LTA in chloroform in the presence of catalytic mercury(II) chloride resulted in the recovery of unreacted starting material.

5.3 Summary

This Chapter has discussed the investigation of alternative catalysts in Pinhey's arylation procedure.[68] Fluoride ion catalysis, as used in the palladium-mediated boronic acid coupling reactions, was found to give the required products, but in very low yields. Mercury(II) chloride was shown to be an effective catalyst for the arylation reaction, and lead NMR spectroscopy demonstrated that, in contrast to mercury(II) acetate, this catalyst did not induce ligand exchange reactions of the lead complex. Lead(II) acetate was also found to be a potential catalyst for the reaction. This was particularly important as it may allow the use

of chiral lead(II) analogues of the complexes described in Chapter Three as catalysts for the phenylation reaction.

Finally, the use of tetraphenylphosphonium bromide in place of phenylboric acid in the arylation procedure was investigated. However, it did not prove possible to achieve α-phenylation in reactions using this compound.

CHAPTER SIX

Experimental

6.1 General procedures

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on Varian Gemini (200MHz), Bruker AM-200 (200MHz), Bruker AM-500 (500MHz) and Bruker AMX-500 (500MHz) spectrometers. Chemical shifts (δ_H) are reported in parts per million (p.p.m.) and are referenced to the residual solvent peak. Multiplicities are reported as broad (br), singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Coupling constants (*J*) are reported in Hertz (Hz) to the nearest 0.5Hz (for spectra recorded at 200MHz) or the nearest 0.1Hz (for spectra recorded at 500MHz). Two dimensional COSY spectra were recorded on a Bruker AM-500 (500MHz) spectrometer. Proton decoupling and heteronuclear multiple bond correlation (HMBC) experiments were recorded on a Bruker AMX-500 (500MHz) spectrometer.

Proton chiral shift nuclear magnetic resonance spectra were recorded on Bruker AM-250 (250MHz) or Bruker AM-300 (300MHz) spectrometers. The shift reagent used was $Eu(tfc)_3$ (tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato], europium(III) derivative), 0.5 eq. being added to separate enantiomers of methyl 1-phenyl-2-oxocyclopentanecarboxylate and 0.2 eq. being added to separate enantiomers of methyl 1-phenyl-2-oxocycloheptanecarboxylate.

Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Varian Gemini and Bruker AM-200 (50.3MHz) and Bruker AM-500 (125.8MHz) spectrometers. Chemical shifts are quoted in p.p.m. and are referenced to the residual solvent peak.

Lead nuclear magnetic resonance (^{207}Pb NMR) spectra were recorded on Bruker AM-250 (52.3MHz) and Bruker AMX-500 (104.6MHz) spectrometers using $CDCl_3$ as an internal lock. Chemical shifts are recorded in p.p.m. from Me_4Pb, using a literature value for LTA,[131] and referenced to LTA. Spectra recorded on the Bruker AM-250 spectrometer were recorded at 223K and 253K, corresponding to probe temperatures of 208K and 244K respectively.

Infra-red spectra were recorded as $CHCl_3$ or $CDCl_3$ solutions, as thin films or as Nujol mulls using a Perkin-Elmer 1750 FT-IR spectrometer. Absorption maxima are quoted in wavenumbers (cm^{-1}) and are described as strong (s), medium (m), weak (w) and broad (br). Only selected peaks are recorded.

Low resolution mass spectra (*m/z*) were recorded on VG Micromass ZAB1F, VG Masslab 20-250 and VG BIO-Q spectrometers using ammonia desorption chemical ionisation (DCI), chemical ionisation (CI) or negative electrospray (ES^-) techniques. Gas chromatography mass spectra (GCMS) were recorded on a VG Trio-1 spectrometer. Major peaks are listed with intensities quoted as a percentage of the base peak.

Optical rotations were recorded on a Perkin-Elmer 241 polarimeter, at the temperature stated, using a path length of 1dm with concentrations given in g/cm^3.

Microanalyses were performed by the microanalytical service of the Dyson Perrins Laboratory.

Melting points were recorded on a Stuart Scientific SMP1 melting point device and are uncorrected.

Thin layer chromatography (t.l.c.) was performed using Merck aluminium foil backed sheets precoated with Kieselgel 60 F_{254}. Plates were visualised using UV light (254nm), a solution of 5% $^{w}/_{v}$ *dodeca*-molybdophosphoric acid in EtOH followed by heat, a solution of

40mg bromocresol purple in 100ml 50% EtOH adjusted to pH10 with alkali[132] or by iodine vapour. Flash column silica chromatography was carried out using Janssen Chimica silicagel (35-70μm).

Chiral gas chromatography (GC) was performed by the technical staff of The Associated Octel Company, Ellesmere Port. Enantiomers of methyl 1-phenyl-2-oxocyclopentanecarboxylate were separated by diluting a few microlitres of sample in 200μl of EtOH in a vial insert and injecting 0.5μl into a split injector. Separation was achieved on an FS-Lipodex E column (length=25m, id=0.25mm) and determined using an FID detector. A racemic sample was used as the standard. Enantiomers of methyl 1-phenyl-2-oxocycloheptanecarboxylate were separated in a similar way using a Chiraldex Gamma-Cyclodextrin Trifluoroacetyl column (length=10m, id=0.25mm) (Appendix 6).

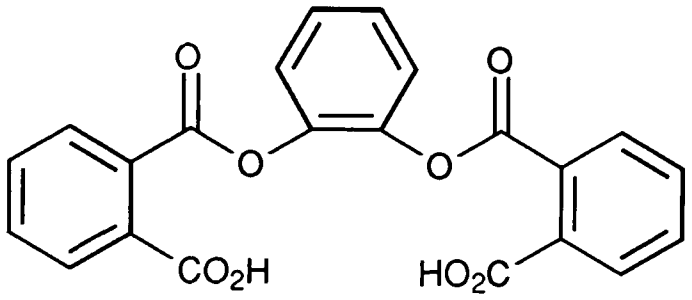
Short path reduced pressure distillations were performed using a horizontal Kugelröhr apparatus at 0.3mmHg.

Reagents were obtained from Aldrich, Lancaster and Fluka chemical companies. LTA was obtained containing acetic acid which was not removed prior to use. LTA used in reactions was assumed to have 95% purity. Ethyl 2-oxocyclopentanecarboxylate and methyl 2-oxocyclopentanecarboxylate were purified by short path distillation prior to use. Solvents were distilled prior to use using standard procedures. Toluene was dried by distillation, discarding the first 15%, and storage over activated 4Å molecular sieves. Petrol refers to that portion of petroleum ether which boils at 30-40°C. Ethanol in chloroform was removed by passing the solvent through an alumina column.

Reaction times are recorded in hours (h) and minutes (min). Solvents were removed at 35°C using a Büchi RE111 rotary evaporator attached to a Vacuubrand CVC2 pump and pressure controlling system.

6.2 Experimental details for Chapter Two

Attempted preparation of dicarboxylic acid (111)



Phthalic anhydride (0.50g, 3.38mmol) and catechol (0.19g, 1.69mmol) were heated at reflux in toluene (40ml) for 20 h. Solvent removal *in vacuo* yielded only starting materials.

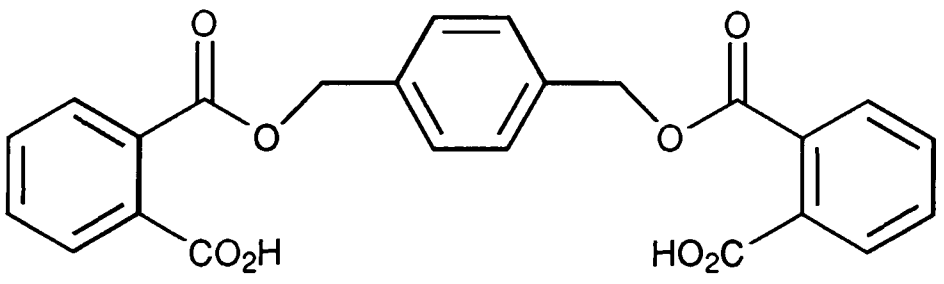
Phthalic anhydride (0.50g, 3.38mmol), catechol (0.19g, 1.69mmol) and *p*-toluenesulphonic acid (0.16g, 0.85mmol) were heated at reflux in ethanol-free $CHCl_3$ (40ml) overnight.[93] Solvent removal *in vacuo* yielded only starting materials.

Phthalic anhydride (0.40g, 2.70mmol), catechol (0.15g, 1.35mmol) and DMAP (33mg, 0.27mmol) were heated at reflux in ethanol-free $CHCl_3$ (40ml) overnight. Solvent removal *in vacuo* yielded only starting materials.

Phthalic anhydride (0.20g, 1.35mmol) and catechol (0.08g, 0.68mmol) were heated at reflux in pyridine for 5 h.[94] Solvent removal *in vacuo* yielded only starting materials.

Phthalic anhydride (0.20g, 1.35mmol) and catechol (0.08g, 0.68mmol) were heated together at 130°C for 1 h and then cooled. The resulting white solid was recrystallised from EtOAc, but was not found to contain the required product.

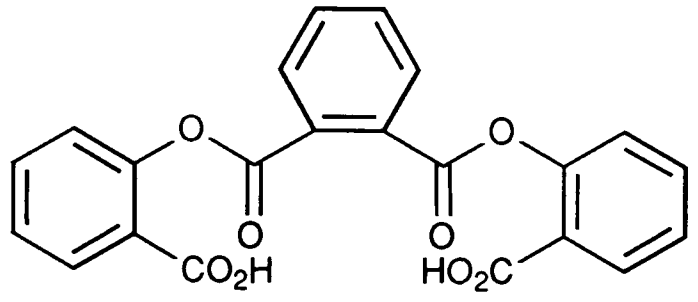
1,1'-(Benzene-1,4-dimethyl)diphthalate (113)



Phthalic anhydride (1.00g, 6.75mmol) and benzene-1,4-dimethanol (0.47g, 3.37mmol) were heated together at 150°C[95] until a solid was obtained which was recrystallised from EtOAc to give the title compound as a white solid (0.45g, 31%).

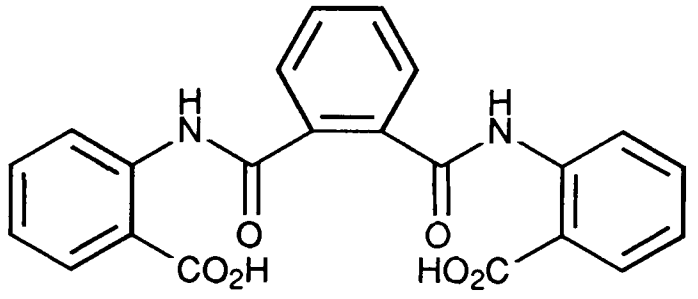
m.p. 160-162°C (from EtOAc); ν_{max} (Nujol/cm^{-1}) 1714 (s, ester C=O), 1686 (s, acid C=O), 1600 (m), 1580 (m), 1490 (m), 1289 (s), and 1129 (s); δ_H (200MHz, $CDCl_3$) 5.30 (4H, s, 2x$C\underline{H}_2$), 7.44 (4H, s, benzenedimethyl-Ar$\underline{H}$), 7.55-7.67 (6H, m, Ar$\underline{H}$) and 7.76-7.80 (2H, m, Ar$\underline{H}$); δ_C (125.8 MHz, $CDCl_3$) 68.25 ($\underline{C}H_2$), 129.51, 129.64, 130.23, 132.15, 132.45 (Ar$\underline{C}$H), 133.46, 133.92, 137.22 (Ar$\underline{C}$), 169.69 (ester $\underline{C}$=O) and 170.47 (acid $\underline{C}$=O); *m/z* (Electrospray, ES^-) 435 (7%, MH^+), 434 (30, M) and 433 (100, M-H).

Attempted preparation of dicarboxylic acid (114)



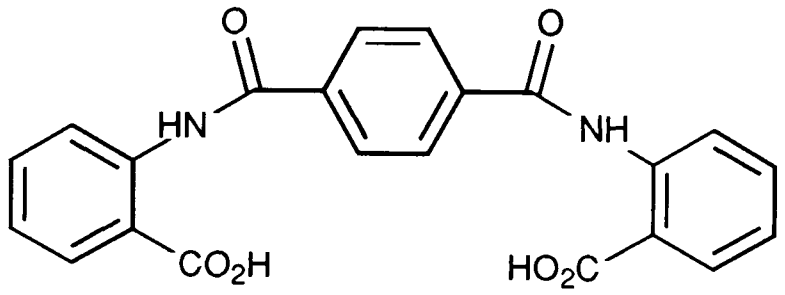
Phthalic anhydride (0.27g, 1.81mmol) and 2-hydroxybenzoic acid (0.50g, 3.62mmol) were heated together at 150°C for 3 h. Analysis of the product by t.l.c. showed no reaction to have occurred.

Attempted preparation of dicarboxylic acid (115)



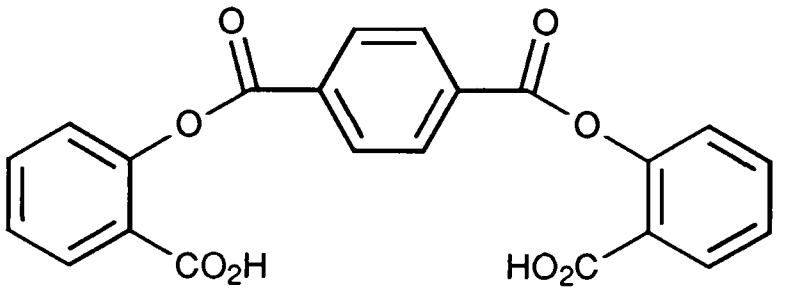
Phthalic anhydride (0.27g, 1.82mmol) and 2-aminobenzoic acid (0.50g, 3.65mmol) were heated together at 165°C for 5 h. A black solid was obtained which did not contain the required product.

Attempted preparation of dicarboxylic acid (117)[97]



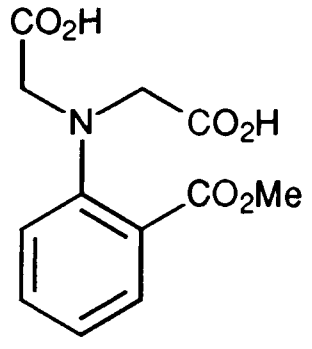
To a solution of 2-aminobenzoic acid (0.20g, 1.46mmol) and Na_2CO_3 (0.16g, 1.46mmol) in water (30ml) at 20-30°C was added a solution of terephthaloyl chloride (0.15g, 0.73mmol) in acetone (10ml). The mixture was stirred at room temperature for 2 h. The solution was then heated at reflux for 3 h, after which time the solvent was removed *in vacuo*. A proton NMR spectrum of the crude material showed it to contain none of the required product.

Attempted preparation of dicarboxylic acid (118)



Terephthaloyl chloride (0.40g, 1.97mmol), 2-hydroxybenzoic acid (0.54g, 3.94mmol) and triethylamine (0.40g, 3.94mmol) were heated at reflux in ethanol-free $CHCl_3$ overnight. Solvent removal *in vacuo* yielded none of the required product.

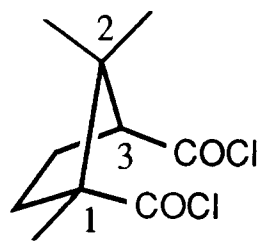
Attempted synthesis of (2-carboxymethylphenylimino)diacetic acid (121)



Methyl 2-aminobenzoate (0.54g, 3.54mmol), chloroacetic acid (0.67g, 7.07mmol) and NaOH (0.28g, 7.07mmol) were heated at reflux in water (50ml) for 7 h.[98] On cooling, brown crystals precipitated out of the solution which were filtered and dried. T.l.c. and NMR spectroscopic analysis of this product showed it to consist of methyl 2-aminobenzoate and chloroacetic acid.

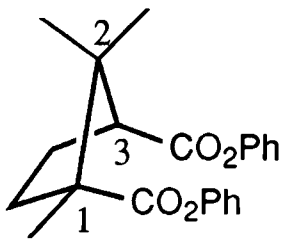
The aqueous filtrate was acidified (2M HCl) and extracted into DCM (50ml) which was dried ($MgSO_4$) and the solvent was removed *in vacuo* to yield only unreacted starting materials.

*(1*R, *3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarbonyl chloride* (127)[100]



To a suspension of PCl_5 (10.40g, 49.94mmol) in petrol at 0°C was added (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid (5.00g, 24.97mmol) in portions. The solution was allowed to stir at 0°C for 1 h and then warmed to room temperature and allowed to stir overnight. Any remaining solid PCl_5 was filtered off and the solvent was removed *in vacuo* to give the crude product as a pale yellow oil. This was purified by short path distillation at 75°C (lit.[100] 90°C at 0.5mmHg) to give the title compound as a colourless oil (5.13g, 87%). $[\alpha]_D^{22}$ +35.7 (*c* 0.97 in $CHCl_3$), lit.[100] $[\alpha]_D^{25}$ +14.0 (*c* 4 in benzene); ν_{max} (Film/cm^{-1}) 2980 (m, CH), 1790 (s, C=O), 1459 (m), 1398 (m) and 802 (s); δ_H (200MHz, $CDCl_3$) 1.06, 1.37, 1.45 (3x3H, 3xs, 3x$\underline{C}H_3$), 1.63-1.76 (1H, m, C(5)H), 1.94-2.29 (2H, m, 2xC(4)H), 2.49-2.65 (1H, m, C(5)H) and 3.29 (1H, t, *J* = 9.5Hz, C(3)H); δ_C (50.3MHz, $CDCl_3$) 20.42, 21.74, 22.62 (3x$\underline{C}H_3$), 23.63 (C(4)), 33.43 (C(5)), 47.57 (C(2)), 64.67 (C(3)), 65.56 (C(1)) and 174.71, 177.08 (2x$\underline{C}$OCl).

*(1*R, *3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid diphenyl ester* (129)

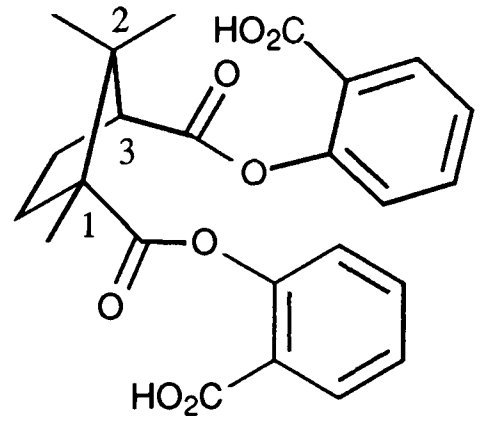


A solution of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarbonyl chloride (127) (0.20g, 0.85mmol), phenol (0.17g, 1.80mmol), triethylamine (0.18g, 1.80mmol) and DMAP (22mg, 0.18mmol) in toluene (50ml) was heated at reflux for 3 h. The solution was cooled and the solvent was removed *in vacuo*. The resulting solid was dissolved in $CHCl_3$ (50ml) and

washed with 2M HCl (50ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo*. The crude product was purified by silica chromatography (1:1 DCM:petrol) to give the title compound as a white solid (0.30g, 66%).

m.p. 88-91°C; R_f 0.47 (1:1 DCM:petrol); $[\alpha]_D^{22}$ +37.2 (*c* 1.05 in $CHCl_3$); ν_{max} (Nujol/cm^{-1}) 1744 (s, C=O), 1592 (w), 1197 (s) and 1167 (s); δ_H (500MHz, $CDCl_3$) 1.18, 1.49, 1.56 (3x3H, 3xs, 3x$\underline{C}H_3$), 1.72-1.77 (1H, m, C(5)H), 2.01-2.09 (1H, m, C(4)H), 2.37-2.44 (1H, m, C(4)H), 2.76-2.83 (1H, m, C(5)H), 3.17 (1H, t, J = 9.4Hz, C(3)H), 7.11-7.15 (4H, m, Ar$\underline{H}$), 7.25-7.28 (2H, m, Ar$\underline{H}$) and 7.40-7.44 (4H, m, Ar$\underline{H}$); δ_H (500MHz, $CDCl_3$, COSY) 1.72-1.77 C(5)H crosspeak with 2.01-2.09 C(4)H, 2.37-2.44 C(4)H and 2.76-2.83 C(5)H; 2.01-2.09 C(4)H crosspeak with 1.72-1.77 C(5)H, 2.37-2.44 C(4)H, 2.76-2.83 C(5)H and 3.17 C(3)H; 2.37-2.44 C(4)H crosspeak with 1.72-1.77 C(5)H, 2.01-2.09 C(4)H, 2.76-2.83 C(5)H and 3.17 C(3)H; 2.76-2.83 C(5)H crosspeak with 1.72-1.77 C(5)H, 2.01-2.09 C(4)H and 2.37-2.44 C(4)H; 3.17 C(3)H crosspeak with 2.01-2.09 C(4)H and 2.37-2.44 C(4)H; δ_C (50.3MHz, $CDCl_3$) 21.53, 21.63 (2x$\underline{C}H_3$), 22.62 (C(4)), 23.15 ($\underline{C}H_3$), 32.62 (C(5)), 47.47 (C(2)), 53.00 (C(3)), 56.61 (C(1)), 121.76, 126.06, 129.72 (Ar$\underline{C}$H), 151.02, 151.09 (Ar$\underline{C}$) and 172.84, 174.49 ($\underline{C}O_2Ph$); *m/z* (CI, NH_3, GCMS) 370 (8%, MNH_4^+), 353 (8, MH^+), 259 (100), 231 (18), 137 (23) and 109 (41).

*Attempted preparation of (1*R, *3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester as the free acid* (124)



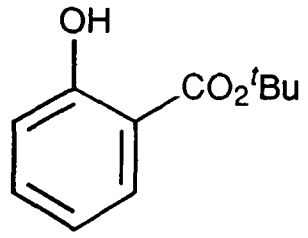
(1*R* , 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarbonyl chloride (127) (0.20g, 0.87mmol), 2-hydroxybenzoic acid (0.24g, 1.74mmol) and triethylamine (0.18g, 1.74mmol) were heated at reflux in ethanol-free $CHCl_3$ (40ml) for 5 h after which the solvent was removed *in vacuo*.

The residue obtained was dissolved in DCM (25ml) and washed with 2M HCl (25ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to yield a white solid. The crude product proved to be a complex mixture which was impossible to purify.

*Attempted preparation of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester as the free acid* (125)

(1*R* , 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarbonyl chloride (127) (0.20g, 0.85mmol), 3-hydroxybenzoic acid (0.25g, 1.80mmol), triethylamine (0.18g, 1.80mmol) and DMAP (22mg, 0.18mmol) were heated at reflux in toluene (30ml) for 8 h and then the solvent was removed *in vacuo* to yield a solid. It was not possible to identify the correct product in the crude reaction mixture.

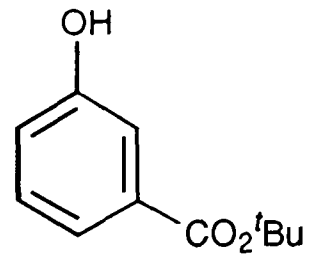
t-*Butyl 2-hydroxybenzoate* (130)[103]



2-Hydroxybenzoic acid (0.30g, 2.17mmol) was suspended in dry benzene (50ml) and the mixture heated to reflux. *N,N'*-Dimethylformamide di-*t*-butyl acetal (1.77g, 8.69mmol) was added dropwise over 20 min and the mixture heated at reflux for a further 30 min. The cooled solution was washed with water (50ml), $NaHCO_3$ (sat. aq.) (2x50ml) and brine (50ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo*. The crude product was then purified by silica chromatography (1:1 DCM:petrol) to give the title compound as a colourless oil (0.26g, 61%)

R_f 0.61 (DCM); δ_H (200MHz, $CDCl_3$) 1.62 (9H, s, ^{t}BuH), 6.82-6.98 (2H, m, ArH), 7.39-7.47 (1H, m, ArH) and 7.77-7.82 (1H, m, ArH); *m/z* (CI, NH_3, GCMS) 212 (2%, MNH_4^+), 195 (45, MH^+), 156 (89), 155 (41), 138 (100) and 121 (54).

t-*Butyl 3-hydroxybenzoate* (131)[103]



3-Hydroxybenzoic acid (0.40g, 2.90mmol) was suspended in dry benzene (50ml) and the mixture heated to reflux. *N,N'*-Dimethylformamide di-*t*-butyl acetal (2.36g, 11.58mmol) was added dropwise over 20 min and the mixture was heated at reflux for a further 30 min. The cooled solution was washed with water (50ml), $NaHCO_3$ (sat. aq.) (2x50ml) and brine (50ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo*. The crude product was then purified by silica chromatography (3:1 DCM:petrol, gradient to 1:9 EtOAc:DCM) to give the title compound as a colourless oil which solidified to a white solid under high vacuum (0.31g, 56%)

A repeat of the above procedure using 3-hydroxybenzoic acid (0.80g, 5.84mmol) and *N,N'*-dimethylformamide di-*t*-butyl acetal (2.38g, 11.69mmol) gave the title compound (0.56g, 50%).

m.p. 97-99°C; R_f 0.60 (1:1 EtOAc:petrol); ν_{max} ($CHCl_3$/cm^{-1}) 3413 (w, br, OH), 1709 (m, C=O), 1601 (w), 1592 (w), 1453 (w), 1370 (w), 1304 (s), 1167 (s) and 1108 (m); δ_H (200MHz, $CDCl_3$) 1.60 (9H, s, ^{t}BuH), 6.79 (1H, s, br, OH), 7.04-7.10 (1H, m, ArH), 7.25-7.33 (1H, m, ArH) and 7.53-7.65 (2H, m, ArH); δ_C (50.3MHz, $CDCl_3$) 28.12 (CH_3), 81.60 ($C(CH_3)_3$), 116.23, 119.87, 121.59, 129.49 (ArCH), 133.06, 155.95 (ArC) and 166.16 ($CO_2{}^t$Bu); *m/z* (CI, NH_3, GCMS) 212 (58%, MNH_4^+), 195 (75, MH^+), 156 (89), 138 (40) and 121 (100).

Alternative preparations of t-*butyl 3-hydroxybenzoate* (131)

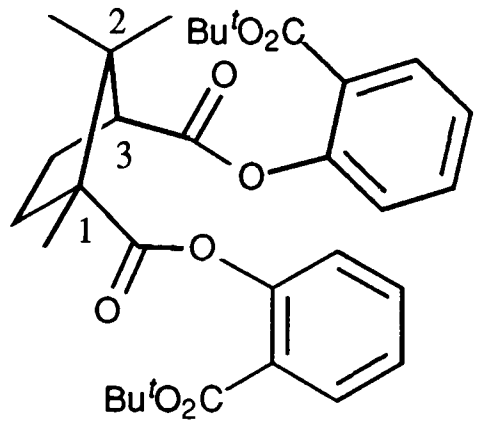
DCCI (1.00g, 4.85mmol), *t*-BuOH (0.37g, 5.00mmol) and copper(I) chloride (1mg, 0.01mmol) were stirred at room temperature overnight in a flask fitted with a drying tube ($CaCl_2$). The resulting solution was filtered through Celite® and the solid was washed with DCM (20ml). 3-Hydroxybenzoic acid (0.21g, 1.50mmol) was then added to the solution and

the mixture was stirred at room temperature for 15 h.[105] The solution was filtered, and the solvent was removed *in vacuo*. None of the required product could be isolated from the crude reaction mixture.

3-Hydroxybenzoic acid (0.20g, 1.45mmol) was dissolved in DCM (1.5ml, 1ml/mmol). To this solution was added *t*-butyl trichloroacetimidate (0.63g, 2.90mmol) in cyclohexane (3ml, 2ml/mmol) followed by boron trifluoride etherate (2.9µl, 2µl/mmol). The resulting solution was stirred at room temperature for 12 h in a flask fitted with a drying tube ($CaCl_2$), after which solid $NaHCO_3$ (0.50g, 5.95mmol) was added and the mixture filtered through a silica plug to remove excess *t*-butyl trichloroacetimidate.[106] None of the required product could be isolated from the crude reaction mixture.

3-Hydroxybenzoic acid (0.20g, 1.45mmol) was dissolved in EtOAc (10ml, 7ml/mmol) and cyclohexane (20ml, 14ml/mmol). To this solution was added *t*-butyl trichloroacetimidate (0.63g, 2.90mmol) in cyclohexane (20ml, 7ml/mmol) followed by boron trifluoride etherate (2.9µl, 2µl/mmol). The resulting solution was stirred at room temperature for 16 h in a flask fitted with a drying tube ($CaCl_2$), after which solid $NaHCO_3$ (0.50g, 5.95mmol) was added and the mixture filtered through a silica plug to remove excess *t*-butyl trichloroacetimidate. The solvent was removed *in vacuo*, and the crude material purified by silica chromatography (1:9 EtOAc:petrol) to give the title compound as a white solid (15mg, 5%).

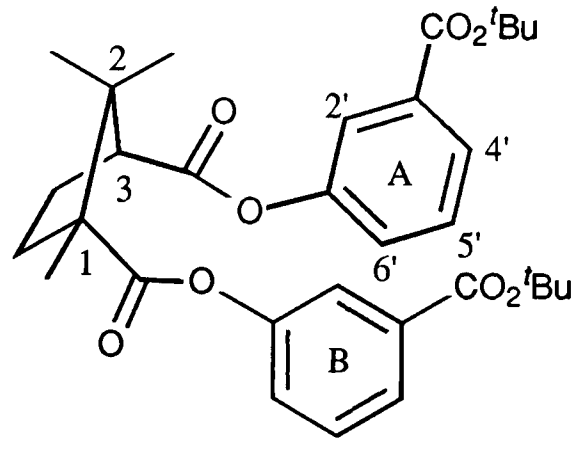
*Attempted preparation of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(*t*-butyl 2-hydroxybenzoate) ester* (132)



(1*R*, 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarbonyl chloride (127) (0.05g, 0.35mmol), *t*-butyl 2-hydroxybenzoate (130) (0.15g, 0.77mmol), triethylamine (0.08g, 0.77mmol) and

DMAP (10mg, 0.08mmol) were heated at reflux in toluene (40ml) for 24 h. The solvent was then removed *in vacuo* and the residue dissolved in EtOAc (50ml). The organic layer was washed with 2M HCl (50ml), 1M NaOH (50ml), water (50ml) and brine (50ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give a mixture of unreacted starting materials.

*(1*R*, 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid di(*t*-butyl 3-hydroxybenzoate) ester* (133)

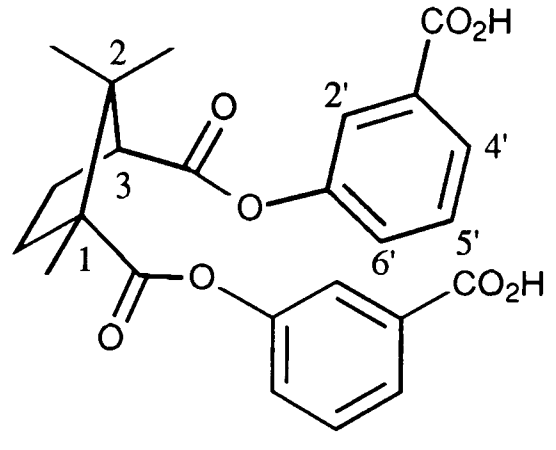


(1*R* , 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarbonyl chloride (127) (0.53g, 3.86mmol), *t*-butyl 3-hydroxybenzoate (131) (1.50g, 7.71mmol), triethylamine (0.78g, 7.71mmol) and DMAP (0.09g, 0.77mmol) were heated at reflux in toluene (50ml) for 35 h. After this time, the solvent was removed *in vacuo* and the resulting residue dissolved in Et_2O (50ml). The organic layer was washed with 2M HCl (50ml) and 2M NaOH (50ml), dried ($MgSO_4$) and the solvent was removed *in vacuo* to yield the title compound as a yellow oil (0.84g, 39%).

ν_{max} ($CHCl_3$/cm^{-1}) 1751 (s, C=O), 1712 (s, C(3') C=O), 1370 (m) and 1303 (s, CO); δ_H (500MHz, $CDCl_3$) 1.16, 1.48, 1.54 (3x3H, 3xs, 3x$C\underline{H}_3$), 1.61 (18H, s, 2x^{t}Bu$\underline{H}$), 1.71-1.77 (1H, m, C(5)H), 2.01-2.09 (1H, m, C(4)H), 2.33-2.42 (1H, m, C(4)H), 2.74-2.80 (1H, m, C(5)H), 3.16 (1H, t, J = 9.4Hz, C(3)H), 7.25-7.29 (2H, m, 2xC(6')H), 7.45 (2H, t, J = 7.9Hz, 2xC(5')H), 7.68 (1H, t, J = 2.0Hz, 1xC(2')H_A or 1xC(2')H_B), 7.70 (1H, t, J = 2.0Hz, 1xC(2')H_A or 1xC(2')H_B) and 7.88 (2H, dq, J_d = 7.8Hz, J_q = 1.4Hz, 2xC(4')H); Selective ^{1}H decoupling experiment (500MHz, $CDCl_3$) Irradiation of C(6')H δ 7.25-7.29 collapses coupling of C(5')H (m), C(2')H_A (d), C(2')H_B (d) and C(4')H (dt); Irradiation of C(5')H δ 7.45 collapses coupling of C(4')H (m); Irradiation of C(2')H δ 7.69 collapses coupling of C(6')H_A (m),

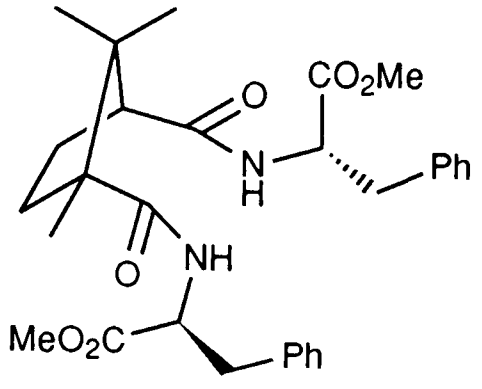
$C(6')H_B$ (m) and C(4')H (dm); Irradiation of C(4')H δ 7.88 collapses coupling of $C(6')H_A$ (m), $C(6')H_B$ (m), C(5')H (m), $C(2')H_A$ (d) and $C(2')H_B$ (d); *m/z* (CI, NH_3, Probe) 570 (53%, MNH_4^+), 514 (7), 458 (24), 359 (44), 331 (16), 303 (39), 275 (18), 137 (83) and 109 (100).

(1R, 3S)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester (125)



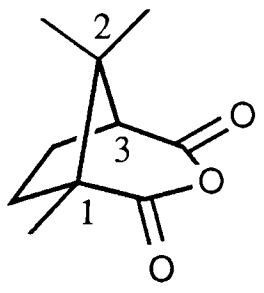
(1*R*, 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid di(*t*-butyl 3-hydroxybenzoate) ester (133) (0.84g, 1.52mmol) was dissolved in $CHCl_3$ (5ml) and TFA (5ml) and stirred at room temperature overnight (or until t.l.c. analysis showed that there was no remaining ester). Removal of the solvent *in vacuo* gave the title compound as a white solid (0.67g, quantitative). m.p. 230-232°C; (Found: C, 64.45; H, 5.36%. $C_{24}H_{24}O_8$ requires C, 65.45; H, 5.49%.); $[\alpha]_D^{22}$ +28.6 (*c* 1.01 in MeOH); ν_{max} (Nujol/cm^{-1}) 3436 (m, br, OH), 1757 (s, ester C=O), 1687 (s, acid C=O), 1590 (m) and 1302 (s); δ_H (500MHz, CD_3OD) 1.15, 1.50, 1.55 (3x3H, 3xs, 3x$C\underline{H}_3$), 1.72-1.77 (1H, m, C(5)H), 2.01-2.15 (1H, m, C(4)H), 2.29-2.37 (1H, m, C(4)H), 2.70-2.77 (1H, m, C(5)H), 3.26-3.30 (1H, m, C(3)H), 7.33-7.37 (2H, m, 2xC(6')H), 7.51-7.55 (2H, m, 2xC(5')H), 7.70-7.73 (2H, m, 2xC(2')H) and 7.92 (2H, d, *J* = 7.7Hz, 2xC(4')H); δ_C (125.8MHz, CD_3OD) 22.05, 22.17, 23.72 (3x$\underline{C}H_3$), 33.79 (C(5)), 54.16 (C(3)), 57.94 (C(1)), 123.89, 127.31, 127.39, 128.25, 130.75 (Ar$\underline{C}$H) and 152.34 (Ar$\underline{C}$) (remaining peaks not observed); *m/z* (DCI, NH_3) 458 (6%, MNH_4^+), 414 (5), 320 (5), 303 (16), 294 (20), 259 (11), 200 (29), 139 (38), 138 (53), 137 (62), 121 (64) and 109 (100).

*Attempted preparation of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(L-phenylalanine methyl ester) ester* (137)[107]



To a stirred solution of L-phenylalanine methyl ester (0.20g, 0.93mmol) and triethylamine (0.36g, 3.59mmol) in DCM (30ml) at -5°C was added slowly a solution of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarbonyl chloride (127) (0.06g, 0.46mmol) in DCM (10ml). The temperature was kept below 0°C throughout the addition. The solution was then allowed to warm to room temperature after which the organic layer was washed with water (50ml), 1M HCl (50ml) and brine (50ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to yield a crude product which did not contain the title compound.

*(1*R, 3S*)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic anhydride* (126)[99]

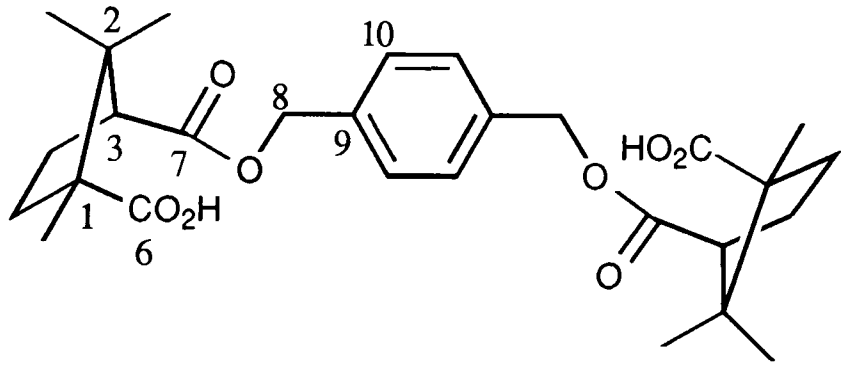


To a solution of (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid (10.00g, 49.94mmol) in CCl_4 (60ml) and DMF (1ml) at 40-50°C was added thionyl chloride (7.29ml, 99.88mmol) dropwise. The resulting solution was heated at reflux for 3 h. The cooled solution was poured onto ice (250ml) and left to stand overnight. The organic layer was then separated, washed with water (100ml) and the solvent was removed *in vacuo*. The resulting greenish solid was recrystallised from ethanol to give the title compound as white needles (5.98g, 66%).

m.p. 224-225°C (from EtOH), lit.[108] 222-223°C (from acetone); R_f 0.31 (DCM); $[\alpha]_D^{22}$ -0.90 (*c* 5.13 in $CHCl_3$) lit.[108] $[\alpha]_D^{22}$ -3.76 (*c* 0.60 in benzene); ν_{max} (Nujol/cm^{-1}) 1804 (s, C=O),

1761 (s, C=O), 1180 (m), 1151 (w), 1129 (m), 1110 (w), 1042 (s), 982 (s) and 943 (m); δ_H (200MHz, $CDCl_3$) 1.01, 1.10, 1.28 (3x3H, 3xs, 3xC$\underline{H}_3$) 1.89-2.38 (4H, m, 2xC(4)H and 2xC(5)H) and 2.85 (1H, d, J = 6.5Hz, C(3)H); δ_C (50.3MHz, $CDCl_3$) 13.95, 20.02, 20.61 (3xC$\underline{H}_3$), 24.32 (C(4)), 33.36 (C(5)), 43.62 (C(2)), 53.76 (C(1)), 54.27 (C(3)) and 170.38, 173.04 (2xC$\underline{O}$); *m/z* (CI, NH_3, GCMS) 200 (100%, MNH_4^+), 183 (11, MH^+), 172 (8), 155 (15), 138 (18), 137 (6) and 109 (10).

*3,3'-(Benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]* (139)

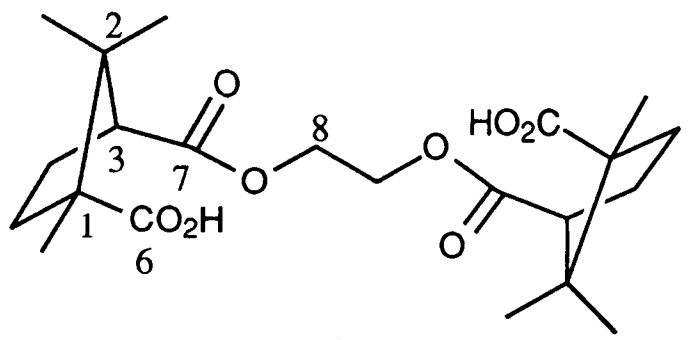


(1*R*, 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic anhydride (126) (5.98g, 32.30mmol) and benzene-1,4-dimethanol (1.51g, 10.93mmol) were heated together at 150°C for 24 h.[95] The resulting solid was dissolved in EtOAc (50ml) and extracted with $NaHCO_3$ (sat. aq.) (3x50ml) and 3M NaOH (50ml). The combined aqueous layers were acidified (conc. HCl) and re-extracted with DCM (2x100ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the title compound as its monohydrate as a pale yellow foam (3.56g, 65%).

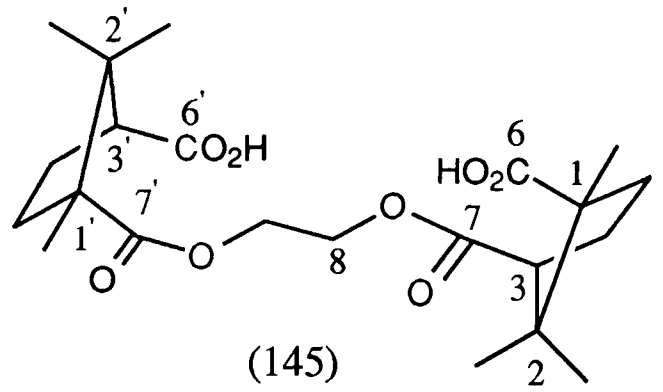
m.p. 52-54°C; R_f 0.46 (EtOAc); (Found: C, 64.34; H, 7.70%. $C_{28}H_{38}O_8.H_2O$ requires C, 64.59; H, 7.74%.); $[\alpha]_D^{22}$ +10.9 (*c* 5.02 in $CHCl_3$); ν_{max} ($CHCl_3$/cm^{-1}) 3400-2800 (m, br, OH), 1728 (s, ester C=O), 1699 (s, acid C=O), 1460 (w), 1379 (w), 1168 (s) and 1119 (m); δ_H (500MHz, $CDCl_3$) 0.82, 1.24, 1.25 (3x6H, 3xs, 6xC$\underline{H}_3$), 1.49-1.54 (2H, m, 2xC(5)H), 1.80-1.88 (2H, m, 2xC(4)H), 2.17-2.26 (2H, m, 2xC(4)H), 2.50-2.57 (2H, m, 2xC(5)H), 2.85 (2H, t, J = 9.4Hz, 2xC(3)H), 5.10 (2H, d, J = 12.4Hz, 2xC(8)H), 5.16 (2H, d, J = 12.4Hz, 2xC(8)H) and 7.36 (4H, s, Ar$\underline{H}$); δ_C (125.8MHz, $CDCl_3$) 21.15, 21.56 (4xC$\underline{H}_3$), 22.57 (2xC(4)), 22.73 (2xC$\underline{H}_3$), 32.23 (2xC(5)), 46.82 (2xC(2)), 52.79 (2xC(3)), 56.15 (2xC(1)), 65.85 (2xC(8)), 128.50 (4xC(10)), 136.06 (2xC(9)), 173.60 (2xC(7)) and 181.99 (2xC(6));

HMBC experiment (500MHz, $CDCl_3$) Irradiation of C(2)C$\underline{H}_3$ δ 0.8 shows correlation with C(2)$\underline{C}H_3$, C(2), C(3) and C(1); Irradiation of C(1)C$\underline{H}_3$ and C(2)C$\underline{H}_3$ δ 1.3 shows correlation with C(2)$\underline{C}H_3$, C(5) [from C(1)C$\underline{H}_3$], C(2), C(3), C(1) and C(6) [from C(1)C$\underline{H}_3$]; Irradiation of C(5)H δ 1.6 shows correlation with C(5)$\underline{C}H_3$, C(4), C(2), C(3) and C(1); Irradiation of C(4)H δ 1.9 shows correlation with C(5), C(2) and C(3); Irradiation of C(4)H δ 2.2 shows correlation with C(5), C(3), C(1) and C(7); Irradiation C(5)H δ 2.5 shows correlation with C(4), C(1)$\underline{C}H_3$, C(1) and C(6); Irradiation of C(3)H δ 2.9 shows correlation with 2xC(2)$\underline{C}H_3$, C(2) and C(7); Irradiation of C(8)H δ 5.3 shows correlation with C(10), C(9) and C(7); *m/z* (DCI, NH_3) 503 (5%, MH^+), 320 (55), 303 (12), 200 (14), 183 (10), 155 (16), 138 (56) and 120 (100).

3,3'-(Ethylene-1,2-dioxy)di[(1R, 3S)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (142)



(142)



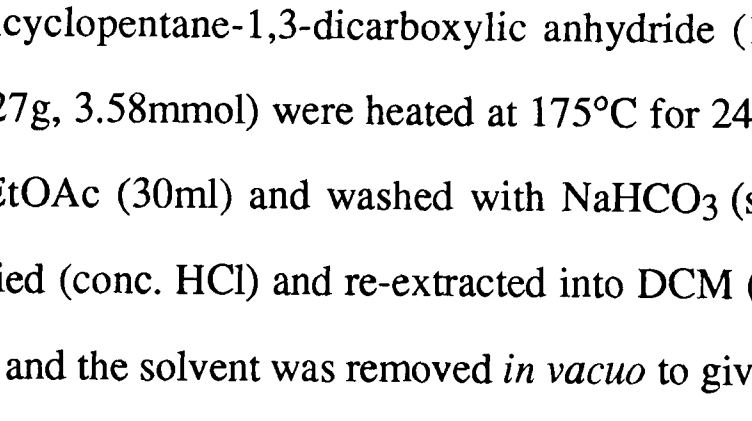
(145)

(1*R*, 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic anhydride (126) (1.47g, 8.08mmol) and ethane-1,2-diol (0.17g, 2.69mmol) were heated together at 180°C for 24 h. The resulting brown solid was dissolved in EtOAc (30ml) and washed with 3M NaOH (3x15ml). The combined aqueous layers were acidified (conc. HCl) and re-extracted with DCM (3x50ml). The organic layers were then dried ($MgSO_4$) and the solvent was removed *in vacuo*. The resulting brown oil was purified by silica chromatography (1:3 EtOAc:petrol, gradient to EtOAc). Those fractions which gave a yellow stain with bromocresol purple were combined to give the product as a mixture of isomers (142) and (145), with (142) being the major isomer, as a hygroscopic white foam (0.17g, 15%).

$[\alpha]_D^{22}$ +22.9 (*c* 1.19 in $CHCl_3$); ν_{max} ($CDCl_3$/cm^{-1}) 3075 (br, OH), 1731 (s, ester C=O), 1698 (s, acid C=O), 1460 (w), 1284 (m) and 1167 (m); δ_H (500MHz, $CDCl_3$) 0.84-0.95 (6H, m, 2xC$\underline{H}_3$), 1.05-1.42 (12H, m, 4xC$\underline{H}_3$), 1.50-1.57 (2H, m, 2xC(5)H), 1.80-1.90 (2H, m,

2xC(4)H), 2.15-2.26 (2H, m, 2xC(4)H), 2.52-2.59 (2H, m, 2xC(5)H), 2.79-3.00 (2H, m, 2xC(3)H), 4.22-4.38 (4H, m, 4xC(8)H); δ_C (50.3MHz, $CDCl_3$) 21.08, 21.43 (4x$\underline{C}H_3$), 22.30 (2xC(4)), 22.58 (2x$\underline{C}H_3$), 32.00 (2xC(5)), 46.71 (2xC(2)), 52.64 (2xC(3)), 56.06 (2xC(1)), 62.24 (2xC(8)), 174.05 (2xC(7)) and 182.64 (2xC(6)). Minor isomer also gives 53.67 (C(1')), 54.21 (C(3')), 175.70 (C(7')) and 180.65 (C(6')); *m/z* (Electrospray, ES^-) 425 ($M-H^-$); *m/z* (DCI, NH_3) 444 (6%, MNH_4^+), 427 (4, MH^+), 262 (8), 245 (99), 227 (100), 201 (28), 183 (19), 181 (13), 155 (11), 137 (17), 136 (30) and 109 (49); Exact mass 449.2159. $C_{22}H_{34}O_8Na$ requires 449.2151.

*3,3'-(Propylene-1,3-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]* (143)

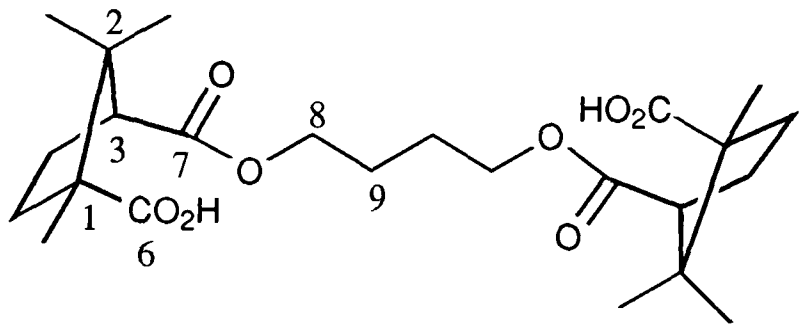


(1*R*, 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic anhydride (126) (1.50g, 8.23mmol) and propane-1,3-diol (0.27g, 3.58mmol) were heated at 175°C for 24 h. The resulting brown solid was dissolved in EtOAc (30ml) and washed with $NaHCO_3$ (sat. aq.) (3x50ml). The aqueous layer was acidified (conc. HCl) and re-extracted into DCM (2x100ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give a brown oil which was purified by silica chromatography (1:1 EtOAc:petrol, gradient to 3:1 EtOAc:petrol) to give the title compound as a white hygroscopic foam (0.32g, 20%).

R_f 0.26 (1:1 EtOAc:petrol); $[\alpha]_D^{22}$ +44.1 (*c* 0.98 in $CHCl_3$); ν_{max} ($CDCl_3$/cm^{-1}) 3000 (br, OH), 1728 (s, ester C=O), 1698 (s, acid C=O), 1173 (m) and 1126 (w); δ_H (500MHz, $CDCl_3$) 0.86 (6H, s, 2x$\underline{C}H_3$), 1.23-1.30 (12H, m, 4x$\underline{C}H_3$), 1.50-1.55 (2H, m, 2xC(5)H), 1.79-1.87 (2H, m, 2xC(4)H), 1.99-2.05 (2H, m, 2xC(9)H), 2.18-2.25 (2H, m, 2xC(4)H), 2.52-2.59 (2H, m, 2xC(5)H), 2.82 (2H, t, *J* = 9.4Hz, 2xC(3)H) and 4.15-4.25 (4H, m, 4xC(8)H); δ_C (50.3MHz, $CDCl_3$) 21.16, 21.44 (4x$\underline{C}H_3$), 22.34 (2xC(4)), 22.67 (2x$\underline{C}H_3$), 27.87 (C(9)), 32.03 (2xC(5)), 46.67 (2xC(2)), 52.73 (2xC(3)), 56.10 (2xC(1)), 60.94

(2xC(8)), 174.24 (2xC(7)) and 182.74 (2xC(6)); *m/z* (Electrospray, ES^-) 439 ($M-H^-$); *m/z* (DCI, NH_3) 458 (4%, MNH_4^+), 441 (2, MH^+), 276 (4), 259 (60), 241 (100), 225 (6), 213 (4), 200 (20), 183 (7), 155 (8), 136 (12) and 109 (35); Exact mass 463.2286. $C_{23}H_{36}O_8Na$ requires 463.2307.

*3,3'-(Butylene-1,4-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]* (144)



(1*R*, 3*S*)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic anhydride (126) (1.67g, 9.14mmol) and butane-1,4-diol (0.28g, 3.05mmol) were heated together at 170°C for 10 h. The resulting brown solid was dissolved in EtOAc (30ml) and washed with $NaHCO_3$ (sat. aq.) (3x50ml). The combined aqueous layers were acidified (conc. HCl) and re-extracted with DCM (3x50ml) which was dried ($MgSO_4$) and the solvent was removed *in vacuo*. The resulting brown oil was purified by silica chromatography (1:1 EtOAc:petrol, gradient to EtOAc). Those fractions which gave a yellow stain with bromocresol purple were combined to give the product as a hygroscopic white foam (0.55g, 40%).

$[\alpha]_D^{22}$ +28.9 (*c* 0.97 in $CHCl_3$); ν_{max} ($CHCl_3/cm^{-1}$) 2900 (br, OH), 1726 (m, ester C=O), 1699 (s, acid C=O), 1284 (w), 1175 (m) and 1125 (w); δ_H (200MHz, $CDCl_3$) 0.84 (6H, s, 2xC$\underline{H}_3$), 1.24 (6H, s, 2xC$\underline{H}_3$), 1.25 (6H, s, 2xC$\underline{H}_3$), 1.45-1.55 (2H, m, 2xC(5)H), 1.72-1.90 (6H, m, 2xC(4)H and 4xC(9)H), 2.05-2.34 (2H, m, 2xC(4)H), 2.50-2.60 (2H, m, 2xC(5)H), 2.75-2.84 (2H, t, J = 9.0Hz, 2xC(3)H), 4.11 (4H, br, s, 4xC(8)H) and 10.86 (2H, br, s, 2xO$\underline{H}$); δ_C (50.3MHz, $CDCl_3$) 21.24, 21.54 (4x$\underline{C}H_3$), 22.42 (2xC(4)), 22.74 (2x$\underline{C}H_3$), 25.47 (2xC(9)), 32.12 (2xC(5)), 46.68 (2xC(2)), 52.76 (2xC(3)), 56.10 (2xC(1)), 63.91 (2xC(8)), 173.95 (2xC(7)) and 182.36 (2xC(6)); *m/z* (Electrospray, ES^-) 453 ($M-H^-$); *m/z* (DCI, NH_3) 455 (2%, MH^+), 273 (38), 255 (48), 200 (53), 183 (30), 182 (15), 155 (36) and 109 (100); Exact mass 477.2465. $C_{24}H_{38}O_8Na$ requires 477.2464.

6.3 Experimental details for Chapter Three

6.3.1 General procedures for the preparation of lead(IV) complexes[86]

General procedure A: The preparation of bis- *lead(IV) complexes*

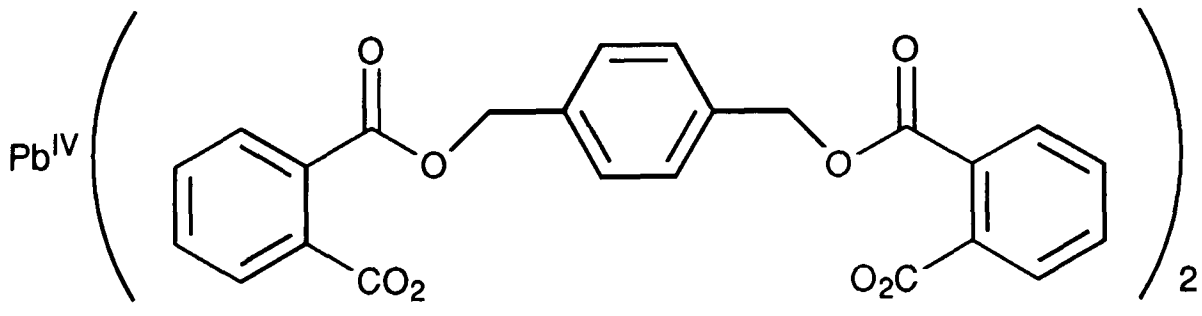
LTA (1 eq.) and a dicarboxylic acid (2 eq.) were combined in dry toluene (20-40ml) and acetic acid (*ca.* 1ml) added to aid dissolution if required. The solvent was removed *in vacuo* (20-70mbar, 35°C) to give a solid which was then redissolved in toluene (20-40ml) and the solvent was removed *in vacuo.* This procedure was repeated until complexation was complete (acetate groups no longer present by proton NMR spectroscopy). Yields of lead(IV) complexes were assumed to be quantitative.

General procedure B: The preparation of mixed ligand lead(IV) complexes

LTA (1 eq.), a dicarboxylic acid (1 eq.) and benzoic or *p*-toluic acid (2 eq.) were combined in dry toluene (20-40ml) and acetic acid (*ca.* 1ml) added to aid dissolution if required. The solvent was removed *in vacuo* (20-70mbar, 35°C) to give a solid which was then redissolved in toluene (20-40ml) and the solvent was removed *in vacuo*. This procedure was repeated until complexation was complete (acetate groups no longer present by proton NMR spectroscopy). Yields of lead(IV) complexes were assumed to be quantitative.

6.3.2 Preparation of novel lead(IV) complexes

Lead(IV) bis*[1,1'-(benzene-1,4-dimethyl)diphthalate]* (153)

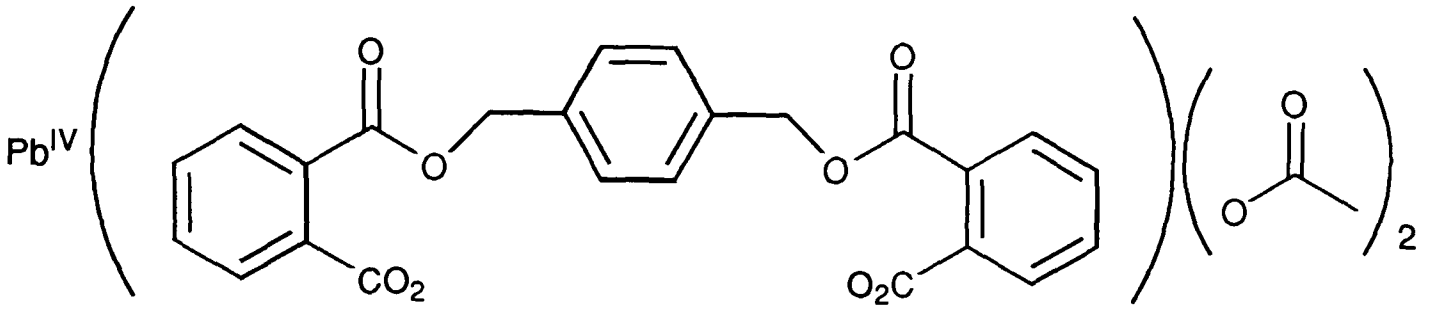


LTA (0.20g, 0.46mmol) and 1,1'-(benzene-1,4-dimethyl)diphthalate (0.40g, 0.92mmol) (113) were reacted according to General procedure A to give the title compound as a pale yellow

solid.

m.p. 105-110°C (decomposed and decarboxylated); ν_{max} (Nujol/cm^{-1}) 1724 (s, C=O), 1581 (w), 1536 (m), 1285 (s), 1123 (m) and 1075 (m); δ_H (200MHz, $CDCl_3$) 5.40 (8H, s, Ar<u>H</u> of benzene-1,4-dimethanol) 7.49-7.69 (20H, m, Ar<u>H</u>) and 7.99-8.03 (4H, d, J = 7.5Hz, Ar<u>H</u>).

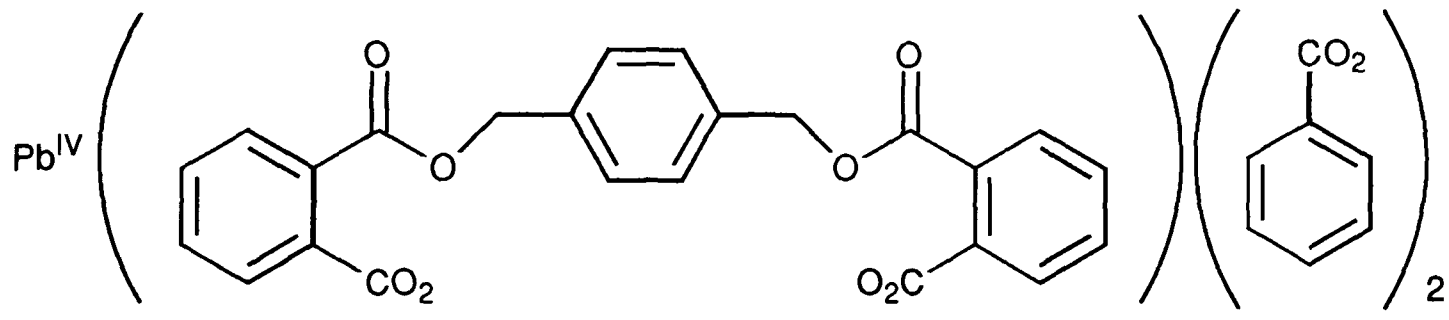
Lead(IV) [1,1'-(benzene-1,4-dimethyl)diphthalate] diacetate (154)



LTA (0.20g, 0.46mmol) and 1,1'-(benzene-1,4-dimethyl)diphthalate (113) (0.20g, 0.46mmol) were reacted according to General procedure B to give the title compound as a pale brown solid which began to decompose immediately in the solid state and in solution.

δ_H (200MHz, $CDCl_3$) 2.16 (6H, s, 2xC<u>H</u>$_3$), 5.40 (4H, s, 2xC<u>H</u>$_2$), 7.54-7.65 (10H, m, Ar<u>H</u>) and 8.00 (2H, d, J = 7.5Hz, Ar<u>H</u>).

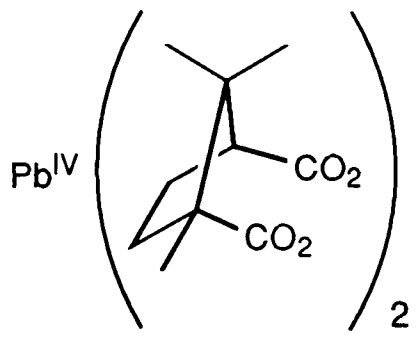
Lead(IV) [1,1'-(benzene-1,4-dimethyl)diphthalate] dibenzoate (155)



LTA (0.22g, 0.50mmol), 1,1'-(benzene-1,4-dimethyl)diphthalate (113) (0.22g, 0.50mmol) and benzoic acid (0.12g, 1.00mmol) were reacted according to General procedure B to give the title compound as a yellow solid.

m.p. 115-118°C ; ν_{max} (Nujol/cm^{-1}) 1728 (s, C=O), 1600 (w), 1530 (s), 1284 (m), 1123 (m) and 1074 (s); δ_H (200MHz, $CDCl_3$) 5.39 (4H, s, 2xC<u>H</u>$_2$), 7.43-7.87 (16H, m, Ar<u>H</u>), 8.01 (2H, d, J = 7.0Hz, Ar<u>H</u>) and 8.13 (4H, d, J = 7.0Hz, Ar<u>H</u>); δ_{Pb} (52.3MHz, $CDCl_3$, 253K) -1893.30 and -1889.92.

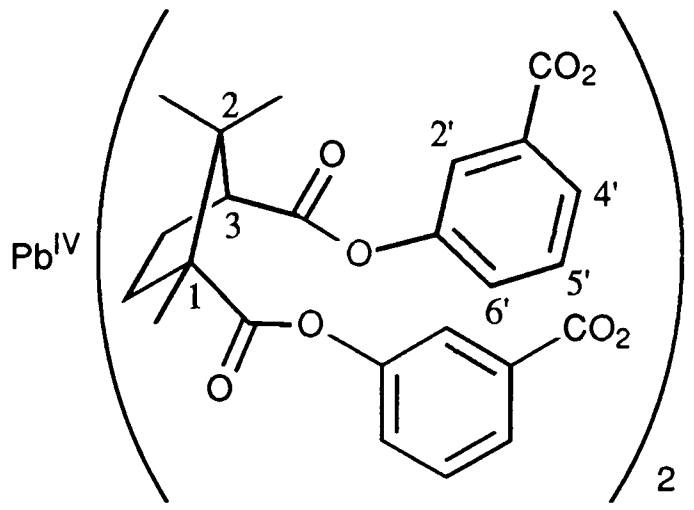
Lead(IV) bis*[(1*R, *3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]* (123)



LTA (0.20g, 0.46mmol) and (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid (0.20g, 1.00mmol) were reacted according to General procedure A to give a crude product which was washed with Et_2O (3x10ml) to give the title compound as a white powder.

m.p. >250°C; (Found C, 39.90; H, 4.89%. $C_{20}H_{28}O_8Pb$ requires C, 39.79; H, 4.67%.); ν_{max} (Nujol/cm^{-1}) 1541 (s), 1300 (m), 1171 (w) and 1129 (w); δ_H (500MHz, d_6-DMSO, 373K) 0.94, 1.14, 1.24 (3x6H, 3xs, 6x$C\underline{H}_3$), 1.63-1.70 (2H, m, $C\underline{H}_2$), 1.96-2.05 (4H, m, 2x$C\underline{H}_2$), 2.37-2.43 (2H, m, $C\underline{H}_2$) and 2.52 (2H, t, J = 9.8Hz, 2x$C\underline{H}$).

Lead(IV) bis*[(1*R, *3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester]* (164)

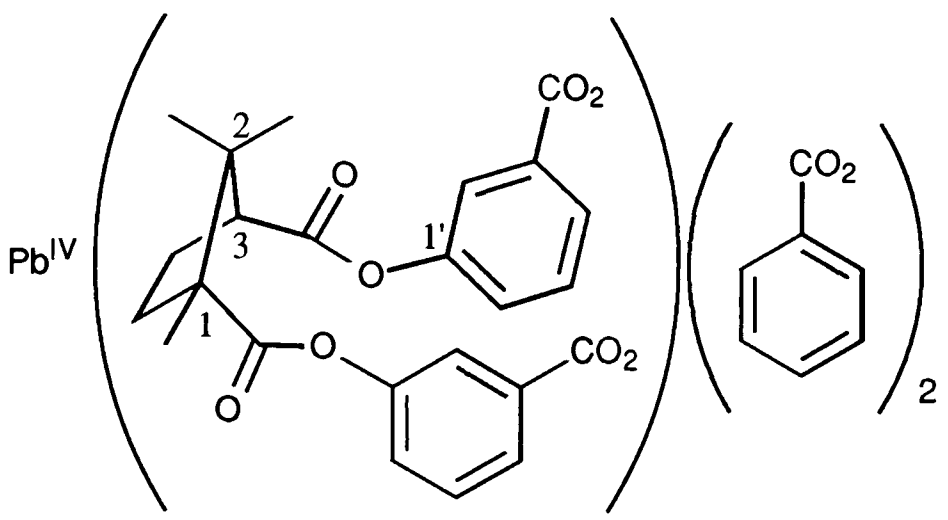


LTA (0.20g, 0.45mmol) and (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester (125) (0.40g, 0.91mmol) were reacted according to General procedure A to give a pale yellow solid which was washed with Et_2O (3x10ml) to give the title compound as a yellow solid.

m.p. 133-135°C (decarboxylated and decomposed); (Found C, 53.45; H, 4.16%. $C_{48}H_{44}O_{16}Pb$ requires C, 53.18; H, 4.09%.); ν_{max} (Nujol/cm^{-1}) 1752 (s, C=O), 1536 (w), 1209 (s), 1140 (s), 1115 (m) and 1079 (m); δ_H (500MHz, d_6-DMSO) 1.04 (6H, s, 2x$C\underline{H}_3$), 1.42 (6H, s, 2x$C\underline{H}_3$), 1.45 (6H, s, 2x$C\underline{H}_3$), 1.64-1.69 (2H, m, 2xC(5)H), 1.98-2.05 (2H, m, 2xC(4)H), 2.15-2.22

(2H, m, 2xC(4)H), 2.56-2.62 (2H, m, 2xC(5)H), (C(3)H obscured by DMSO peak), 7.31-7.35 (4H, m, 4xC(4')H), 7.53 (4H, t, J = 7.9Hz, 4xC(2')H), 7.58-7.62 (4H, m, 4xC(5')H) and 7.82 (4H, d, J = 7.8Hz, 4xC(6')H); δ_C (125.8MHz, $CDCl_3$) 21.27, 21.46 (4x$\underline{C}H_3$), 22.39 (2xC(4)), 23.08 (2x$\underline{C}H_3$), 32.32 (2xC(5)), 47.00 (2xC(2)), 52.22 (2xC(3)), 56.24 (2xC(1)), 122.20, 125.37, 126.62, 129.72 (Ar$\underline{C}$H), 137.10 (C(3')), 150.44 (C(1')), 169.28 ($\underline{C}O_2$Pb), 172.26, 173.76 ($\underline{C}O_2$Ar) and 175.00 ($\underline{C}O_2$Pb).

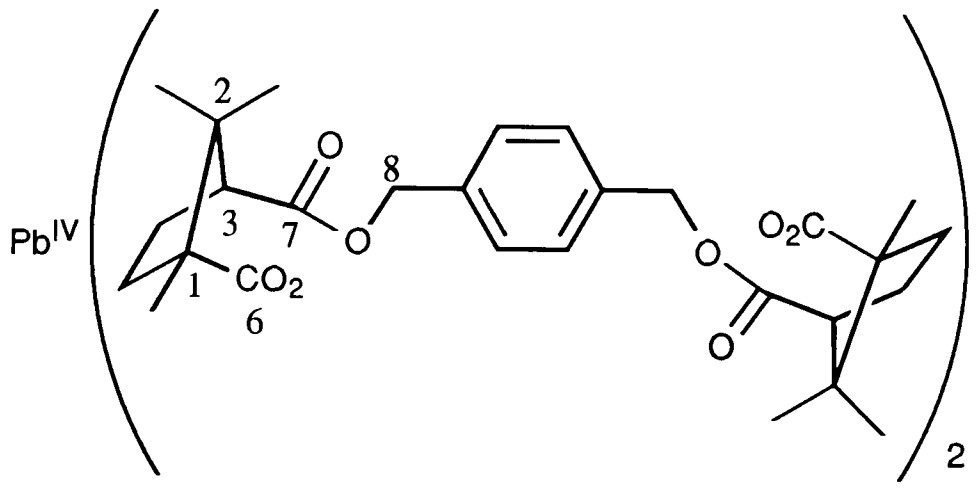
Lead(IV) [(1R, 3S)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester] dibenzoate (165)



LTA (0.13g, 0.29mmol), (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester (125) (0.13g, 0.29mmol) and benzoic acid (0.07g, 0.58mmol) were reacted according to General procedure B to give the title compound as a yellow solid.

m.p. 153-154°C (decomposed); (Found C, 48.56; H, 3.83%. $C_{38}H_{32}O_{12}Pb$ requires C, 51.40; H, 3.63%.); $[\alpha]_D^{24}$ +0.36 (*c* 0.28 in $CHCl_3$); ν_{max} (Nujol/cm^{-1}) 1753 (s, C=O), 1601 (w), 1535 (s), 1309 (m), 1212 (s), 1116 (s) and 1078 (m); δ_H (200MHz, $CDCl_3$) 1.12, 1.43, 1.49 (3x3H, 3xs, 3x$\underline{C}H_3$), 1.59-1.84 (1H, m, C(5)H), 1.87-2.15 (1H, m, C(4)H), 2.15-2.52 (1H, m, C(4)H), 2.57-2.89 (1H, m, C(5)H), 3.12 (1H, t, J = 9.0Hz, C(3)H), 7.36-7.77 (10H, m, Ar$\underline{H}$), 7.89 (2H, s, Ar$\underline{H}$), 8.04 (2H, d, J = 7.5Hz, Ar$\underline{H}$) and 8.14 (4H, d, J = 7.5Hz, Ar$\underline{H}$ *o*- to benzoate CO_2Pb); δ_C (50.3MHz, $CDCl_3$) 21.62 (2x$\underline{C}H_3$), 22.49 (C(4)), 23.07 ($\underline{C}H_3$), 32.61 (C(5)), 47.43 (C(2)), 52.66 (C(3)), 56.57 (C(1)), 125.23, 128.15, 128.82, 129.62, 129.96, 132.19, 134.75 (Ar$\underline{C}$ and Ar$\underline{C}$H), 150.84, 150.92 (2xC(1')) and 172.38, 174.06 ($\underline{C}O_2$Ar); δ_{Pb} (52.3MHz, $CDCl_3$, 223K) -1900.30, -1899.09, -1897.51, -1896.12 and -1895.40.

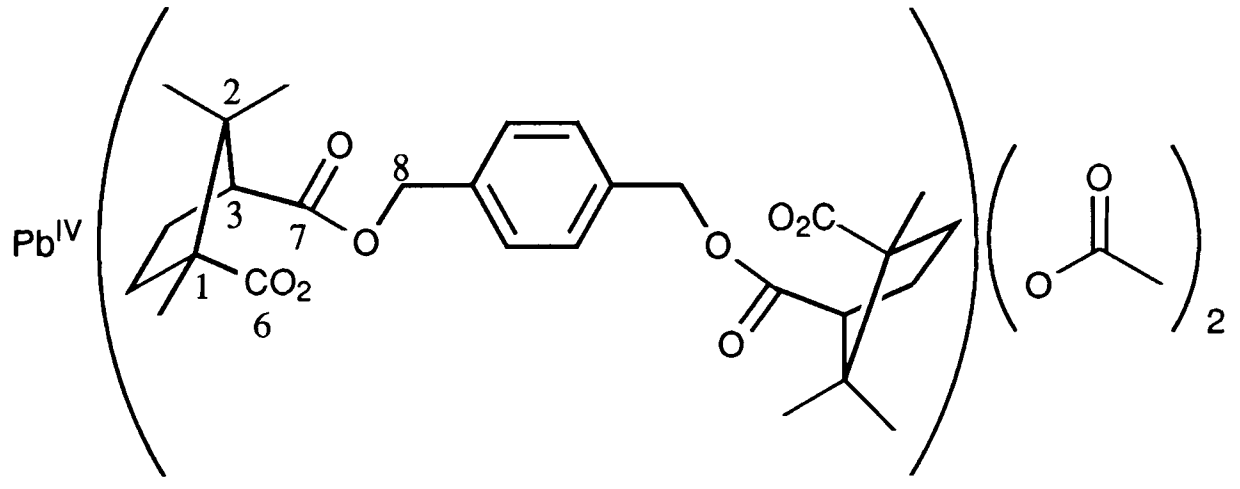
Lead(IV) bis*{3,3'-(benzene-1,4-dimethyl)di[(1*R, *3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]}* (166)



LTA (0.22g, 0.50mmol) and 3,3'-(benzene-1,4-dimethyl)di[(1*R* , 3*S*)-1,2,2-trimethyl cyclopentane-1,3-dicarboxylate] (139) (0.50g, 1.00mmol) were reacted according to General procedure A to give the title compound as a yellow foamy solid.

$[\alpha]_D^{22}$ -3.78 (*c* 0.98 in $CHCl_3$); ν_{max} (Nujol/cm^{-1}) 1733 (w), 1306 (s), 1156 (m) and 973 (m); δ_H (500MHz, $CDCl_3$) 0.35, 0.98, 1.15 (3x12H, 3xs, 12xC<u>H</u>$_3$), 1.56-1.64 (4H, m, 4xC(5)H), 1.74-1.93 (4H, m, 4xC(4)H), 2.23-2.36 (4H, m, 4xC(4)H), 2.39-2.46 (4H, m, 4xC(5)H), 2.70 (4H, t, *J* = 9.1Hz, 4xC(3)H), 4.59 (4H, d, *J* = 11.3Hz, 4xC(8)H), 5.80 (4H, d, *J* = 11.3Hz, 4xC(8)H) and 7.46 (8H, s, Ar<u>H</u>).

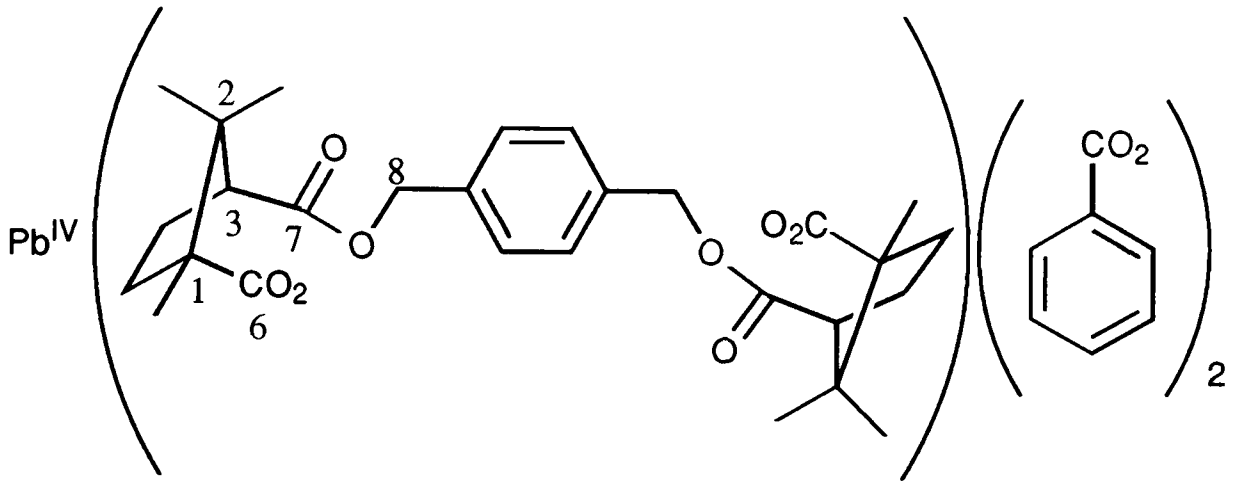
*Lead(IV) {3,3'-(benzene-1,4-dimethyl)di[(1*R, *3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} diacetate* (167)



LTA (0.22g, 0.5mmol) and 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethyl cyclopentane-1,3-dicarboxylate] (139) (0.25g, 0.5mmol) were reacted according to General procedure B to give the title compound as a yellow solid which decomposed rapidly in the solid state and in solution.

δ_H (200MHz, $CDCl_3$) 0.34 (6H, s, 2x$C\underline{H}_3$), 0.97 (6H, s, 2x$C\underline{H}_3$), 1.01-1.28 (10H, m, 2x$C\underline{H}_3$ and 2x$C\underline{H}_2$), 1.56-2.86 (12H, m, 2x$CO_2C\underline{H}_3$ and 2x$C\underline{H}_2$), 4.56-4.68 (2H, m, 2xC(8)H), 5.74-5.83 (2H, m, 2xC(8)H) and 7.35-7.46 (4H, m, Ar$\underline{H}$).

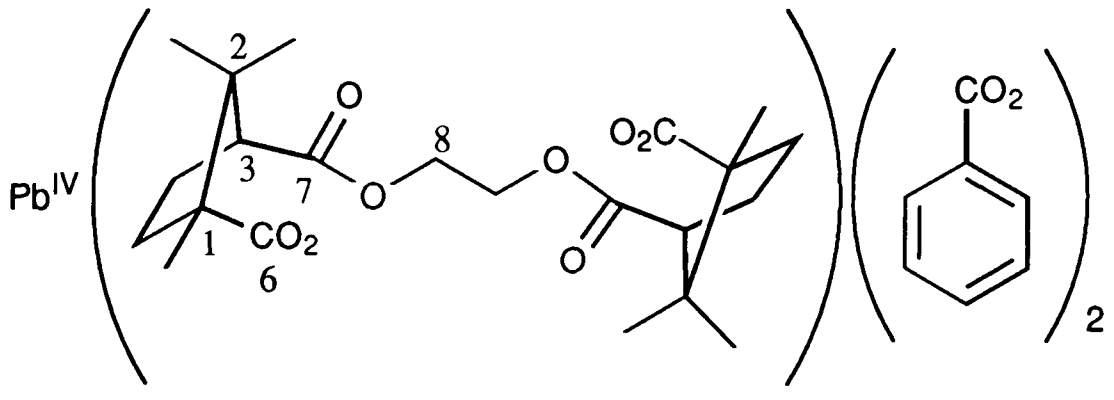
*Lead(IV) {3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} dibenzoate* (168)



LTA (0.22g, 0.50mmol), 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139) (0.25g, 0.50mmol) and benzoic acid (0.12g, 1.00mmol) were reacted according to General procedure B to give the title compound as a yellow foamy solid.

$[\alpha]_D^{22}$ +3.02 (*c* 1.00 in $CHCl_3$); δ_H (500MHz, $CDCl_3$) 0.36-0.43 (6H, m, 2x$C\underline{H}_3$), 0.98-1.28 (12H, m, 4x$C\underline{H}_3$), 1.60-2.85 (10H, m, 2xC(3)H, 4xC(4)H and 4xC(5)H), 4.59-4.72 (2H, m, 2xC(8)H), 5.11-5.82 (2H, m, 2xC(8)H), 7.31-7.47 (8H, m, Ar$\underline{H}$), 7.61 (2H, t, J = 7.4Hz, Ar$\underline{H}$) and 8.10 (4H, d, J = 6.8Hz, Ar$\underline{H}$).

*Lead(IV) {3,3'-(ethylene-1,2-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} dibenzoate* (169)

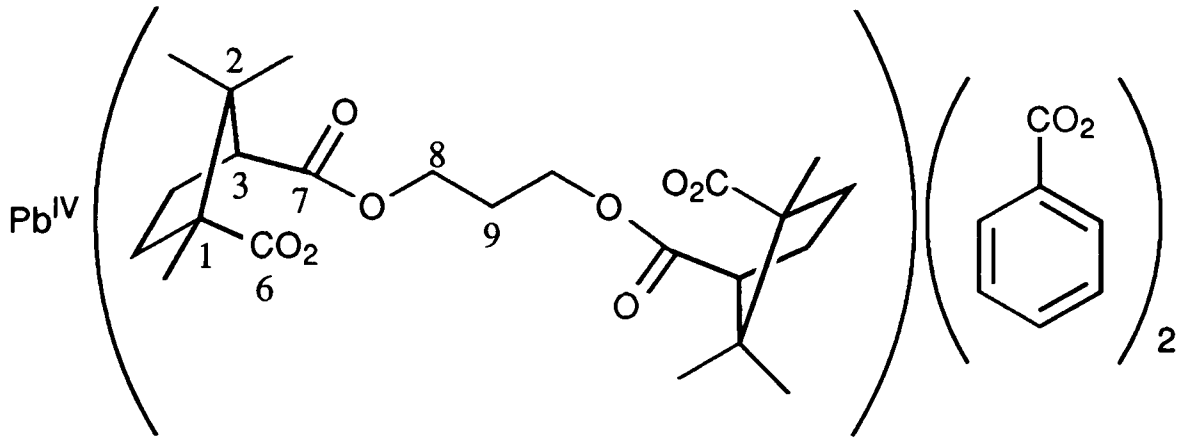


LTA (0.16g, 0.35mmol), 3,3'-(ethylene-1,2-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (142) (0.15g, 0.35mmol) and benzoic acid (0.09g, 0.70mmol) were reacted

according to General procedure B to give the title compound as a foamy yellow hygroscopic solid.

$[\alpha]_D^{22}$ +0.20 (*c* 1.00 in $CHCl_3$); ν_{max} (Nujol/cm^{-1}) 1730 (s, C=O), 1593 (w), 1530 (s) and 1174 (m); δ_H (200MHz, $CDCl_3$) 0.91 (6H, br, s, 2x$C\underline{H}_3$), 1.27 (12H, br, s, 4x$C\underline{H}_3$), 1.54-1.76 (2H, br, m, 2xC(5)H), 1.79-2.01 (2H, br, m, 2xC(4)H), 2.04-2.18 (2H, br, m, 2xC(4)H), 2.43-2.56 (2H, br, m, 2xC(5)H), 2.75-2.84 (2H, br, m, 2xC(3)H), 4.17-4.32 (4H, br, m, 4xC(8)H), 7.28-7.52 (6H, br, m, Ar$\underline{H}$) and 7.90-8.13 (4H, br, m, Ar$\underline{H}$); δ_C (50.3MHz, $CDCl_3$) 21.17 (2x$\underline{C}H_3$), 22.49 (4x$\underline{C}H_3$ and C(4)), 33.51 (C(5)), 47.14 (C(2)), 52.27 (C(3)), 56.57 (C(1)), 62.29 (C(8)), 128.68, 131.47, 134.17 (Ar$\underline{C}$ and Ar$\underline{C}$H), 173.81 (C(7)), 175.14 (br, Ar$\underline{C}O_2$Pb) and 185.29 (br, C(6)); δ_{Pb} (52.3MHz, $CDCl_3$, 223K) -1895.32, -1892.74, -1890.20, -1887.80 and -1883.74.

*Lead(IV) {3,3'-(propylene-1,3-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} dibenzoate* (170)

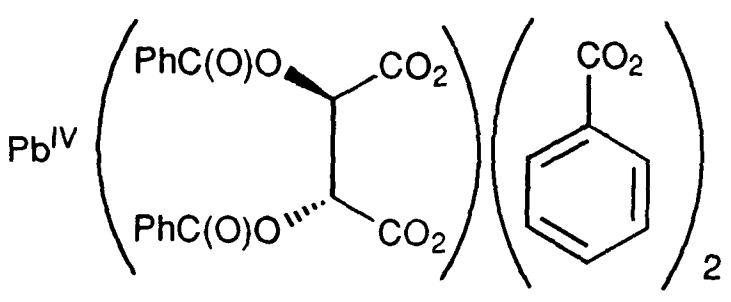


LTA (0.18g, 0.40mmol), 3,3'-(propylene-1,3-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (143) (0.17g, 0.40mmol) and benzoic acid (0.10g, 0.79mmol) were reacted according to General procedure B to give the title compound as an orange solid.

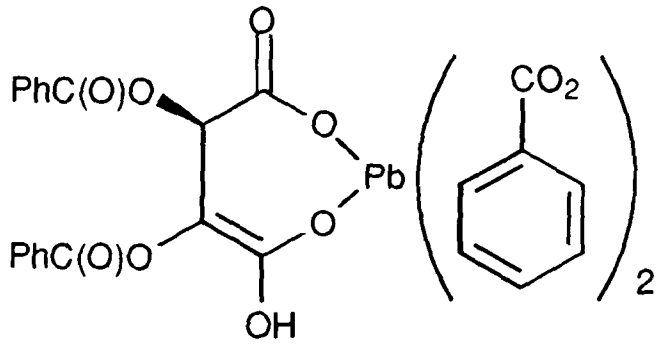
m.p. 101-103°C (decomposed); (Found C, 49.80; H, 5.31%. $C_{37}H_{44}O_{12}Pb$ requires C, 50.05; H, 5.00%.); $[\alpha]_D^{26}$ +17.5 (*c* 1.02 in $CDCl_3$); ν_{max} (Nujol/cm^{-1}) 1729 (s, C=O), 1593 (w), 1531 (m), 1308 (m), 1171 (s), 884 (s) and 816 (m); δ_H (200MHz, $CDCl_3$) 0.86-1.02 (6H, br, m, 2x$C\underline{H}_3$), 1.09-1.27 (12H, br, m, 4x$C\underline{H}_3$), 1.39-2.33 (8H, m, 2xC(5)H, 4xC(4)H and 2xC(9)H), 2.45-2.56 (2H, m, 2xC(5)H), 2.80 (2H, t, *J* = 9.0Hz, 2xC(3)H), 4.06-4.17 (4H, br, m, 4xC(8)H), 7.33-7.66 (6H, m, Ar$\underline{H}$) and 8.10 (4H, d, *J* = 7.0Hz, Ar$\underline{H}$); δ_C (50.3MHz, $CDCl_3$) 21.33, 22.64 (6x$\underline{C}H_3$, C(4)), 28.00 (C(9)), 33.65 (C(5)), 47.13 (C(2)),

52.29 (C(3)), 56.50 (C(1)), 60.99 (C(8)), 125.26, 128.19, 128.55, 128.99, 131.64, 134.28 (Ar<u>C</u>H and Ar<u>C</u>) and 173.54 (C(7)).

Lead(IV) dibenzoyl-L-tartrate dibenzoate (173) *or* (175)



(173)

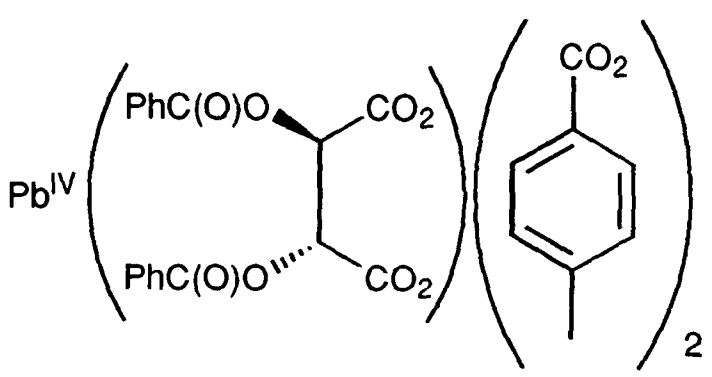


(175)

LTA (0.22g, 0.50mmol), dibenzoyl-L-tartaric acid (0.18g, 0.50mmol) and benzoic acid (0.12g, 1.00mmol) were reacted according to General procedure B to give the title compound as a yellow solid.

m.p. 127-129°C; (Found C, 47.71; H, 2.27%. $C_{32}H_{22}O_{12}Pb$ requires C, 47.70; H, 2.75%.); $[\alpha]_D^{22}$ +25.2 (*c* 1.01 in $CHCl_3$); ν_{max} (Nujol/cm^{-1}) 1735 (s, C=O), 1693 (w), 1600 (m), 1414 (s), 1260 (s) and 1241 (s); δ_H (200MHz, $CDCl_3$) 5.02 (1H, br, s, O<u>H</u>), 6.14 (1H, br, s, C<u>H</u>), 7.33-7.84 (12H, m, Ar<u>H</u>) and 8.02 (8H, d, J = 7.0Hz, Ar<u>H</u>); δ_C (50.3MHz, $CDCl_3$) 72.17 (<u>C</u>H), 126.04, 128.32, 128.53, 129.04, 130.13, 131.83, 133.59, 134.46 (Ar<u>C</u> and Ar<u>C</u>H), 164.72 (Ph<u>C</u>=O) and 175.36 (<u>C</u>=O); δ_{Pb} (52.3MHz, $CDCl_3$, 223K) -1894.07 and -1890.18.

Lead(IV) dibenzoyl-L-tartrate di-p-*toluate* (174)



LTA (0.33g, 0.75mmol), dibenzoyl-L-tartaric acid (0.27g, 0.75mmol) and *p*-toluic acid (0.20g, 1.5mmol) were reacted according to General procedure B to give the title compound as a yellow solid.

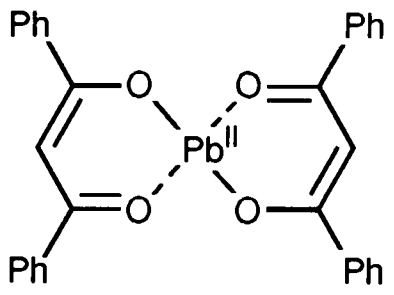
m.p. 128-130°C (decarboxylated); (Found C, 48.63; H, 3.19%. $C_{34}H_{26}O_{12}Pb$ requires

C, 48.98; H, 3.14%.); $[\alpha]_D^{22}$ +20.5 (*c* 1.00 in $CHCl_3$); ν_{max} (Nujol/cm^{-1}) 1734 (s, C=O), 1604 (m), 1587 (m), 1413 (s), 1261 (s) and 1241 (s); δ_H (200MHz, $CDCl_3$) 2.38 (6H, s, 2x$C\underline{H}_3$), 6.11 (2H, s, 2x$C\underline{H}$), 7.05-7.49 (10H, m, Ar$\underline{H}$), 7.74 (4H, br, s, Ar$\underline{H}$) and 7.99 (4H, d, J = 7.5Hz, Ar$\underline{H}$); δ_C (50.3MHz, $CDCl_3$) 21.76 (2x$\underline{C}H_3$), 72.41 ($\underline{C}$H), 123.61, 128.50, 129.48, 130.27, 130.38, 132.12, 133.70 (Ar$\underline{C}$ and Ar$\underline{C}$H), 145.70 (Ar$\underline{C}CH_3$), 165.14 (Ph$\underline{C}$=O) and 174.85 ($\underline{C}$=O); δ_{Pb} (52.3MHz, $CDCl_3$, 223K) -1893.16, -1891.60 and -1888.87.

Attempted preparation of lead(IV) tetra(dibenzoylmethane)

Dibenzoylmethane (0.99g, 5.06mmol) was dissolved in 1,2-dichlorobenzene[84] and warmed to 60°C. The solution was degassed by placing under high vacuum and dried LTA (0.45g, 1.02mmol) added, giving a deep orange-red solution. The vacuum was reapplied and the mixture heated at reflux for 3 h. The solvent was removed *in vacuo* to give a yellow solid, some of which was organic soluble. The remaining solid was recrystallised from DMSO, and by single crystal X-ray analysis was shown to be lead(II) di(dibenzoylmethane) (177).

An attempt to prepare the complex by dissolving the ligand and LTA in toluene, followed by solvent removal *in vacuo* gave the same products.



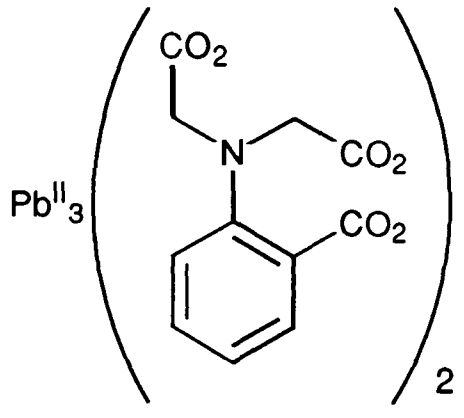
(177)

m.p. 232-234°C (from DMSO); ν_{max} (Nujol/cm^{-1}) 1597 (m), 1554 (s), 1510 (s), 1275 (m) and 1219 (w); δ_H (200MHz, d_6-DMSO) 6.36 (2H, s, 2x$C\underline{H}$), 7.26-7.44 (12H, m, Ar$\underline{H}$) and 7.82 (8H, d, J = 7.5Hz, Ar$\underline{H}$).

Attempted preparation of lead(IV) di[(2-carboxyphenylimino)diacetate]

LTA (0.20g, 0.46mmol) and (2-carboxyphenylimino)diacetic acid (0.23g. 0.92mmol) were dissolved in dry toluene (40ml) and the solvent was removed *in vacuo*. The residue was dissolved in dry toluene (40ml) and the solvent was removed *in vacuo* to give a yellow solid

which was washed with MeOH (3x10ml) to give a pale brown solid which was found to be the trimeric complex (120).

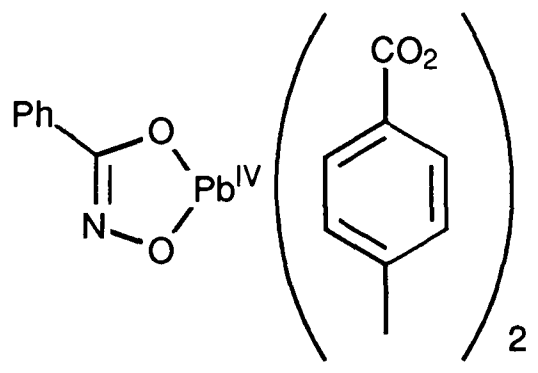


(120)

m.p. >250°C; (Found C, 23.74; H, 1.48; N, 2.47%. $C_{22}H_{16}N_2O_{12}Pb_3$ requires C, 23.55; H, 1.44; N, 2.50%.); ν_{max} (Nujol/cm^{-1}) 1559 (s), 1314 (m), 1278 (m) and 1172 (w); δ_H (500MHz, d_6-DMSO, 373K) 3.82 (8H, s, 4x$C\underline{H}_2$), 7.06 (2H, t, J = 7.4Hz, Ar$\underline{H}$), 7.14 (2H, d, J = 8.2Hz, Ar$\underline{H}$), 7.32 (2H, t, J = 7.8Hz, Ar$\underline{H}$) and 7.79 (2H, d, J = 7.9Hz, Ar$\underline{H}$).

Attempted preparation of lead(IV) dibenzohydroxamate di-p-*toluate* (181)

LTA (0.22g, 0.50mmol), benzohydroxamic acid (0.14g, 1.00mmol) and *p*toluic acid (0.14g, 1.00mmol) were combined in dry toluene and the solution was heated at reflux for 1h. The solvent was removed *in vacuo* to give a pale brown solid which was triturated with Et_2O (20ml) to give a white solid, identified as complex (182)

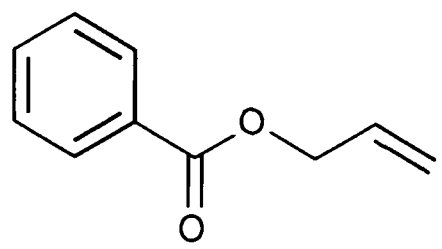


(182)

m.p. 85-90°C; (Found C, 45.35; H, 2.87; N, 1.11%. $C_{23}H_{19}NO_6Pb$ requires C, 45.09; H, 3.13; N, 2.29%.); ν_{max} (Nujol/cm^{-1}) 1676 (m), 1652 (w), 1610 (m), 1593 (m) and 1500 (s); δ_H (200MHz, $CDCl_3$) 2.30 (6H, s, 2x$C\underline{H}_3$), 7.03 (4H, d, J = 7.5Hz, Ar$\underline{H}$), 7.25-7.46 (3H, m, Ar$\underline{H}$) and 7.71-7.83 (6H, m, Ar$\underline{H}$); δ_C (50.3MHz, $CDCl_3$) 21.53 (2x$\underline{C}H_3$), 127.90, 128.70, 129.74, 129.86, 132.36, 143.11 (Ar$\underline{C}$ and Ar$\underline{C}$H) and 175.00 ($\underline{C}O_2$).

6.3.3 Reaction of lead(IV) complexes with allyltributyltin

Allyl Benzoate (156)[115]



To triethylamine (2.50g, 25mmol) dissolved in DCM (40ml) was added allyl alcohol (1.15g, 20mmol) with stirring. Benzoyl chloride (2.80g, 20mmol) was added dropwise to this solution over 30 min. The resulting solution was stirred for 2.5 h after which a cloudy yellow solution was obtained which was washed with NH_4Cl (sat. aq.) (2x30ml), water (2x30ml) and dried (Na_2SO_4). The solvent was removed *in vacuo* to give a pale yellow liquid which was purified by short path distillation to give the title compound as a colourless oil (2.62g, 81%).

ν_{max} (Film/cm^{-1}) 3072 (w, CH), 2945 (w, CH), 1719 (s, C=O), 1650 (w, C=C), 1602 (m), 1452 (m), 1362 (m), 1315 (m), 1270 (s), 1177 (m) and 1111 (s); δ_H (200MHz, $CDCl_3$) 4.81 (2H, d, J = 5.5Hz, $OC\underline{H}_2CH=CH_2$), 5.24-5.44 (2H, m, $OCH_2CH=C\underline{H}_2$), 5.93-6.12 (1H, m, $OCH_2C\underline{H}=CH_2$), 7.36-7.63 (3H, m, Ar$\underline{H}$) and 8.06 (2H, d, J = 7.0Hz, Ar$\underline{H}$ *o*- to ester); δ_C (50.3MHz, $CDCl_3$) 65.45 ($OCH_2CH=\underline{C}H_2$), 118.26 ($O\underline{C}H_2CH=CH_2$), 128.53, 129.80 (Ar$\underline{C}$H), 130.35 (Ar$\underline{C}$), 132.48, 133.15 ($OCH_2\underline{C}H=CH_2$ and Ar$\underline{C}$H) and 166.41 ($\underline{C}$=O); *m/z* (CI, NH_3, GCMS) 180 (58%, MNH_4^+), 163 (24, MH^+), 105 (100) and 94 (7).

Reaction of lead(IV) bis*[1,1'-(benzene-1,4-dimethyl)diphthalate]* (153) *with allyltributyltin*[86]

Complex (153) (0.15g, 0.14mmol) and allyltributyltin (46mg, 0.14mmol) were combined in $CDCl_3$ (3ml) and stirred for 12 h, after which time proton NMR spectroscopy indicated that no reaction had taken place.

Reaction of lead(IV) [1,1'-(benzene-1,4-dimethyl)diphthalate] dibenzoate (155) *with allyltributyltin*

Complex (155) (0.35g, 0.34mmol) was dissolved in $CDCl_3$ (2ml) and allyltributyltin (0.13g, 0.34mmol) in $CDCl_3$ (3ml) added. The solution was stirred at room temperature under N_2

overnight to give a white suspension. Proton NMR spectroscopy of the crude reaction mixture showed that allyl ester formation had occurred. The crude material was purified by silica chromatography (1:1 DCM:petrol) to give allyl benzoate as a colourless oil (7mg, 14%).

Reaction of lead(IV) bis*[(1*R, 3S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]* (123) *with allyltributyltin*

Complex (123) (47mg, 0.08mmol) and allyltributyltin (26mg, 0.08mmol) were shaken in $CDCl_3$ (3ml). After stirring at room temperature for 4h, proton NMR spectroscopy indicated that no reaction had taken place.

Reaction of lead(IV) bis*[(1*R, 3S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester]* (164) *with allyltributyltin*

Complex (164) (77mg, 0.07mmol) and allyltributyltin (24mg, 0.07mmol) were suspended in $CDCl_3$ (3ml) and stirred at room temperature under N_2 for 44 h. Proton NMR spectroscopy of the crude reaction mixture indicated that some allyl ester formation had occurred, but the required ester could not be isolated.

*Reaction of lead(IV) [(1*R, 3S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester] dibenzoate* (165) *with allyltributyltin*

Complex (165) (88mg, 0.10mmol) and allyltributyltin (33mg, 0.10mmol) were stirred in $CHCl_3$ (3ml) under N_2 overnight. The solvent was removed *in vacuo*, giving a crude product which by proton NMR spectroscopy was shown to contain allyl benzoate, although this was not isolated.

*Reaction of lead(IV) {3,3'-(benzene-1,4-dimethyl)di[(1*R, 3S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} dibenzoate* (168) *with allyltributyltin*

Complex (168) (0.18g, 0.19mmol) and allyltributyltin (62mg, 0.19mmol) were dissolved in $CDCl_3$ (3ml) and stirred at room temperature under N_2 overnight. A proton NMR spectrum of the crude material showed formation of allyl benzoate, although this was not isolated.

6.4 Experimental details for Chapter Four and Chapter Five

6.4.1 Attempted allylation of nucleophiles using lead(IV) {3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} dibenzoate (168) and allyltributyltin

Ethyl 2-oxocyclopentanecarboxylate[61,71]

To complex (168) (0.20g, 0.21mmol) in $CHCl_3$ (3ml) was added allyltributyltin (77mg, 0.23mmol) in $CHCl_3$ (2ml) and the mixture was stirred for 15 min. Ethyl 2-oxocyclopentanecarboxylate (33mg, 0.21mmol) in $CHCl_3$ (3ml) was added dropwise. The resulting mixture was stirred under N_2 for 4 h, after which time the solution was diluted with Et_2O (15ml). The organic layer was then washed with water (2x20ml) and brine (20ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Proton NMR spectroscopy of the crude product showed that the required allylated product had not been formed.

To complex (168) (0.40g, 0.42mmol) in $CHCl_3$ (15ml) was added ethyl 2-oxocyclopentanecarboxylate (66mg, 0.42mmol) in pyridine (33mg, 0.42mmol) and $CHCl_3$ (5ml) and the reaction mixture was stirred for 30 min. Allyltributyltin (0.14g, 0.42mmol) in $CHCl_3$ (5ml) was added and the mixture was stirred overnight. The organic layer was then washed with 2M HCl (3x25ml), water (25ml) and brine (25ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Proton NMR spectroscopy of the crude product showed that the required allylated product had not been formed.

Complex (168) (0.33g, 0.34mmol) was dissolved in toluene (20ml) and allyltributyltin (0.11g, 0.34mmol) was added giving a cloudy solution. Ethyl 2-oxocyclopentanecarboxylate (53mg, 0.34mmol) and DBU (52mg, 0.34mmol) in toluene (10ml) were then added and the resulting cloudy solution was stirred at room temperature for 2 h.[121] The crude mixture was washed with 1M HCl (4x25ml), water (2x25ml) and brine (25ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Purification of the crude material was achieved by silica chromatography (petrol, gradient to EtOAc) which yielded only unreacted ethyl 2-oxocyclopentanecarboxylate and allyl benzoate.

Dibenzoylmethane

Complex (168) (0.20g, 0.21mmol) and dibenzoylmethane (47mg, 0.21mmol) were stirred in $CHCl_3$ (15ml) and pyridine (17mg, 0.21mmol) for 10 min. Allyltributyltin (70mg, 0.21mmol) in $CHCl_3$ (5ml) was added and the solution was stirred at room temperature for 24 h. The reaction mixture was diluted with Et_2O (20ml) and washed with 1M HCl (3x25ml), water (25ml) and brine (25ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Proton NMR spectroscopy of the crude product showed none of the required allylated product to be present. Complex (168) (0.16g, 0.17mmol) and dibenzoylmethane (34mg, 0.15mmol) were heated at reflux in $CHCl_3$ (30ml) for 20 min. Allyltributyltin (61mg, 0.18mmol) was added and the mixture was heated at reflux for a further 4 h. The crude reaction mixture was washed with 1M HCl (25ml), water (25ml) and brine (25ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Proton NMR spectroscopy of the crude product showed none of the required allylated product to be present.

Diethyl malonate

Complex (168) (0.20g, 0.21mmol) and diethyl malonate (34mg, 0.21mmol) were stirred in $CHCl_3$ (15ml) and pyridine (17mg, 0.21mmol) for 10 min. Allyltributyltin (70mg, 0.21mmol) in $CHCl_3$ (5ml) was added and the solution was stirred at room temperature for 24 h. The reaction mixture was diluted with Et_2O (20ml) and washed with 1M HCl (3x25ml), water (25ml) and brine (25ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Proton NMR spectroscopy of the crude product showed none of the required allylated product to be present.

Attempted allylation by pre-complexing dibenzoylmethane

LTA (0.18g, 0.40mmol), 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139) (0.20g, 0.40mmol) and dibenzoylmethane (0.18g, 0.80mmol) were reacted according to General procedure B. Proton NMR spectroscopy of the resulting lead(IV) compound was not conclusive, but did not show any signs of remaining acetate groups. A portion of this product (0.19g, 0.20mmol) was stirred in $CHCl_3$ (15ml) with allyltributyltin (66mg, 0.20mmol) at room temperature overnight. The solvent was removed *in vacuo* and the

residue was dissolved in Et_2O, whereupon a yellow precipitate formed immediately. The organic layer was washed with 1M HCl (3x25ml), water (2x25ml) and brine (25ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Proton NMR spectroscopy of the crude product showed none of the required allylated product to be present.

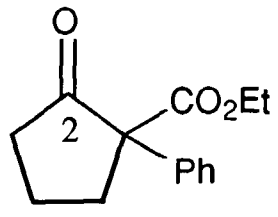
6.4.2 General procedure for phenylation reactions[68]

Stage One : A lead(IV) complex (1 eq.), phenylboric acid (1 eq.) and a catalyst (0.1 eq.) were dissolved in dry $CHCl_3$ (20-40ml) and then stirred at 40°C for 1 h. The resulting cloudy solution was then stirred overnight at room temperature.

Stage Two: A nucleophile (0.91 eq.) in pyridine (3.03 eq.) was added to the above solution, which was stirred at 40°C for 1 h and at room temperature overnight. The resulting solution was filtered through Celite® and the solid was washed with $CHCl_3$ (2x25ml). The combined organic layers were washed with 3M H_2SO_4 (25-50ml) and the $CHCl_3$ layer was separated. The aqueous phase was extracted with $CHCl_3$ (2x15ml), the combined organic layers were dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the crude product.

6.4.3 Phenylations using LTA

Ethyl 1-phenyl-2-oxocyclopentanecarboxylate (187)

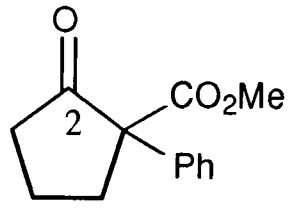


LTA (2.22g, 5.00mmol), phenylboric acid (0.61g, 5.00mmol) and mercury(II) acetate (0.16g, 0.50mmol) were reacted according to the General procedure Stage One; ethyl 2-oxocyclopentanecarboxylate (0.71g, 4.55mmol) in pyridine (1.20g, 15.15mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was dissolved in Et_2O and the solution was cooled to 0°C and shaken briefly with 3M NaOH (50ml) at 0°C. The organic layer was then washed further with water (50ml) and

brine (50ml), dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the title compound as a colourless oil (0.71g, 67%).

R_f 0.45 (1:3 EtOAc:petrol); ν_{max} (Film/cm^{-1}) 1752 (s, ring C=O), 1730 (s, ester C=O), 1499 (m), 1466 (m), 1254 (s), 1235 (s), 1219 (s), 1179 (m) and 1125 (m); δ_H (200MHz, $CDCl_3$) 1.24 (3H, t, J = 7.0Hz, $CH_2C\underline{H}_3$), 1.94-2.05 (2H, m, $C\underline{H}_2$), 2.37-2.62 (3H, m, $C\underline{H}_2$), 2.87-2.94 (1H, m, $C\underline{H}_2$), 4.20 (2H, q, J = 7.0Hz, $C\underline{H}_2CH_3$) and 7.30-7.40 (5H, m, Ar$\underline{H}$); δ_C (50.3MHz, $CDCl_3$) 13.86 ($CH_2\underline{C}H_3$), 19.21, 34.78, 37.68 (3x$\underline{C}H_2$), 61.87 ($\underline{C}H_2CH_3$), 65.03 (C(1)), 127.58, 127.83, 128.68 (3xAr$\underline{C}$H), 136.44 (Ar$\underline{C}$), 170.97 ($\underline{C}O_2Et$) and 212.04 ($\underline{C}$=O); *m/z* (CI, NH_3, GCMS) 250 (54%, MNH_4^+), 233 (100, MH^+), 204 (15), 175 (10) and 159 (10).

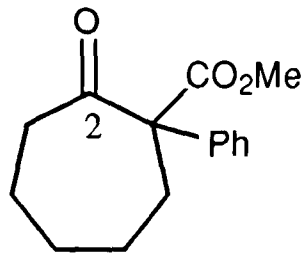
Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191)



LTA (2.22g, 5.00mmol), phenylboric acid (0.61g, 5.00mmol) and mercury(II) acetate (0.16g, 0.50mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (0.65g, 4.55mmol) in pyridine (1.20g, 15.15mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (3:1 DCM:petrol, gradient to DCM) to give the title compound as a colourless oil (0.70g, 70%).

R_f 0.34 (DCM); ν_{max} (Film/cm^{-1}) 2954 (m, CH), 1750 (s, ring C=O), 1722 (s, ester C=O), 1449 (m) and 1256 (s); δ_H (200MHz, $CDCl_3$) 1.82-2.13 (2H, m, $C\underline{H}_2$), 2.28-2.62 (3H, m, $C\underline{H}_2$), 2.83-2.93 (1H, m, $C\underline{H}_2$), 3.72 (3H, s, $C\underline{H}_3$) and 7.30-7.41 (5H, m, Ar$\underline{H}$); δ_C (50.3MHz, $CDCl_3$) 19.19, 34.92, 37.75 (3x$\underline{C}H_2$), 53.00 ($\underline{C}H_3$), 65.05 (C(1)), 127.54, 127.92, 128.78 (3xAr$\underline{C}$H), 136.32 (Ar$\underline{C}$), 171.52 ($\underline{C}O_2Me$) and 211.95 ($\underline{C}$=O); *m/z* (CI, NH_3, GCMS) 236 (53%, MNH_4^+), 219 (100, MH^+), 204 (8), 190 (12) and 159 (13).

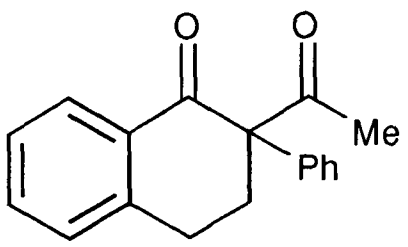
Methyl 1-phenyl-2-oxocycloheptanecarboxylate (193)



LTA (0.20g, 0.46mmol), phenylboric acid (0.06g, 0.46mmol) and mercury(II) acetate (15mg, 0.05mmol) were reacted according to the General procedure Stage One; methyl 2-oxocycloheptanecarboxylate (0.07g, 0.42mmol) in pyridine (0.11g, 1.40mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:2 Et_2O:petrol) to give the title compound as a white solid (0.08g, 77%).

m.p. 63-65°C; R_f 0.43 (1:1 Et_2O:petrol); ν_{max} (Nujol/cm^{-1}) 1731 (s, ring C=O), 1703 (s, ester C=O), 1235 (s), 1157 (m) and 1070 (m); δ_H (200MHz, $CDCl_3$) 1.26-1.97 (6H, m, 3x$\underline{C}H_2$), 2.13-2.25 (1H, m, $C\underline{H}_2$), 2.58 (2H, t, J = 6.0Hz, $C\underline{H}_2$), 2.73-2.84 (1H, m, $C\underline{H}_2$), 3.70 (3H, s, $C\underline{H}_3$) and 7.18-7.41 (5H, m, Ar$\underline{H}$); δ_C (50.3MHz, $CDCl_3$) 25.37, 26.36, 30.33, 33.63, 41.86 (5x$\underline{C}H_2$), 52.49 ($\underline{C}H_3$), 68.21 (C(1)), 127.65, 128.63 (2xAr$\underline{C}$H), 139.00 (Ar$\underline{C}$), 172.86 ($\underline{C}O_2Me$) and 208.61 ($\underline{C}$=O); *m/z* (CI, NH_3, GCMS) 247 (100%, MH^+), 206 (40), 189 (95) and 173 (15).

α–Phenyl-α-acetyl-1-tetralone (195)

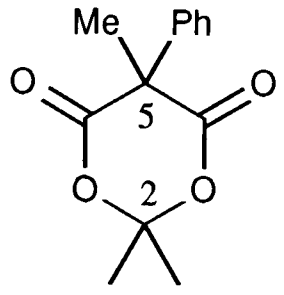


LTA (0.22g, 0.50mmol), phenylboric acid (0.06g, 0.50mmol) and mercury(II) acetate (16mg, 0.05mmol) were reacted according to the General procedure Stage One; 2-acetyl tetralone (0.09g, 0.46mmol) in pyridine (0.12g, 1.52mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:9 EtOAc:petrol) to give the title compound as a yellow oil (0.06g, 50%).

R_f 0.23 (1:19 EtOAc:petrol); ν_{max} ($CDCl_3$/cm^{-1}) 1709 (s, ring C=O), 1678 (s, ketone C=O),

1601 (m), 1455 (m), 1354 (m) and 1297 (m); δ_H (200MHz, $CDCl_3$) 2.17 (3H, s, C<u>H</u>$_3$), 2.63-2.86 (4H, m, 2xC<u>H</u>$_2$), 7.14-7.18 (3H, m, Ar<u>H</u>), 7.30-7.48 (5H, m, Ar<u>H</u>) and 8.16 (1H, d, J = 8.0Hz, Ar<u>H</u>); δ_C (50.3MHz, $CDCl_3$) 25.69, 29.49, 31.20 (2x<u>C</u>H$_2$ and <u>C</u>H$_3$), 126.83, 127.54, 127.81, 127.91, 128.68, 128.98, 132.50 (Ar<u>C</u>H), 133.72, 136.71, 143.38 (Ar<u>C</u>), 196.93 (ketone <u>C</u>=O) and 207.05 (<u>C</u>=O); *m/z* (CI, NH_3, GCMS) 265 (100%, MH^+), 240 (2), 223 (41), 193 (2), 131 (4), 118 (8) and 106 (2).

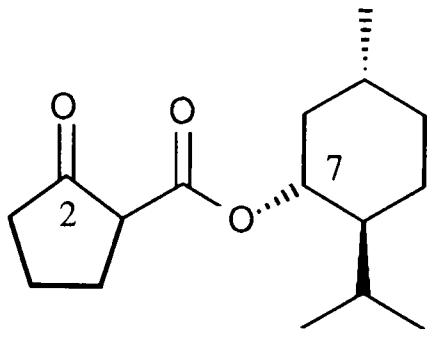
5-Phenyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (196)



LTA (0.20g, 0.46mmol), phenylboric acid (0.06g, 0.46mmol) and mercury(II) acetate (15mg, 0.05mmol) were reacted according to the General procedure Stage One; 2,2,5-trimethyl-1,3-dioxane-4,6-dione (0.07g, 0.42mmol) in pyridine (0.11g, 1.40mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (DCM) to give the title compound as a white solid (0.08g, 71%).

m.p. 133-135°C; R_f 0.44 (DCM); ν_{max} (Nujol/cm^{-1}) 1776 (m, C=O), 1735 (s, C=O), 1302 (s), 1159 (s) and 1070(m); δ_H (200MHz, $CDCl_3$) 1.28 (3H, s, C(5)C<u>H</u>$_3$), 1.74, 1.89 (2x3H, 2xs, 2xC(2)C<u>H</u>$_3$) and 7.33-7.47 (5H, m, Ar<u>H</u>); δ_C (50.3MHz, $CDCl_3$) 26.22, 27.12, 29.34 (3x<u>C</u>H$_3$), 55.47 (C(5)), 105.70 (C(2)), 125.88, 129.02, 129.94 (3xAr<u>C</u>H), 137.20 (Ar<u>C</u>) and 167.76 (<u>C</u>=O); *m/z* (CI, NH_3, Probe) 252 (82%, MNH_4^+), 150 (13), 132 (100), 122 (15), 104 (51) and 76 (83).

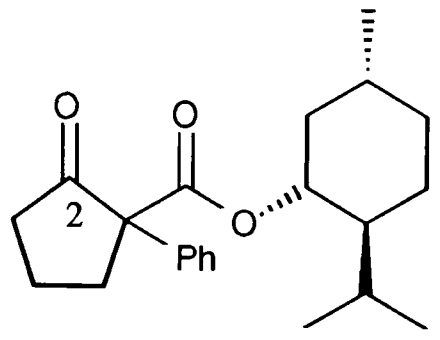
(1R, 2S, 5R)-(-)-Menthyl 2-oxocyclopentanecarboxylate (200)[125]



(1*R*, 2*S*, 5*R*)-(-)-Menthol (1.56g, 10.00mmol) and DMAP (0.06g, 0.50mmol) were dissolved in toluene (40ml) and ethyl 2-oxocyclopentanecarboxylate (0.78g, 5.00mmol) was added dropwise. The resulting solution was heated at reflux for 24 h after which time the solvent was removed *in vacuo*. The crude product was purified by silica chromatography (1:24 EtOAc:petrol) to give the title compound as a single diastereomer as a white solid (0.74g, 56%).

m.p. 59-61°C, lit.[126] 63-64°C; R_f 0.34 (1:9 EtOAc:petrol); $[\alpha]_D^{24}$ -107.0 (*c* 1.00 in $CHCl_3$), lit.[126] $[\alpha]_D^{22}$ -226 (*c* 0.27 in $CHCl_3$); ν_{max} (Nujol/cm^{-1}) 1757 (m, ring C=O), 1713 (s, ester C=O), 1662 (w), 1300 (m) and 1184 (m); δ_H (500MHz, $CDCl_3$) 0.76 (3H, d, J = 6.9Hz, C$\underline{H}_3$), 0.84-1.10 (9H, m, 2xC$\underline{H}_3$, C$\underline{H}_2$ and C$\underline{H}$ of rings), 1.38-1.52 (2H, m, C$\underline{H}_2$ and C$\underline{H}$ of rings), 1.66-1.71 (2H, m, C$\underline{H}_2$ and C$\underline{H}$ of rings), 1.83-1.91 (1H, m, C$\underline{H}_2$ and C$\underline{H}$ of rings), 1.98-2.06 (2H, m, C$\underline{H}_2$ and C$\underline{H}$ of rings), 2.11-2.16 (1H, m, C$\underline{H}_2$ and C$\underline{H}$ of rings), 2.25-2.33 (4H, m, C$\underline{H}_2$ and C$\underline{H}$ of rings), 3.13 (1H, t, J = 8.9Hz, C(1)H) and 4.40 (1H, dt, J_d = 4.4Hz, J_t = 10.9Hz, C(7)H); δ_C (50.3MHz, $CDCl_3$) 15.79, 20.70 (2x$\underline{C}H_3$), 20.85 ($\underline{C}H_2$ of cyclopentane ring), 21.86 ($\underline{C}H_3$), 22.97 ($\underline{C}H_2$ of menthyl ring), 25.63 ($\underline{C}$H), 27.27 ($\underline{C}H_2$ of cyclopentane ring), 31.28 ($\underline{C}$H), 34.09 ($\underline{C}H_2$ of menthyl ring), 37.90 ($\underline{C}H_2$ of cyclopentane ring), 40.63 ($\underline{C}H_2$ of menthyl ring), 46.85 ($CH_3\underline{C}$H), 55.12 (C(1)), 75.38 (O$\underline{C}$H), 169.32 (ester $\underline{C}$=O) and 212.69 ($\underline{C}$=O); *m/z* (CI, Probe, NH_3) 284 (100%, MNH_4^+), 267 (MH^+, 28), 156 (10), 146 (85), 138 (53), 128 (41), 111 (38), 95 (30) and 81 (28).

(1R, 2S, 5R)-(-)-Menthyl 1-phenyl-2-oxocyclopentanecarboxylate (201), *mercury(II) chloride catalysed*



LTA (0.44g, 1.00mmol), phenylboric acid (0.12g, 1.00mmol) and mercury(II) chloride (27mg, 0.10mmol) were reacted according to the General procedure Stage One; (1*R*, 2*S*, 5*R*)-(-)-menthyl 2-oxocyclopentanecarboxylate (200) (0.24g, 0.91mmol) in pyridine (0.24g, 3.03mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:49 EtOAc:petrol) to give the title compound as a mixture of diastereomers (*ca.* 1:1) as a colourless oil (0.31g, 47%).

R_f 0.39 (1:9 EtOAc:petrol); $[\alpha]_D^{26}$ -59.1 (*c* 1.01 in $CHCl_3$); ν_{max} ($CDCl_3$/cm^{-1}) 1752 (m, ring C=O), 1719 (s, ester C=O), 1498 (w), 1457 (w), 1258 (s) and 1127 (m); δ_H (200MHz, $CDCl_3$) 0.67 (3H, d, J = 7.0Hz, C$\underline{H}_3$), 0.80 (3H, 2xd, J = 2.0Hz, C$\underline{H}_3$), 0.85-1.11 (6H, m, C$\underline{H}_3$, C$\underline{H}_2$ and C$\underline{H}$ of rings), 1.26-1.75 (5H, m, C$\underline{H}_2$ and C$\underline{H}$ of rings), 1.92-2.13 (3H, m, C$\underline{H}_2$ and C$\underline{H}$ of rings), 2.25-2.61 (3H, m, C$\underline{H}_2$ and C$\underline{H}$ of rings), 2.82-2.94 (1H, m, C$\underline{H}_2$ of cyclopentane ring), 4.67 (1H, dt, J_d = 4.5Hz, J_t = 11.0Hz, C(7)H) and 7.26-7.44 (5H, m, Ar$\underline{H}$); δ_C (50.3MHz, $CDCl_3$) 15.71 ($\underline{C}H_3$), 19.19 ($\underline{C}H_2$ of cyclopentane ring), 20.59, 21.86 (2x$\underline{C}H_3$), 22.90 ($\underline{C}H_2$ of menthyl ring), 25.63, 25.74, 31.27 (3x$\underline{C}$H), 34.04 ($\underline{C}H_2$ of menthyl ring), 34.36, 34.83, 37.53, 37.75 ($\underline{C}H_2$ of cyclopentane ring), 40.12, 40.22 ($\underline{C}H_2$ of menthyl ring), 46.69 ($CH_3\underline{C}$H), 65.15 ($\underline{C}$Ph), 75.99 (O$\underline{C}$H), 127.55, 127.72, 128.56 (Ar$\underline{C}$H), 136.37, 136.68 (Ar$\underline{C}$), 170.47, 170.58 (ester $\underline{C}$=O) and 212.02, 212.26 (ring $\underline{C}$=O); *m/z* (CI, Probe, NH_3) 360 (70%, MNH_4^+), 343 (MH^+, 36), 222 (76), 204 (100) and 160 (20).

6.4.4 Phenylations using LTA with the addition of free chiral ligands

*Added (1*R, *3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid* (122)

LTA (0.44g, 1.00mmol), phenylboric acid (0.12g, 1.00mmol) and mercury(II) acetate (32mg, 0.10mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (0.13g, 0.91mmol) and (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid (0.20g, 1.00mmol) in pyridine (0.24g, 3.03mmol) were added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:4 EtOAc:petrol) to give methyl 1-phenyl-2-oxocyclopentanecarboxylate (191) as a yellow oil (0.13g, 61%). Chiral shift NMR spectroscopy indicated that the product was racemic.

The above procedure was repeated using (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid (0.40g, 2.00mmol). The crude product was purified by silica chromatography (1:4 EtOAc:petrol) to give methyl 1-phenyl-2-oxocyclopentanecarboxylate (191) as a yellow oil (0.12g, 57%). Chiral shift NMR spectroscopy indicated that the product was racemic.

*Added 3,3'-(benzene-1,4-dimethyl)di[(1*R, *3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]* (139)

LTA (0.33g, 0.75mmol), phenylboric acid (0.10g, 0.75mmol) and mercury(II) acetate (24mg, 0.08mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (0.10g, 0.68mmol) and 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139) (0.38g, 0.75mmol) in pyridine (0.18g, 2.27mmol) were added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (3:1 DCM:petrol) to give methyl 1-phenyl-2-oxocyclopentanecarboxylate (191) as a yellow oil (46mg, 28%), data as above. Chiral shift NMR spectroscopy indicated that the product was racemic.

The above procedure was repeated using 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139) (0.75g, 1.50mmol). The crude product was purified by silica chromatography (3:1 DCM:petrol) to give methyl 1-phenyl-2-oxocyclopentanecarboxylate (191) as a yellow oil (55mg, 34%), data as above. Chiral shift NMR spectroscopy indicated that the product was racemic.

6.4.5 Phenylation using lead(IV) [1,1'-(benzene-1,4-dimethyl)diphthalate] dibenzoate (155)

5-Phenyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (196)

Complex (155) (0.40g, 0.45mmol), phenylboric acid (55mg, 0.45mmol) and mercury(II) acetate (16mg, 0.05mmol) were reacted according to the General procedure Stage One; 2,2,5-trimethyl-1,3-dioxane-4,6-dione (65mg, 0.41mmol) in pyridine (0.11g, 1.36mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (DCM) to give the title compound as a white solid (0.50g, 52%), data as above.

6.4.6 Phenylations using lead(IV) [(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester] dibenzoate (165)

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191)

Complex (165) (0.18g, 0.20mmol), phenylboric acid (25mg, 0.20mmol) and mercury(II) acetate (6mg, 0.02mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (26mg, 0.19mmol) in pyridine (0.05g, 0.62mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was dissolved in EtOAc (25ml) and washed with $NaHCO_3$ (sat. aq.) (2x25ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give a crude product which was purified by silica chromatography (2:3 DCM:petrol, gradient to 2:1 DCM:petrol) to give the title compound as a yellow oil (18mg, 44%), data as above. The enantiomeric excess was found to be 0% by chiral shift NMR spectroscopy.

5-Phenyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (196)

Complex (165) (0.18g, 0.20mmol), phenylboric acid (25mg, 0.20mmol) and mercury(II) acetate (6mg, 0.02mmol) were reacted according to the General procedure Stage One; 2,2,5-trimethyl-1,3-dioxane-4,6-dione (29mg, 0.19mmol) in pyridine (0.05g, 0.62mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:3 EtOAc:petrol) to give the title compound as a white solid (27mg, 62%), data as above.

6.4.7 Phenylations using lead(IV) *bis*{3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} (166)

Ethyl 1-phenyl-2-oxocyclopentanecarboxylate (187)

Complex (166) (0.56g, 0.46mmol), phenylboric acid (61mg, 0.46mmol) and mercury(II) acetate (15mg, 0.05mmol) were reacted according to the General procedure Stage One; ethyl 2-oxocyclopentanecarboxylate (66mg, 0.42mmol) in pyridine (0.11g, 1.40mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:9 EtOAc:petrol) to give the title compound as a yellow oil (18mg, 18%), data as above.

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191)

Complex (166) (0.62g, 0.51mmol), phenylboric acid (0.06g, 0.51mmol) and mercury(II) acetate (16mg, 0.05mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (66mg, 0.47mmol) in pyridine (0.12g, 1.55mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was dissolved in Et_2O and the solution cooled to 0°C and shaken briefly with 3M NaOH (50ml) at 0°C. The organic layer was then washed further with water (50ml) and brine (50ml), dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the crude product. Attempted purification of this product by silica chromatography (3:1 DCM:petrol) resulted in the isolation of the title compound contaminated with around 90% of (1*R*, 3*S*)-1,2,2-

trimethylcyclopentane-1,3-dicarboxylic anhydride (126).

Complex (166) (0.60g, 0.50mmol), phenylboric acid (0.06g, 0.50mmol) and mercury(II) acetate (16mg, 0.05mmol) were reacted according to the General procedure Stage One, heating at 40°C for 2 h and then at room temperature for 48 h; methyl 2-oxocyclopentanecarboxylate (65mg, 0.46mmol) in pyridine (0.12g, 1.52mmol) was added and the reaction continued according to Stage Two of the General procedure, heating at 40°C for 2 h and then at room temperature for 48 h. The crude product was purified by silica chromatography (1:6 EtOAc:petrol) to give the title compound as a yellow oil (10mg, 10%), data as above. The enantiomeric excess was found to be 12% by chiral shift NMR spectroscopy, 4% by chiral GC.

Methyl 1-phenyl-2-oxocycloheptanecarboxylate (193)

Complex (166) (0.54g, 0.45mmol), phenylboric acid (55mg, 0.45mmol) and mercury(II) acetate (16mg, 0.05mmol) were reacted according to the General procedure Stage One; methyl 2-oxocycloheptanecarboxylate (70mg, 0.41mmol) in pyridine (0.11g, 1.36mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by dissolving in EtOAc (25ml) and washing with $NaHCO_3$ (sat. aq.) (2x25ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the title compound as a yellow oil (8mg, 8%, estimated from proton NMR spectroscopy), data as above, which it was not possible to purify further by silica chromatography.

5-Phenyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (196)

Complex (166) (0.25g, 0.21mmol), phenylboric acid (25mg, 0.21mmol) and mercury(II) acetate (7mg, 0.02mmol) were reacted according to the General procedure Stage One; 2,2,5-trimethyl-1,3-dioxane-4,6-dione (30mg, 0.19mmol) in pyridine (0.05g, 0.63mmol) was added and the reaction continued according to Stage Two of the General procedure. Proton NMR spectroscopy of the crude reaction mixture showed a small quantity (<5%) of the title compound to be present, but purification by silica chromatography (DCM) failed to isolate this.

6.4.8 Phenylation using lead(IV) {3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} diacetate (167)

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191)

Complex (167) (0.36g, 0.45mmol), phenylboric acid (55mg, 0.45mmol) and mercury(II) acetate (16mg, 0.05mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (58mg, 0.41mmol) in pyridine (0.11g, 1.36mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:9 EtOAc:petrol) to give the title compound as a yellow oil (33mg, 37%), data as above. The enantiomeric excess was found to be 8% by NMR spectroscopy, 1% by chiral GC.

6.4.9 Phenylations using lead(IV) {3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} dibenzoate (168)

Ethyl 1-phenyl-2-oxocyclopentanecarboxylate (187)

Complex (168) (0.30g, 0.32mmol), phenylboric acid (39mg, 0.32mmol) and mercury(II) acetate (10mg, 0.03mmol) were reacted according to the General procedure Stage One; ethyl 2-oxocyclopentanecarboxylate (49mg, 0.42mmol) in pyridine (0.11g, 1.40mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was dissolved in Et_2O (100ml) and washed with water (50ml) and brine (50ml), dried (Na_2SO_4) and the solvent was removed *in vacuo*. GCMS analysis of this crude product showed the presence of the title compound.

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191)

Complex (168) (0.46g, 0.49mmol), phenylboric acid (0.59g, 0.49mmol) and mercury(II) acetate (16mg, 0.05mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (63mg, 0.44mmol) in pyridine (0.12g, 1.47mmol) was added and the reaction continued according to Stage Two of the General procedure to give the title

compound (21mg, 20%), data as above.

In a repeat of the above reaction, complex (168) (0.48g, 0.50mmol), phenylboric acid (61mg, 0.5mmol), mercury(II) acetate (16mg, 0.05mmol), methyl 2-oxocyclopentanecarboxylate (64mg, 0.45mmol) and pyridine (0.12g, 1.52mmol) were reacted according to the General procedure, heating at 40°C for 2 h and then for 48 h at room temperature at each stage. The crude product was purified by silica chromatography (1:4 EtOAc:petrol) to give the title compound (21mg, 21%), data as above. The enantiomeric excess was found to be 8% by NMR spectroscopy, 4% by chiral GC.

In a further reaction, complex (168) (0.43g, 0.45mmol), phenylboric acid (55mg, 0.45mmol), mercury(II) acetate (16mg, 0.05mmol), methyl 2-oxocyclopentanecarboxylate (58mg, 0.41mmol) and pyridine (0.11g, 1.36mmol) were reacted according to the General procedure, heating at 40°C for 3 h and then overnight at room temperature at each stage. The crude product was purified by silica chromatography (1:9 EtOAc:petrol) to give the title compound (29mg, 33%), data as above. The enantiomeric excess was found to be 5% by chiral shift NMR spectroscopy.

Methyl 1-phenyl-2-oxocycloheptanecarboxylate (193)

Complex (168) (0.54g, 0.45mmol), phenylboric acid (55mg, 0.45mmol) and mercury(II) acetate (16mg, 0.05mmol) were reacted according to the General procedure Stage One; methyl 2-oxocycloheptanecarboxylate (70mg, 0.41mmol) in pyridine (0.11g, 1.36mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by dissolving in EtOAc (25ml) and washing with $NaHCO_3$ (sat. aq.) (4x25ml) and a solution of 0.5M $NaHCO_3$ (aq.)/ 0.5M $CuSO_4$ (aq.) (2x25ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the title compound as a yellow oil (17mg, 17%), data as above. The enantiomeric excess was found to be 6% by NMR spectroscopy, 4% by chiral GC.

α–Phenyl-α-acetyl-1-tetralone (195)

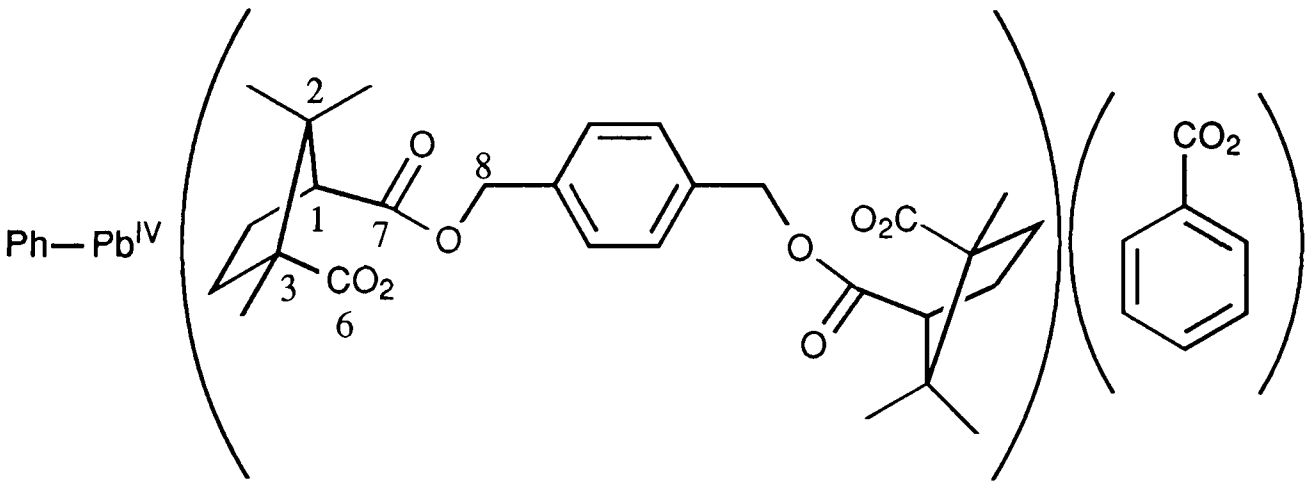
Complex (168) (0.47g, 0.50mmol), phenylboric acid (61mg, 0.50mmol) and mercury(II) acetate (16mg, 0.05mmol) were reacted according to the General procedure Stage One; 2-acetyl tetralone (86mg, 0.46mmol) in pyridine (0.12g, 1.52mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was dissolved in EtOAc (25ml) and washed with $NaHCO_3$ (sat. aq.) (25ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to yield a crude product which was purified by silica chromatography (1:19 EtOAc:petrol) to give the title compound as a yellow oil (10mg, 8%), data as above.

5-Phenyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (196)

Complex (168) (0.20g, 0.21mmol), phenylboric acid (25mg, 0.21mmol) and mercury(II) acetate (7mg, 0.02mmol) were reacted according to the General procedure Stage One; 2,2,5-trimethyl-1,3-dioxane-4,6-dione (30mg, 0.19mmol) in pyridine (0.05g, 0.63mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:3 EtOAc:petrol) to give the title compound as a white solid (23mg, 52%), data as above.

6.4.10 Phenylation *via* initial formation of intermediate phenyllead species[68]

*Phenylation using phenyllead(IV) {3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} monobenzoate* (197)



Lead(IV) {3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-

dicarboxylate]} dibenzoate (0.48g, 0.5mmol) (168) and mercury(II) acetate (16mg, 0.05mmol) were dissolved in $CHCl_3$ (25ml) giving a clear yellow solution. To this was added a solution of phenylboric acid (61mg, 0.50mmol) in $CHCl_3$ (10ml) over 15 min, *via* a dropping funnel, giving a cloudy solution which was stirred at 40°C for 1 h and then at room temperature overnight. The reaction mixture was then filtered through Celite®, and the solid was washed with $CHCl_3$ (2x30ml). The $CHCl_3$ filtrate was washed with water (40ml) and the aqueous layer was extracted with $CHCl_3$ (2x80ml). The combined organic layers were filtered through Celite® and concentrated to 50ml *in vacuo*. The solution was diluted with petrol (300ml) and left to stand at 0°C overnight. This solution was filtered to give phenyllead(IV) {3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} mono benzoate (197) as a white solid (61mg, 13%). A satisfactory proton NMR spectrum of this product could not be obtained, but the crude material was taken on to the next stage of the reaction.

Complex (197) (20mg, 0.02mmol) was dissolved in $CHCl_3$ (10ml) and a solution of methyl 2-oxocyclopentanecarboxylate (3mg, 0.02mmol) and pyridine (5mg, 0.06mmol) in $CHCl_3$ (5ml) added. The resulting solution was heated at 40°C for 1 h and then at room temperature overnight. The organic layer was then washed with 2M HCl (25ml) and water (25ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Proton NMR spectroscopy of the crude material (11mg) showed *ca.* 3mg of this to be methyl 1-phenyl-2-oxocyclopentanecarboxylate (191) (70%), giving around 10% yield over two steps.

6.4.11 Phenylations using lead(IV) {3,3'-(ethylene-1,2-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} dibenzoate (169)

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191)

Complex (169) (0.17g, 0.19mmol), phenylboric acid (24mg, 0.19mmol) and mercury(II) acetate (6mg, 0.02mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (26mg, 0.19mmol) in pyridine (0.05g, 0.62mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude

product was purified by silica chromatography (1:9 EtOAc:petrol) to give the title compound as a yellow oil (29mg, 69%), data as above. The enantiomeric excess was found to be 10% by NMR spectroscopy, 6% by chiral GC.

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191), *mercury(II) chloride catalysed*
Complex (169) (82mg, 0.09mmol), phenylboric acid (12mg, 0.09mmol) and mercury(II) chloride (2mg, 0.01mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (12mg, 0.09mmol) in pyridine (23mg, 0.29mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was dissolved in EtOAc (25ml) and washed with $NaHCO_3$ (sat. aq.) (2x25ml). The crude product was purified by silica chromatography (1:3 EtOAc:petrol) to give the title compound as a yellow oil (3mg, 16%), data as above. The enantiomeric excess was found to be 6% by chiral GC.

6.4.12 Phenylation using lead(IV) {3,3'-(propylene-1,3-dioxy)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} dibenzoate (170)

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191), *mercury(II) chloride catalysed*
Complex (170) (0.31g, 0.35mmol), phenylboric acid (43mg, 0.35mmol) and mercury(II) chloride (10mg, 0.04mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (45mg, 0.32mmol) in pyridine (0.08g, 1.06mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was dissolved in EtOAc (25ml) and washed with $NaHCO_3$ (sat. aq.) (2x25ml) and water (2x25ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. The product obtained was further purified by silica chromatography (1:3 EtOAc:petrol) to give the title compound as a yellow oil (39mg, 57%), data as above. The enantiomeric excess was found to be 6% by chiral GC.

6.4.13 Phenylations using lead(IV) dibenzoyl-L-tartrate dibenzoate (173)

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191)

Complex (173) (0.25g, 0.31mmol), phenylboric acid (38mg, 0.31mmol) and mercury(II) acetate (10mg, 0.03mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (40mg, 0.28mmol) in pyridine (0.07g, 0.94mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was dissolved in EtOAc (25ml) and washed with $NaHCO_3$ (sat. aq.) (2x25ml) and water (2x25ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. The product obtained was purified by silica chromatography (1:4 Et_2O:petrol, gradient to 3:7 Et_2O:petrol) to give the title compound as a yellow oil (44mg, 71%), data as above. The enantiomeric excess was found to be 4% by chiral shift NMR spectroscopy, 4% by chiral GC.

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191), *mercury(II) chloride catalysed*

Complex (173) (0.36g, 0.45mmol), phenylboric acid (55mg, 0.45mmol) and mercury(II) chloride (0.12g, 0.45mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (58mg, 0.41mmol) in pyridine (0.11g, 1.36mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:19 EtOAc:petrol, gradient to 1:9 EtOAc:petrol) to give the product contaminated with a small quantity of benzoic acid. The fractions containing the product were washed with $NaHCO_3$ (sat. aq.) (2x25ml), the organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the title compound as a yellow oil (58mg, 65%). The enantiomeric excess was found to be 6% by chiral shift NMR spectroscopy, 3% by chiral GC.

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191), *mercury(II) chloride catalysed with addition of dibenzoyl-L-tartaric acid*[78]

Complex (173) (0.25g, 0.30mmol), phenylboric acid (37mg, 0.30mmol), mercury(II) chloride (33mg, 0.12mmol) and dibenzoyl-L-tartaric acid (0.11g, 0.30mmol) were reacted according to

the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (39mg, 0.28mmol) in pyridine (73mg, 0.92mmol) was added and the reaction continued according to Stage Two of the General procedure. The $CHCl_3$ was not removed, the organic layer being washed further with $NaHCO_3$ (sat. aq.) (50ml), dried ($MgSO_4$) and the solvent being removed *in vacuo*. The recovered material was found to be almost exclusively methyl 2-oxocyclopentanecarboxylate.

6.4.14 Phenylations using lead(IV) dibenzoyl-L-tartrate di-*p*-toluate (174)

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191)

Complex (174) (0.46g, 0.55mmol), phenylboric acid (67mg, 0.55mmol) and mercury(II) acetate (18mg, 0.06mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (71mg, 0.50mmol) in pyridine (0.13g, 1.67mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was dissolved in EtOAc (25ml) and washed with $NaHCO_3$ (sat. aq.) (2x20ml), water (20ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. The product obtained was further purified by silica chromatography (1:3 Et_2O:petrol) to give the title compound as a yellow oil (64mg, 58%), data as above. The enantiomeric excess was found to be 4% by NMR spectroscopy, 4% by chiral GC.

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191), *mercury(II) chloride catalysed*

Complex (174) (0.10g, 0.12mmol), phenylboric acid (15mg, 0.12mmol) and mercury(II) chloride (33mg, 0.12mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (16mg, 0.11mmol) in pyridine (29mg, 0.37mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was dissolved in EtOAc (25ml) and washed with $NaHCO_3$ (sat. aq.) (2x25ml). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo*. The product obtained was further purified by silica chromatography (1:3 Et_2O:petrol) to give the title compound as a yellow oil (13mg, 54%). The enantiomeric excess was found to be 8% by

chiral shift NMR spectroscopy, 5% by chiral GC.

*(1*R, 2S, *5*R*)-(-)-Menthyl phenyl-2-oxocyclopentanecarboxylate* (201), *mercury(II) chloride catalysed*

Complex (174) (0.75g, 0.90mmol), phenylboric acid (0.11g, 0.90mmol) and mercury(II) chloride (24mg, 0.09mmol) were reacted according to the General procedure Stage One; (1*R*, 2*S*, 5*R*)-(-)-menthyl 2-oxocyclopentanecarboxylate (200) (0.22g, 0.82mmol) in pyridine (0.22g, 2.72mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:49 EtOAc:petrol) to give the title compound as a mixture of diastereomers (*ca.* 1:1) as a white solid (90mg, 32%).

6.4.15 Attempted phenylations using lead(IV) benzohydroxamate di-*p*-toluate (182)

5-Phenyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (196)

Complex (182) (0.10g, 0.13mmol), phenylboric acid (16mg, 0.13mmol) and mercury(II) acetate (4mg, 0.01mmol) were reacted according to the General procedure Stage One; 2,2,5-trimethyl-1,3-dioxane-4,6-dione (19mg, 0.12mmol) in pyridine (32mg, 0.40mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was found to contain none of the title compound.

5-Phenyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (196), *mercury(II) chloride catalysed*

Complex (182) (60mg, 0.10mmol), phenylboric acid (12mg, 0.10mmol) and mercury(II) chloride (3mg, 0.01mmol) were reacted according to the General procedure Stage One; 2,2,5-trimethyl-1,3-dioxane-4,6-dione (14mg, 0.09mmol) in pyridine (23mg, 0.29mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was found to contain none of the title compound.

6.4.16 Catalyst studies

Phenylation in the absence of catalyst

LTA (2.22g, 5.00mmol) and phenylboric acid (0.61g, 5.00mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (0.65g, 4.55mmol) in pyridine (1.20g, 15.15mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was found to contain starting material (*ca.* 18%), methyl 1-phenyl-2-oxocyclopentanecarboxylate (191) (*ca.* 20%), and at least three other side products.

Phenylation using fluoride ion catalysis[124]

LTA (0.20g, 0.46mmol), phenylboric acid (56mg, 0.46mmol) and cesium fluoride (0.14g, 0.92mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (60mg, 0.42mmol) in pyridine (0.11g, 1.40mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was shown by proton NMR spectroscopy to contain approximately 5% of phenylated product (191).

A repeat of the above reaction using potassium fluoride (54mg, 0.92mmol) gave none of the required phenylated product (191).

Phenylation using mercury(II) chloride catalysis

LTA (0.22g, 0.50mmol), phenylboric acid (61g, 0.50mmol) and mercury(II) chloride (0.14g, 0.50mmol) were reacted according to the General procedure Stage One; methyl 2-oxocyclopentanecarboxylate (71mg, 0.50mmol) in pyridine (0.12g, 1.52mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (1:19 EtOAc:petrol) to give methyl 1-phenyl-2-oxocyclopentanecarboxylate (191) as a colourless oil (58mg, 53%), data as above.

A repeat of the above reaction using LTA (0.22g, 0.50mmol), mercury(II) chloride (14mg, 0.05mmol) and methyl 2-oxocyclopentanecarboxylate (65mg, 0.46mmol) gave, after silica

chromatography (1:9 EtOAc:petrol), the same product (191) as a yellow oil (57mg, 58%).

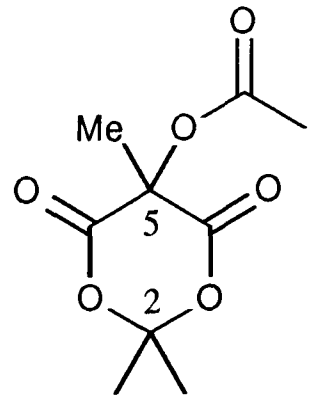
Phenylation using lead(II) acetate catalysis

LTA (0.22g, 0.50mmol), phenylboric acid (61mg, 0.50mmol) and lead(II)) acetate trihydrate (0.16g, 0.50mmol) were reacted according to the General procedure Stage One; 2,2,5-trimethyl-1,3-dioxane-4,6-dione (72mg, 0.46mmol) in pyridine (0.12g, 1.52mmol) was added and the reaction continued according to Stage Two of the General procedure. The crude product was purified by silica chromatography (3:1 DCM:petrol) to give 5-phenyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (196) as a white solid (42mg, 39%).

6.4.17 Studies towards a different source of phenyl group

Use of tetraphenylphosphonium bromide[128]

LTA (0.24g, 0.55mmol), tetraphenylphosphonium bromide (0.23g, 0.55mmol) and 2,2,5-trimethyl-1,3-dioxane-4,6-dione (79mg, 0.50mmol) were combined in DMF, giving a clear yellow solution. The solution was then heated to 105°C under N_2 whereupon the solution became colourless. Heating at 105°C was continued for 24 h, after which time the DMF solution was partitioned between Et_2O (50ml) and water (50ml). The organic layer was washed with water (2x50ml), dried ($MgSO_4$) and the solvent was removed *in vacuo* to give 5-acetyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione (207) as a white solid (45mg, 42%).



(207)

m.p. 91-95°C; R_f 0.49 (1:1 EtOAc:petrol); ν_{max} (Nujol/cm^{-1}) 1789 (m, C=O), 1751 (s, C=O), 1311 (s), 1244 (w), 1204 (w) and 1151 (m); δ_H (200MHz, $CDCl_3$) 1.82, 1.86 (2x3H, 2xs, 2xC(2)C$\underline{H}_3$), 1.92 (3H, s, C(5)C$\underline{H}_3$) and 2.22 (3H, s, $CO_2C\underline{H}_3$); δ_C (50.3MHz, $CDCl_3$) 19.70,

23.34, 28.29, 28.58 (4x$\underline{C}H_3$), 72.47 (C(5)), 108.03 (C(2)) and 165.47 (3x$\underline{C}$=O); *m/z* (CI, NH_3, Probe) 234 (49%, MNH_4^+), 193 (3), 176 (99), 149 (10), 132 (85), 115 (100) and 107 (9).

LTA (0.24g, 0.55mmol) and tetraphenylphosphonium bromide (0.23g, 0.55mmol) were combined in DMF giving a deep red solution. The solution was warmed to 105°C under N_2 whereupon the solution became colourless. 2,2,5-Trimethyl-1,3-dioxane-4,6-dione (79mg, 0.50mmol) in DMF was added after 30 min and the solution heated at 105°C overnight. A small quantity was removed and partitioned between Et_2O and water. The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo*. Proton NMR spectroscopy of the resulting material showed no identifiable products to be present. Removal of the solvent *in vacuo* from the remaining reaction mixture gave no identifiable products.

Use of tetraphenylphosphonium bromide with mercury(II) chloride catalysis

LTA (0.22g, 0.50mmol), tetraphenylphosphonium bromide (0.21g, 0.50mmol) and mercury(II) chloride (14mg, 0.05mmol) were combined in DMF giving a deep red solution which was heated at 40°C for 1 h and then stirred at room temperature overnight. A colourless solution was obtained to which was added 2,2,5-trimethyl-1,3-dioxane-4,6-dione (72mg, 0.46mmol) in DMF. The mixture was stirred at 40°C for 1 h and then at room temperature overnight. The resulting solution was partitioned between $CHCl_3$ (50ml) and water (50ml), the organic layer was washed with 3M H_2SO_4 (50ml) and water (50ml), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Proton NMR spectroscopy of the crude material showed none of the required product (196) to be present.

CHAPTER SEVEN

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APPENDICES

Appendix 1: Selective ^{1}H decoupling experiment on (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(*t*-butyl 3-hydroxybenzoate) ester (133)

Appendix 2: HMBC experiment on 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139)

Appendix 3: ^{207}Pb NMR spectra

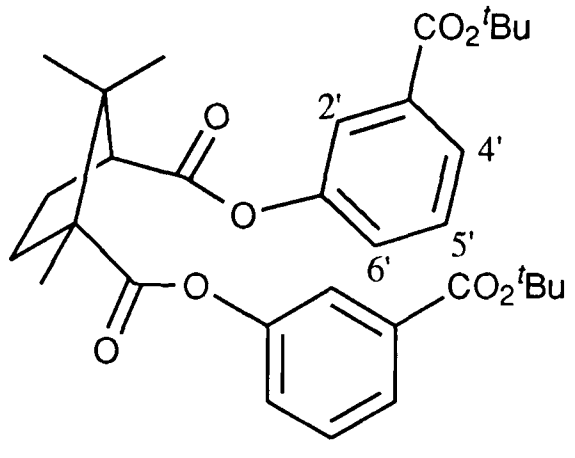
Appendix 4: ^{1}H NMR spectra of 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139) and lead(IV) *bis*{3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} (166)

Appendix 5: Atomic coordinates, thermal parameters, bond lengths and angles for lead(II) di(dibenzoylmethane) (177)

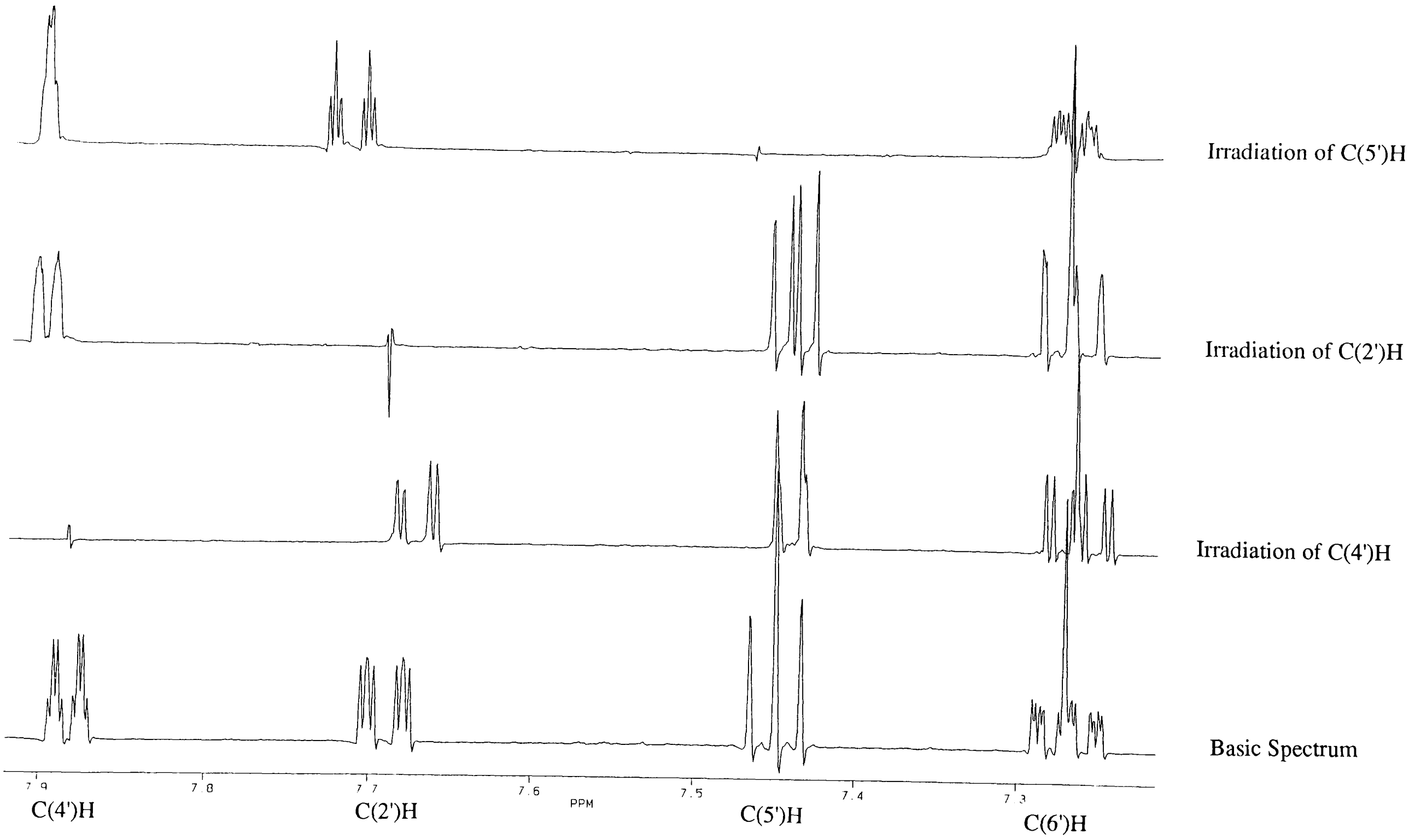
Appendix 6: Analysis of optically active compounds

APPENDIX 1

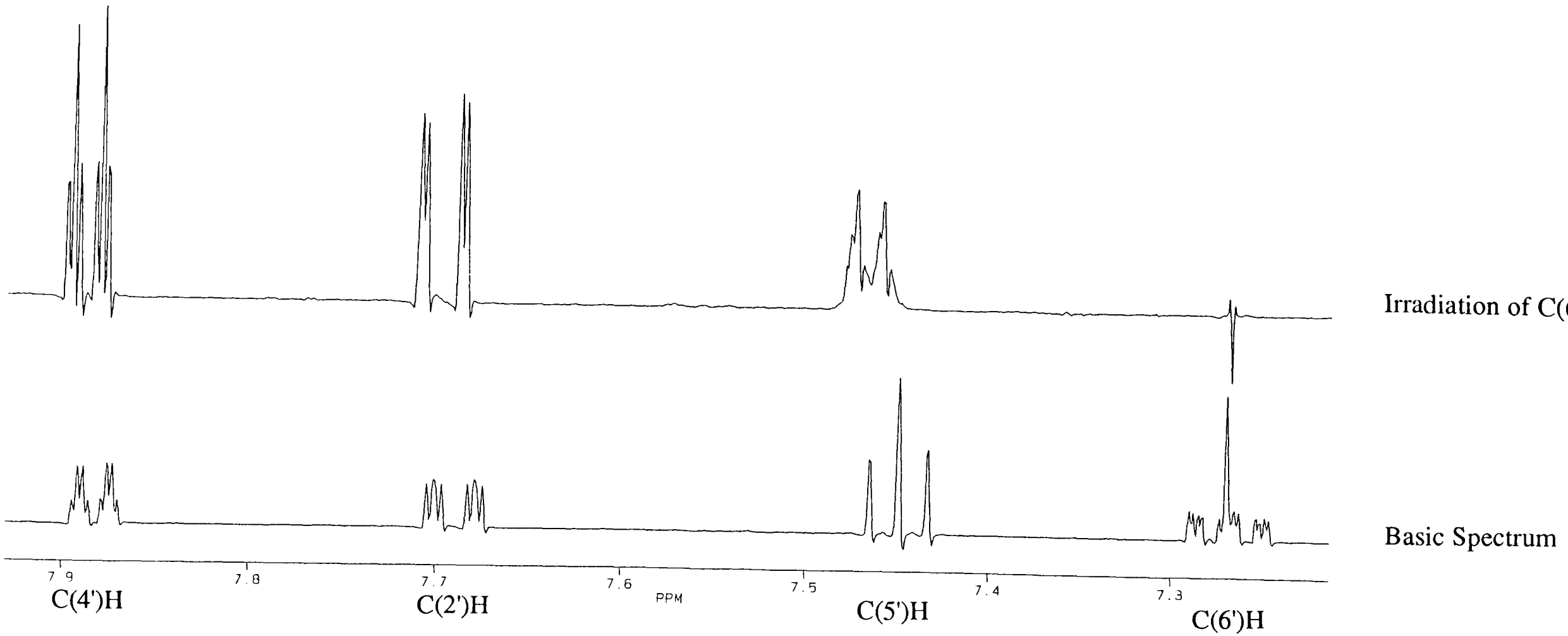
Selective ^{1}H decoupling experiment on (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(*t*-butyl 3-hydroxybenzoate) ester (133)



APPENDIX 1 : Selective ^1H decoupling experiment on (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(*t*-butyl 3-hydroxybenzoate) ester (133)

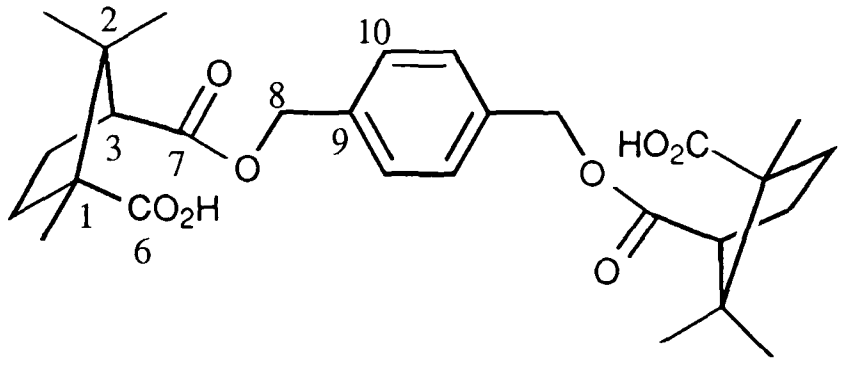


APPENDIX 1 : Selective ^1H decoupling experiment on (1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(*t*-butyl 3-hydroxybenzoate) ester (133)



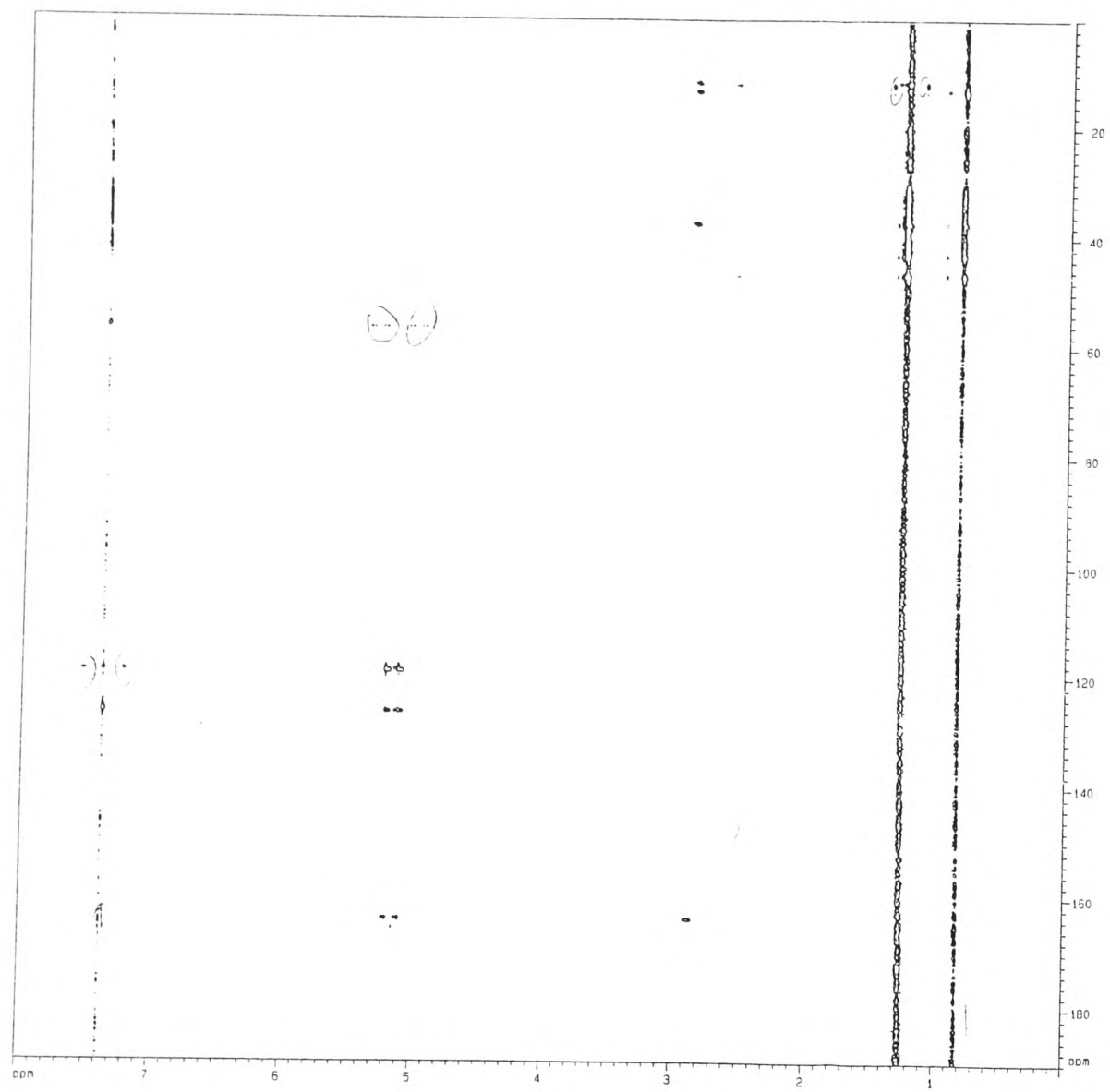
APPENDIX 2

HMBC experiment on 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139)



APPENDIX 2 : HMBC experiment on 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139)

HMBC for $^{2}J_{CH}$ or $^{3}J_{CH}$



Current Data Parameters

NAME	emma
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date	950126
Time	18.46
PULPROG	inv4lplrnd
SOLVENT	CDCl3
AQ	0.2560200 sec
FIDRES	1.953125 Hz
DW	125.0 usec
RG	512
NUCLEUS	1H
HL1	1 dB
D1	1.0000000 sec
P1	6.5 usec
D2	0.0038500 sec
P3	12.0 usec
SFO2	125.7332215 MHz
D6	0.0600000 sec
D0	0.0000030 sec
P2	12.0 usec
DE	178.6 usec
SFO1	499.9819999 MHz
SWH	4000.00 Hz
TD	2048
NS	64
DS	4
INO	0.0000209 sec

F1 - Acquisition parameters

NDO	2
TD	512
SFO1	125.7223 MHz
FIDRES	46.654766 Hz
SW	190.000 ppm

F2 - Processing parameters

SI	1024
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WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0
PC	1.00

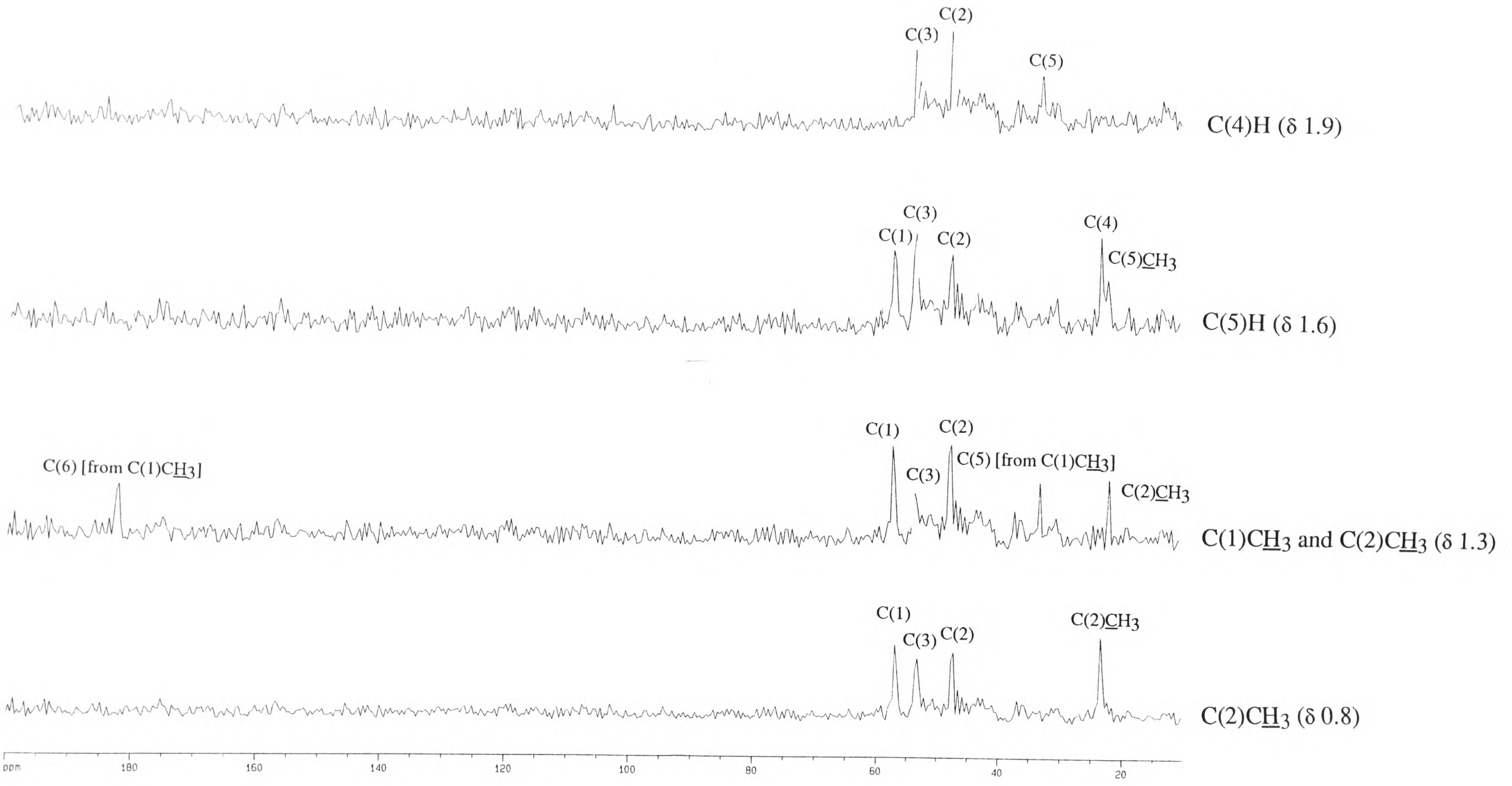
F1 - Processing parameters

SI	512
WDW	QF
SF	125.7102765 MHz
SSB	0
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GB	0

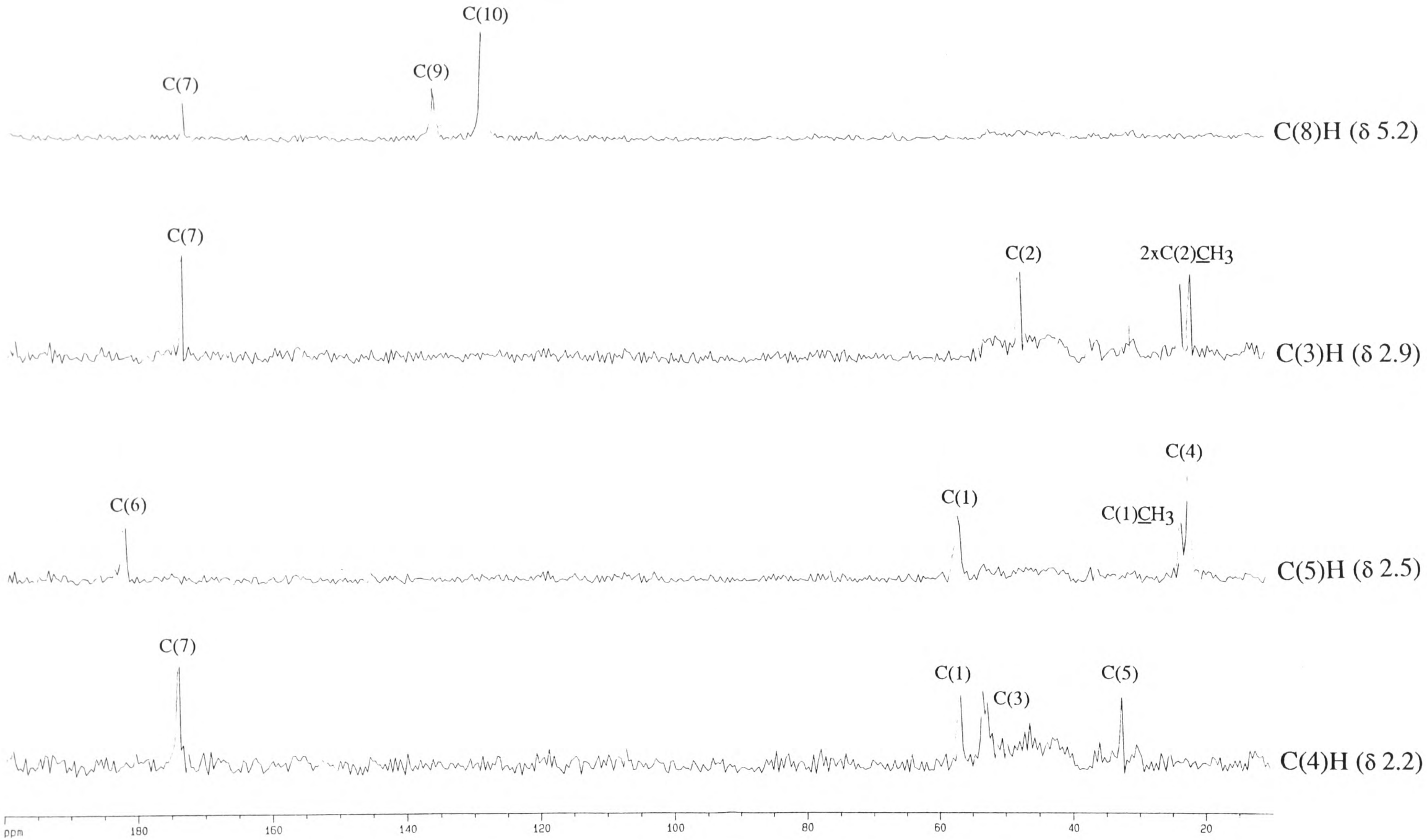
2D NMR plot parameters

CX2	25.00 cm
CX1	25.00 cm
F2PLO	8.000 ppm
F2LO	3999.84 Hz
F2PHI	0.000 ppm
F2HI	-0.16 Hz
F1PLO	190.000 ppm
F1LO	23884.97 Hz
F1PHI	-0.018 ppm
F1HI	-2.27 Hz
F2PPMCM	0.32001 ppm/cm
F2HZCM	160.00000 Hz/cm
F1PPMCM	7.60072 ppm/cm
F1HZCM	955.48962 Hz/cm

APPENDIX 2 : HMBC experiment on 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139)



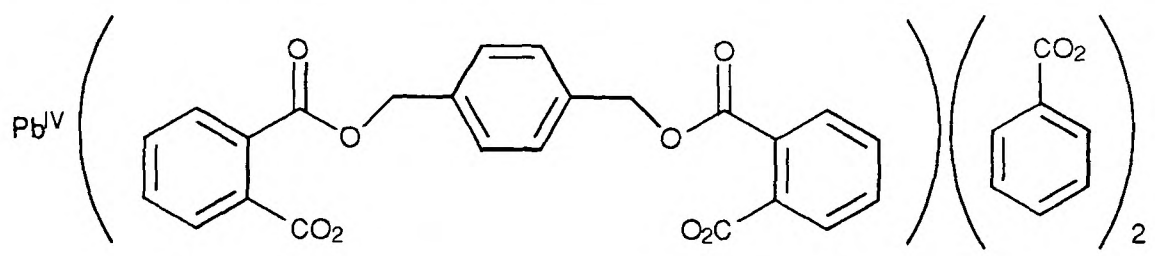
APPENDIX 2 : HMBC experiment on 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139)

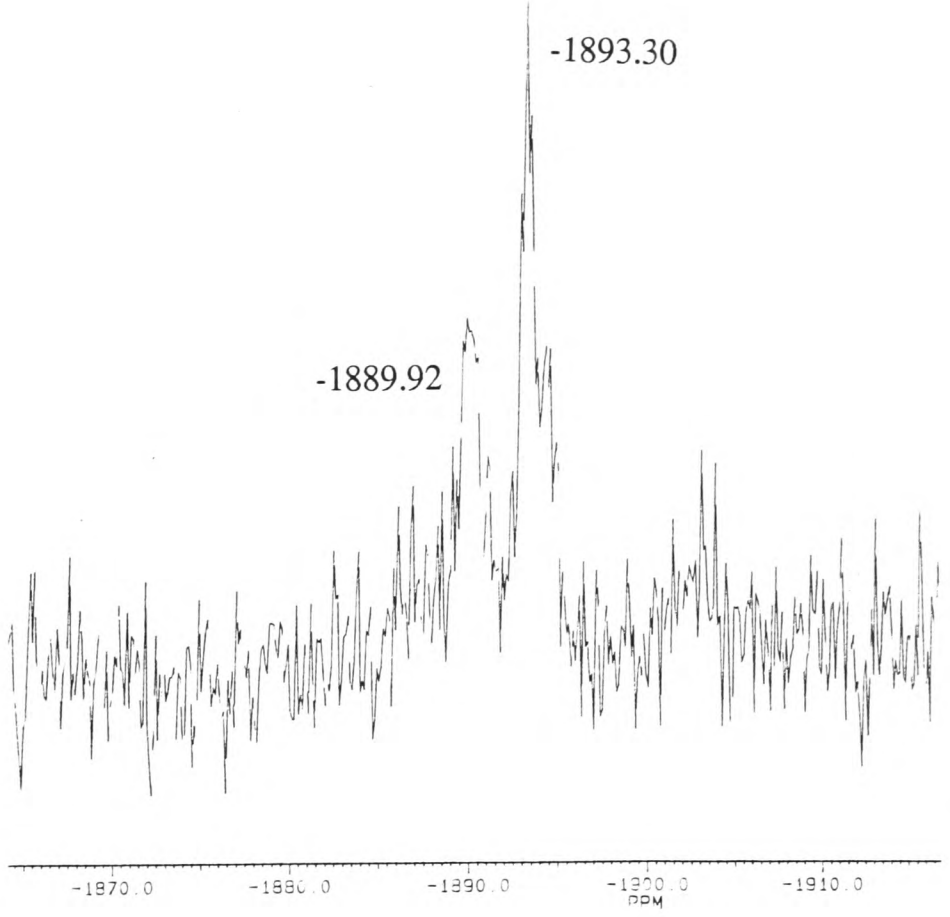


APPENDIX 3

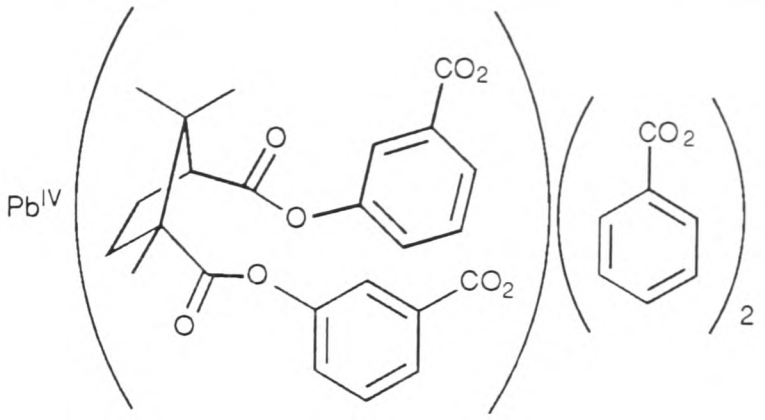
^{207}Pb NMR spectra

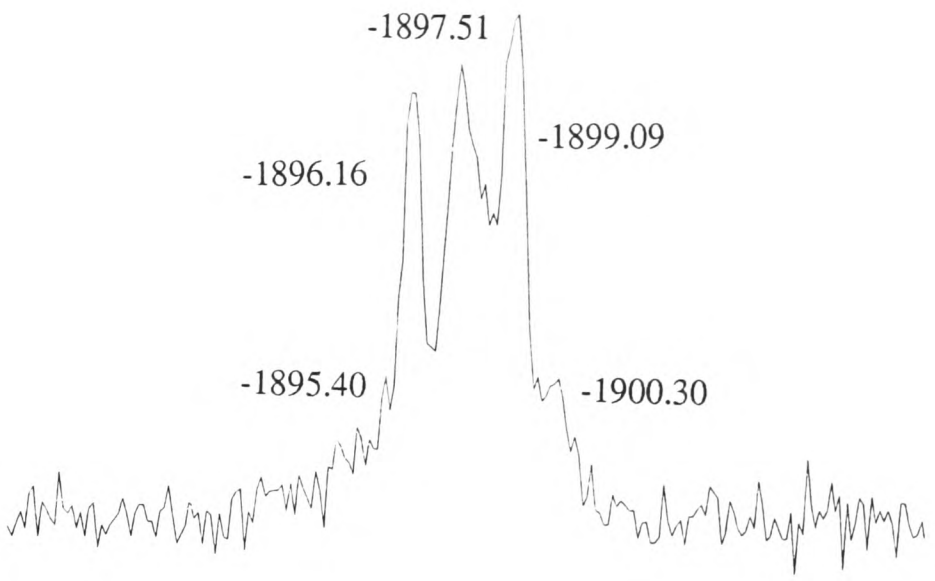
Appendix 3 : Lead(IV) [1,1'-(benzene-1,4-dimethyl)diphthalate] dibenzoate (**155**) *(253K)*



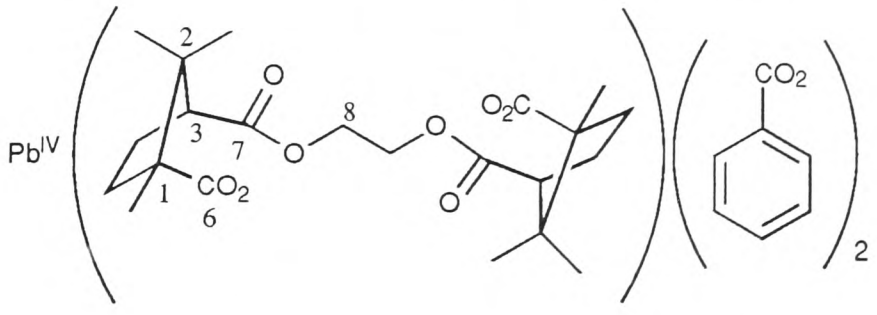


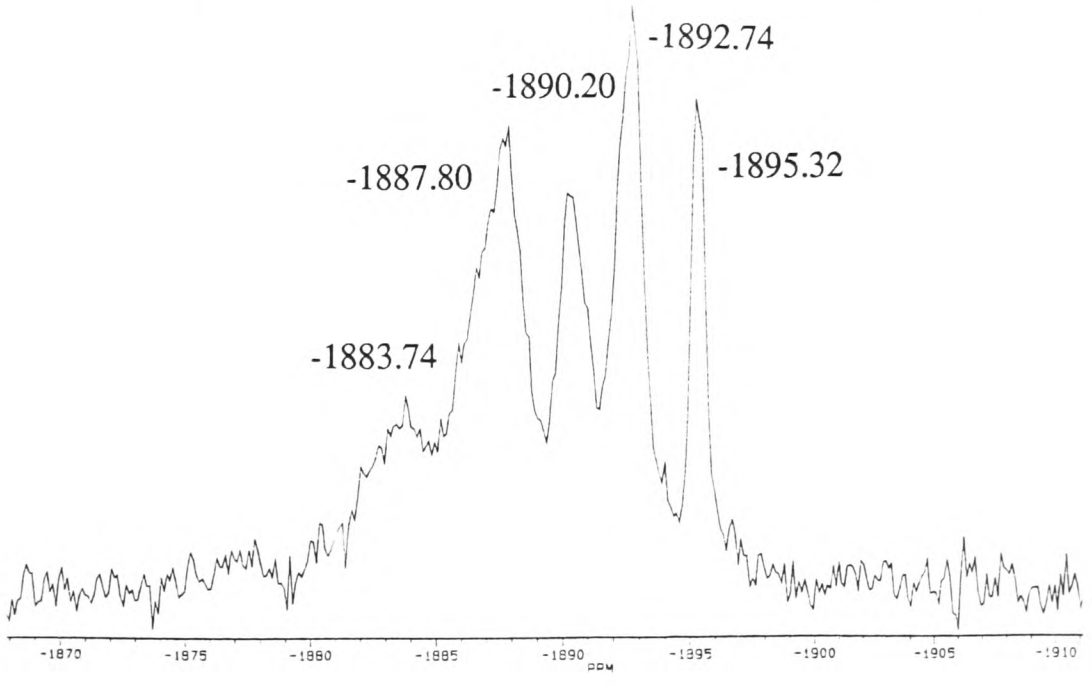
Appendix 3 : Lead(IV) [(1R, 3S)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid di(3-hydroxybenzoic acid) ester] dibenzoate* (165) *(223K)



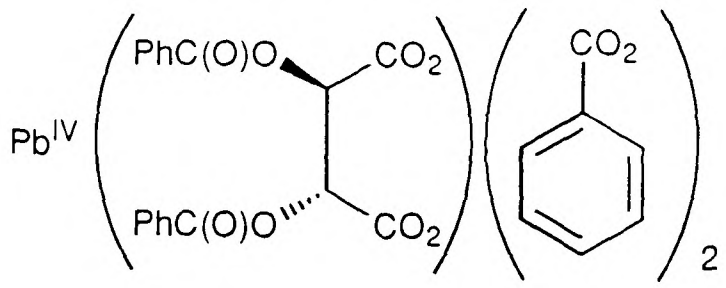


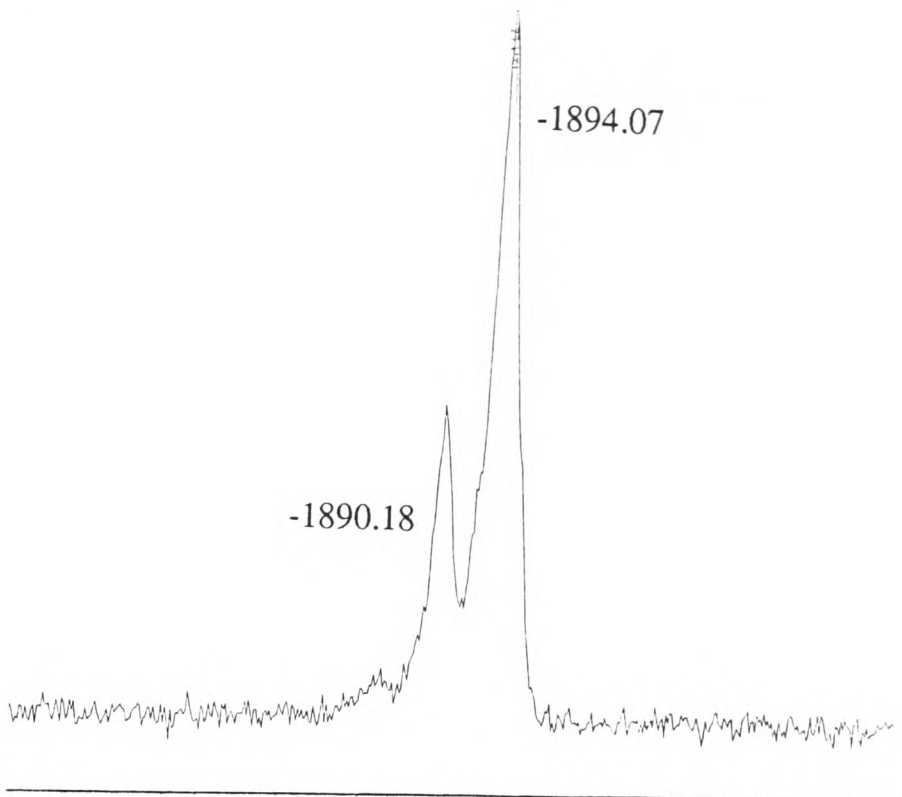
Appendix 3 : Lead(IV) {3,3'-(ethylene-1,2-dioxy)di[(1R, 3S)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} dibenzoate* (169) *(223K)



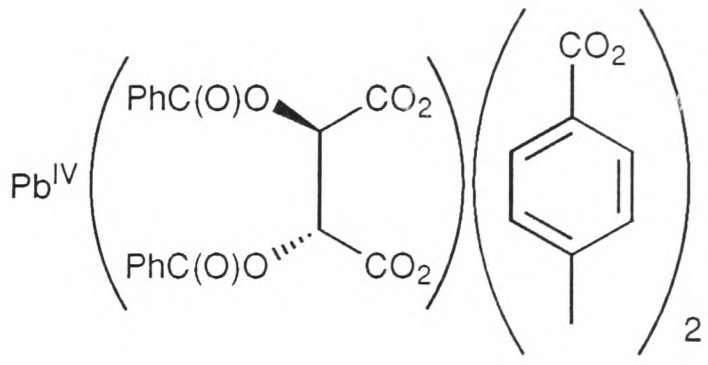


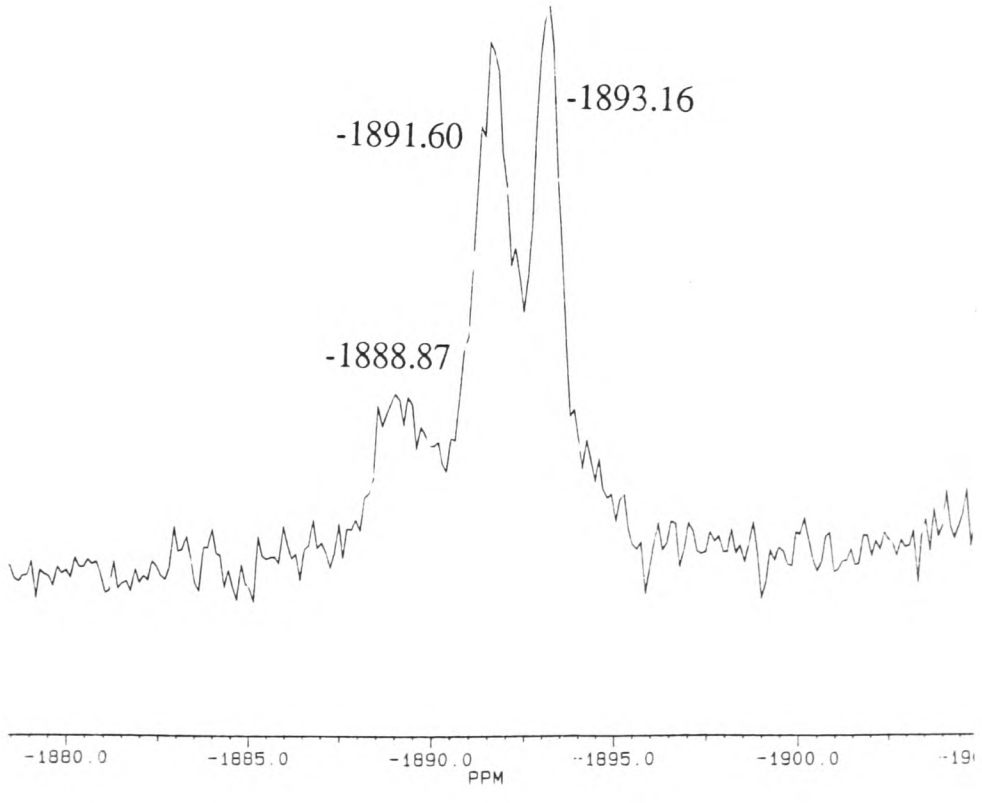
Appendix 3 : Lead(IV) dibenzoyl-L-tartrate dibenzoate (173) *(223K)*





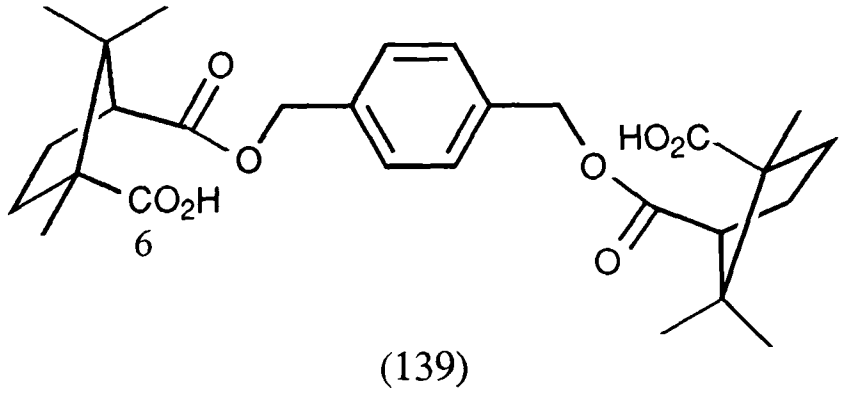
*Appendix 3 : Lead(IV) dibenzoyl-L-tartrate di-*p*-toluate* (174) *(223K)*



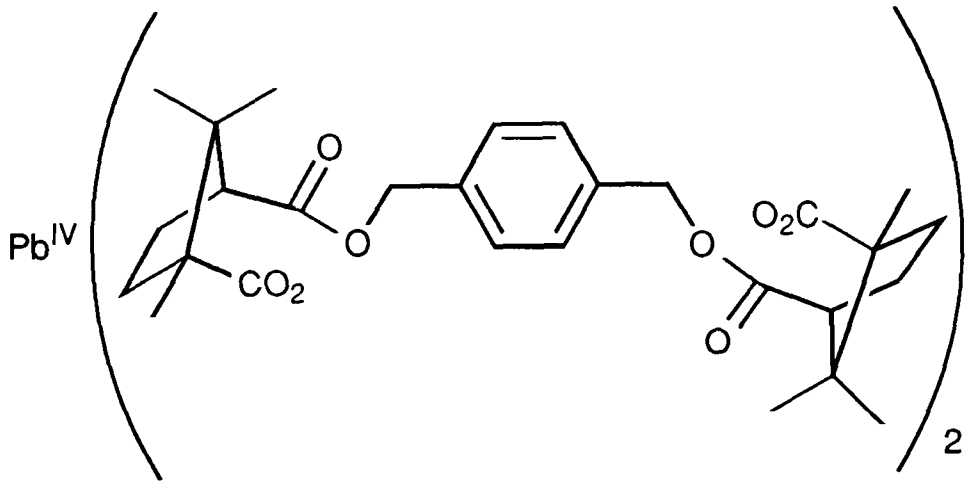


APPENDIX 4

^{1}H NMR spectra of 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139) and lead(IV) *bis*{3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} (166)

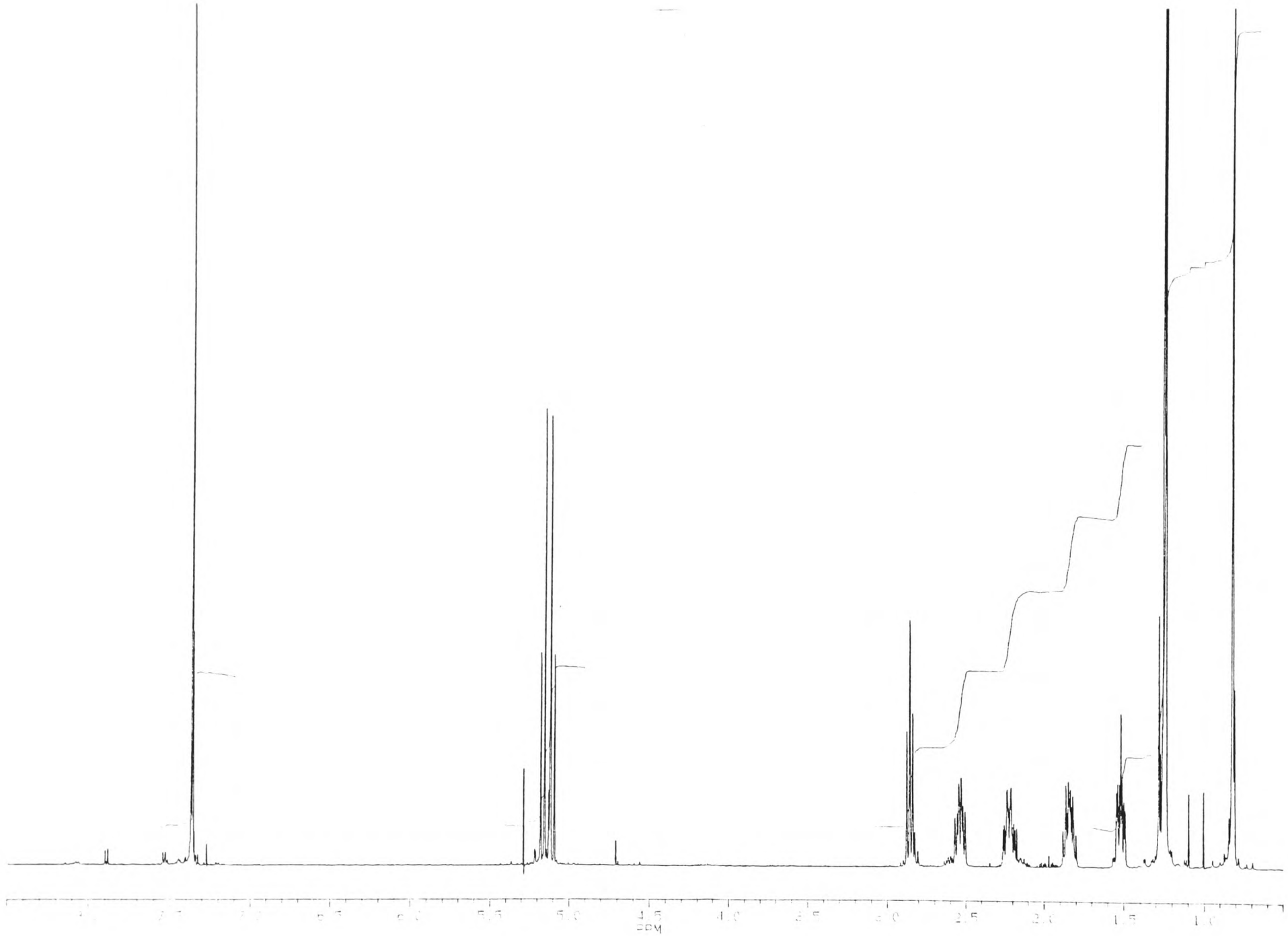


(139)

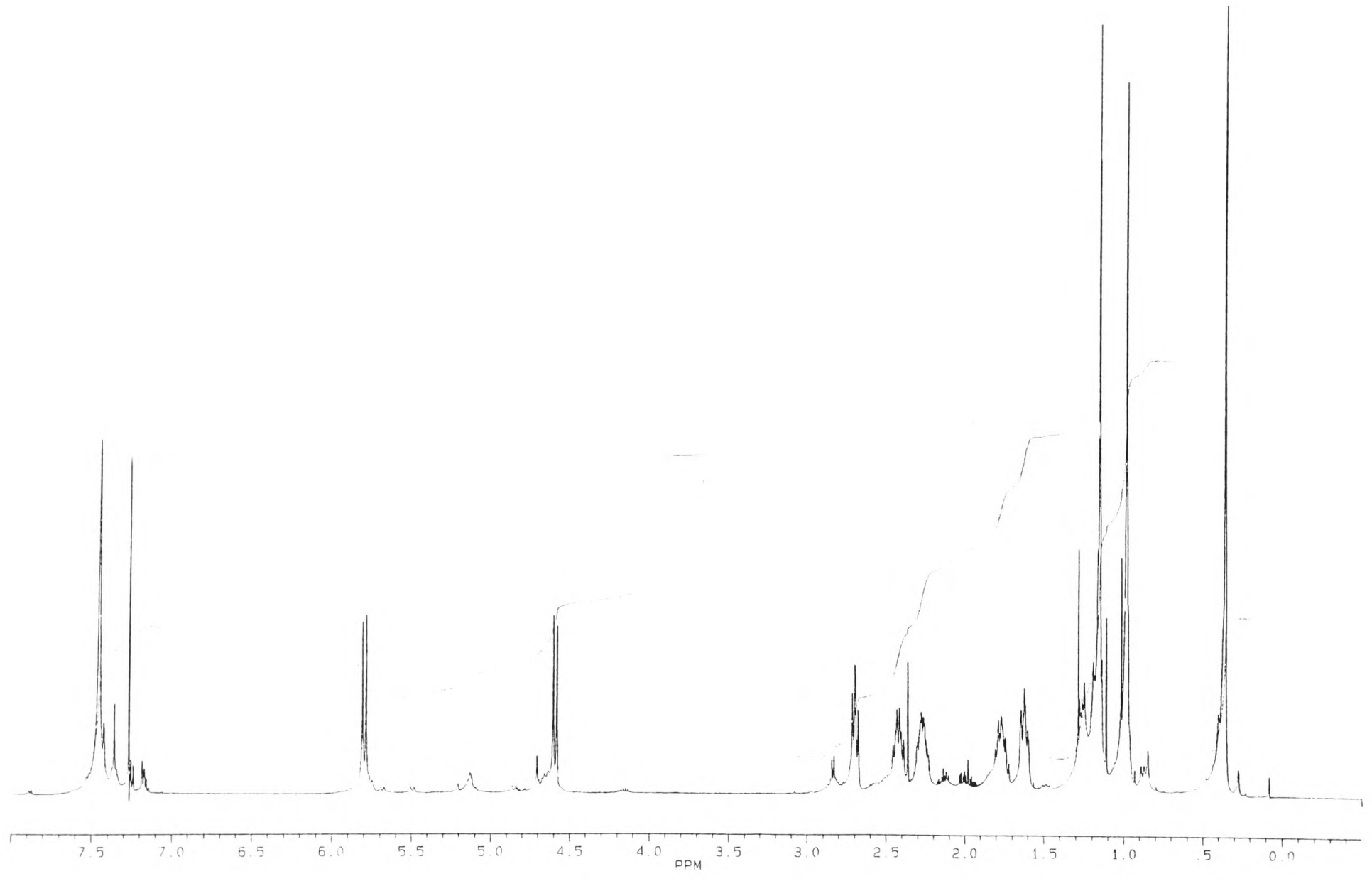


(166)

APPENDIX 4 : ^{1}H NMR spectrum of 3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate] (139)

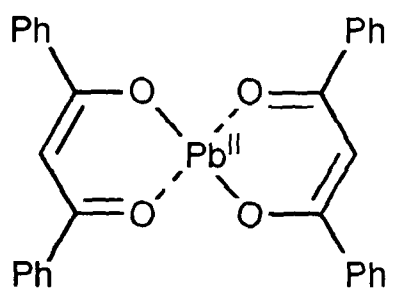


APPENDIX 4 : ^{1}H NMR spectrum of lead(IV) *bis*{3,3'-(benzene-1,4-dimethyl)di[(1*R*, 3*S*)-1,2,2-trimethylcyclopentane-1,3-dicarboxylate]} (166)



APPENDIX 5

Atomic coordinates, thermal parameters, bond lengths and angles for lead(II) di(dibenzoylmethane) (177)



Atom	x/a	y/b	z/c	U(iso)
O(1)	0.0279(5)	-0.1067(4)	0.0089(2)	0.0338
O(2)	0.1868(6)	-0.0558(4)	0.1270(2)	0.0379
O(3)	0.3341(5)	-0.0558(5)	0.0080(3)	0.0403
O(4)	0.2099(6)	0.0490(5)	-0.0860(3)	0.0490
PB(5)	0.20149(3)	0.06005(2)	0.02778(1)	0.0289
C(6)	-0.0556(7)	-0.3041(6)	-0.0191(3)	0.0309
C(7)	0.0212(7)	-0.2106(6)	0.0262(4)	0.0347
C(8)	0.2089(7)	-0.2156(6)	0.1843(3)	0.0364
C(9)	0.1557(7)	-0.1633(6)	0.1291(3)	0.0356
C(10)	-0.1179(8)	-0.4150(7)	0.0026(4)	0.0404
C(11)	0.4309(7)	-0.1927(6)	-0.0272(4)	0.0393
C(12)	0.0769(8)	-0.2394(6)	0.0811(4)	0.0372
C(13)	-0.0678(8)	-0.2797(7)	-0.0841(4)	0.0414
C(14)	0.4680(8)	-0.2028(7)	0.0370(4)	0.0452
C(15)	0.2570(7)	-0.0100(6)	-0.1246(4)	0.0349
C(16)	0.3583(8)	-0.1076(6)	-0.0419(4)	0.0376
C(17)	0.2384(8)	0.0110(7)	-0.1954(4)	0.0438
C(18)	0.1348(9)	-0.3189(7)	0.2123(4)	0.0445
C(19)	0.4613(8)	-0.2634(7)	-0.0741(5)	0.0452
C(20)	-0.1898(9)	-0.5007(7)	-0.0404(5)	0.0484
C(22)	0.188(1)	-0.3682(7)	0.2620(4)	0.0525
C(23)	-0.1388(9)	-0.3632(8)	-0.1264(4)	0.0504
C(24)	0.3382(9)	-0.1621(8)	0.2073(4)	0.0515
C(25)	-0.2004(8)	-0.4737(7)	-0.1047(5)	0.0457
C(27)	0.158(1)	0.119(1)	-0.2757(6)	0.0694
C(28)	0.3246(9)	-0.0866(7)	-0.1057(4)	0.0458
C(34)	0.320(1)	-0.3159(8)	0.2816(5)	0.0581
C(35)	0.396(1)	-0.2124(9)	0.2546(5)	0.0581
C(36)	0.278(1)	-0.0444(9)	-0.2459(5)	0.0644
C(37)	0.196(1)	0.062(1)	-0.3253(5)	0.0651
C(38)	0.174(1)	0.0928(9)	-0.2112(5)	0.0644
C(39)	0.259(1)	-0.017(1)	-0.3099(6)	0.0753
C(40)	0.528(1)	-0.3407(8)	-0.0562(6)	0.0557
C(41)	0.533(1)	-0.2834(8)	0.0536(5)	0.0538
C(42)	0.5646(9)	-0.3516(8)	0.0067(6)	0.0536

Atom	x/a	y/b	z/c	U(iso)
H(101)	-0.122(8)	-0.446(7)	0.050(4)	0.0414
H(121)	0.070(8)	-0.300(7)	0.088(4)	0.0376
H(131)	-0.024(8)	-0.204(7)	-0.099(4)	0.0420
H(141)	0.446(7)	-0.148(6)	0.079(4)	0.0445
H(181)	0.045(9)	-0.354(7)	0.199(4)	0.0443
H(191)	0.433(8)	-0.250(7)	-0.125(4)	0.0468
H(201)	-0.238(9)	-0.593(8)	-0.023(4)	0.0502
H(221)	0.131(8)	-0.450(7)	0.287(4)	0.0516
H(231)	-0.161(9)	-0.358(7)	-0.167(5)	0.0547
H(241)	0.380(9)	-0.091(8)	0.190(4)	0.0506
H(251)	-0.258(8)	-0.533(7)	-0.137(4)	0.0502
H(271)	0.10(1)	0.169(9)	-0.284(5)	0.0711
H(281)	0.342(8)	-0.130(7)	-0.135(4)	0.0479
H(341)	0.366(9)	-0.352(8)	0.314(4)	0.0620
H(351)	0.50(1)	-0.185(8)	0.262(4)	0.0605
H(361)	0.32(1)	-0.094(8)	-0.234(5)	0.0629
H(371)	0.192(9)	0.094(8)	-0.370(5)	0.0679
H(381)	0.151(9)	0.136(8)	-0.173(5)	0.0662
H(391)	0.28(1)	-0.050(9)	-0.347(5)	0.0727
H(401)	0.542(9)	-0.386(8)	-0.093(4)	0.0576
H(411)	0.547(9)	-0.287(8)	0.095(5)	0.0556
H(421)	0.631(9)	-0.403(8)	0.012(4)	0.0561

ANISOTROPIC TEMPERATURE FACTORS

Atom	U(11)	U(22)	U(33)	U(23)	U(13)	U(12)
O(1)	0.043(3)	0.024(2)	0.042(3)	0.003(2)	-0.008(2)	0.011(2)
O(2)	0.066(3)	0.023(3)	0.038(3)	-0.006(2)	-0.006(2)	0.013(2)
O(3)	0.041(3)	0.049(3)	0.043(3)	-0.002(2)	0.000(2)	0.025(3)
O(4)	0.065(4)	0.050(3)	0.047(3)	0.009(3)	-0.004(3)	0.029(3)
PB(5)	0.0310(2)	0.0223(2)	0.0366(2)	-0.0013(1)	-0.0037(1)	0.0093(1)
C(6)	0.037(4)	0.027(4)	0.035(4)	-0.009(3)	-0.006(3)	0.014(3)
C(7)	0.036(4)	0.038(4)	0.037(4)	-0.003(3)	0.001(3)	0.019(3)
C(8)	0.040(4)	0.035(4)	0.032(4)	-0.003(3)	-0.003(3)	0.006(3)
C(9)	0.044(4)	0.034(4)	0.031(4)	-0.001(3)	0.002(3)	0.012(3)
C(10)	0.044(4)	0.030(4)	0.051(4)	-0.005(3)	-0.000(4)	0.012(3)
C(11)	0.032(4)	0.040(4)	0.053(5)	0.009(4)	0.009(4)	0.013(3)
C(12)	0.048(4)	0.027(3)	0.042(4)	0.003(3)	-0.008(4)	0.012(3)
C(13)	0.044(4)	0.040(4)	0.042(4)	-0.001(4)	0.001(4)	0.015(3)
C(14)	0.033(4)	0.039(4)	0.069(6)	0.002(4)	0.001(4)	0.008(3)
C(15)	0.030(4)	0.031(4)	0.043(4)	0.002(3)	0.007(3)	0.000(3)
C(16)	0.033(4)	0.031(4)	0.050(5)	0.002(3)	0.003(3)	0.007(3)
C(17)	0.032(4)	0.050(5)	0.049(5)	0.005(4)	-0.006(3)	-0.005(4)
C(18)	0.044(5)	0.047(5)	0.041(4)	0.000(4)	-0.008(3)	0.004(4)
C(19)	0.036(4)	0.040(4)	0.071(6)	-0.008(4)	0.009(4)	0.012(3)
C(20)	0.052(5)	0.033(4)	0.075(7)	-0.005(4)	-0.008(4)	0.018(4)
C(22)	0.074(6)	0.036(5)	0.052(5)	0.009(4)	-0.009(4)	0.006(4)
C(23)	0.063(6)	0.072(6)	0.038(5)	-0.021(4)	-0.011(4)	0.029(5)
C(24)	0.060(5)	0.049(5)	0.044(5)	0.009(4)	-0.003(4)	0.008(4)
C(25)	0.039(4)	0.039(5)	0.079(7)	-0.026(4)	-0.014(4)	0.009(4)
C(27)	0.075(7)	0.080(7)	0.060(7)	0.019(6)	-0.014(5)	0.009(6)
C(28)	0.067(6)	0.044(5)	0.038(4)	-0.009(3)	-0.003(4)	0.024(4)
C(34)	0.079(7)	0.065(6)	0.047(5)	0.011(4)	-0.021(5)	0.019(5)
C(35)	0.052(5)	0.069(7)	0.061(6)	0.012(5)	-0.022(5)	0.002(5)
C(36)	0.070(7)	0.070(7)	0.052(6)	-0.004(5)	-0.002(5)	0.015(5)
C(37)	0.075(7)	0.078(8)	0.054(6)	0.018(6)	-0.012(6)	-0.028(6)
C(38)	0.073(7)	0.069(7)	0.057(6)	0.005(5)	-0.019(5)	0.016(5)
C(39)	0.083(8)	0.094(9)	0.050(6)	-0.005(6)	0.000(6)	0.003(7)
C(40)	0.056(6)	0.039(5)	0.089(7)	-0.010(5)	0.012(5)	0.017(4)

C(41)	0.054(6)	0.047(5)	0.070(6)	0.013(5)	-0.002(5)	0.019(4)
C(42)	0.041(5)	0.039(5)	0.109(9)	0.010(5)	0.003(5)	0.017(4)

BOND LENGTHS (Å)

O(1) - PB(5)	2.295(5)
O(1) - C(7)	1.299(9)
O(2) - PB(5)	2.459(5)
O(2) - C(9)	1.253(8)
O(3) - PB(5)	2.290(5)
O(3) - C(16)	1.270(9)
O(4) - PB(5)	2.345(6)
O(4) - C(15)	1.265(9)
C(6) - C(7)	1.50(1)
C(6) - C(10)	1.38(1)
C(6) - C(13)	1.38(1)
C(7) - C(12)	1.36(1)
C(8) - C(9)	1.49(1)
C(8) - C(18)	1.38(1)
C(8) - C(24)	1.38(1)
C(9) - C(12)	1.43(1)
C(10) - C(20)	1.40(1)
C(10) - H(101)	1.03(8)
C(11) - C(14)	1.39(1)
C(11) - C(16)	1.49(1)
C(11) - C(19)	1.39(1)
C(12) - H(121)	0.73(8)
C(13) - C(23)	1.37(1)
C(13) - H(131)	0.94(8)
C(14) - C(41)	1.40(1)
C(14) - H(141)	1.15(8)
C(15) - C(17)	1.50(1)
C(15) - C(28)	1.39(1)
C(16) - C(28)	1.40(1)
C(17) - C(36)	1.37(1)
C(17) - C(38)	1.40(1)
C(18) - C(22)	1.38(1)
C(18) - H(181)	0.93(8)
C(19) - C(40)	1.38(1)
C(19) - H(191)	1.11(8)
C(20) - C(25)	1.37(1)
C(20) - H(201)	1.14(9)
C(22) - C(34)	1.38(1)
C(22) - H(221)	1.12(8)
C(23) - C(25)	1.38(1)
C(23) - H(231)	0.87(9)
C(24) - C(35)	1.38(1)
C(24) - H(241)	0.91(9)
C(25) - H(251)	1.03(8)
C(27) - C(37)	1.36(2)
C(27) - C(38)	1.38(1)
C(27) - H(271)	1.0(1)
C(28) - H(281)	0.85(8)
C(34) - C(35)	1.38(1)
C(34) - H(341)	1.00(9)
C(35) - H(351)	1.00(9)
C(36) - C(39)	1.38(2)
C(36) - H(361)	0.85(9)
C(37) - C(39)	1.36(2)
C(37) - H(371)	1.0(1)
C(38) - H(381)	1.0(1)
C(39) - H(391)	0.9(1)
C(40) - C(42)	1.36(2)

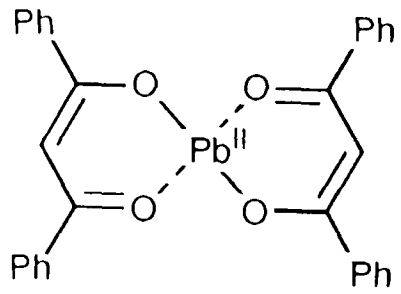
C(40) - H(401)	0.98(9)
C(41) - C(42)	1.38(2)
C(41) - H(411)	0.86(9)
C(42) - H(421)	1.07(9)

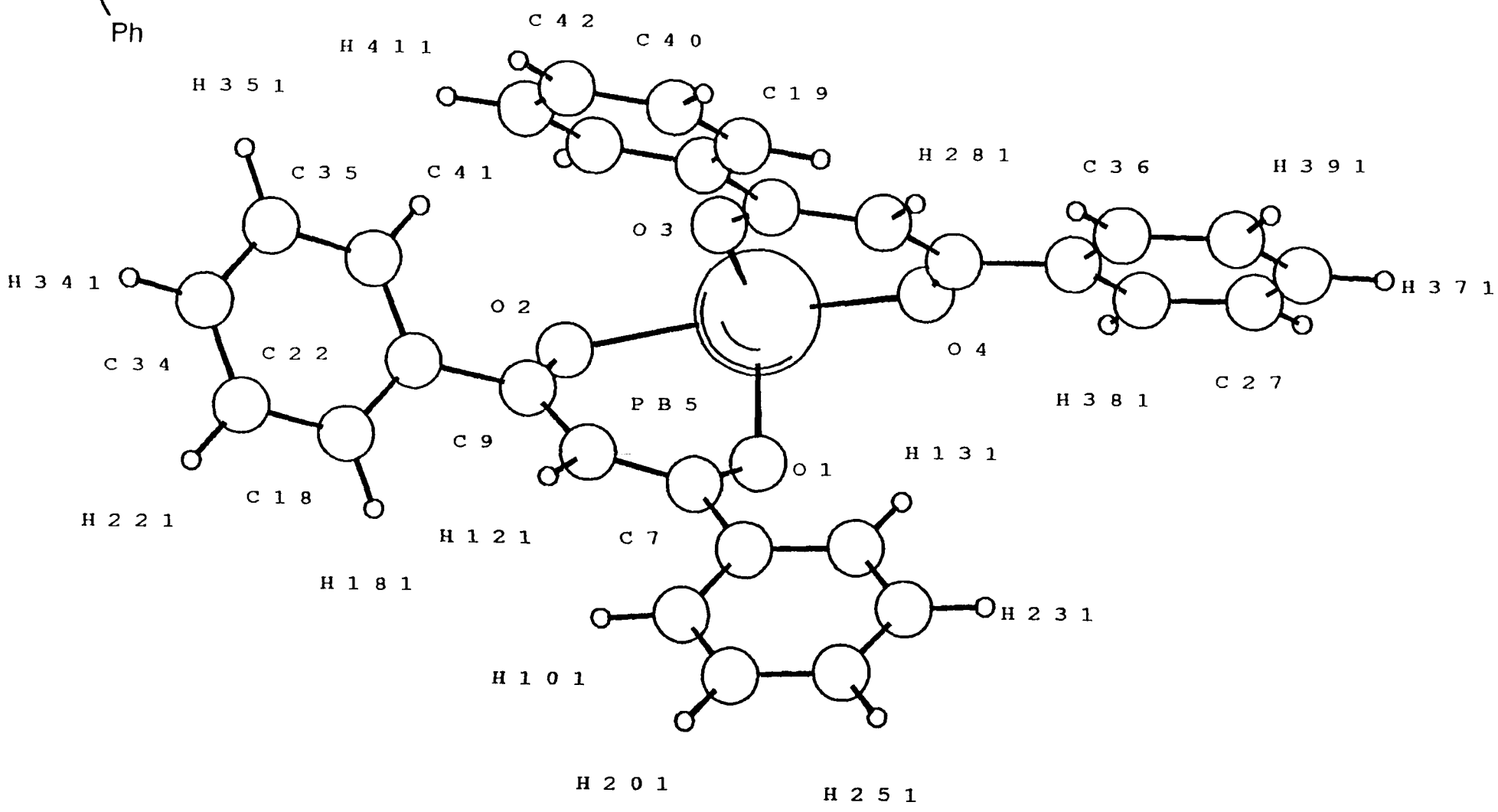
BOND ANGLES (DEGREES)

C(7) - O(1) - PB(5)	127.8(4)
C(9) - O(2) - PB(5)	125.6(4)
C(16) - O(3) - PB(5)	134.3(5)
C(15) - O(4) - PB(5)	133.2(5)
O(2) - PB(5) - O(1)	74.7(2)
O(3) - PB(5) - O(1)	82.8(2)
O(3) - PB(5) - O(2)	74.6(2)
O(4) - PB(5) - O(1)	79.3(2)
O(4) - PB(5) - O(2)	142.2(2)
O(4) - PB(5) - O(3)	75.4(2)
C(10) - C(6) - C(7)	121.5(7)
C(13) - C(6) - C(7)	119.9(6)
C(13) - C(6) - C(10)	118.6(7)
C(6) - C(7) - O(1)	115.5(6)
C(12) - C(7) - O(1)	125.3(7)
C(12) - C(7) - C(6)	119.1(6)
C(18) - C(8) - C(9)	122.3(7)
C(24) - C(8) - C(9)	119.5(7)
C(24) - C(8) - C(18)	118.2(7)
C(8) - C(9) - O(2)	117.8(6)
C(12) - C(9) - O(2)	124.8(6)
C(12) - C(9) - C(8)	117.4(6)
C(20) - C(10) - C(6)	120.6(8)
H(101)- C(10) - C(6)	128.3(44)
H(101)- C(10) - C(20)	111.0(43)
C(16) - C(11) - C(14)	117.9(7)
C(19) - C(11) - C(14)	118.7(7)
C(19) - C(11) - C(16)	123.4(8)
C(9) - C(12) - C(7)	127.4(7)
H(121)- C(12) - C(7)	120.1(67)
H(121)- C(12) - C(9)	112.5(66)
C(23) - C(13) - C(6)	121.0(8)
H(131)- C(13) - C(6)	118.0(49)
H(131)- C(13) - C(23)	121.0(49)
C(41) - C(14) - C(11)	120.0(8)
H(141)- C(14) - C(11)	123.6(38)
H(141)- C(14) - C(41)	116.4(38)
C(17) - C(15) - O(4)	114.7(7)
C(28) - C(15) - O(4)	124.9(7)
C(28) - C(15) - C(17)	120.4(7)
C(11) - C(16) - O(3)	113.8(7)
C(28) - C(16) - O(3)	124.5(7)
C(28) - C(16) - C(11)	121.8(7)
C(36) - C(17) - C(15)	125.2(8)
C(38) - C(17) - C(15)	117.6(8)
C(38) - C(17) - C(36)	117.2(9)
C(22) - C(18) - C(8)	121.5(8)
H(181)- C(18) - C(8)	119.5(49)
H(181)- C(18) - C(22)	118.9(50)
C(40) - C(19) - C(11)	119.7(9)
H(191)- C(19) - C(11)	115.8(41)
H(191)- C(19) - C(40)	124.5(41)
C(25) - C(20) - C(10)	119.5(8)
H(201)- C(20) - C(10)	120.7(42)
H(201)- C(20) - C(25)	119.8(42)
C(34) - C(22) - C(18)	119.0(8)

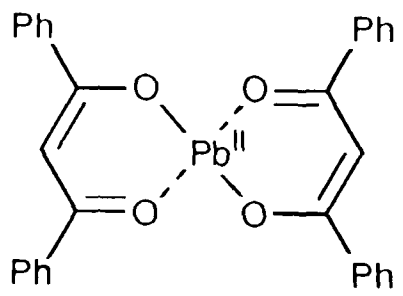
H(221)- C(22) - C(18)	124.5(43)
H(221)- C(22) - C(34)	116.5(42)
C(25) - C(23) - C(13)	120.4(9)
H(231)- C(23) - C(13)	130.2(61)
H(231)- C(23) - C(25)	109.2(60)
C(35) - C(24) - C(8)	121.5(8)
H(241)- C(24) - C(8)	114.8(54)
H(241)- C(24) - C(35)	123.7(55)
C(23) - C(25) - C(20)	119.9(8)
H(251)- C(25) - C(20)	121.8(46)
H(251)- C(25) - C(23)	118.2(47)
C(38) - C(27) - C(37)	121.8(12)
H(271)- C(27) - C(37)	120.9(60)
H(271)- C(27) - C(38)	116.3(61)
C(16) - C(28) - C(15)	126.4(7)
H(281)- C(28) - C(15)	118.3(57)
H(281)- C(28) - C(16)	115.2(57)
C(35) - C(34) - C(22)	120.6(8)
H(341)- C(34) - C(22)	122.2(52)
H(341)- C(34) - C(35)	117.2(52)
C(34) - C(35) - C(24)	119.1(9)
H(351)- C(35) - C(24)	120.5(53)
H(351)- C(35) - C(34)	118.9(53)
C(39) - C(36) - C(17)	120.9(11)
H(361)- C(36) - C(17)	113.5(69)
H(361)- C(36) - C(39)	125.6(70)
C(39) - C(37) - C(27)	117.9(11)
H(371)- C(37) - C(27)	115.5(56)
H(371)- C(37) - C(39)	125.2(55)
C(27) - C(38) - C(17)	120.3(11)
H(381)- C(38) - C(17)	115.8(56)
H(381)- C(38) - C(27)	123.6(57)
C(37) - C(39) - C(36)	121.8(12)
H(391)- C(39) - C(36)	128.4(68)
H(391)- C(39) - C(37)	109.7(66)
C(42) - C(40) - C(19)	122.1(9)
H(401)- C(40) - C(19)	111.9(53)
H(401)- C(40) - C(42)	126.0(53)
C(42) - C(41) - C(14)	120.8(10)
H(411)- C(41) - C(14)	113.3(63)
H(411)- C(41) - C(42)	125.9(63)
C(41) - C(42) - C(40)	118.7(8)
H(421)- C(42) - C(40)	113.9(47)
H(421)- C(42) - C(41)	126.5(47)

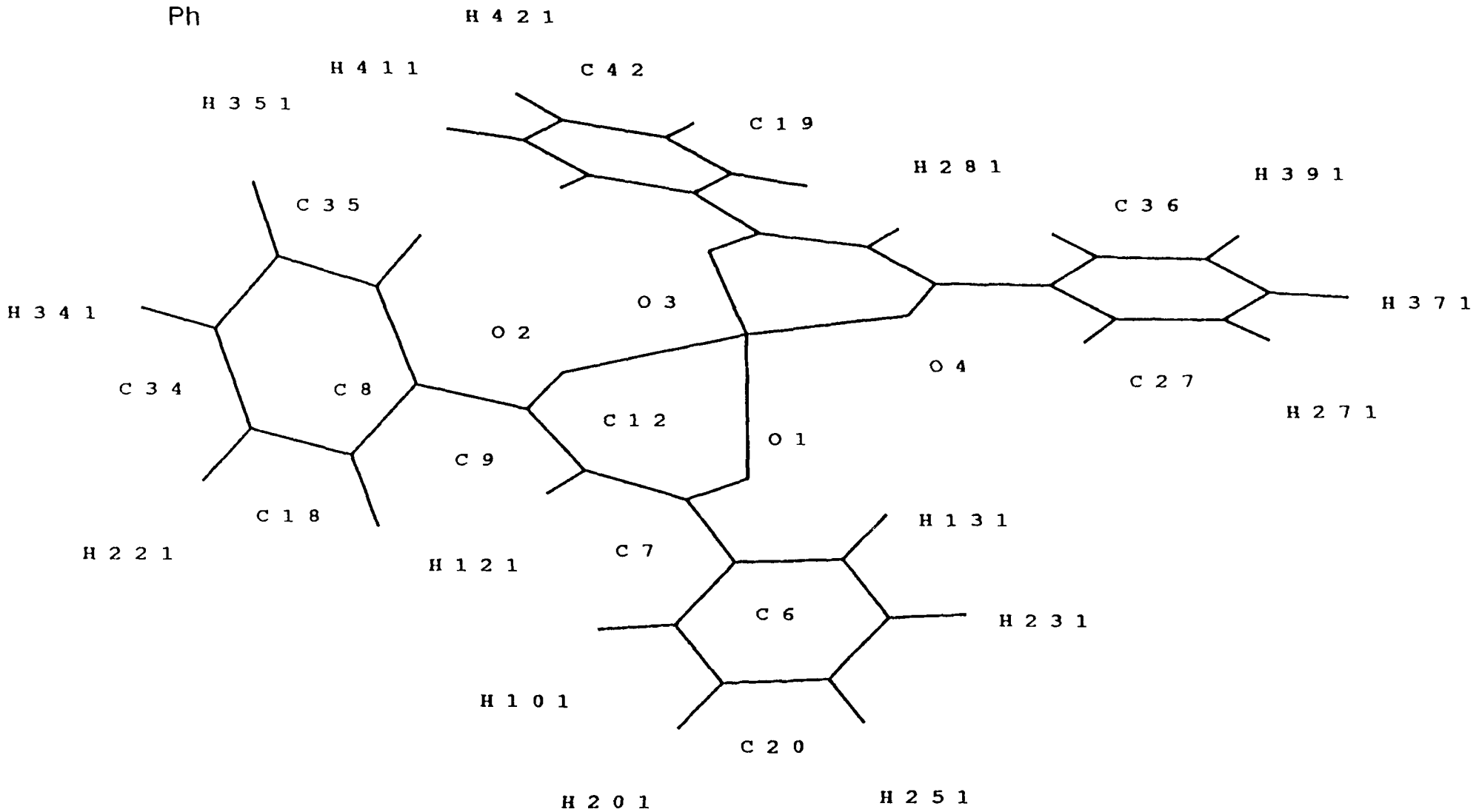
APPENDIX 5 : X-ray crystal structure of lead(II) di(dibenzoylmethane) (177)





APPENDIX 5 : X-ray crystal structure of lead(II) di(dibenzoylmethane) (177)





APPENDIX 6

Analysis of optically active compounds

Methyl 1-phenyl-2-oxocyclopentanecarboxylate (191)

Method summary

A few microlitres of sample were diluted in 200µl of ethanol in a vial insert and 0.5µl was injected into a split injector. The enantiomers were separated on an FS-Lipodex E column and were determined using an FID detector.

Standard

A racemic mixture was used (Spectrum overleaf).

Apparatus

2ml Hewlett Packard autosampler vials

2ml vial crimpers

100µl pipettor

1µl syringe

HP5890 Series 11 GC with FID detector and packed column injector

HP3396 Integrator

Chrom Perfect (version 6) data system

Chromatographic conditions

Column FS-LIPODEX E length=25m, id=0.25mm

Injection 0.5µl

Carrier gas Helium 1ml/min, 27.5cm/sec, 100:1 split

Hydrogen 30ml/min

Air 400ml/min

Injector temperature 150°C

Detector temperature 200°C

Oven temperature 70°C for 0.5 min then to 110°C at 20°C/min followed by an increase of 1°C/min to 130°C

GC Input Range=0 (autorange)

Methyl 1-phenyl-2-oxocycloheptanecarboxylate (193)

Method summary

A few microlitres of sample were diluted in 200µl of ethanol in a vial insert and 0.5µl was injected into a split injector. The enantiomers were separated on a Chiraldex Gamma-Cyclodextrin Trifluoroacetyl column and were determined using an FID detector.

Standard

A racemic mixture was used (Spectrum overleaf).

Apparatus

2ml Hewlett Packard autosampler vials

2ml vial crimpers

100µl pipettor

1µl syringe

HP5890 Series 11 GC with FID detector and packed column injector

HP3396 Integrator

Chrom Perfect (version 6) data system

Chromatographic conditions

Column Chiraldex Gamma-Cyclodextrin Trifluoroacetyl length=10m, id=0.25mm

Injection 0.5µl

Carrier gas Helium 1ml/min, 36.9cm/sec, 100:1 split

Hydrogen 30ml/min

Air 400ml/min

Injector temperature 150°C

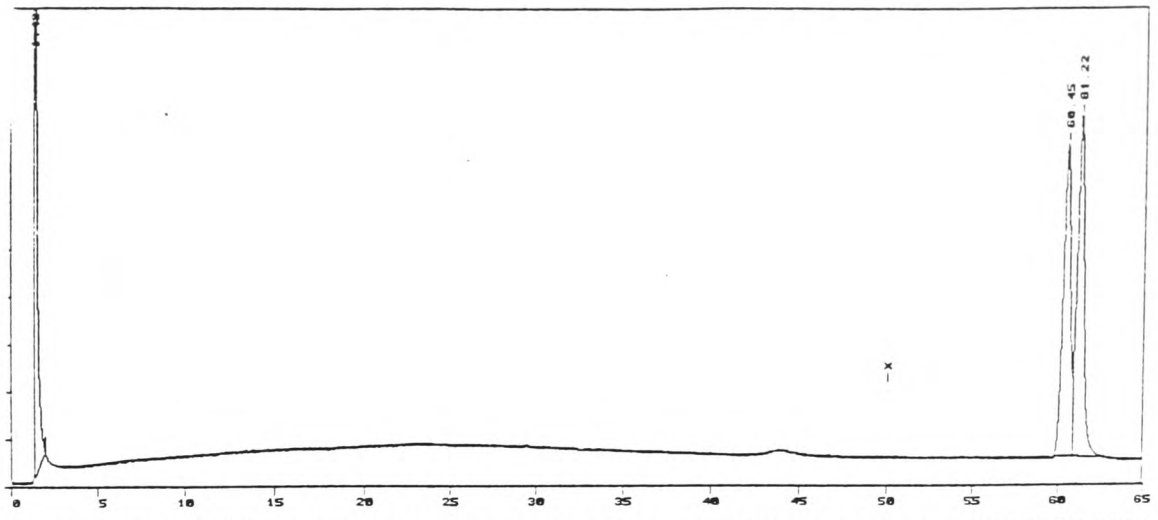
Detector temperature 200°C

Oven temperature 70°C for 0.5 min then to 130°C at 20°C/min

GC Input Range=0 (autorange)

Appendix 6 : Racemic methyl 1-phenyl-2-oxocyclopentanecarboxylate (191)

ile=D:\CP\DATA1\OPTICAL.30R Date printed=09-19-1994 Time= 13:02:13
ample Name=E132 LIPODEX COLUMN
.0 to 65.0 min. Low Y=0.339 High Y=0.739 mv Span=0.4

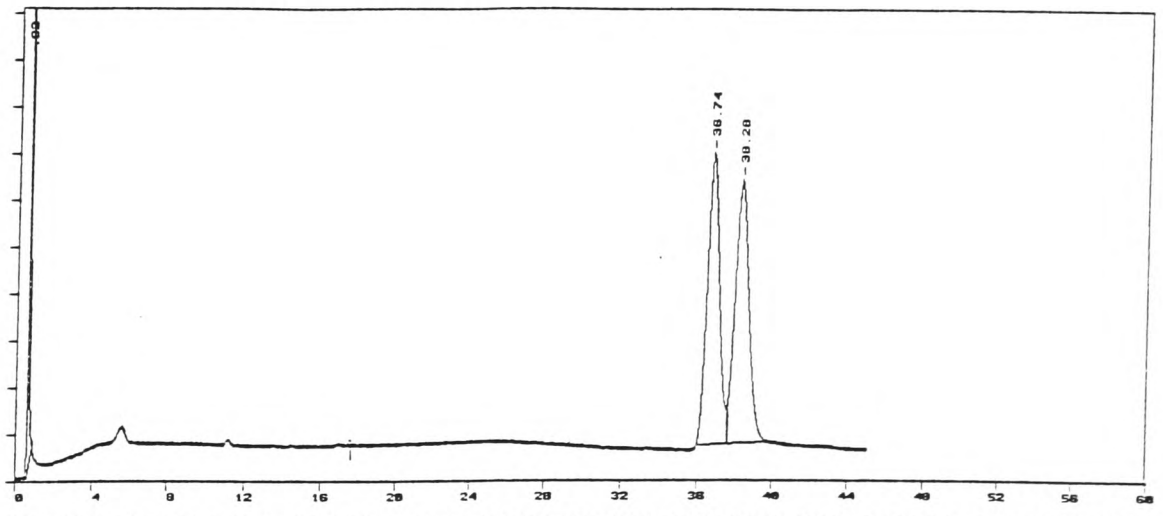



```
**************************************************************************
* METHOD....UNCALIBRATED SAMPLES      CAL.FILE....D:\CP\DATA1\UNKNOWNS.CAL*
* TODAY'S DATE....09-19-1994          TIME.....13:02:30                   *
* AREA FILE D:\CP\DATA1\OPTICAL.30R  DATE TAKEN SEP 19, 1994  11:48:15   *
* SAMPLE NAME.....E132 LIPODEX COLUMND:\CP\DATA1\OPTICAL.30R  Dil= 1     *
**************************************************************************
```

Ret Time (min)	Peak Type	Peak Height	Peak Area		Peak Name	Normalized Amount
1.430	BB	859351	1101542	1101541.75		98.6%
60.446	BV	262	7679	7679.10		0.7%
61.224	VB	285	8384	8383.79		0.8%

Appendix 6 : Racemic methyl 1-phenyl-2-oxocycloheptanecarboxylate (193)

D:\CP\DATA1\OPTICAL.18R Date printed=09-19-1994 Time= 11:24:26
ample Name=E152 RACEMATE
0.0 to 60.0 min. Low Y=0.332 High Y=0.482 mv Span=0.15




```
**************************************************************************
* METHOD....UNCALIBRATED SAMPLES      CAL.FILE....D:\CP\DATA1\UNKNOWNS.CAL*
* TODAY'S DATE....09-19-1994          TIME.....11:24:51                   *
* AREA FILE D:\CP\DATA1\OPTICAL.18R  DATE TAKEN OCT  9, 1994  10:56:05   *
* SAMPLE NAME.....E152 RACEMATE       D:\CP\DATA1\OPTICAL.18R  Dil= 1     *
**************************************************************************
```

Ret Time (min)	Peak Type	Peak Height	Peak Area		Peak Name	Normalized Amount
0.618	BB	579544	868790	868789.81		99.1%
36.740	BV	93	4065	4065.25		0.5%
38.280	VB	84	4231	4231.26		0.5%