The Synthetic Applications of Organomercurials Arising by the Cleavage of Cyclopropane Derivatives

by

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Abstract

Organomercurial esters 2a-c obtained from cyclopropyl alcohols 1a-c in three or five (depending on whether the system is cis or trans) steps, react with organocuprates via an intramolecular addition across the carbonyl bond to generate the corresponding lactolate. Quenching of the latter intermediate with water leads to the lactol 3a,c in the cycloheptane and cyclopentane series, whereas the open hydroxyketone 4b is formed in the cyclohexane series. Quenching of the lactolate with BF$_3$Et$_2$O gives different products, as demonstrated for the cyclohexane series.

The Pd(II)-catalysed carbonylation of chloromercurio alcohols 5a-c allows the construction of either cis- or trans-fused lactone rings 6a-c. The stereochemistry of the lactone annulation is controlled by the Hg(II) reagent to initially open the cyclopropane ring, in conjunction with orthogonal protection.
To Mum and Dad
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**Abbreviations**

**Ac** - COCH$_3$

**NOE** - Nuclear Overhauser Effect

**LUMO** - Lowest Unoccupied Molecular Orbital

**HOMO** - Highest Occupied Molecular Orbital

**Me** - Methyl

**Et** - Ethyl

**Bu** - Butyl

**'Bu** - Tertiary Butyl

**Ph** - Phenyl

**THF** - Tetrahydrofuran

**Δ** - Heat

**DME** - 1,2-Dimethoxyethane

**TFA** - Trifluoroacetate

**acac** - Acetylacetonate

**TLC** - Thin Layer Chromatography

**DMSO** - Dimethyl Sulfoxide

**PCC** - Pyridinium Chlorochromate

**DMAP** - 4-Dimethylaminopyridine

**p-BQ** - *para*-Benzoquinone

**TMS** - Tetramethysilane
Chapter 1

Introduction
1.1 The Stereochemistry of Cyclopropane Cleavage

The use of metals in organic synthesis often allows synthetic goals to be achieved that cannot be attained by traditional methods. Due to their exceptional steric and electronic properties metals have the potential to control reactivity and to enhance the selectivity and efficiency of chemical reactions. Further avenues may be opened by transmetallation, a methodology that combines (often in one pot) the benefits of specific reactivities of two or more metals in tandem reactions.

Stereocontrolled cyclopropanation, which is often metal catalysed, followed by ring opening with metal complexes serves as an attractive strategy for the construction of up to three contiguous chiral centres. The value of this strategy may be increased if cleavage by the metal produces a stable organometallic which can then undergo further transformations e.g. transmetallations. However the mechanism for the cleavage of cyclopropanes was poorly understood until very recently, and this considerably hampered a wider synthetic application of this methodology.

Scheme I

There are two possible mechanisms for the electrophilic opening of cyclopropanes, "edge" or "corner" attack (scheme I). Edge (or syn) attack occurs with retention of configuration at the centre of electrophilic attachment. This was known to occur with
transition metals (Pd, Pt, Rh)\(^9\) and halogens (Cl\(_2\) and Br\(_2\))\(^1\), which are reagents capable of back donation. The alternative is corner\(^6,11\) (or anti) attack, which occurs with inversion of configuration. Until recently, there was a lack of direct evidence in support of this mechanism. Then in the late eighties and early nineties, evidence was found to show that mercury(II), thallium(III)\(^15\) and proton,\(^12\) all of which are poor back donors, are capable of stereospecific corner activation.

Scheme II

Coxon et al.\(^12\) reacted the tricyclic derivative 1 (Scheme II) with mercury acetate in methanol to show that mercury opened the cyclopropane with inversion at C4. To prove the configuration, they reduced the mercury (with retention of configuration) with sodium mercury amalgam in sodium deuteroxide to produce the deuterated ether 3. They then compared this with an authentic sample of 3, made by known methods, to show they were identical. They also demonstrated that protons attack via a corner mechanism by reacting the same system with D\(^+\).
Lambert et al.\(^2\) also showed using cis-trideuterated cyclopropane 4 (Scheme III) that mercury opens cyclopropanes by a corner mechanism. This conclusion was based on the magnitude and temperature dependence of the proton-proton vicinal coupling constants, which complied with inversion at the centre of mercury attack.

At the same time Kocovsky and co-workers showed that using the cyclopropanated steroid skeleton 6 thallium(III) was also capable of corner attack\(^1\) (Scheme IV). Utilising isotopic labelling (\(^2\)H and \(^18\)O) and NOE experiments on the resulting lactols, 10 and 11, they were able to show the reaction occurs by a double inversion pathway. This was achieved by labelling the β position of the cyclopropane with deuterium to produce 7. Upon reaction with thallium(III) lactol 11 was produced, which was also shown to be labelled in the β position. This can be explained by initial corner attack by thallium, with inversion, followed by the nucleophilic substitution of thallium by oxygen, which is known to occur with inversion, to give the lactol. Reaction of the \(^18\)O labelled aldehyde produced a lactol with a labelled ether oxygen ruling out the possibility of the thallium being substituted by water to produce an hydroxyaldehyde which would cyclise to give the same lactol.
This methodology was repeated using mercury(II). It was found that, unlike the thallium example, the organomercurial intermediate 12 was a stable, isolable compound that did not instantaneously convert to the lactol (Scheme V). Due to the rotation about the C(3)-C(4) bond the configuration at C(4) could not be assigned, therefore the conformation about this bond had to be fixed. This was achieved by catalytically transmetallating the mercury with palladium(II) (which is known to occur with retention of configuration) to furnish the lactol 10. The use of deuterium labelling again showed that mercury must open the cyclopropane with inversion i.e. by corner attack.
Scheme V

6. R=H
7. R=D

1. Hg(NO₃)₂
2. KBr
Inversion

12. R=H
13. R=D

Retention

Pd²⁺

10. R=H
11. R=D

H₂O
Inversion

14. R=H
15. R=D
1.2 The mechanism of cyclopropane cleavage

Why do poor back donors prefer corner attack? Coxon offered an explanation\textsuperscript{12} which took orbital considerations into account.

**Scheme VI**

1. Interaction of the LUMO of the electrophile with the degenerate HOMOs of cyclopropane

- **corner**

- **edge**

2. Back donation of the d\textsubscript{p}-electrons to the LUMOs of cyclopropane

Attack at the corner of the cyclopropane by the electrophiles deuteron and mercuric ion is due to the favourable interaction of both of the degenerate HOMOs of the cyclopropane with the H 1s and the d\textsubscript{p} LUMO of the electrophile respectively (Scheme VI part 1.). For edge attack only the HOMO / LUMO interaction of the symmetrical Walsh
orbital is favourable, the interaction with the unsymmetrical orbital being unfavoured. Therefore since corner attack gives favourable interactions with both degenerate molecular orbitals it will be the preferred mode of attack. However a favourable interaction of the LUMO Walsh orbital of cyclopropane with the d-orbitals from transition metals capable of back donation (Pd, Pt, Rh) allows oxidative addition at the edge (part 2). This interaction compensates for the more favoured σ-interaction at the corner of cyclopropane between the HOMO Walsh orbital and the LUMO orbitals of the electrophile. In the case of mercury the donor ability\(^7\) of the d- orbitals is small, so the d- HOMO / cyclopropane LUMO interaction has little or no effect.

1.3 Applications of organomercurials

It should be noted that organometallics vary vastly in their reactivities; some are highly reactive e.g. alkylolithiums, Grignard reagents, organocuprates etc., while others are relatively stable e.g. R-Hg, R-B and R-Sn. This fact gives us a very useful tool for the further tuning of reactivity. Until recently only a few types of transformations of organomercurials were known.\(^8\) These are illustrated in scheme VII below.

Scheme VII

\[ \text{RCH}_2\text{HgX} \quad \text{(a) oxidation} \quad \text{RCH}_2\text{Y} \]
\[ \quad \text{(b) reduction} \quad \text{RCH}_3 \]
\[ \quad \text{(c) transmetallation} \quad \text{RCH}_2[M] \]
Pathways (a) and (b) (Scheme VII) have been widely studied. Pathway (a), oxidation, can lead to useful heteroatom substitutions allowing the mercury to be replaced by halogens, oxygen, sulphur, nitrogen and phosphorus functionalities. The reduction of mercury, pathway (b), is easily achieved by the use of the hydrides of boron, aluminium or tin, sodium borohydride being the most common reagent. The most important use of reduction reactions is in the substitution of mercury for hydrogen in solvomercuration products, although this reaction may sometimes be considered a waste of the functionality introduced by mercury. These reactions of organomercurials are well documented, further information about them may be found within the several reviews. Pathway (c), the transmetallation of mercury, is a poorly explored area. Once the transmetallation has taken place the intermediate may react further. How this intermediate reacts will depend on the nature of [M].

Scheme VIII

There are three possible ways for the organometallic intermediate to react (Scheme VIII). If the metal is electrophilic (hard metals) it will cause the carbon attached to it to become cationic in nature and thus susceptible to nucleophilic attack (type a). On the other hand if the metal is nucleophilic (soft metals) the attached carbon will become anionic and
thus may attack nucleophilic centres (type b). The other possibility is for $\beta$-elimination producing a double bond (type c).

Part of the research of our group is to explore the applications of organomercurials, especially transmetallations. Previous work done in the group by Dr Jiri Srogl\textsuperscript{7,19} has provided examples of these reactions. The reaction of organomercurio aldehyde 12 with palladium(II) (Scheme V) is an example of reaction type (a). The transmetallation with palladium provides an electrophilic centre which is attacked by the nucleophilic oxygen of the aldehyde group.

In contrast, the reaction with the cuprate\textsuperscript{7,19} $\text{Me}_2\text{CuLi}_2$ (Scheme IX) produces a nucleophilic centre which is attacked by the electrophilic carbon of the aldehyde. This is an example of reaction type (b). This reaction was initially performed using an excess of $\text{Me}_2\text{CuLi}$, but subsequent investigation has shown that $\text{Me}_2\text{CuLi}_2$ is the reagent required. This will be discussed in more detail later as it contributes to part of this thesis.
This reaction also allowed the intramolecular conjugate addition to an activated carbon-carbon double bond (Scheme X). The \(\alpha,\beta\)-unsaturated ester 21 was prepared from the aldehyde 12 by Horner-Emmons olefination with \((\text{EtO})_2\text{P(O)}\text{CH}_2\text{CO}_2\text{Et}\) and \(\text{BuLi}\) in refluxing THF. The reaction of 21 with the cuprate produced the cyclobutane derivative 24 in good yield. As in the above reaction the \(\beta\)-carbon is acting as an electrophile which is attacked by the nucleophilic centre adjacent to the metal. The mechanism of the transmetallation will be discussed in chapter 3. Comparing the reaction of palladium and the cuprate with the organomercurial aldehyde demonstrates the potential of transmetallation reactions. They show that by simply changing the metal complex used as a reagent completely different transformations can occur. This is why this type of reaction is so potentially useful.
These reactions are all taking place on the sterically hindered steroid skeleton, which may have some influence on the course of the reactions. It was the aim of this project to explore the applications of organomercurials on much simpler systems in order to test the generality of these types of reactions.
Chapter 2
Synthesis of Organomercurials
2.1 Synthesis of the cis Organomercurial Series

To explore the reactivity of organomercurials, cyclopropanated allylic alcohols were chosen as precursors. The use of this type of system would give, after cyclopropane cleavage, an easily manipulated functionality in the close proximity to the attached mercury. The mercury cleavage of cyclopropylcarbinols was first studied by Collum\textsuperscript{20} et al. to synthesise acyclic and cyclic 2-methyl 1,3 diols (scheme XI).

\textbf{Scheme XI}

They opened the cyclopropanes using electrophilic mercury(II) salts to give the organomercurials, which were then reduced \textit{in situ} to give their desired products. This chemistry was used to isolate the organomercurials and study their further reactions. Initially an attempt to cleave a cyclopropanated cholestane skeleton was tried.
Cholestenone was reduced to form the β-allylic alcohol (scheme XII, 25), which was stereoselectively cyclopropanated. Several methods of cyclopropanation were tried, Sm(Hg)/CH$_2$I$_2$, Zn/CuCl$_2$/CH$_2$I$_2$, ZnEt$_2$/CH$_2$I$_2$, but it was found that the Simmons-Smith cyclopropanation$^{19,20}$ (zinc/copper couple and methylene iodide) gave the best results. Unfortunately cleaving of this cyclopropane 26 gave several products, presumably due to the generated cationic centre causing rearrangements within the steroid skeleton.

**Scheme XII**

![Scheme XII](image)

Our attention turned to simpler monocyclic allylic alcohols$^{21}$ (scheme XIII). The cyclopropanes were prepared by reducing the corresponding conjugated ketones to form the alcohols which were again cyclopropanated using the Simmons-Smith reaction.$^{24a}$

**Scheme XIII**

![Scheme XIII](image)

Mercury(II)-mediated cleavage of the 6-membered cyclopropane 34 in a non-nucleophilic solvent (DME, CH$_2$Cl$_2$) yielded the product as expected according to
Collum\textsuperscript{20} (Scheme XIV, A). The reaction rate of ring opening is dependent on the nature of the mercury salt used. Three salts were tested, acetate, trifluoroacetate and nitrate. Acetate, which is the least electrophilic, was very slow to react with virtually no reaction at room temperature, nitrate was the fastest.

Scheme XIV

Further study of the conditions of this reaction showed that by using different solvents and by changing the mercury salt different products could be obtained (Scheme XIV). In a nucleophilic solvent such as methanol, competition with the metal ligand arises to quench the newly formed electrophilic centre (Scheme XIV [B and C] and
Scheme XV. If Hg(NO$_3$)$_2$ is used the nitrate anion is sufficiently nucleophilic to quench the cation in the presence of methanol; on the other hand if Hg(O$_2$CCF)$_2$ is used the electrophilic centre is quenched by methanol to afford the methoxy derivative. This demonstrates the low nucleophilicity of trifluoroacetate.$^{36}$

![Scheme XV](image)

The configuration of the carbon bearing the CH$_3$HgX is determined by the stereochemistry of the cyclopropanation, which along with the oxymercuration, also defines the orientation of the newly attached nucleophile. The inductive effect of the hydroxy group presumably controls the regiochemistry of the transformation.

The investigation was extended to try to quench the electrophilic centre with nitrogen and carbon nucleophiles, instead of oxygen. This did not prove too successful. The cleavage of cyclopropane 34 with Hg(O$_2$CCF)$_2$ in acetonitrile (a Ritter type reaction$^{37}$) afforded the amide 38 (scheme XVI). This reaction was not as clean as those
performed in DME or MeOH. The product was also very polar which caused problems in purification. The use of acetylacetonate as a carbon nucleophile also proved unrewarding. The attempted ring scission using \( \text{Hg(O}_2\text{CCF}_3)_2 \) in DME in the presence of \( \text{Cu(acac)}_2 \) or \( \text{Fe(acac)}_3 \) produced no reaction.

**Scheme XVI**

In view of the above facts the methoxy derivative is the substrate of choice. It is produced cleanly and in good yields (~90%), also the low reactivity of the methoxy group would avoid potential complications that may be associated with the more reactive nitrate and amide groups in further reactions.

The above methodology was applied to the analogous seven and five membered ring systems (scheme XVII). The cycloheptane derivative 35 was regioselectively
to produce the organomercurial chloride 40, which can be methylated using MeCu\(^7\) to form the methylorganomercurial 41. Cleavage of the cyclopentane analogue 33 turned out to be less regioselective producing a mixture of 42 and 43 in a 2:1 ratio (82%).

**Scheme XVII**

The desired derivative 44 was obtained by methylating with MeCu to furnish the methylmercurio derivatives which were separated by chromatography. Separation after
methylation was required as some of the chloromericurial derivatives are not very stable under column chromatography conditions. The cyclohexane derivative can also be methylated in the same manner to yield the methylmercurio derivative (Scheme XIX, 48). The organomercurial compounds are very stable, the chloro derivatives can be kept for months at room temperature in air; the methylmercurials are stable for long periods of time if stored in a freezer. Purification is not usually a problem, most derivatives can be purified by column chromatography although there are some exceptions. Recrystallisation, in my experience, of the solid chloro derivatives (the methyl derivatives are usually oils) causes the mercurials to decompose, although each compound should be considered individually in this respect.

2.2 Synthesis of the Trans Series

Having synthesised a series of cis-organomercurials (with respect to the hydroxy and mercury groups) we wished to produce the corresponding trans series. Initially a Corey-Chaykovsky\textsuperscript{20} type synthesis of cyclopropenated ketone was attempted, followed by a selective reduction (Scheme XVIII).

It was found that reduction with L-Selectride gave the best selectivity for the trans isomer (the cis isomer was not observed by TLC). Unfortunately cleavage of this cyclopropane gave at least three products which could not be easily identified. This approach was abandoned and an alternative method was looked for. Two methods were investigated in achieving our aim.
The first method was to invert the hydroxy group in the existing cis-series of methylmercurio derivatives (Scheme XIX). This was achieved by oxidising the alcohol to the ketone with PCC followed by reduction, with NaBH₄, back to the alcohol. This is an interesting reaction as the methyl on the mercury is acting as a protecting group. Under normal circumstances it would not be possible to use a reducing agent in the presence of mercury functionality; in fact, as mentioned in the introduction (1.3), sodium borohydride is often used to remove mercury after solvomercuration reactions. Here we have an example of mercury surviving in the presence of a reducing agent. More recent work shows that this protection allows the use of several reducing agents,
LiAlH(tert-BuO)_3, L-Selectride, or Super hydride. By contrast, on treatment with LiAlH_4 the expected reduction of mercury is observed. In the case of the six and five membered ring systems, this methodology worked well. The cyclohexane derivative was reduced to give a 4.8:1 ratio in favour of the trans alcohol 52. The cyclopentane derivative gave an even better ratio of 5.2:1 in favour of trans alcohol 54. In the case of the cycloheptane derivative, this method failed to produce the trans isomer 53. Reduction with NaBH_4 yielded exclusively the cis alcohol 41.

Scheme XIX
The methyl mercury derivatives can be converted to the chloromercurials (55 and 56) by simply stirring with mercury(II) chloride in DME at room temperature. This is a transmetallation reaction, -HgMe being exchanged for -HgCl. This methodology represents a true protection / deprotection reaction sequence.

The second method for the synthesis of the trans series was to try to open the cyclopropane using mercury acetate to incorporate a functional group trans to the mercury derivative, which can then be further manipulated. First of all the hydroxy groups in the cyclopropyl alcohols, 34 and 35, which are initially required to stereo-direct the cyclopropanation, were protected by methylation using sodium hydride and methyl iodide to give the methoxy cyclopropanes 57 and 58. These cyclopropane derivatives were then cleaved using Hg(OAc)$_2$. Mercury acetate is a poor reagent for the oxymercuration of cyclopropanes. At room temperature its reaction in DME does not proceed, probably due to its poor solubility and low electrophilicity. An alternative to this reaction would be mercury trifluoroacetate in acetic acid. This reaction also failed to proceed. Eventually it was found that mercury acetate in acetic acid, heated to 60°C for four hours, was capable of cleaving the cyclopropane to give the desired products 59 and 60. The acetates can be hydrolysed to give the alcohol derivatives 63 and 64; or since the acetate functionality was also required for further reactions, the chloromercurials can be methylated to give the methylmercurials 61 and 62.
Compound 63 was used to prepare an all-cis configured series of compounds using the oxidation/reduction methodology developed earlier. Reduction of ketone 66
gave almost exclusively alcohol 67, with only a trace of 65 (16:1), this alcohol was then either acetylated to give 68 or deprotected to give the chloromercurio alcohol 69.

**Scheme XXI**

Having made the *cis* and *trans* series of organomercurials we were now in a position to explore their further reactions.
Chapter 3
Reactions of Organomercurials
with Cuprates
3.1 Reactions with Cuprates followed by Quenching with Water.

Addition of Grignard and alkylithium reagents to carbonyl groups is one of the most widely used applications of organometallics in organic synthesis. However its intramolecular version has never been fully developed, owing to the high reactivity of the reagents required to generate the RMgX or RLi group in the molecule already containing an unprotected carbonyl function. Alternatives involving less reactive organometallic species (B, Si, Sn, Zn, Cr and Ni) are confined to allylic, benzylic or vinylic halides and enol triflates as precursors. Much more successful is the Sm(II)- and Yb(II)-mediated cyclisation of halo ketones and halo esters. As discussed earlier it has recently been shown that the intramolecular addition to an aldehyde group can be accomplished via activating the neighbouring C-HgX moiety by organocuprates (Scheme IX). Similarly, intramolecular addition across an activated double bond (1,4-addition) has also been observed (Scheme X).

It was of interest to explore whether the cuprate activated organomercurials were prone to add intramolecularly across an ester carbonyl as they are in the case of aldehydes. Whereas esters react rapidly with Grignard and alkylithium reagents they are essentially inert towards organocuprates. However an intramolecular reaction of this type has rarely been attempted, presumably in view of the difficulties associated with generating a suitable precursor. Since carbonyl- containing organomercurials can be prepared as stable compounds, it was reasoned that they might serve as the starting material of choice.

The 6-membered ring acetate 70, obtained by acylation of alcohol 48 was treated with an excess of Me₂CuLi (Scheme XXII) the reported conditions for the reaction with
aldehyde 12. This afforded a fast, clean conversion to the hydroxy ketone 73 (70% isolated yield).\(^\text{25}\)

**Scheme XXII**

The acyl migration can be rationalised as follows: the organometallic species 71 generated from 70 reacts via attack on the neighbouring ester group to form intermediate 72, which subsequently collapses to 73 on aqueous workup.

Although this reaction was clean and fast it was found to be unreliable (i.e. sometimes it failed to work); it also required a large excess of cuprate (5 equiv.); 1 equivalent gave no reaction. The conditions of this reaction were extensively examined.
It was found that the further purification of copper iodide and extensive drying of solvent had no effect, but the titration of methyl lithium did. It was found that excess Me$_2$CuLi, made from freshly titrated MeLi would not react with the organomercurial acetate, but the further addition of MeLi initiated the reaction. This suggested that either MeLi was the actual reagent or a higher order cuprate was involved. The reaction of 70 with MeLi gave a complex mixture of products, indicating that copper must play a crucial role in the reaction. When 1 equivalent of "Me$_3$CuLi" was used as the reagent the usual fast clean reaction was observed.

Equation 1

\[
\text{CuI} + X \text{MeLi} \rightarrow \begin{cases} \text{MeCu} & X=1 \\ \text{Me}_2\text{CuLi} & X=2 \\ \text{Me}_3\text{CuLi}_2 & X=3 \\ \end{cases}
\]

This prompted an investigation into the conditions required to initiate the intramolecular addition to the steroidal aldehyde. Again it was found that there was no reaction with 1 equiv. of Me$_2$CuLi made with titrated MeLi, but the reaction would proceed when Me$_3$CuLi$_2$ was utilised.

The initially observed reaction of organomercurials with excess Me$_2$CuLi, made from non-titrated MeLi, can be explained by excess MeLi being present in the reaction mixture to form Me$_3$CuLi$_2$ which is the reactive species. These reactions stress the importance of using titrated alkylithiums in the synthesis of organocuprates. The appearance of the MeLi also has an effect on the reaction. For a good reaction the MeLi should be clear; cuprates made with "active" MeLi but with a cloudy appearance will not
react with the organomercurial (it can be used in MeCu mercury methylation reactions).

Presumably the insoluble lithium salts block the reaction in some way. The cuprate

"Me₃CuLi₂" will be discussed at the end of this chapter.

It was found that the ligand on the mercury was important. As previously discussed the methylmercurio acetate gave a clean reaction, but the reaction of the chloromercurio acetate 74 (Scheme XXIII) is less successful.

Scheme XXIII

![Scheme XXIII diagram]

1. Me₃CuLi₂
2. H₂O

OH

OMe
This reaction required 2 equiv. of cuprate; the first equivalent methylates the mercury, the second activates the mercury moiety to initiate the addition to the ester. Unfortunately this reaction has a tendency to stop at the methylmercury intermediate and not to proceed any further. For this reason the reaction of the methylmercury acetate is superior.

The addition was repeated on the benzoate 75 and pivalate 76 (Scheme XXIV, prepared from alcohol 48 by acylation with (PhCO)₂O / Et₂O (rt) or t-BuCOCl /THF(reflux) respectively, in the presence of DMAP). Both exhibited the same behaviour as the acetate, producing hydroxy ketones 77 (60%) and 78 (55%).

Scheme XXIV

In analogy to the above series the cycloheptane and cyclopentane derivatives were tested (Scheme XXV). The 5-membered ring acetate analogue 79 gave a successful reaction upon treatment with the cuprate to afford the acetal 80 (57%) as the sole isolable product. In this case the cyclic intermediate proved to be stable enough not to collapse on work up.
Scheme XXV

1. Me$_3$CuLi$_2$
2. H$_2$O

81 R = Me
82 R = Ph
83 R = "Bu
84 R = Me
85 R = Ph
86 R = "Bu

87
The reaction of the 7-membered ring acetate $81$ with $\text{Me}_3\text{CuLi}_2$ gave rise to a mixture of acetal $84'$ (37%) and the hydrolysis product $87$ (23%). The corresponding benzoate $82$ and pivalate $83$ gave the acetals $85$ (65%) and $86$ (59%) respectively as the sole isolable products.

The hydrolysis product afforded an opportunity to explore the mechanism of these reactions, for which three possible pathways can be envisaged.

In pathway 1 (Scheme XXVI) the methylmercury is transmetallated for copper to produce intermediate $88$. The coordinated copper has two possible alkyl groups it can transfer to the ester carbonyl. If the main skeleton alkyl is transferred, intermediate $89$ will be produced which will give the acetal $84$ on workup, but if a methyl group is transferred $90$ will result. This can then breakdown to give acetone and $87$ on workup.
To test this theory mixed cuprates were prepared with non-transferable ligands. Such mixed cuprates $R_R R_T Cu Li$ (where $R_R$ = non transferable ligand, $R_T$ = transferable ligand) are generally prepared via prior formation of $R_R Cu$ to which is added the organolithium $R_T Li$ (Eq. 2).

**Equation 2**

\[
R_R Li + CuX \rightarrow R_R Cu + LiX \rightarrow R_R R_T Cu Li + LiX
\]

Lithium methyl ($α$-thiophenyl) cuprate gave a similar mixture of $84$ (41%) and $87$ (22%) (excess MeLi present in the reaction mixture may have produced a higher order cuprate causing this reaction). MeCuCNLi$^{38}$ effected simple deacylation. Finally cuprates containing $1$-pentynyl or dibutylphosphide ligands proved to be unreactive. These results suggest that competition for alkyl transfer is not the correct mechanism for this reaction.

The second possible mechanism (pathway 2; Scheme XXVI) is that the mercury could be activated to produce an anionic centre which could act as a base to extract a proton to form an enolate, this again would give $87$ on workup. To test this theory the deuterium labelled acetate $92$ was prepared from alcohol $41$ (Scheme XXVII).
If this mechanism was correct a deuterium would be transferred to the newly formed methyl. The methyl of 87 produces a doublet at δ 1.07 in the ¹H NMR which integrates to 3 protons. If deuterium is transferred the integration should be reduced to 2 protons. The reaction of 92 with the cuprate did not produce the labelled alcohol 93, but produced the unlabelled alcohol 87, therefore this mechanism can also be ruled out.

The last possible mechanism (path 3) is that the cuprate activates the mercury moiety but due to the flexible nature of the 7-membered ring the acetate may not be in a close enough position to react with it. Therefore the carbonyl has time to react with another molecule of the cuprate reagent in the system. The nature of this reagent could be complex and could contain copper, lithium and/or mercury.
In the trans-series, the cyclohexane derived acetate 94 reacted with Me$_2$CuLi$_2$ in an analogous way to the cis-acetate 70 (Scheme XXVIII).

However the expected methyl ketone 97 was only obtained in low yield (15%), the main product being the tertiary alcohol 98 (40%). In this case the cyclic intermediate 95 is apparently less stable than its cis-counterpart 72. As a consequence 95 can be assumed to open up immediately, generating the carbonyl species 96, which can freely react with the remaining cuprate to give 98. The latter reaction resulted in a significant amount of starting material being recovered (30%), which indicates that Me$_2$CuLi$_2$ must react with the newly formed carbonyl in preference to Me$_2$CuLi (which is presumably formed after Me$_2$CuLi$_2$ has reacted with the mercury). By contrast the cis-lactolate 72 presumably survives in the reaction mixture until the aqueous quench, protecting the carbonyl group from further reacting with cuprate.
Scheme XXVIII

\[ \text{Ac}_2\text{O} \]
\[ \text{Me}_3\text{CuLi}_2 \]
\[ \text{H}_2\text{O} \]
Under the same conditions the isomeric 6-membered ring acetate 61 afforded mainly the ketone 101 (39%), whereas the tertiary alcohol 102 was obtained as a by-product (8%) along with some starting material (8%). The 7-membered ring homologue 62 gave solely acetal 103 (62%) as a mixture of two anomers (3.6:1).

The all-cis-acetate 68 gave a complex mixture of at least seven products on reaction with Me₂CuLi₂.
Can other cuprates be used? It was found that acetate 94 will react with excess 
$\text{Ph}_3\text{CuLi}_2$ under the same conditions. This reaction gave mainly the tertiary alcohol 104.
(51%) as a 5:2 mixture of epimers. An attempt was made to define the stereochemistry of the two epimers. It was thought that oxidation of the secondary alcohol would form ketone 105 which could then cyclise to form acetal 107 fixing the conformation of the molecule. Unfortunately it was found that the predominant pathway is to eliminate methanol possibly to produce the conjugated ketone 108 which further reacted to give a complex mixture of products. This process obviously scrambled the known stereocentres making it impossible to define the stereocentre we were interested in.
3.2 Reactions with Cuprates Followed by Quenching with BF₃·Et₂O.

Protonation of the intermediate 72 in the aqueous workup leads to the corresponding acetal which then affords the hydroxy ketone 73 (scheme XXII). It was reasoned that this methodology could be broadened if 72 is quenched by a reagent capable of abstracting the acetal oxygen, since the resulting intermediate should collapse to products different to 73. Lewis acids seemed to be the prime candidates for this purpose.⁶⁶a

Scheme XXX
In a model experiment the *cis*-acetate 70 was treated with Me$_3$CuLi and the reaction was quenched by BF$_3$Et$_2$O (Scheme XXX). The product mixture turned out to contain the usual ketone 73 (19%) the cyclic ether 112 (35%) and the olefin 113 (26%). The corresponding pivalate 76 afforded a mixture of the ketone 78 (21%) and the expected alkene 114 (24%), which was isolated as a single (E)-isomer; the (E)-configuration was established by NOE experiments.

The formation of 112 can be attributed to the oxygen abstraction from intermediate 111 (Scheme XXXI, path a) followed by a reaction of the resulting oxonium species 115 with the remaining organocuprate (presumably MeCu.BF$_3$). The formation of 113 is less obvious. One possible mechanism is that the ether oxygen of 112 reacts with BF$_3$ to form intermediate 117 (Scheme XXXII) which could undergo an elimination reaction to form 113 via 118. Treatment of 112 with BF$_3$.Et$_2$O yielded no reaction, therefore this mechanism can be ruled out. Another possible mechanism is for elimination in the intermediate 111 (scheme XXXI, path b) to generate enol ether 116 followed by a reaction with cuprate (Scheme XXXII) to form intermediate 119 which can reductively eliminate to form 120 which would collapse to yield 113 upon work up. This process is preceded by the insertion of alkyls into the C-O bond of enol ethers with Grignard reagents in the presence of nickel(II) or copper(I) salts. The stereochemical outcome of the pivalate reaction is in accord with this proposed stereospecific insertion of "CH$_3\) into the C-O bond.
Scheme XXXI
3.3 Reaction of Organomercurial Carbonates with Cuprates

The intermediate acetal species 72 (Scheme XXII) collapses to the open form 73 employing the ring-oxygen as a leaving group. This outcome suggests that, if a better leaving group was adjacent to the acetal carbon, in place of the alkyl group R, the reaction may produce a lactone. Thus starting with a carbonate, such as 121, it can be assumed that the corresponding intermediate 124 should prefer to eject the OR group (rather than the cyclic oxygen) to afford the lactone 125 (Scheme XXXIII). Note that in the competition between OR and the ring oxygen (the potential leaving groups), the latter expulsion would be reversible, whereas the former ejection is, de facto, irreversible. The required carbonate 121 was obtained from alcohol 48 on treatment with EtOCOCl, and indeed the reaction of the latter compound with Me₃CuLi₂ afforded the expected lactone 125, though as a mixture with the usual ketone 73 in a 1:3 ratio.

It was reasoned that this unsatisfactory outcome may be due to the insufficient leaving capability of EtO⁻. In order to generate a better leaving group the phenyl and p-nitrophenyl carbonates 122 and 123 were employed. The p-NO₂ group of 123 was found to react with the cuprate which resulted in the formation of a complex mixture of products. The phenyl carbonate 122 produced only the ketone 73 (in the presence of excess cuprate). Apparently, the introduction of a better leaving group into the starting carbonate increased the electrophilicity of the carbonyl group, so that it became more prone to react directly with Me₃CuLi₂. This finding suggests that, in the reaction of ethyl carbonate, there is a competition between ring closure and attack at the carbonate by cuprate to form intermediate 126; -OR can then be expelled to form acetate 71 which further reacts to generate 73.
Scheme XXXIII

121 R = Et
122 R = Ph
123 R = p-N0₂-C₆H₄

48 ClCO₂R

121

122

123

126

[Me]

124

125

126

[Me]

71

73

OH

OMe

OMe

OMe
3.4 Reaction of Organomercurial Acetates with Lewis Acids

Another possible approach to gain acetal 84 would be to activate the carbonyl of ester 81 using a Lewis acid such as MoCl₅ or AlCl₃ [195-197] (Scheme XXXIV).

**Scheme XXXIV**

This was found not to be the case. Two products were observed upon reaction with 1 equiv. of MoCl₅: the chloromercurial 74a (14%) and the chloro-derivative 128 (60%). The mechanism (Scheme XXXV) for this reaction may consist of a
transmetallation, possibly via transition state 133, to produce an alkylmercury chloride (74a or 130) and an alkylmolybdenum species (129 or 131) which can reductively eliminate to produce alkyl chloride (128 or 132) and molybdenum trichloride. Since only 1 equivalent of MoCl₅ was used the 60:13 ratio of products in favour of the alkyl chloride 128 shows that transmetallation of mercury to insert molybdenum between the methylmercury and the main skeleton bond is the most favoured pathway. Previous work done within the group⁷ shows that alkylmercury halides will react with MoCl₅ to give alkyl chlorides, which supports this mechanism.
3.5 Discussion

The structure of the reactive species, generated by treatment of the organomericurials with $\text{Me}_2\text{CuLi}_2$ deserves some comment. To explore this species an NMR study was undertaken. The $^{1}H$, $^{7}Li$ and $^{13}C$ NMR spectra were recorded for $\text{MeLi}$, $\text{Me}_2\text{CuLi}$, $\text{Me}_3\text{CuLi}_2$, model compound 136 (scheme XXXVI) and a mixture of
The reactions of cuprates with organomercurial acetates are very fast (instantaneous), therefore it would be impossible to follow this reaction by NMR. The model compound 136, synthesised from bromomethylcyclohexane 134, contains only the mercury functionality which should mean that the activated intermediate will be stable enough to be analysed by NMR.

**Scheme XXXVI**

\[
\begin{align*}
\text{Br} & \quad \text{HgBr} & \text{HgMe} \\
134 & \xrightarrow{1. \text{Mg}} 135 & \xrightarrow{2. \text{HgBr}_2} 136
\end{align*}
\]

The cuprate $\text{Me}_3\text{CuLi}_2$ has been found in several studies to give superior results to $\text{Me}_2\text{CuLi}$. So what is the nature of $\text{Me}_3\text{CuLi}_2$? There have been two major studies into the structure of this cuprate. Ashby et al. suggested that $\text{Me}_3\text{CuLi}_2$ is a discrete species. This is based on the $^1\text{H}$ NMR studies of various mixtures of $\text{MeLi:MeCu}$. For $\text{Me}_3\text{CuLi}_2$, they found 2 peaks which corresponded to $\text{Me}_2\text{CuLi}$ and $\text{MeLi}$, but they argued that the integration of the peaks was not consistent with "free" $\text{MeLi}$ and $\text{Me}_2\text{CuLi}$ and concluded through an equilibrium study that $\text{Me}_3\text{CuLi}_2$ is a discrete species.

The other major study is by Lipshutz et al. They suggested that $\text{Me}_2\text{CuLi}_2$ is a mixture of a cuprate species ($\text{Me}_2\text{CuLi}$) and "free" $\text{MeLi}$. This proposal is based on the $^1\text{H}$ and $^7\text{Li}$ NMR. They observed similar peaks to Ashby but argued in favour of
the above proposal. It should be noted that the cuprates used in both these studies are 
LiI free.

In the NMR studies that we undertook the $^1$H NMR for Me$_2$CuLi$_2$ supported 

the Lipshutz proposal. Two signals were discerned at -0.49 and -1.20 ppm (in ca. 2:1 

ratio) corresponding to the spectra of Me$_2$CuLi and MeLi. However the $^7$Li NMR 

spectrum exhibited broad singlets at 0.15, -0.61 and -1.67 ppm (in 0.8:1.0:10 ratio), 

whereas MeLi shows a signal at 0.21 ppm and Me$_2$CuLi at 1.92 ppm. This is clearly in 

conflict with the simple MeLi + Me$_2$CuLi structure for "MegCuLi$_2"$. However it should 

be noted that Lipshutz suggested that the various species present in cuprates are "not 

readily detected by standard ($^1$H, $^{13}$C) NMR techniques in samples containing LiI". 

Indeed it has been shown that the presence of LiI has a substantial effect on the 

structure, and thus on the reactivity of cuprates.$^{35,52}$ If Gilman's test is carried out on 

Me$_2$CuLi in THF/Et$_2$O a positive result (free MeLi) is obtained when LiI is absent, but 

when present a negative result is seen.$^{52}$

The aim of our experiments was to observe the effect of cuprates on alkyl 

mercurials rather than to study the structure of cuprates. Therefore our NMR solutions 

were prepared in the same manner as for our reactions, and thus contain LiI. It is clear 

that the composition of cuprates is complex. Lipshutz summed up the situation by 

suggesting that copper halide based cuprates should be thought of as RLi-to-RCu ratios, 

and that by fine-tuning this ratio different results may be obtained.$^{52}$

The next question is: What happens when "Me$_3$CuLi$_2"$ is mixed with 

organomercurials
More than 20 years ago Whitesides proposed the cluster R-[Hg,Cu,Li,Me] as a possible structure for the product of an organomercurial with a cuprate. Indeed, assuming the complex 137 (Scheme XXXVII) to be an intermediate would explain the
observed reactivity. On the other hand, the straightforward transmetallation \( \text{R-HgMe} \rightarrow \text{R-Li} \) can be ruled out since the reactions in order to be successful require the presence of copper. Another possibility would comprise a direct methylation on mercury, generating the anion \( \text{139} \). In order to test this hypothesis an endeavour to generate \( \text{139} \) (or a like species) by other means was tried. Thus, methylation with the thallium ate complex \( \text{[Me}_4\text{Ti]}^+\text{Li}^- \) was attempted. However, no reaction was observed and unchanged \( \text{70} \) was recovered in high yield. Another attempt was inspired by the work of Iwata, who has recently shown that \( \text{R-Hgl} \) reacts with excess \( \text{R}_2\text{N}^-\text{I}^- \) to generate \( \text{[R-Hgl}_2]^+ \). The latter species is capable of effecting an intramolecular 1,4-addition across an electron-deficient C=C bond. However \( \text{74} \) turned out to be inert under those reaction conditions (except the exchange of Cl by I). Even adding Lewis acids, in order to increase the electrophilicity of the carbonyl group was to no avail. These experiments show that simple methylation to give \( \text{139} \) is an unlikely mechanism as well. Yet another mechanism, involving the cuprate intermediate \( \text{138} \), was studied by NMR using the model compound \( \text{136} \).

Two questions arise when the organomercurial and cuprate are mixed. Firstly: Are there any changes to the cuprate signals? There was no observed change in the \(^1\text{H}\) or \(^7\text{Li}\) NMR signals associated with \( \text{Me}_2\text{CuLi}_2 \). The \(^1\text{H}\) NMR still showed peaks at -0.49 and -1.20 ppm in the same ratio as observed before, while the \(^7\text{Li}\) NMR showed peaks at 0.13, -0.67 and -1.72 ppm essentially identical to those observed prior to the addition of \( \text{136} \). The \(^{13}\text{C}\) NMR of \( \text{Me}_2\text{CuLi}_2 \) was not very useful due to the low sensitivity of carbon NMR.
Secondly: Are there any changes to the organomercurial signals? There were some distinct changes to signals in both the $^1$H and $^{13}$C NMR of the organomercurial. In the $^1$H NMR the signal for $\text{-HgMe}$ of 136 appears as a singlet at 0.83 ppm with mercury satellite peaks at 0.99 and 0.67 ppm ($J = 96$Hz). When the cuprate was added the singlet split into two peaks at 0.80 and 0.83 (in 1.0:1.4 ratio); no satellite peaks were discernible. Unfortunately the signal for $\text{-CH}_2\text{HgMe}$ was swamped by solvent signals in the $^1$H NMR. The $^{13}$C NMR spectrum showed an interesting pattern: the $\text{CH}_2\text{HgMe}$ signal that appears at 52.12 ppm for 136 turned into two distinct peaks at 53.76 and 51.81 ppm in ~ 1:1 ratio. The $\text{-HgMe}$ peak at 23.48 ppm disappeared upon addition of the cuprate. This signal was weak in the spectra of 136; it may be that this signal was also split on addition of cuprate but was too weak to distinguish. The position of the methylene signals excludes structures such as $[\text{RCH}_2\text{-HgMe}_2]^+$, $\text{RCH}_2\text{Li}$ or $\text{(RCH}_2)\text{CuLi}$, as the corresponding signal for the $\text{CH}_2$ would be expected to appear at a much higher field. All these observations suggest that neither methylation of mercury nor simple transmetallation occurs. Therefore, the original Whitesides' suggestion, namely the formation of a cluster, such as 137, still seems to be the most reasonable explanation of this intriguing process.
Chapter 4
Carbonylation Reactions
4.1 Palladium (II)-Catalysed Carbonylation Reaction

The 5-membered lactone, annulated to another ring in a cis or trans-fashion, is a typical structural motif encountered in a number of natural products.\textsuperscript{57} Whereas the stereoselective synthesis of cis-lactones is usually accomplished via halolactonisation and related reactions,\textsuperscript{58,59} trans isomers are more difficult to obtain.\textsuperscript{11} The frequent requirement for the presence of another substituent in a stereo-defined position may produce additional synthetic problems.

The attempt to synthesise lactones by applying the cuprate methodology (scheme XXXIII) was met with limited success; therefore an alternative strategy was sought. Since organomercurials can be transmetallated with palladium(II) salts to generate organopalladium species,\textsuperscript{14,15,60} which, in turn, are known to undergo carbonylation,\textsuperscript{61} it was thought that combining these two processes in one pot might produce the desired lactones more efficiently.\textsuperscript{52}

Initial experiments to explore the transmetallation of mercury by palladium on our systems were not very encouraging. The organomercurial chloride 37 was treated with a stoichiometric amount of Li\textsubscript{2}PdCl\textsubscript{4}, generated \textit{in situ} from PdCl\textsubscript{2} and LiCl, to try to synthesise the 4-membered cyclic ether 143 (Scheme XXXVIII, path a).
It was found that 2-methylcyclohex-2-enone 148 was the major product of this reaction. This expensive formation of a relatively cheap chemical can be rationalised as follows: the initial transmetallation of mercury in 37 was followed by β-elimination (path b) and the resulting allylic alcohol 144 was isomerised, presumably by palladium, to the enol 146, whose transformation into the conjugated ketone 148 is trivial. In a similar way, the cycloheptane homologue 40 furnished the methoxyketone 149. Hence it is obvious that, although transmetallation by Pd(II) has been achieved, the resulting complex preferred to react via β-elimination. This may be because the formation of the oxetane is less energetically favourable than elimination due to the angle strain within the 4-membered ring. The palladium(II) carbonylation of this system should be more successful than the above reaction as the 5-membered lactone is a less strained system and should therefore be more favoured.

Treatment of 37 with stoichiometric Li₂PdCl₄ under a carbon monoxide atmosphere did indeed yield lactone 125, but the reaction mixture was very messy and purification difficult as a result. It was reasoned that tuning of the coordination sphere of palladium might improve the result. Therefore further attempts to carbonylate 37 were carried out in the presence of stoichiometric quantities of (AcO)₂Pd, (CF₃CO₂)₂Pd, (Ph₃P)₂PdCl₂ or (MeCN)₂PdCl₂. The latter complex (Scheme XXXIX) turned out to be the most promising, mediating an essentially quantitative and clean conversion of 37 into 125 (rt,12hr), it was therefore selected for the development of the catalytic cycle.
Scheme XXXIX

56

HgCl, (MeCN)₂PdCl₂, CO, p-BQ, THF, Δ

37 n = 1
40 n = 2
42 n = 0

125 n = 1
130 n = 2
151 n = 0

HgCl, (MeCN)₂PdCl₂, CO, p-BQ, THF, Δ

52 n = 1
54 n = 0

152 n = 1
153 n = 0

HgCl, (MeCN)₂PdCl₂, CO, p-BQ, THF, Δ

63 n = 1
64 n = 2

154 n = 1
155 n = 2

HgCl, (MeCN)₂PdCl₂, CO, p-BQ, THF, Δ

69 n = 1

156
Since in this reaction Pd(II) is converted to Pd(0) (Scheme XL) a successful catalytic process would require that a stoichiometric amount of an efficient oxidant be present. Among mild oxidants known to serve this purpose, copper(II) salts seem to play a prominent role, as documented by their successful use in methoxycarbonylation reactions. However, after numerous test experiments, p-benzoquinone was found to be superior to CuCl₂, (AcO)₂Cu or Cu(NO₃)₂ for this system. Thus on heating at 60°C with (MeCN)₂PdCl₂ (10 mol %) and p-benzoquinone (2 equiv) in THF under an atmosphere of carbon monoxide for 4 days the organomercurial yielded lactone 125 in 60% isolated yield. Similarly, organomercurials 40 and 42 showed high conversions affording the respective lactones 150 (59%) and 151 (52%).

The trans-isomeric chloromercurio alcohols 52, 54, 63 and 64 behaved in a similar manner and produced the trans-fused lactones 152 (58%), 153 (47%), 154 (63%) and 155 (58%) respectively, under the same conditions. Finally, carbonylation of the all-cis-organomercurial 69 resulted in the formation of the cis-lactone 156 (58%). Thus these experiments have demonstrated that both the cis and trans-fused lactones can be synthesised using this methodology.
Another possible method to carbonylate alkylmercury halides is to use octacarbonyldicobalt as the reagent. Seyferth and Spohn\textsuperscript{46} reported that alkylmercury halides react with $\text{Co}_2(\text{CO})_8$ to produce symmetrical ketones ($2 \text{RHgX} \rightarrow \text{RCOR}$). It was thought that the cobalt carbonyl may provide an additional method to generate lactones. It was found that when 37 was mixed with cobalt carbonyl, in the manner as
reported by Seyferth, carbonylation did not take place; instead a ligand exchange reaction occurred (scheme XLII) to form the stable bimetallic complex 159.

**Scheme XLII**

Seyferth proposed an intermediate such as 159 in the mechanism for the carbonylation reaction, but was unable to isolate such a species or generate one by other methods. A brief note has mentioned the preparation of CH$_2$HgCo(CO)$_4$ by reaction of Na[Co(CO)$_4$] with excess methylmercuric chloride in methanol, but no details or properties other than the carbonyl stretching frequencies were reported. Compound 159 offers evidence for the Seyferth mechanism (scheme XLII).
An attempt was made to try to synthesise the lactone directly from cyclopropane 34 by cleaving with palladium in a carbon monoxide atmosphere to try to initiate a cleavage and carbonylation in one pot (scheme XLIII, path a).

Scheme XLIII
The reaction of 34 with (MeCN)$_2$PdCl$_2$ (10 mol %) and CuCl$_2$ as an oxidant and nucleophile source under a CO atmosphere in dichloromethane yielded the chlorocycloheptene 164 as the major product and not the lactone. This can be explained by the most substituted bond of the cyclopropane being cleaved$^{6c,d}$ to give the 7-membered ring intermediate 163 which loses the hydroxy group to generate a double bond. The cationic centre formed during the cyclopropane cleavage is quenched by nucleophilic chloride. The use of different palladium complexes and oxidants had little effect on the course of this reaction; even the use of a different metal, (PhCN)$_2$PtCl$_2$, gave the same product. Therefore this is obviously not a viable approach.

4:2 Discussion

The palladium carbonylation described above offers a versatile, stereocontrolled method that allows the construction of either the cis- or trans-annulated 5-membered lactones with three adjacent chiral centres on the parent ring (Scheme XXXIX). Noteworthy is the simplicity of manipulating the relative configurational pattern, in particular, the stereochemistry control by employing orthogonal protection in concert with the choice of the reagent, used to effect the initial cyclopropane cleavage. Thus, with the free OH in the starting cyclopropyl derivative (to be later implemented in the lactone ring), the second oxygen is introduced in a protected form (MeO in the cases we have described) by means of (CF$_3$CO$_2$)$_2$Hg/MeOH. This strategy eventually leads to a cis-fused lactone. On the other hand, if the original hydroxyl is orthogonally protected (again, as MeO in our case), we can use the acetate anion of (AcO)$_2$Hg in order to introduce a masked hydroxyl to C-3; after saponification of the respective product,
carbonylation will provide the corresponding trans-fused lactone. An alternative approach to the trans-fused lactones involves inversion of configuration of the hydroxyl. The all-cis-lactone can also be synthesised via this approach.

This methodology offers an expedient route to any of the four combinations of the relative configuration at the three centers; all of them have been described in this thesis. This protocol can be used in the synthesis of a number of isoprenoids and other naturally occurring 5-membered lactones and might further be enhanced by introducing a nitrogen substituent, e.g., in the cyclopropane opening via the Ritter reaction. Such an approach would be likely to find application in alkaloid chemistry.
Conclusion

Reaction of the organomercurials 70, 75, 76, 79, 81-83, and 94 having a neighbouring ester group (which are readily obtained from cyclopropyl alcohols 33-35 by the Hg\(^{2+}\)-mediated ringopening; Chapter 2) with MesCuLi\(_2\) results in an instantaneous, intramolecular addition across the carbonyl bond to generate the corresponding lactolate (e.g., 70→ 71→ 72; Scheme XXII). Quenching of the latter intermediate with water leads either to an open hydroxyketone (e.g., 72→ 73 and 99→ 101; Schemes XXII and XXVIII) or to a lactol (80, 84-86 or 103; Schemes XXV and XXVIII), depending on the actual structural pattern. On the other hand, quenching with BF\(_3\)EtO gives different products, as shown for the cyclohexane series (111→ 112 + 113; Scheme XXX). Although this approach can, in principle, be used to synthesise lactones (if a carbonate group is employed as the electrophilic acceptor), a more efficient and versatile alternative has been developed. The method relies on the Pd(II)-catalysed carbonylation of the chloromercurio alcohols (37, 40, 42, 52, 54, 63, 64 and 69), and works with comparable efficiency for the construction of either cis- or trans-fused lactone rings (125, 150-156; Scheme XXXIX). The choice of the Hg(II) reagent to initially open the cyclopropane ring, in conjunction with orthogonal protection, controls the final stereochemistry of the lactone annulation.
Experimental
Experimental Section

**General Methods.** Melting points were determined on a Kofler block and are uncorrected. The IR spectra were recorded on a Perkin-Elmer 298 spectrometer in CHCl₃. The NMR spectra were recorded for CDCl₃ solutions at 25 °C on Bruker ARX-250 or Bruker AM-300. Chemical shifts were referenced to TMS or the solvent signal (CHCl₃ at 7.27ppm). The coupling constants were obtained by first-order analysis. The mass spectra were measured on a Kratos Concept H instrument using direct inlet and the lowest temperature enabling evaporation or in a thermospray mode; chemical ionization was used in certain cases (with NH₃). GC Analysis was carried out using capillary columns (BP10 25m x 2.65 μm). Elemental analysis was carried out by Butterworth Laboratories, Teddington, Middlesex.

Flash chromatography was carried out according to the method of Still et al⁷⁰ using silica gel manufactured by Merck & Co., Kiesel 60, 230-400 mesh (ASTM). TLC was conducted on precoated aluminium sheets (60-254) with a 0.2 mm layer thickness, manufactured by Merck and Co..

All reactions were carried out under nitrogen. Standard workup of an ethereal solution means washing three times with 5% HCl (aqueous), water, and three times with 5% KHCO₃ (aqueous) and drying with MgSO₄. Petroleum ether refers to the fraction boiling in the range 40-60 °C. THF was distilled from sodium metal in the presence of benzophenone. Ether refers to diethyl ether and was distilled from LiAlH₄. Dichloromethane was distilled from calcium hydride. Triethylamine and pyridine were dried over sodium hydroxide. The identity of samples prepared by different routes was checked by TLC and IR and NMR spectra.

**General Procedure for the Cyclopropane Cleavage (Procedure A).** The cyclopropyl alcohol (4.5 mmol) in methanol (15 mL) was treated with mercury(II) trifluoroacetate (2.3 g; 5.4 mmol) at rt for 12 h. The reaction was then quenched with brine (15 mL), the product was
extracted into ether and the ethereal solution was worked up. The crude product was dissolved in a petroleum ether-acetone mixture (4:1) and passed through a column of silica gel (10 g) to give the pure product.

**General Procedure for the Methylation of Mercury Halides (Procedure B).** To a stirred suspension of copper(I) iodide (304 mg; 1.6 mmol) in ether (10 mL) or THF (10 mL) was added a 1.4 M solution of methyllithium in ether (1.1 mL; 1.6 mmol) at -20 °C and the mixture was stirred for 15 min to form the bright-yellow methylcopper. The mixture was then cooled to -78 °C and the organomercurial chloride (0.54 mmol), either solid or dissolved in THF (in the case of B), was added. The mixture was stirred at -78 °C for 10 min and then quenched with 5% HCl and diluted with ether and water. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel (30 g) using a petroleum ether-acetone mixture (95:5) as the eluent to give the pure methylmercurio derivative.

**Reaction of the Organomercurials with Organocuprates (Procedure C).** To a stirred suspension of copper(I) iodide (410 mg; 2.2 mmol) in ether (10 mL) was added a 1.4M solution of methyllithium in ether (4.6 mL; 6.5 mmol) at -20 °C. The mixture was stirred at -20 °C for 10 min and then cooled to -78 °C. A solution of the organomercurial (1.8 mmol) in ether (5 mL) was added and the mixture was stirred at -78 °C for 10 min and then quenched with 5% aqueous HCl. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel (30 g) using first a petroleum ether-acetone mixture (95:5) to elute impurities and then a 9:1 mixture to obtain the pure product.

**General Procedure for the Palladium(II)-Catalyzed Carbonylation (Procedure D).** In a 10 mL flask, fitted with a condenser connected to a balloon containing carbon monoxide, was stirred a solution of the organomercurial (0.52 mmol), p-benzoquinone (113 mg; 1.0 mmol), and \((\text{CH}_3\text{CN})_2\text{PdCl}_2\) (13 mg; 0.052 mmol) in THF (3 mL) at 60 °C for 4 d. The
reaction was then quenched with sodium dithionite, the product was taken up into ether, and the ethereal solution was worked up. The solvent was evaporated and the residue was chromatographed on silica gel (20 g) with a petroleum ether-acetone mixture (98:2) to give the pure lactone.

**General Procedure for the Synthesis of Cyclopropanes.**

**Preparation of the Zinc/Copper couple.** 32 g of zinc powder was washed by stirring in a conical flask with 30 mL of 3% HCl. The liquid was decanted off and the procedure repeated with 3 x 3% HCl (30 mL), 4 x H₂O (30 mL), 2 x CuSO₄(50 mL), 4 x H₂O (30 mL), 4 x absolute ethanol (30 mL). The zinc was then transferred to a Buchner funnel and washed with dry ether 4 times. The couple was then dried overnight under vacuum.

![OH](image)

**The Cyclopropanation Reaction.** 6.2 g (9.6 mmol) of zinc/copper couple, a crystal of iodine and dry diethyl ether (100 mL) were stirred in a 3-necked flask fitted with a condenser and dropping funnel. To the colourless solution 17.9 g (6.7 mmol) of diiodomethane was added. The mixture was gently heated until an exothermic reaction occurred, a gentle reflux was maintained with the use of an ice bath for 30 min. The alcohol (1.9 mmol) was then added dropwise and the reaction was refluxed for a further 2 hrs. The solution was then cooled in an ice bath and quenched by the cautious addition of saturated ammonium chloride solution. The liquid was filtered and extracted with ether and subsequently washed with brine and water and dried with MgSO₄. The ether was evaporated and the crude oil purified by column chromatography, eluting with dichloromethane, on the same day to yield the pure cyclopropane. 33 (59%), 34 (62%), 35 (80%).
(1R*,2R*,3R*)-2-[(Chloromercurio)methyl]-3-nitroyclohexan-1-ol (36).

Prepared as by procedure A except; DME was used in place of methanol and mercury(II) nitrate (1.7g, 5.4 mmol) was used instead of mercury trifluoroacetate to yield 36 in 71% yield. IR ν(OH) 1275 and 1625 cm⁻¹; v(ONO₂) 1350 cm⁻¹; ¹H NMR 1.80 (dd, J₂-H=12.4, J₁-H=4.1 Hz, 1H, CH₂HgCl), 2.08 (dd, J₂-H=12.4, J₁-H=6.1 Hz, 1H, CH₂HgCl), 2.31 (m, 1H, CHCH₂Hg), 4.06 (m, 1H, CHOH); ¹³C NMR 18.6 (t), 28.8 (t), 29.6 (t), 33.1 (t), 46.1 (d), 56.2 (q), 71.3 (d), 80.6 (d).

(1R*,2R*,3R*)-2-[(Chloromercurio)methyl]-3-methoxycyclohexan-1-ol (37).

Obtained from 34 in 86% yield using procedure A; mp 119-121 °C (acetone-heptane); IR ν(OH) 3460 and 3615 cm⁻¹; ¹H NMR (300 MHz) δ 1.05-1.27 (m, 2 H), 1.50-1.75 (m, 5 H), 1.78 (dd, J₁-H=11.3 Hz, J₂-H=7.4 Hz, 1H, CH₂HgCl), 2.03 (dd, J₁-H=11.3 Hz, J₂-H=4.7 Hz, 1H, CH₂HgCl), 3.11 (ddd, J=9.8, 9.7, 4.1 Hz, 1H, CH-OCH₃), 3.36 (s, 3 H, CH₃O), 3.96 (dd, J=2.8 and 3.3 Hz, 1H, CHOH); ¹³C NMR (75 MHz) δ 18.47 (t), 28.50 (t), 29.51 (t), 32.98 (t), 46.04 (d), 56.12 (q), 71.32 (d), 80.45 (d); HRMS (El) m/z 380.04667 (calcd for C₉H₁₄ClO₂Hg: 380.04669). Anal. Calcd. for C₉H₁₄ClO₂Hg: C, 25.34; H, 3.99. Found: C, 25.11; H, 3.70.
(1R*,2R*,3R*)-2-[(Chloromercurio)methyl]-3-methoxycycloheptan-1-ol (40)

![Chemical Structure]

Obtained from 35 in 90% yield using procedure A; mp 111-113 °C (acetone-heptane); IR v(OH) 3460 and 3610 cm⁻¹; ¹H NMR δ 1.48 (m, 1 H), 1.56-1.79 (m, 5 H), 1.80-1.84 (m, 3 H), 1.86 (dd, J_gem = 11.5 Hz, J₂-H₈-H = 6.7 Hz, 1 H, CH₂HgCl), 2.02 (dd, J_gem = 11.5 Hz, J₂-H₈-H = 6.7 Hz, 1 H, CH₂HgCl), 2.21 (ddd, J₂-H₈-H = 6.7 Hz, J₂-H₃-H = 6.7 Hz, J₂-H₁-H = 2.5 Hz, 1 H, CH₂HgCl), 3.02 (ddd, J₃-H₅-H = 7.5 Hz, J₃-H₄-H = 6.7 Hz, J₃-H₄-H = 3.5 Hz, 1 H, CH₂HgCl), 3.32 (s, 3 H, CH₃O), 4.03 (dt, J₁-H₇-H = 7.9 Hz, J₁-H₂-H = 2.5 Hz, J₁-H₇-H = 2.5 Hz, 1 H, CH₂HgCl); ¹³C NMR δ 22.29 (t), 23.56 (t), 29.40 (t), 33.92 (t), 48.25 (d), 56.60 (q), 72.35 (d), 85.04 (d); HRMS (EI) m/z 394.06239 (calcd for C₉H₁₇ClO₂Hg: 394.06234). Anal. Calcd for C₉H₁₇ClO₂Hg: C, 27.48; H, 4.35. Found: C, 27.23; H, 3.95.

(1R*,2R*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]cycloheptan-1-ol (41)

![Chemical Structure]

Obtained from 40 in 80% yield using procedure B; ¹H NMR δ 0.26 (s (83%) and d (17%), J₄-H₂ = 102.5 Hz), 0.91 (dd, J_gem = 12.5 Hz, J₂-H₈-H = 8.1 Hz, 1 H, CH₂Hg), 1.02 (dd, J_gem = 12.5 Hz, J₂-H₈-H = 7.5 Hz, 1 H, CH₂Hg), 1.36-1.49 (m, 1 H), 1.53-1.70 (m, 4 H), 1.73-1.88 (m, 4 H), 2.30 (dq, J₂-H₃-H = 7.5 Hz, J₂-H₈-H = 7.5 Hz, J₁-H₃-H = 2.5 Hz, 1 H, CH₂Hg), 3.03 (m, J₁-H₂-H = 2.5 Hz, 1 H, 2-H), 3.32 (s, 3 H, CH₃O), 4.09 (m, W = 17 Hz, 1 H, 1-H); ¹³C NMR δ 19.10 (q), 22.30 (t), 24.32 (t), 29.32 (t), 32.93 (t), 41.48 (t), 49.01 (d), 56.31 (q), 73.66 (d), 86.82 (q).
(d); MS m/z 392 (MNH₄⁺). Anal. Calcd for C₁₀H₂₂O₂Hg: C, 32.21; H, 5.41. Found, C, 32.36; H, 5.31

\((1R^*,2R^*,3R^*)-2\{\text{(Chloromercurio)methyl}\}-3\text{-methoxycyclopentan-1-ol (42)}\).

\[
\begin{align*}
\text{OH} & \\
\text{HgCl} & \\
\text{OMe} & \\
\end{align*}
\]

Obtained from 33 (in a mixture with 43) using procedure A; mp 57-59 °C (acetone-heptane); IR ν(OH) 3460 and 3615 cm⁻¹; ¹H NMR δ 1.85 (m, 2 H, CH₂Hg), 3.37 (s, 3 H, CH₃O), 3.42 (m, 1 H, CHOCH₃), 4.12 (dd, J = 5.2, 2.1 Hz, 1 H, CHOH); ¹³C NMR δ 26.90 (t), 28.05 (t), 32.46 (t), 50.21 (d), 58.07 (q), 74.12 (d), 87.50 (d); MS (Cl) m/z 384 (M⁺-NH₄), 348 (M⁺- H₂O); HRMS (EI) m/z 129.09157 (calcd for C₇H₁₃O₂: 129.09155). Anal. Calcd. for C₇H₁₃ClO₂Hg: C, 23.02; H, 3.59. Found: C, 22.83; H, 3.42.

\((1R^*,2R^*,3S^*)-3\{\text{(Chloromercurio)methyl}\}-2\text{-methoxycyclopentan-1-ol (43)}\).

\[
\begin{align*}
\text{OH} & \\
\text{OMe} & \\
\text{HgCl} & \\
\end{align*}
\]

Obtained from 33 (in a mixture with 42) using procedure A; ¹H NMR (in a mixture with 42) δ 3.36 (s, 3 H, CH₃O), 3.56 (m, CHOCH₃), 4.05 (m, 1 H, CHOH); ¹³C NMR δ 26.62 (t), 32.49 (t), 33.53 (t), 53.50 (d), 55.94 (q), 71.92 (d), 72.19 (d).
(1R*,2R*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cyclopentanol (44).

Obtained in 45% yield by methylation (procedure B) of a mixture of 42 and 43, followed by separation from the product of methylation of 43 via chromatography on silica gel (20 g) using a petroleum ether-acetone mixture (95:5 followed by 90:10) as eluent; IR ν(OH) 3420 and 3605 cm⁻¹; ¹H NMR δ 0.27 (s (83%) and d (17%), J₃-H,₅-H = 102.5 Hz, 3 H, CH₃Hg), 0.91 (dd, J₆-H = 12.4 Hz, J₆-H,₃-H = 10.1 Hz, 1 H, CH₂Hg), 1.04 (dd, J₇-H = 12.4 Hz, J₂-H,₅-H = 6.0 Hz, 1 H, CH₂Hg), 1.48 (m, 1 H), 1.70 (m, 1 H), 2.05 (m, 3 H), 3.35 (s, 3 H, CH₃O), 3.37 (m, 1 H, OCH₃), 3.98 (m, W2 = 11.9 Hz, 1 H, CHOCH₃); ¹³C NMR δ 19.55 (q), 27.80 (t), 31.56 (t), 37.50 (t), 51.01 (d), 57.52 (q), 75.90 (d), 88.42 (d); HRMS (EI) m/z 346.0856 (calcd for C₉H₁₄O₂Hg: 346.0856). Anal. Calcd for C₉H₁₄O₂Hg: C, 27.87; H, 4.68. Found: C, 27.59; H, 4.95.

(1S*,2R*,3R*)-Bicyclo[4.1.0]heptan-2-ol (47).

To a stirred solution of the ketone 46 (5.00 g; 45 mmol) in ether (175 mL) was added 1M solution of L-Selectride® (55 mL; 55 mmol) in THF at -78 °C. The stirred mixture was allowed to warm to rt and then quenched at 0 °C by water. Aqueous 30% solution of H₂O₂ (30 mL) and a solution of KOH (5 g) in water (20 mL) were then added and the resulting mixture was stirred at rt for 2 h. The product was then extracted into ether and the ethereal
solution was worked up. The crude product was chromatographed on silica gel (120 g) using first a petroleum ether-ether mixture (95:5) to elute impurities, followed by the 80:20 mixture to obtain pure 47 (3.03 g; 60%): \(^1\)H NMR \(\delta\) 0.43 (m, 2 H, cycloprop), 0.7-2.2 (m, 8 H), 4.35 (m, \(W/2 = 18\) Hz, 1 H, CH(OH)).

\((1R^*,2R^*,3R^*)\)-3"Methoxy"2-[(methylmercurio)methyl]-cyclohexan-1-ol (48).

\[
\begin{array}{c}
\text{OMe} \\
\text{HgMe}
\end{array}
\]

Obtained from 37 in 88% yield using procedure B; \(^1\)H NMR \(\delta\) 0.24 (s (83%) and d (17%), \(J_{1H,Hg} = 102.5\) Hz, 3 H, CH\(_2\)Hg), 0.85 (dd, \(J_{gem} = 12.5\) Hz, \(J_{2H,7-H} = 9.4\) Hz, 1 H, CH\(_2\)Hg), 0.96 (dd, \(J_{gem} = 12.5\) 7Hz, \(J_{2H,7-H} = 5.9\) Hz, 1 H, CH\(_2\)Hg), 1.05-1.21 (m, 1 H), 1.39-1.85 (m, 5 H), 1.90-2.01 (m, 1 H), 2.06-2.18 (m, 1 H), 3.06 (dt, \(J = 10.3\) and 4.4 Hz, 1 H, CH-OCH\(_3\)), 3.36 (s, 3 H, CH\(_2\)O), 3.88 (m, \(W = 9.0\) Hz, 1 H, CH-OH); \(^{13}\)C NMR \(\delta\) 18.51 (q), 19.01 (t), 29.85 (t), 32.59 (t), 40.46 (t), 47.06 (d), 56.20 (q), 74.03 (d), 82.04 (d); MS m/z 362 (M\(^+\) - 18).

Anal. Caled for C\(_9\)H\(_{19}\)O\(_2\)Hg: C, 30.13; H, 5.06. Found: C, 30.11; H, 5.06.

\((2S^*,3R^*)\)-3"Methoxy"2-[(methylmercurio)methyl]-cyclohexan-1-one (49).

\[
\begin{array}{c}
\text{OMe} \\
\text{HgMe}
\end{array}
\]

To a stirred solution of 48 (1.00 g; 2.78 mmol) in dichloromethane (20 mL) was added pyridinium chlorochromate (PCC; 643 mg; 3.06 mmol) and the mixture refluxed for 2 h. After cooling, the mixture was filtered through a 5 cm pad of silica gel and the colorless filtrate was evaporated. The crude product was chromatographed on silica gel (40 g) using a
petroleum ether-acetone mixture (9:1) as eluent to furnish 49 (711 mg; 71%): IR ν(C=O) 1700 cm⁻¹; ¹H NMR δ 0.26 (s (83%) and d (17%), J₉₂.₇₃₇ = 104.1 Hz, 3 H, CH₂Hg), 2.97 (m, 1 H, CHOCH₃), 3.35 (s, 3 H, CH₃O); ¹³C NMR δ 19.7 (q), 21.0 (t), 29.3 (t), 38.7 (t), 41.1 (t), 57.1 (q), 58.0 (d) 87.6 (d), 214.1 (s).

(25°,3R°)-3-Methoxy-2-[(methylmercurio)methyl]-cycloheptan-1-one (50).

![Chemical structure of (25°,3R°)-3-Methoxy-2-[(methylmercurio)methyl]-cycloheptan-1-one (50).]

To a stirred solution of 41 (1.05 g; 2.78 mmol) in dichloromethane (20 mL) was added pyridinium chlorochromate (PCC; 663 mg; 3.06 mmol) and the mixture refluxed for 2 h. After cooling, the mixture was filtered through a 5 cm pad of silica gel and the colorless filtrate was evaporated. The crude product was chromatographed on silica gel (40 g) using a petroleum ether-acetone mixture (9:1) as eluent to furnish 50 (647 mg; 62%): IR ν(C=O) 1694 cm⁻¹; ¹H NMR δ 0.19 (s (83%) and d (17%), J₉₂.₇₃₇ = 107.0 Hz, 3 H, CH₂Hg), 0.91 (dd, J₉₂.₇₃₇ = 12.6 Hz, J₂₂.₇₃₇₂₂ = 9.8 Hz, 1 H, CH₂Hg), 1.02 (dd, J₉₂.₇₃₇ = 12.6 Hz, J₂₂.₇₃₇₂₂ = 5.5 Hz, 1 H, CH₂Hg), 2.45 (m, 2 H, CH₂CO), 2.88 (m, 1 H, CHCO), 3.03 (dt, J = 7.9 and 1.0 Hz, 1 H, CHOCH₃), 3.33 (s, 3 H, CH₃O); ¹³C NMR δ 18.6 (q), 22.7 (t), 23.0 (t), 31.2 (t), 41.7 (t), 43.6 (t), 56.8 (d), 59.1 (q), 85.9 (d), 217.2 (s); HRMS m/z 372.10130 (calcd for C₁₀H₁₅O₂Hg: 372.10131).
(2S*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cyclopentan-1-one (51).

![Chemical structure of 51](image)

To a stirred solution of 44 (970 mg; 2.78 mmol) in dichloromethane (20 mL) was added pyridinium chlorochromate (PCC; 643 mg; 3.06 mmol) and the mixture refluxed for 2 h. After cooling, the mixture was filtered through a 5 cm pad of silica gel and the colorless filtrate was evaporated. The crude product was chromatographed on silica gel (40 g) using a petroleum ether-acetone mixture (9:1) as eluent to furnish 51 (523 mg; 76%): IR ν(C=O) 1740 cm⁻¹; ¹H NMR δ 0.32 (s (83%) and d (17%), J₇H₅ = 107.0 Hz, 3 H, CH₂Hg), 0.89 (dd, J₉H₉ = 12.8 Hz, J₂₆H₆H = 9.1 Hz, 1 H, CH₂Hg), 1.08 (dd, J₉H₅ = 12.8 Hz, J₂₄H₆H = 7.7 Hz, 1 H, CH₂Hg), 3.43 (s, 3 H, CH₃O), 3.43 (m, 1 H, CH-OCH₃); ¹³C NMR δ 19.4 (q), 26.7 (t), 36.5 (t), 39.8 (t), 57.0 (d), 57.1 (q), 88.1 (d), 220.9 (s); HRMS (EI) m/z 344.07001 (calcd for C₇H₁₄O₂Hg: 344.06999).

(1S*,2R*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cyclohexan-1-ol (52).

![Chemical structure of 52](image)

To a stirred solution of the ketone 49 (200 mg; 0.56 mmol) in a mixture of ether (20 mL) and ethanol (5 mL) was added sodium borohydride (158 mg; 4.1 mmol) and the mixture was stirred at rt for 2 h. The excess of the reagent was decomposed by water and the ethereal solution was worked up. The crude product mixture was chromatographed on silica gel (20 g) using a petroleum ether-acetone mixture (95:5) to give 48 as the less polar component (25 mg; 12%). The more polar component was identified as 52 (120 mg; 60%): mp 39-42 °C.
(acetone-heptane); IR ν(OH) 3415 and 3603 cm⁻¹; ¹H NMR δ 0.26 (s (83%) and d (17%), J_H-Hg = 102.5 Hz 3 H, CH₃Hg), 0.80 (dd, J_gem = 12.8 Hz, J₂₃-H₂ = 8.7 Hz, 1 H, CH₂Hg), 0.88 (dd, J_gem = 12.8 Hz, J₂₃-H₂ = 5.8 Hz 2.73 (dt, J = 9.3 and 3.9 Hz, 1 H, CH₃OH), 3.14 (dt, J = 9.8 and 5.5 Hz 1 H, CH₃-OCH₃); ¹³C NMR δ 19.46 (q), 20.20 (t), 29.69 (q), 34.44 (t), 41.18 (t), 51.26 (d), 56.85 (q), 77.53 (d), 85.17 (d); HRMS m/z 360.10131 (calcd for C₆H₁₃O₂Hg: 360.10132). Anal. Calcd. for C₆H₁₃O₂: C, 30.13; H, 5.06. Found: C, 29.96; H, 5.01.

(1S⁰,2R⁰,3R⁰)-3-Methoxy-2-[(methylmercurio)methyl]-cyclopentan-1-ol (54).

![Chemical Structure](image)

To a stirred solution of the ketone 51 (192 mg; 0.56 mmol) in a mixture of ether (20 mL) and ethanol (5 mL) was added sodium borohydride (158 mg; 4.1 mmol) and the mixture was stirred at rt for 2 h. The excess of the reagent was decomposed by water and the ethereal solution was worked up. The crude product mixture was chromatographed on silica gel (20 g) using a petroleum ether-acetone mixture (95:5) to give 44 as the less polar component (14 mg; 7%). The more polar component was identified as 54 (74 mg; 38%): IR ν(OH) 3465 and 3600 cm⁻¹; ¹H NMR δ 0.25 (s (83%) and d (17%), J_H-Hg = 101.9 Hz 3 H, CH₃Hg), 0.88 (dd, J_gem = 12.6 Hz, J₂₃-H₂ = 8.5 Hz, 1 H, CH₃Hg), 1.04 (dd, J_gem = 12.6 Hz, J₂₃-H₂ = 7.6 Hz, 1 H, CH₃Hg), 2.60 (br s, 1 H, OH), 3.20 (dt, J = 6.3 and 4.7 Hz, 1 H, CH₃OCH₃), 3.30 (s, 3 H, CH₃O), 3.56 (dd, J = 12.0 and 5.7 Hz, 1 H, CH₃OH); ¹³C NMR δ 21.0 (q), 27.7 (t), 32.1 (t), 43.7 (t), 54.0 (d), 57.2 (q), 80.9 (d), 89.8 (d); HRMS (EI) m/z 346.08566 (calcd for C₆H₁₄O₂Hg: 346.08560). Anal. Calcd. for C₆H₁₄ClO₂Hg: C, 25.34; H, 3.99. Found: C, 25.12; H, 3.71.
To a stirred solution of 52 (400 mg; 1.13 mmol) in 1,2-dimethoxyethane (10 mL) was added mercury(II) chloride (331 mg; 1.22 mmol) and the resulting mixture was stirred at rt for 20 min. The mixture was then diluted with water and the product was taken up into ether. The ethereal solution was washed with brine and the solvent was evaporated. The solid residue was extracted with a petroleum ether-ether mixture (8:2) in order to separate the desired organic product from other mercurial residues. The extract was evaporated and the residue was chromatographed on silica gel (20 g) using a petroleum ether-ether mixture (9:1) to give pure 55 (401 mg; 95%); mp 67-69 °C (ether-heptane); IR ν(OH) 3465 and 3600 cm⁻¹; ¹H NMR δ 1.79 (dd, J₆₇.7-H = 11.9 Hz, J₂-₇-₇-H = 8.3 Hz, 1 H, CH₂HgCl), 2.10 (dd, J₆₇.₇-H = 11.9 Hz, J₂-7-7-H = 6.0 Hz, 1 H, CH₂HgCl), 2.70 (dt, J = 10.1 and 4.7 Hz, 1 H, CH-OH), 3.18 (dt, J = 9.8 and 4.4 Hz, 1 H, CH-OCH₃), 3.38 (s, 3 H, CH₃O); ¹³C NMR δ 20.4 (t), 29.9 (t), 30.1 (t), 32.3 (t), 50.9 (d), 57.0 (q), 75.4 (d), 83.7 (d); HRMS m/z 143.10720 (M⁺ - HgCl; calcd for C₈H₁₅O₂: 143.10720).

(1S⁰,2R⁰,3R⁰)-3-Methoxy-2-[chloromercurio)methyl]-cyclohexan-1-ol (55).
min. The mixture was then diluted with water and the product was taken up into ether. The ethereal solution was washed with brine and the solvent was evaporated. The solid residue was extracted with a petroleum ether-ether mixture (8:2) in order to separate the desired organic product from other mercurial residues. The extract was evaporated and the residue was chromatographed on silica gel (20 g) using a petroleum ether-ether mixture (9:1) to give pure 56 (457 mg; 97%): 1H NMR δ 2.73 (m, 1H, OH), 3.01 (m, 1H, CH-OCH3), 3.12 (s, 3H, CH3O), 3.40 (m, 1H, CH-O); 13C NMR δ 27.5 (t), 31.7 (2 x t), 53.3 (d), 57.6 (q), 78.2 (d), 87.0 (d); HRMS m/z 129.09153 (M+ - HgCl; calcd for C7H13O2: 129.09155).

(1S*,2S*,6R*)-2-Methoxybicyclo[4.1.0]heptane (57).5n

To a stirred mixture of sodium hydride (0.58 g; 13.4 mmol; obtained from a 60% oil suspension by washing with petroleum ether) in THF (10 mL) was added a solution of the alcohol 34 (1.00 g; 8.93 mmol) in THF (5 mL) and the mixture was heated at 45 °C for 5 min. The mixture was then cooled to rt and a solution of methyl iodide (1.9 g; 1.34 mmol) in THF (5 mL) was added over a period of 20 min while stirring. The mixture was stirred at 45 °C for an additional 30 min, then cooled to 0 °C, and the excess of the reagent was decomposed by water. The crude product was chromatographed on silica gel using a petroleum ether-ether mixture (98:2) to afford 57 (0.78 g; 69%): 1H NMR δ 0.26 (m, 1H), 0.52 (m, 1H), 1.72 (m, 1H), 3.30 (s, 3H, OCH3), 3.67 (m, 1H, CHOME); 13C NMR δ 7.4 (t), 12.5 (d), 14.5 (d), 20.1 (t), 23.7 (t), 28.2 (t), 55.6 (q), 75.8 (d).
To a stirred mixture of sodium hydride (0.58 g; 13.4 mmol; obtained from a 60% oil suspension by washing with petroleum ether) in THF (10 mL) was added a solution of the alcohol 35 (1.13 g; 8.93 mmol) in THF (5 mL) and the mixture was heated at 45 °C for 5 min. The mixture was then cooled to rt and a solution of methyl iodide (1.9 g; 1.34 mmol) in THF (5 mL) was added over a period of 20 min while stirring. The mixture was stirred at 45 °C for an additional 30 min, then cooled to 0 °C, and the excess of the reagent was decomposed by water. The crude product was chromatographed on silica gel using a petroleum ether-ether mixture (98:2) to afford 58 (0.83 g; 66%): \(^1\)H NMR \(\delta\) 0.35-0.58 (m, 2 H, cycloprop), 3.26 (s, 3 H, CH\(_3\)O), 3.61 (dt, \(\delta = 7.9\) and 3.4 Hz, 1 H, CH-\(\text{OCH}_3\)) \(^1^\)C NMR \(\delta\) 4.4 (t), 14.0 (d), 18.7 (d), 24.1 (t), 26.5 (t), 29.6 (t), 31.5 (t), 55.4 (q), 78.6 (d).

\((1R^\circ,2S^\circ,7R^\circ)-2-[(\text{Chloromercurio})\text{methyl}]\text{-1-methoxycyclohexan-3-yl} \text{Acetate (59)}\). A stirred solution of 57 (2.27 g; 18.0 mmol) and mercury(II) acetate (5.0 g; 19.8 mmol) in glacial acetic acid (20 mL) was refluxed for 4 h. The mixture was then cooled to rt and quenched with brine. The product was extracted into CH\(_2\)Cl\(_2\) (5x) and the organic layer was washed with 5% aqueous KHCO\(_3\) and water, and dried with Na\(_2\)SO\(_4\). The solvent was evaporated and the residue was dissolved in petroleum ether-ether mixture (2:1) and filtered through a pad of silica gel. The filtrate was evaporated to yield pure 59 (5.62 g; 74%): IR
\(v(C=O)\) 1722 cm\(^{-1}\); \(^1H\) NMR \(\delta\) 1.55 (dd, \(J_{\text{gem}} = 12.5\) Hz, \(J_{2,4,7,8\text{-H}} = 4.3\) Hz, 1 H, CH\(_2\)Hg), 1.86 (dd, \(J_{\text{gem}} = 12.5\) Hz, \(J_{2,4,7,8\text{-H}} = 4.9\) Hz, 1 H, CH\(_2\)Hg), 2.00 (s, 3 H, CH\(_3\)CO\(_2\)), 3.25 (s, 3 H, CH\(_3\)O), 3.34 (m, \(W/2 = 11\) Hz, 1 H, CH-OCH\(_3\)), 4.72 (dt, \(J = 9.9\) and 4.4 Hz, 1 H, CH-O\(_2\)CO); \(^{13}C\) NMR \(\delta\) 17.5 (t), 20.3 (q), 25.7 (t), 27.4 (t), 29.8 (t), 44.6 (d), 55.1 (q), 74.3 (d), 78.3 (d), 169.9 s; MS (El) \(m/z\) 422 (M\(^+\)), 362 (M\(^+\) - OAc); HRMS (El) \(m/z\) 185.1176 (M\(^+\) - HgCl; caleed for C\(_{10}\)H\(_{17}\)O\(_3\): 185.11777).

\((1R^*,2R^*,3R^*)\)-2-[(Chloromercurio)methyl]-1-methoxycycloheptan-3-yl Acetate (60).

\[
\begin{align*}
\text{OMe} & \quad \text{HgCl} \\
& \quad \text{OAc}
\end{align*}
\]

A stirred solution of 58 (2.57 mg; 18.0 mmol) and mercury(II) acetate (5.0 g; 19.8 mmol) in glacial acetic acid (20 mL) was refluxed for 4 h. The mixture was then cooled to rt and quenched with brine. The product was extracted into CH\(_2\)Cl\(_2\) (5x) and the organic layer was washed with 5% aqueous KHCO\(_3\) and water, and dried with Na\(_2\)SO\(_4\). The solvent was evaporated and the residue was dissolved in a petroleum ether-ether mixture (2:1) and filtered through a pad of silica gel. The filtrate was evaporated to yield pure 60 (5.65 g; 72%): IR \(v(C=O)\) 1725 cm\(^{-1}\); \(^1H\) NMR \(\delta\) 1.77 (dd, \(J_{\text{gem}} = 12.0\) Hz, \(J_{2,4,7,8\text{-H}} = 4.4\) Hz, 1 H, CH\(_2\)Hg), 1.87 (dd, \(J_{\text{gem}} = 12.0\) Hz, \(J_{2,4,7,8\text{-H}} = 6.0\) Hz, 1 H, CH\(_2\)Hg), 2.06 (s, 3 H, CH\(_3\)CO\(_2\)), 2.41 (m, \(W = 22\) Hz, 1 H, CH-CH\(_2\)Hg), 3.34 (s, 3 H, CH\(_3\)O), 3.42 (m, \(W/2 = 15\) Hz, 1 H, CH-O\(_2\)CO), 4.74 (dt, \(J = 7.1\) and 4.1 Hz, 1 H, CH-O\(_2\)Ac); \(^{13}C\) NMR \(\delta\) 21.9 (q), 22.6 (t), 23.6 (t), 25.5 (t), 32.6 (t), 47.6 (d), 57.2 (q), 79.1 (d), 81.6 (d), 171.1 (s); MS (El) \(m/z\) (%): 376 (M\(^{**}\) - OAc, 83), 344 (M\(^{**}\) - OAc - OMe, 100); HRMS (El) \(m/z\) 199.13344 (M\(^+\) - HgCl; caleed for C\(_{11}\)H\(_9\)O\(_3\); 199.13342).
(1R*2R*3R*)-2-[(Methylmercurio)methyl]-1-methoxycyclohexan-3-yl Acetate (61).

Obtained from 59 in 74% yield using procedure B; 1H NMR δ 0.20 (s (83%) and d (17%), J_{H,Hg} = 103.5 Hz, 3 H, CH_{3}Hg), 0.71 (dd, J_{gem} = 13.3 Hz, J_{2-H,7-H} = 4.7 Hz, 1 H, CH_{2}Hg), 1.04 (dd, J_{gem} = 13.3 Hz, J_{2-H,7-H} = 6.5 Hz, 1 H, CH_{2}Hg), 2.03 (s, 3 H, CH_{3}CO), 2.57 (m, W = 24 Hz, 1 H, CH-CH_{2}Hg), 3.28 (s, 3 H, CH_{3}O), 77773.38 (m, W/2 = 9 Hz, 1 H, CH-OCH_{3}), 4.82 (dt, J = 9.1 and 4.1 Hz, 1 H, CH-OAc); 13C NMR δ 19.2 (q), 19.4 (t), 21.8 (q), 27.1 (t), 30.6 (t), 40.1 (t), 46.6 (d), 55.6 (q), 77.0 (d), 81.7 (d), 171.2 (s); HRMS (El) m/z 402.11188 (calcd for C_{11}H_{20}O_{3}Hg: 402.11185). Anal. Calcd for C_{11}H_{20}O_{3}Hg: C, 32.96; H, 5.03. Found: C, 32.70; H, 5.29.

(1R*2R*3R*)-2-[(Methylmercurio)methyl]-1-methoxycycloheptan-3-yl Acetate (62).

Obtained from 60 in 72% yield using procedure B; mp 48-51 °C (acetone-heptane); 1H NMR δ 0.22 (s (83%) and d (17%), J_{H,Hg} = 103.2 Hz, 3 H, CH_{3}Hg), 0.98 (dd, J_{gem} = 12.9 Hz, J_{2-H,8-H} = 6.9 Hz, 1 H, CH_{2}Hg), 2.72 (m, W = 22 Hz, 1 H, CH(CH_{2})Hg), 3.27 (s, 3 H, CH_{3}O), 3.42 (dt, J = 8.2 and 1.9 Hz, 1 H, CH-OCH_{3}), 4.78 (m, W = 18 Hz, 1 H, CH-OAc); 13C NMR δ 19.6 (q), 22.5 (q), 23.0 (t), 24.3 (t), 29.3 (t), 32.6 (t), 42.8 (t), 47.5 (d), 56.9 (q), 80.3 (d), 83.1 (d), 171.1 (s); HRMS (El) m/z 416.12753 (calcd for C_{12}H_{22}O_{3}Hg: 416.12755).
(1R*,2S*,3R*)-2-[(Chloromercurio)methyl]-1-methoxycyclohexan-3-ol (63).

Solid 59 (2.24 g; 5.3 mmol) was added to a solution NaOH (0.3 g; 6 mmol) in methanol (10 mL) and water (0.5 mL) and the mixture was stirred at rt for 20 min. The mixture was then diluted with ether and the resulting solution was worked up. The crude product was dissolved in ether and the solution was filtered through a pad of silica gel. The filtrate was evaporated to afford pure 63 (1.96 g; 98%); IR ν(OH) 3487, 3609 cm⁻¹; ¹H NMR δ 1.69 (dd,  1 J G = 11.9 Hz, 1 H, CH₂Hg), 2.15 (dd,  1 J G = 11.9 Hz, 1 H, CH₂Hg), 3.23 (s, 3 CH₃O), 3.31 (m,  1 J W = 8.5 Hz, 1 H, CH₂CH₃), 3.38 (s, 3 H, CH₃O), 3.43 (dt,  1 J W = 10.1 and 4.4 Hz, 1 H, CH₂Hg); ¹³C NMR δ 17.78 (t), 26.18 (t), 28.31 (t), 34.16 (t), 47.07 (d), 55.30 (q), 71.68 (d), 79.03 (d); MS (El) m/z 362 (M⁺ - HgO), 345 (M⁺ - Cl); HRMS (El) m/z 143.10720 (M⁺ - HgCl; calcd for C₈H₁₅O₂: 143.10720). Anal. Calcd for C₈H₁₅O₂Hg: C, 25.34; H, 3.99. Found: C, 25.13; H, 3.72.

(1R*,2S*,3R*)-2-[(Chloromercurio)methyl]-1-methoxycycloheptan-3-ol (64).

Solid 60 (2.30 mg; 5.3 mmol) was added to a solution NaOH (0.3 g; 6 mmol) in methanol (10 mL) and water (0.5 mL) and the mixture was stirred at rt for 20 min. The mixture was then diluted with ether and the resulting solution was worked up. The crude product was dissolved in ether and the solution was filtered through a pad of silica gel. The filtrate was evaporated to afford pure 64 (2.02 g; 97%); mp 43-46 °C (ether); IR ν(OH) 3480 and 3610
cm⁻¹; ¹H NMR δ 3.30 (s, 3 H, CH₃O), 3.37 (br d, J = 7.6 Hz, 1 H, CH-OCH₃), 3.49 (dt, J = 6.9 and 3.5 Hz, 1 H, CH-OH); ¹³C NMR δ 22.7 (t), 23.6 (t), 29.3 (t), 33.4 (t), 36.7 (t), 50.1 (d), 57.3 (q), 76.7 (d), 82.4 (d); MS (EI) m/z 358 (M⁺ - Cl), 157 (M⁺ - HgCl); HRMS (EI) m/z 157.12283 (M⁺ - HgCl; calcd for C₁₁H₃₄O₄: 157.12285).

(lR*,2S*,3R*)-2-[(Methylmercurio)methyl]-1-methoxycyclohexan-3-ol (65).

Obtained from 63 (3.0 g) in 87% yield using procedure B; IR v(OH) 3420, 3610 cm⁻¹; ¹H NMR δ 0.22 (s (83%) and d (17%), JₜHg = 102 Hz; 3 H, CH₃Hg), 0.83-0.90 (m, 2 H, CH₂Hg), 2.38 (m, W = 25 Hz, 1 H, 2-H), 3.29 (s, 3 H, CH₃O), 3.37 (m, W/2 = 10 Hz, 1 H, CH-OCH₃), 3.55 (dt, J = 9.4, 4.1 Hz, 1 H, CH-OH); ¹³C NMR δ 19.2 (t), 19.6 (q), 27.2 (t), 34.3 (t), 40.3 (t), 49.3 (d), 56.4 (q), 74.4 (d), 82.1 (d); HRMS (EI) m/z 360.10128 (calcd for C₁₁H₁₉O₃Hg: 360.10131). Anal. Calcd for C₁₁H₁₉O₃Hg: C, 30.13; H, 5.06. Found: C, 30.02; H, 5.31.

(1R*,2R*)-1-Methoxy-2-[(methylmercurio)methyl]-cyclohexan-3-one (66).

To a stirred solution of 65 (2.50 g; 6.95 mmol) in dichloromethane (50 mL) was added pyridinium chlorochromate (PCC; 2.0 g; 9.3 mmol) and silica gel (3 g) and the mixture stirred at rt overnight. The solvent was then evaporated and the residue was chromatographed on silica gel (30 g) using a petroleum ether-acetone mixture (95:5) as eluent to furnish 66.
(1.79 g; 71%): IR ν(C=O) 1700 cm⁻¹; ¹H NMR δ 0.19 (s (83%) and d (17%), J₉,H₉ = 106 Hz, 3 H, CH₃Hg), 0.64 (dd, J₉,H₉ = 12.9 Hz, J₂,H₇,H₇ = 5.0 Hz, 1 H, CH₃Hg), 0.92 (dd, J₉,H₉ = 12.9 Hz, J₂,H₇,H₇ = 5.7 Hz, 1 H, CH₃Hg), 3.26 (s, 3 H, CH₃O), 3.40 (m, W/2 = 15 Hz, 1 H, CH-OCH₃); ¹³C NMR δ 17.7 (q), 21.4 (t), 27.4 (t), 37.1 (t), 41.5 (t), 56.2 (d), 56.7 (q), 85.0 (d), 214.0 (s); HRMS m/z 358.08565 (calcd for C₉H₁₆O₂H₂g: 358.08566). Anal. Calcd for C₉H₁₆O₂H₂g: C, 30.30; H, 4.52. Found: C, 30.17; H, 4.39.

(1R*,2S*,3S*)-1-Methoxy-2-[((methylmercurio)methyl]-cyclohexan-3-ol (67).

To a stirred solution of the ketone 66 (1.24 g; 3.47 mmol) in a mixture of ether (60 mL) and ethanol (15 mL) was added sodium borohydride (157 mg; 4.1 mmol) and the mixture was stirred at rt for 2 h. The excess of the reagent was decomposed by water and the ethereal solution was worked up. The crude product mixture was chromatographed on silica gel (20 g) using a petroleum ether-acetone mixture (95:5) to give 67 (990 mg; 79%) as the less polar component: IR ν(OH) 3490, 3600 cm⁻¹; ¹H NMR δ 0.22 (s (83%) and d (17%), J₉,H₉ = 102 Hz, 3 H, CH₃Hg), 0.96 (dd, J₉,H₉ = 13.2 Hz, J₂,H₇,H₇ = 6.3 Hz, 1 H, CH₃Hg), 1.05 (dd, J₉,H₉ = 13.2 Hz, J₂,H₇,H₇ = 6.6 Hz, 1 H, CH₂Hg), 2.37 (m, W = 25 Hz, 1 H, 2-H), 3.09 (d, J = 9.8 Hz, 1 H, OH), 3.32 (s, 3 H, CH₃O), 3.33 (m, 1 H, CH-OCH₃), 3.66 (m, W/2 = 21 Hz, 1 H, CH-CH₃Hg); ¹³C NMR δ 14.7 (t), 18.9 (q), 27.1 (t), 32.9 (t), 40.5 (t), 44.4 (d), 56.8 (q), 73.2 (d), 83.2 (d); HRMS m/z 360.10128 (calcd for C₉H₁₆O₂H₂g: 360.10131). Anal. Calcd for C₉H₁₆O₂H₂g: C, 30.13; H, 5.06. Found: C, 30.38; H, 4.82. The more polar component was identified as 65 (60 mg; 5%).
(1R*,2R*,3S*)-2-[(Methylmercurio)methyl]-1-methoxycyclohexan-3-yl Acetate (68).

To a solution of the methylmercurio alcohol 67 (300 mg; 0.83 mmol) and triethylamine (0.33 mL; 2.49 mmol) in ether (10 mL) were successively added acetic anhydride (0.31 mL; 2.49 mmol) and 4-N,N-dimethylaminopyridine (101 mg; 0.83 mmol). The mixture was stirred at rt for 20 min and then quenched by ice and 5% aqueous HCl. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel using a petroleum ether-acetone mixture (95:5) as the eluent to give the pure 68 (301 mg; 69%): IR ν(C=O) 1720 cm⁻¹; ¹H NMR δ 0.23 (s (83%) and d (17%), J = 103 Hz, 3 H, CH₂Hg), 0.77 (dd, J₆₋₇,₇-H = 13.3 Hz, J₂₋₇,₇-H = 8.9 Hz, 1 H, CH₂Hg), 0.84 (dd, J₆₋₇,₇-H = 13.3 Hz, J₃₋₇,₇-H = 7.6 Hz, 1 H, CH₂Hg), 2.06 (s, 3 H, CH₃CO₂), 2.67 (m, W = 29 Hz, 1 H, 2-H), 3.26 (m, CH-OCH₃), 3.31 (s, 3 H, CH₃O), 4.81 (dt, J = 10.1 and 4.4 Hz, 1 H, CH-OAc); ¹³C NMR δ 18.3 (q), 19.7 (t), 21.6 (q), 24.7 (t), 25.0 (t), 31.7 (t), 41.3 (d), 56.0 (q), 76.5 (d), 81.2 (d), 170.4 (s); HRMS m/z 402.11185 (calcd for C₁₁H₂₀O₃Hg: 402.11188). Anal. Calcd for C₁₁H₂₀O₃Hg: C, 32.96; H, 5.03. Found: C, 32.73; H, 4.99.

(1R*,2S*,3S*)-2-[(Chloromercurio)methyl]-1-methoxycyclohexan-3-ol (69).

To a stirred solution of 67 (500 mg; 1.39 mmol) in 1,2-dimethoxyethane (10 mL) was added mercury(II) chloride (418 mg; 1.54 mmol) and the resulting mixture was stirred at rt for 30 min. Silica gel (1 g) was then added and the solvent was evaporated. The was
chromatographed on silica gel (20 g) using a petroleum ether-acetone mixture (9:1) to give pure 69 (490 mg; 93%): IR ν(OH) 3510, 3610 cm⁻¹; ¹H NMR δ 2.75 (d, J = 10.4 Hz, 1 H, OH), 3.33 (s, 3 H, CH₃O), 3.34 (m, 1 H, CH-OCH₃), 3.64 (m, W/2 = 21 Hz, 1 H, CH-OH); ¹³C NMR δ 14.5 (t), 27.3 (t), 27.8 (t), 33.0 (t), 43.4 (d), 57.3 (q), 71.4 (d), 81.1 (d); HRMS m/z 380.04666 (calcd for C₉H₁₅ClO₂Hg: 380.04669). Anal. Calcd for C₉H₁₅ClO₂Hg: C, 25.34; H, 3.99. Found: C, 25.17; H, 4.20.

(1R*,2S*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cyclohexan-1-yl Acetate (70).

To a solution of the methylmercurio alcohol 48 (647 mg; 1.8 mmol) and triethylamine (0.7 mL; 5.6 mmol) in ether (10 mL) were successively added acetic anhydride (0.6 mL; 5.6 mmol) and 4-N,N-dimethylaminopyridine (230 mg; 1.8 mmol). The mixture was stirred at rt for 20 min and then quenched by ice and 5% aqueous HCl. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel using a petroleum ether-dichloromethane mixture (1:1) as the eluent to give the pure 70 (679 mg; 94%): IR ν(C=O) 1724 cm⁻¹; ¹H NMR δ 0.25 (s (83%) and d (17%), J₆,Hg = 102.5 Hz, 3 H, CH₃Hg), 0.84 (dd, J₆, gem = 13.1 Hz, J₆,CH₂Hg = 8.4 Hz, 1 H, CH₂Hg), 1.00 (dd, J₆, gem = 13.1 Hz, J₆,CH₂Hg = 6.3 Hz, 1 H, CH₂Hg), 1.07-1.26 (m, 1 H), 1.37-1.65 (m, 3 H), 1.78-1.88 (m, 1 H), 2.08 (s, 3 H, CH₃CO₂), 2.07-2.20 (m, 2 H), 3.06 (dt, J = 9.5 and 4.5 Hz, 1 H, CH-OCH₃), 5.04 (m, W = 9.4 Hz, 1 H, CH-OAc); ¹³C NMR δ 19.28 (q), 19.42 (t), 21.41 (q), 29.62 (t), 29.83 (t), 40.65 (t), 45.82 (d), 56.18 (q), 77.00 (d), 82.38 (d), 170.57 (s); MS m/z 420 (M+NH₄⁺). Anal. Calcd for C₁₁H₂₂O₂Hg: C, 33.96; H, 5.03. Found: C, 33.69; H, 5.01.
(1'R*,2'R*,3'R*)-1-(2'-Hydroxy-6'-methoxy-cyclohexan-1'-yl)-propan-2-one (73).

Obtained from 70 in 70% yield using procedure C; IR $\nu$(C=O) 1721 cm$^{-1}$; $^1$H NMR (300 MHz) $\delta$ 1.05-2.05 (m, 8 H), 2.11 (s, 3 H, CH$_3$CO), 2.55 (dd, $J_{gem}$ = 16.4 Hz, $J_{1-H,2'-H}$ = 7.4 Hz, 1 H, CHCH$_2$CO), 2.64 (dd, $J_{gem}$ = 16.4 Hz, $J_{1-H,2'-H}$ = 5.6 Hz, 1 H, CHCH$_2$CO), 3.14 (dt, $J$ = 9.6 and 4.0 Hz, 1 H, CHOCH$_3$), 3.23 (s, 3 H, CH$_3$O), 3.95 (m, $\omega/2$ = 9.5 Hz, 1 H, CHO), $^1$C NMR (75 MHz) $\delta$ 16.36 (t), 29.35 (t), 30.30 (q), 32.20 (t), 42.36 (t), 43.19 (d), 55.84 (q), 68.78 (d), 78.39 (d), 209.84 (s); HRMS (El) m/z 187.13342 (MH$^+$; calcd for C$_{10}$H$_{19}$O$_3$ 187.13341). Anal. Calcd for C$_{10}$H$_{19}$O$_3$: C, 64.49; H, 9.74. Found: C, 64.22; H, 9.95.

(1'R*,2'S*,3'R*)-2-[(Chloromercurio)methyl]-3-methoxy-cyclohexan-1-yl Acetate (74).

A solution of 37 (492 mg; 1.30 mmol), acetic anhydride (0.25 mL; 2.60 mmol), triethylamine (0.36 mL; 2.60 mmol) and 4-$N,N$-dimethylaminopyridine (164 mg; 1.3 mmol) in ether (10 mL) was stirred at rt for 20 min. The excess of the reagent was then decomposed with ice and water, the product was extracted into ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel (25 g) with a petroleum ether-dichloromethane mixture (1:1) to afford pure 74 (494 mg; 99%); IR $\nu$(C=O) 1725 cm$^{-1}$; $^1$H NMR $\delta$ 1.49 (dd, $J_{gem}$ = 11.9, $J_{2-H,7-H}$ = 9.7 Hz, 1 H, CH$_3$Hg), 1.69 (dd, $J_{gem}$ = 11.9, Hz
72₃₇H = 4.8 Hz, 1 H, CH₂Hg), 2.00 (s, 3 H, CH₃CO₂), 2.94 (dt, J 10.2 and 4.1 Hz, 1 H, CH₂-OCH₃), 3.24 (s, 3 H, CH₃O), 4.92 (m, W/2 = 8.8 Hz, 1 H, CH-OAc); ¹³C NMR δ 19.0 (t), 21.3 (q), 28.1 (t), 29.6 (q), 29.9 (t), 45.0 (d), 56.1 (q), 75.1 (d), 80.1 (d), 170.4 (s); MS (CI) m/z 440 (M⁺-NH₄⁺).

(1R*,2S*,3R*)-2-[(Chloromercurio)methyl]-3-methoxycycloheptan-1-yl Acetate (74a).

Prepared from alcohol 40 (0.50 g, 1.2 mmol) by the same method as 74, to yield pure 74a (0.53 g, 95%): IR v(C=O) 1728 cm⁻¹; ¹H NMR δ 1.83 (dd, J₆₇-H.7 Hz, J₂-H₂-H₂= 8.7 Hz, 1H, CH₂Hg), 2.03 (dd, J₆₇-H = 11.7, J₂-H₂-α= 5.9 Hz, 1H,CH₂Hg), 2.12 (s, 3H, CH₃CO₂), 2.27 (m, W/2 = 15Hz, 1H, CH₂Hg), 3.02 (dt, J = 7.2 and 3.4Hz, 1H, CH₃Hg), 3.17 (s, 3H, OCH₃), 3.36 (s, 3H, OCH₃), 5.09 (m, W/2 = 15Hz, CHOAc); ¹³C NMR δ 21.3 (q), 22.3 (t), 23.7 (t), 28.9 (t), 30.2 (t), 31.3 (t), 46.8 (d), 56.5 (q), 76.0 (d), 85.2 (d), 170.2 (s); MS (CI) m/z 437 (MH⁺, Int. 3%), 454 (M⁺+ NH₄⁺, Int. 17%); Anal Calc. for C₁₁H₁₉ClO₃Hg: C, 30.35; H, 4.40, Found: C, 30.52; H, 4.41.

(1R*,2S*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cyclohexan-1-yl Benzoate (75).

To a solution of the methylmercurio alcohol 48 (647 mg; 1.8 mmol) and triethylamine (0.7 mL; 5.6 mmol) in ether (10 mL) were successively added benzoic anhydride (1.28 g; 5.6 mmol) and 4-N,N-dimethylaminopyridine (230 mg; 1.8 mmol). The mixture was stirred at rt for 20 min and then quenched by ice and 5% aqueous HCl. The product was extracted with ether and the etheral solution was worked up. The crude product was chromatographed on silica gel using a petroleum ether-dichloromethane mixture (1:1) as the eluent to give the pure 75 (724 mg; 87%): IR v(C=O) 1713 cm⁻¹; ¹H NMR δ 0.14 (s (83%) and d (17%), J₆₇Hg
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$= 102.5 \text{ Hz, } Z, \text{ CH}_3\text{Hg}, 0.93 \text{ (dd, } J_{\text{gem}} = 12.5 \text{ Hz, } J_{2,3}\text{-H} = 8.8 \text{ Hz, } 1 \text{ H, CH}_2\text{Hg}, 1.06 \text{ (dd, } J_{\text{gem}} = 12.5 \text{ Hz, } J_{2,3}\text{-H} = 6.3 \text{ Hz, } 1 \text{ H, CH}_2\text{Hg}, 1.21 \text{ (m, } 1 \text{ H, } 1.62 \text{ (m, } 3 \text{ H, } 2.00 \text{ (m, } 1 \text{ H, } 2.22 \text{ (m, } 2 \text{ H, } 3.22 \text{ (dt, } J = 10.1 \text{ and } 4.1 \text{ Hz, } 1 \text{ H, CH-CH}_3\text{Hg), 3.43 \text{ (s, } 3 \text{ H, CH}_2\text{O), } 5.31 \text{ (m, } W/2 = 9.1 \text{ Hz, } 1 \text{ H, CHOBz), 7.33 \text{ (m, } 2 \text{ H, } \pi\text{-arom), } 7.43 \text{ (m, } 1 \text{ H, } \pi\text{-arom), } 7.93 \text{ (m, } 2 \text{ H, } \delta\text{-arom); } ^{13}\text{C NMR } \delta 19.18 \text{ (q), } 19.61 \text{ (t), } 30.01 \text{ (t), } 30.28 \text{ (t), } 46.39 \text{ (d), } 56.25 \text{ (q), } 77.88 \text{ (d), } 82.45 \text{ (d), } 128.37 \text{ (d), } 129.55 \text{ (d), } 130.75 \text{ (s), } 132.86 \text{ (d), } 166.05 \text{ (s); HRMS (El) } m/z 464.12753 \text{ (calcd for } C_{16}H_{22}O_3\text{Hg; } 464.127053).}$

$(RS*,2S*,3R*)$-3-Methoxy-2-[(methylmercurio)methyl]-cyclohexan-1-yl Pivolate (76).

To a solution of the methylmercurio alcohol $48 \text{ (757 mg; } 1.6 \text{ mmol) and triethylamine (0.48 mL; } 4.8 \text{ mmol) in THF (20 mL) was added trimethylacetyl chloride (0.59 mL; } 4.8 \text{ mmol) and } 4-N,N\text{-dimethylaminopyridine (188 mg; } 1.6 \text{ mmol) and the mixture was refluxed for 24 h. The reaction mixture was then decomposed with ice and 5% aqueous HCl, the product was extracted with ether, and the ethereal solution was worked up. The crude product was chromatographed on silica gel using a petroleum ether-dichloromethane mixture (1:1) as the eluent to give the pure 76 (639 mg; 90%): IR $\nu$(C=O) 1712 cm$^{-1}$; $^1$H NMR $\delta$ 0.25 (s (83%), 7H, HgMe), 0.89 (d, $J = 7.7$ Hz, 2 H, CH$_3$Hg), 1.13 (m, 2 H), 1.24 (s, 9 H, t-H), 1.52 (m, 3 H), 1.89 (m, 2 H), 2.23 (m, 1 H), 3.03 (dt, $J = 10.3$ and 4.2 Hz, 1 H, CH-CH$_3$), 3.39 (s, 3 H, CH$_2$O), 5.02 (m, $W/2 = 8.5$ Hz, 1 H, CHO$_2$R); $^{13}$C NMR $\delta$ 17.96 (q), 18.54 (t), 26.14 (t), 26.49 (q), 29.41 (t), 38.27 (s) 39.94 (t), 45.48 (d), 55.30 (q), 76.27 (d), 81.31 (d), 177.13 (s); HRMS (El) $m/z$ 444.15882 (calcd for $C_{14}H_{20}O_3$Hg: 444.15883). Anal. Calcd. for $C_{14}H_{20}O_3$Hg: C, 37.96; H, 5.92. Found: C, 37.72; H, 6.08.
(1'R\(^\ast\),2'R\(^\ast\),6'R\(^\ast\))-2-(2'-Hydroxy-6'-methoxy-cyclohexan-1'-yl)-acetylbenezene (77).

Obtained from 75 in 60% yield using procedure C; IR \(\nu(\text{C}=\text{O})\) 1672, \(\nu(\text{OH})\) 3420, 3618 cm\(^{-1}\);
\(^1\text{H} NMR \delta 3.06 (\text{dd}, J_{\text{gem}} = 15.7 \text{ Hz}, J_{1'-\text{H},2'-\text{H}} = 8.7 \text{ Hz}, 1 \text{ H}, \text{CHCH}_2\text{CO}), 3.27 (\text{s and m}, 4 \text{ H}, \text{CH}_3\text{O and CHOCH}_3), 3.38 (\text{dd}, J_{\text{gem}} = 15.7 \text{ Hz}, J_{1'-\text{H},2'-\text{H}} = 4.6 \text{ Hz}, 1 \text{ H}, \text{CHCH}_2\text{CO}), 4.07 (m, \int/2 = 9.4 \text{ Hz}, 1 \text{ H}, \text{CHOH}), 7.45 (m, 2 \text{ H}, \text{o-arom}), 7.54 (m, 1 \text{ H}, \text{p-arom}), 8.00 (m, 2 \text{ H}, \text{m-arom}); \(^{13}\text{C} NMR \delta 18.59 (t), 29.80 (t), 32.42 (t), 37.24 (t), 44.28 (d), 56.20 (q), 68.88 (d), 78.88 (d), 128.36 (2 x d), 128.80 (2 x d), 133.00 (d), 137.14 (s), 201.47 (s); HRMS (EI) \text{m}/\text{z} 248.14116 (\text{calcd for C}_{15}\text{H}_{20}\text{O}_3: 248.14124).

(1'R\(^\ast\),2'R\(^\ast\),6'R\(^\ast\))-1-(2'-Hydroxy-6'-methoxy-cyclohexan-1'-yl)-3,3'-dimethylbutan-2-one (78).

Obtained from 76 in 55% yield using procedure C; IR \(\nu(\text{C}=\text{O})\) 1695, \(\nu(\text{OH})\) 3400, 3610 cm\(^{-1}\);
\(^1\text{H} NMR \delta 1.12 (\text{s}, 9 \text{ H}, \text{t-Bu}), 2.73 (m, 2 \text{ H}, \text{CH}_2\text{CO}), 3.20 (\text{dt}, J = 9.5 \text{ and } 3.7 \text{ Hz}, 1 \text{ H}, \text{CHOCH}_3), 3.26 (s, 3 \text{ H}, \text{CH}_3\text{O}), 3.96 (m, \int/2 = 10.0 \text{ Hz}, 1 \text{ H}, \text{CHOH}); \(^{13}\text{C} NMR \delta 19.39 (t), 26.80 (q), 29.85 (t), 33.68 (t), 35.82 (t), 43.16 (d), 44.82 (s), 56.34 (q), 69.64 (d), 78.80 (d), 217.32 (s); HRMS (EI) \text{m}/\text{z} 228.17249 (\text{calcd for C}_{13}\text{H}_{24}\text{O}_3: 228.17254). \text{Anal. Caled for C}_{13}\text{H}_{24}\text{O}_3: \text{C}, 83.83; \text{H}, 12.99. \text{Found: C}, 83.70; \text{H}, 13.24.
(1R*,2S*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cyclopentan-1-yl Acetate (79).

To a solution of the methylmercurio alcohol 44 (622 mg; 1.8 mmol) and triethylamine (0.7 mL; 5.6 mmol) in ether (10 mL) were successively added acetic anhydride (0.6 mL; 5.6 mmol) and 4-N,N-dimethylaminopyridine (230 mg; 1.8 mmol). The mixture was stirred at rt for 20 min and then quenched by ice and 5% aqueous HCl. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel using a petroleum ether-dichloromethane mixture (1:1) as the eluent to give the pure 79 (383 mg; 55%): IR v(C=O) 1727 cm⁻¹; ¹H NMR δ 0.26 (s (83%) and d (17%), J_Hg = 102.5 Hz, 3 H, CH₂Hg), 0.91 (dd, J_gem = 12.9 Hz, J₂-H₂-H' = 9.1 Hz, 1 H, CH₂Hg), 1.01 (dd, J_gem = 12.9 Hz, J₂-H₂-H' = 6.5 Hz, 1 H, CH₂Hg), 1.50 (m, 1 H), 1.69 (m, 1 H), 2.05 (s, 3 H, CH₃CO₂), 2.12 (m, 1 H), 2.28 (m, 1 H), 3.36 (s, 3 H, CH₃O), 3.38 (m, 1 H, CHOCH₃), 5.09 (dt, J = 5.1 and 2.0 Hz, 1 H, CHOAc); ¹³C NMR δ 19.8 (q), 21.3 (q), 27.7 (t), 29.4 (t), 38.1 (t), 49.8 (d), 57.5 (q), 78.8 (d), 88.5 (d) 170.7 (s); HRMS (EI) m/z 388.09616 (calcd for C₁₀H₁₄O₂Hg 388.09623).

(2S*,4S*,5R*,8R*)-5-Methoxy-2-methyl-1-oxabicyclo[3.3.0]octan-2-ol (80).

Obtained from 79 in 57% yield using procedure C; IR ν(OH) 3410, 3585 cm⁻¹; ¹H NMR δ
1.26 (dd, $J_{\text{gem}} = 12.9$ Hz, $J_{2,4-H,4-H} = 7.7$ Hz, 1 H, 4-H), 1.44 (s, 3 H, CH$_3$), 1.60-1.90 (m, 4 H), 2.24 (dd, $J_{\text{gem}} = 12.9$ Hz, $J_{2,4-H,4-H} = 9.8$ Hz, 1 H, 4-H’), 2.85 (t, $J = 8.3$ Hz, 1 H, 5-H), 3.19 (s, 3 H, CH$_3$O), 3.41 (d, $J = 3.0$ Hz, 1 H, CH$_2$OCH$_3$), 4.70 (t, $J = 5.5$ Hz, 1 H, 8-H); $^{13}$C NMR δ 27.0 (q), 28.5 (t), 30.6 (t), 43.3 (t), 48.7 (d), 56.4 (q), 84.0 (d), 88.4 (d), 106.4 (s); MS m/z 155 (100, M-H$_2$O). Anal. Calcd for C$_9$H$_{16}$O$_3$: C, 62.77; H, 9.36. Found: C, 62.99; H, 9.12.

(1R*,2S*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cycloheptan-1-yl Acetate (81).

![Chemical Structure](image)

To a solution of the methylmercurio alcohol 41 (672 mg; 1.8 mmol) and triethylamine (0.7 mL; 5.6 mmol) in ether (10 mL) were successively added acetic anhydride (0.6 mL; 5.6 mmol) and 4-N,N-dimethylaminopyridine (230 mg; 1.8 mmol). The mixture was stirred at rt for 20 min and then quenched by ice and 5% aqueous HCl. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel using a petroleum ether-dichloromethane mixture (1:1) as the eluent to give the pure 81 (710 mg; 95%): IR ν(C=O) 1724 cm$^{-1}$; $^1$H NMR δ 0.27 (s (83%) and d (17%), $J_{\text{H-Hg}} = 102.5$ Hz, 2 H, CH$_3$Hg), 0.92 (dd, $J_{\text{gem}} = 13.1$ Hz, $J_{2,4-H,4-H} = 7.8$ Hz, 1 H, CH$_2$Hg), 1.09 (dd, $J_{\text{gem}} = 13.1$ Hz, $J_{2,4-H,4-H} = 7.5$ Hz, 1 H, CH$_2$Hg), 1.38-1.54 (m, 2 H), 1.57-1.60 (m, 3 H), 1.76-1.84 (m, 2 H) 1.87-2.01 (m, 1 H) 2.06 (s, 3 H, CH$_3$CO), 2.41 (dq, $J_{2,3-H,3-H} = 7.5$ Hz, $J_{2,4-H,4-H} = 7.5$ Hz, $J_{1,2,2-H,2-H} = 8.9$ Hz, 1 H, 8-H), 3.02 (m, $W = 19$ Hz, 1 H, CH-OCH$_3$), 3.33 (s, 3 H, CH$_3$O), 5.11 (dt, $J = 8.9$ and 2.5 Hz, 1 H, CH-OAc); $^{13}$C NMR δ 19.67 (q), 21.41 (q), 22.04 (t), 24.06 (t), 29.23 (t), 29.79 (t), 42.61 (t), 47.08 (d), 56.34 (q), 77.23 (d), 86.73 (d), 170.35 (s); MS m/z 434 (M-NH$_4^+$). Anal. Calcd for C$_{12}$H$_{25}$O$_3$Hg: C, 34.74; H, 5.34. Found: C, 34.76; H, 5.34.
(1R*,2S*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cycloheptan-1-yl Benzoate (82).

To a solution of the methylmercurio alcohol 41 (672 mg; 1.8 mmol) and triethylamine (0.7 mL; 5.6 mmol) in ether (10 mL) were successively added benzoic anhydride (1.28 g; 5.6 mmol) and 4-N,N-dimethylaminopyridine (230 mg; 1.8 mmol). The mixture was stirred at rt for 20 min and then quenched by ice and 5% aqueous HCl. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel using a petroleum ether-dichloromethane mixture (1:1) as the eluent to give the pure 82 (737 mg; 86%): IR v(C=O) 1713 cm⁻¹; ¹H NMR δ 0.14 (s (83%) and d (17%), J₉,₁₀H₂ = 102.5 Hz, 3 H, CH₃Hg), 0.80-0.92 (m, 1 H), 1.02 (dd, J₉,₁₀H₂ = 13.0 Hz, J₁₀,₁₀H₂ = 8.0 Hz, 1 H, CH₃HgCH₃), 1.22 (d, J₉,₁₀H₂ = 13.0 Hz, J₁₀,₁₀H₂ = 7.5 Hz, 1 H, CH₃Hg), 1.46-1.61 (m, 2 H), 1.61-1.81 (m, 3 H), 1.80-1.95 (m, 2 H), 2.07-2.21 (m, 1 H), 2.49-2.59 (m, 1-H), 3.12 (m, W = 20 Hz, 1 H, CHOCH₃), 3.37 (s, 3 H, CH₃O), 5.36 (dt, J = 8.1 and 1.9 Hz, 1 H, CH-OBz), 7.45 (m, 2 H, o-arom), 7.57 (m, 1 H, p-arom), 8.06 (m, 2 H, m-arom); HRMS (EI) m/z 478.14318 (caled for C₁₇H₂₃O₃Hg: 478.14318).
(1R*,2S*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cycloheptan-1-yl Pivalate (83).

To a solution of the methylmercurio alcohol 41 (598 mg; 1.6 mmol) and triethylamine (0.48 mL; 4.8 mmol) in THF (20 mL) was added trimethylacetyl chloride (0.59 mL; 4.8 mmol) and 4-N,N-dimethylaminopyridine (188 mg; 1.6 mmol) and the mixture was refluxed for 48 h. The reaction mixture was then decomposed with ice and 5% aqueous HCl, the product was extracted with ether, and the ethereal solution was worked up. The crude product was chromatographed on silica gel using a petroleum ether-dichloromethane mixture (1:1) as the eluent to give the pure 83 (418 mg; 57%): ^H NMR δ 0.27 (s (83%) and d (17%), J = 102.0 Hz, 3 H, CH₃Hg), 0.97 (dd, J₁ = 13.0 Hz, J₂ = 9.2 Hz, 1 H, CH₂Hg), 1.11 (dd, J₁ = 13.0 Hz, J₂ = 6.1 Hz, 1 H, t-Bu), 1.35-1.70 (m, 5 H), 1.85 (m, 2 H), 2.02 (m, 1 H), 2.02 (m, 1 H), 2.26 (m, 1 H), 2.98 (m, W/2 = 15 Hz, 1 H), 3.33 (s, 3 H, CH₃O), 5.06 (dt, J = 7.6 and 2.0 Hz, 1 H, CH-O₂R); ^13C NMR δ 20.05 (q), 22.14 (t), 24.31 (t), 27.36 (q), 29.45 (t), 30.71 (t), 39.01 (s), 44.47 (t), 47.73 (d), 56.36 (q), 78.26 (d), 87.11 (d), 178.09 (s); HRMS (El) m/z 458.17451 (calcd for C₂₅H₄₅O₇Hg: 458.17448).

(2S*,4S*,5R*,10R*)-5-Methoxy-2-methyl-1-oxabicyclo[5.3.0]decan-2-ol (84).

Obtained from 81 in 37% yield along with 87 (23%) using procedure C. 84: IR ν(OH) 3437,
3613, 3672 cm\(^{-1}\); \(^1\)H NMR (400 MHz) \(\delta\) 1.25 (m, 2 H, 7-H\(^{-}\) and 8-H\(^{-}\)), 1.35 (m, 1 H, 6-H\(^{-}\)), 1.46 (m, 1 H, 9-H\(^{-}\)), 1.53 (s, 3 H, CH\(_3\)), 1.67 (dd, \(J_{\text{gem}} = 12.8\) Hz, \(J_{4,6,3,5\text{-pro-S}-H} = 10.2\) Hz, 1 H, 3-pro-S*-H), 1.75 (m, 2 H, 7-H and 8-H), 1.82 (m, 1 H, 9-H), 2.03 (m, 1 H, 6-H), 2.30 (dd, \(J_{\text{gem}} = 12.8\) Hz, \(J_{4,6,3,5\text{-pro-R}-H} = 7.9\) Hz, 1 H, 3-pro-R*-H), 2.75 (ddddd, \(J = 10.8, 9.7, 9.1, 7.9\) Hz, 1 H, 4-H), 3.07 (t, \(J = 9.7\) Hz, 1 H, 5-H), 3.30 (s, 3 H, CH\(_3\)O), 4.29 (ddd, \(J = 11.1, 9.1, 3.6\) Hz, 1 H, 10-H); \(^1^3\)C NMR (100 MHz) \(\delta\) 24.95 (t; C-5 or C-6), 27.05 (q; Me), 27.65 (t; C-5 or C-6), 31.93 (t; C-6), 33.19 (t; C-3), 43.57 (t; C-10), 47.46 (d; C-1), 56.03 (q; MeO), 79.85 (d; C-7), 84.06 (d; C-2), 103.72 (s); MS m/z 201 (5, M), 183 (100, M-H\(_2\)O). NOE difference experiments for the major anomer: irradiation of Me resulted in the increase of 3-pro-S*-R (2.5%), 3-pro-R*-H (0.9%), and 5-H (0.7%); irradiation of 5-H resulted in the increase of 3-pro-S*-H (3%) and 6-H (1%); irradiation of MeO resulted in the increase of 4-H (1%) and 3-pro-S*-H (1%); irradiation of 10-H resulted in the increase of 4-H (8%). Anal. Calcd for C\(_{11}\)H\(_{20}\)O\(_3\): C, 65.97; H, 10.07. Found: C, 65.83; H, 10.15.

\((2^S_*,4^S_*,5^R_*,10^R_*)\)-S-Methoxy-2-phenyl-1-oxabicyclo[5.3.0]decan-2-ol (85).

\[
\begin{align*}
\text{OH} & \quad \text{Ph} \\
\text{OMe} & \quad \text{Me}
\end{align*}
\]

Obtained from 82 in 65% yield using procedure C; \(^1\)H NMR (300 MHz) \(\delta\) 1.73 (dd, \(J_{\text{gem}} = 12.8\) Hz, \(J_{4,6,3,5\text{-pro-S}-H} = 10.4\) Hz, 1 H, 3-H\(^{-}\)), 2.54 (dd, \(J_{\text{gem}} = 12.8\) Hz, \(J_{4,6,3,5\text{-pro-R}-H} = 7.7\) Hz, 1 H, 3-H), 2.84 (m, 1 H, 4-H), 3.06 (m, 1 H, 5-H), 3.24 (s, 3 H, CH\(_3\)O), 3.77 (br s, 1 H, OH), 4.18 (dd, \(J = 11.2, 9.1, 3.3\) Hz, 1 H, 10-H), 7.27-7.32 (m, 2 H, \(\alpha\)-arom), 7.34-7.37 (m, 1 H, \(p\)-arom), 7.55-7.58 (m, 2 H, \(m\)-arom); \(^1^3\)C NMR (75 MHz) \(\delta\) 24.99 (t), 27.61 (t), 31.72 (t), 32.95 (t), 46.20 (t), 47.47 (d), 55.96 (q), 80.00 (d) 84.17 (d), 104.66 (s), 125.213 (2 x d), 127.65 (d), 127.92 (2 x d), 143.78 (s); MS m/z 244 (M-H\(_2\)O, 65.5), 157 (11), 105 (55.6). Anal. Calcd for C\(_{16}\)H\(_{22}\)O\(_3\): C, 73.25; H, 8.45. Found: C, 73.08; H, 8.27.
(2Σ⁰,4S⁰,5R⁰,10R⁰)-2-t-Butyl-5-methoxy-1-oxabicyclo[5.3.0]decan-2-ol (86).  

\[ \text{H NMR} \delta 1.00 (s, 9 H, t-Bu), 1.81 (dd, J_{\text{gem}} = 12.8 Hz, 3 \text{ H}, 3 \text{-H}), 2.09 (dd, J_{\text{gem}} = 12.8 Hz, J_{4\text{H},3\text{H}} = 7.9 Hz, 1 \text{ H}, 3\text{-H}), 2.78 (m, 1 \text{ H}, 4\text{-H}), 3.06 (m, 1 \text{ H}, 5\text{-H}), 3.31 (s, 3 \text{ H}, \text{CH}_3\text{O}), 4.27 (ddd, 1 \text{ H}, J = 11.5, 9.1, \text{ and } 2.8 \text{ Hz}, 1 \text{ H}, 10\text{-H}); \]  
\[ \text{C NMR} \delta 25.34 (q), 25.57 (t), 27.87 (t), 31.89 (t), 32.87 (t), 37.29 (s), 37.70 (t), 47.00 (d), 55.94 (q), 80.32 (d), 84.49 (d), 109.45 (s); \]  
\[ \text{HRMS (EI) } m/z 242.18804 \text{ (calcd for C}_{14}\text{H}_{19}\text{O}_{2}: 242.18819). \]

(1R⁰,2R⁰,3R⁰)-3-Methoxy-2-methylcycloheptanol-1-ol (87).  

\[ \text{IR } \nu(\text{OH}) 3409, 3593 \text{ cm}^{-1}; \]  
\[ \text{H NMR (400 MHz) } \delta 1.03 (d, J = 7.4 \text{ Hz}, 3 \text{ H}, \text{CH}_2\text{CH}), 1.20 \text{ - } 1.80 (m, 9 \text{ H}), 3.04 (q, J = 5.6 \text{ Hz}, 1 \text{ H}, \text{CH}-\text{OCH}_2), 3.26 (s, 3 \text{ H}, \text{CH}_2\text{O}), 4.01 (dt, J = 9.0 \text{ and } 2.6 \text{ Hz}, 1 \text{ H}, \text{CHOH}); \]  
\[ \text{C NMR (100 MHz) } \delta 14.41 (q), 22.14 (t), 23.96 (t), 29.73 (t), 32.64 (t), 43.89 (d), 56.46 (q), 71.82 (d), 83.87 (d); \]  
\[ \text{MS (Cl) } m/z 176 (\text{MNH}_4\text{)}, 159 (\text{MH}^+). \]
(15°,25°,3R°)-3-Methoxy-2-[(methylmercurio)methyl]-cyclohexan-1-yl Acetate (94).

To a solution of the methylmercurio alcohol 52 (650 mg; 1.8 mmol) and triethylamine (0.7 mL; 5.6 mmol) in ether (10 mL) were successively added acetic anhydride (0.6 mL; 5.6 mmol) and 4-N,N-dimethylaminopyridine (230 mg; 1.8 mmol). The mixture was stirred at rt for 20 min and then quenched by ice and 5% aqueous HCl. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel using a petroleum ether-dichloromethane mixture (1:1) as the eluent to give the pure 94 (708 mg; 98%): mp 31-32 °C (hexane); IR \( \nu(C=O) \) 1718 cm\(^{-1}\); \(^1\)H NMR \( \delta \) 0.2 (s (83%) and d (17%), \( J_{\text{gem}} = 102.3 \text{ Hz} \), 3 H, \( \text{CH}_3\text{Hg} \)), 0.71 (dd, \( J_{\text{gem}} = 13.1 \text{ Hz} \), \( J_{2-7-7-H} = 8.6 \text{ Hz} \), 1 H, \( \text{CH}_2\text{Hg} \)), 1.18 (dd, \( J_{\text{gem}} = 13.1 \text{ Hz} \), \( J_{2-7-7-H} = 4.6 \text{ Hz} \), 1 H, \( \text{CH}_2\text{Hg} \)), 2.08 (s, \( \text{CH}_3\text{CO} \)), 2.72 (dt, \( J = 10.3 \text{ and } 4.1 \text{ Hz} \), 1 H, \( \text{CH-CH}_3\)), 3.39 (s, \( \text{CH}_3\text{O} \)), 4.41 (dt, \( J = 10.2 \text{ and } 4.5 \text{ Hz} \), 1 H, \( \text{CH-CH}_2\text{OAc} \)); \(^{13}\)C NMR \( \delta \) 19.4 (q), 20.6 (t), 21.8 (q), 30.3 (t), 31.9 (t), 40.2 (t), 49.4 (d), 56.9 (q), 79.6 (d), 85.0 (d), 171.2 (s); HRMS m/z 402.11188 (calcld for \( \text{C}_{15}\text{H}_{29}\text{O}_{3}\text{Hg} \): 402.11187). Anal. Calcd for \( \text{C}_{15}\text{H}_{29}\text{O}_{3}\text{Hg} \): C, 32.96; H, 5.03. Found: C, 33.06; H, 5.00.

(1'R°,2'S°,6'R°)-1-(2'-Hydroxy-6'-methoxy-cyclohexan-1'-yl)-propan-2-one (97).

Obtained from 94 in 15% yield as a mixture with 98, using procedure C: The crude mixture
was chromatographed on silica gel (25 g) using a petroleum ether-acetone mixture (95:5), which eluted the unreacted 94 (30%), followed by the (90:10) mixture to obtain 97 (15%), contaminated by 98 (5%). Finally, the (80:20) mixture eluted 96 (40%). 95: \(^1\)H NMR \(\delta\) 2.19 (s, 3 H, \(\text{CH}_3\)CO), 2.58 (dd, \(J = 16.4\) and 6.6 Hz, 1 H, CHCH\(_2\)CO), 2.83 (m, 1 H, \(\text{CHOH}\)), 3.21 (dt, \(J = 10.1\) and 4.2 Hz, 1 H, \(\text{CHOMe}\)), 3.29 (s, 3 H, \(\text{CH}_3\)O).

\((1'R^*,2'S^*,6'R^*)-1-(2'-\text{Hydroxy-6'-methoxy-cyclohexan-1'-yl})-2\text{-methylpropan-2-ol}\ (98).\)

![Diagram of 98]

Obtained from 94 in 40% yield as the most polar component, along with 97 (15%) and unreacted 94 (30%) using procedure C. 98: \(^1\)H NMR \(\delta\) 1.24 (s, 3 H, \(\text{CH}_3\)), 1.26 (s, 1 H, \(\text{CH}_3\)), 2.74 (dt, \(J = 9.9\) and 4.1 Hz, 1 H, \(\text{CH-OH}\)), 3.23 (dt, \(J = 9.9\) and 4.1 Hz, 1 H, \(\text{CH-CH}_2\)), 3.35 (s, 3 H, \(\text{CH}_3\)), 3.90 (br s, 2 H, \(\text{OH}\)); \(^1\)C NMR \(\delta\) 20.3 (t), 29.6 (t), 31.5 (t), 34.9 (t), 44.5 (t), 47.0 (t), 57.1 (t), 70.5 (s), 74.2 (d), 83.0 (s); MS (EI) \(m/z\) 169 (MH\(^+\)-2OH, Int. 15%), 137 (169-MeOH, Int. 20%).

\((1'S^*,2'R^*,6'R^*)-1-(2'-\text{Hydroxy-6'-methoxy-cyclohexan-1'-yl})-2\text{-methylpropan-2-one}\ (101).\)

![Diagram of 101]

Obtained from 61 in 39% yield along with the less polar, unreacted 61 (8%) and the more polar 102 (8%), using procedure C; IR \(\nu(C=O)\) 1708, \(\nu(OH)\) 3425 and 3600 cm\(^{-1}\); \(^1\)H NMR \(\delta\)
2.12 (s, 3 H, CH₃CO), 2.55 (dd, J₆₋₇,₁-H = 17.6 Hz, J₃₋₁-H = 6.3 Hz, 1 H, CHCH₂CO), 2.74 (dd, J₆₋₇,₁-H = 17.6 Hz, J₃₋₁-H = 6.3 Hz, CHCH₂CO), 3.17 (s, 3 H, CH₃O), 3.38 (m, W/2 = 8 Hz, 1 H, CH-CH₃), 3.48 (dt, J = 10.2 and 4.1 Hz, 1 H, CH-OH); ¹³C NMR δ 19.2 (t), 27.4 (t), 31.1 (q), 35.7 (t), 43.9 (t), 45.1 (d), 56.8 (q), 70.9 (d), 79.6 (d), 210.8 (s); HRMS (EI) m/z 186.12559 (calcd for C₁₀H₁₈O₃: 186.12556).

(1'S*,2'R*,6'R*)-1-(2'-Hydroxy-6'-methoxy-cyclohexan-1'-yl)-2-methylpropan-2-ol (102).

Obtained from 61 in 8% yield along with 101 (39%) and unreacted 61 (8%) using procedure C; IR ν(OH) 3370 and 3605 cm⁻¹; ¹H NMR δ 1.15 (s, 3 H, CH₃), 1.21 (s, 3 H, CH₃), 3.21 (s, 3 H, CH₃O), 3.35 (m, W/2 = 11.5 Hz, 1 H, CH-OCH₃), 3.56 (dt, J = 9.4 and 4.4 Hz, 1 H, CH-OH); ¹³C NMR δ 18.4 (t), 26.9 (t), 28.5 (q), 31.5 (q), 34.3 (t), 44.1 (d), 44.4 (t), 56.3 (q), 69.7 (s), 71.3 (d), 81.6 (d); MS (CI) m/z 202 (M⁺-H₂O+N⁺), 185 (MH⁺-H₂O). 167 (MH⁺-2H₂O). Anal. Calcd for C₁₁H₂₂O₃: C, 65.31; H, 10.96. Found: C, 65.10; H, 11.23.
(2S*,4R*,5R*,10R*)-5-Methoxy-2-methyl-1-oxabicyclo[5.3.0]decan-2-ol (103).

Obtained from 62 in 62% yield using procedure C; IR ν(OH) 3435 and 3590 cm⁻¹; ¹H NMR δ 1.36 (m, 1 H, 7-H'), 1.46 (m, 1 H, 9-H') 1.50 (s, 3 H, CH₃), 1.55 - 1.75 (m, 4 H), 1.89 (dd, J₉₋₁₀ = 12.8 Hz, J₆₋₈₋₉ = 3.7 Hz, 1 H, 3-pro-R*-H), 1.96 (m, 1 H, 6-H), 2.09 (dd, J₉₋₁₀ = 12.8 Hz, J₆₋₈₋₉ = 12.0 Hz, 1 H, 3-pro-S*-H), 2.10 (m, 1 H, 9-H), 2.28 (ddd, J = 12.0, 8.4, 3.7, 3.1 Hz, 1 H, 4-H), 3.30 (s, CH₃O of the minor anomer), 3.38 (s, CH₃O of major anomer; in ca 3.6:1 ratio to the minor anomer), 3.49 (ddd, J = 6.5, 5.5, 3.1 Hz, 1 H, CHOCH₃), 4.13 (ddd, J = 11.3, 8.4, 3.7 Hz, 1 H, 10-H), 4.79 (s, 1 H, OH); ¹³C NMR of the major anomer: δ 22.1 (t), 25.2 (q), 26.7 (q), 32.4 (t), 33.0 (t), 42.1 (t), 47.8 (d), 57.0 (q), 75.2 (d), 78.0 (d), 103.7 (s); ¹³C of the minor anomer: δ 21.6 (t), 26.2 (t), 27.8 (q), 33.9 (t), 36.1 (t), 41.3 (t), 49.0 (d), 57.4 (q), 76.4 (d), 79.2 (d), 104.7 (s); HRMS (EI) m/z 200.14124 (calcd for C₁₁H₂₀O₃: 200.14125).

NOE difference experiments for the major anomer: irradiation of OH resulted in the increase of 10-H (8%), 3-pro-R*-H (4%), and MeO (1.5%); irradiation of Me resulted in the increase of 3-pro-S*-H (7%) and 3-pro-R*-H (1%); irradiation of 10-H resulted in the increase of OH (4%) and 9-H (4%); irradiation of MeO resulted in the increase of OH (1%).
(2S,2'S,6'R*)-1-(2'-Hydroxy-6'-methoxy-cyclohexan-1'-yl)-2-phenylpropan-2-ol (104).

Obtained from 94, as a 5:2 mixture of C-2 epimers, in 51% yield using a modified procedure C. To a stirred suspension of copper(I) iodide (142 mg; 0.75 mmol) in ether (10 mL) was added a 1.6M solution of phenyllithium in cyclohexane (1.4 mL; 2.24 mmol) at -20 °C. The mixture was stirred at -20 °C for 10 min and then cooled to -78 °C. A solution of the organomercurial 94 (300 mg; 0.75 mmol) in ether (5 mL) was added and the mixture was stirred at -78 °C for 10 min and then quenched with 5% aqueous HCl. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel (25 g) using first a petroleum ether-acetone mixture (95:5) to elute impurities and then a 9:1 mixture to obtain the minor epimer of 104 (29 mg; 15%) followed by the major epimer of 104 (72 mg; 37%). The major epimer: $^1$H NMR δ 1.51 (s, 3 H, CH$_3$), 1.98 (dd, $J = 14.5$ and 3.1 Hz, 1 H, CH$_2$CH), 2.69 (dt, $J = 10.1$ and 3.8 Hz, 1 H, CH-OH), 3.23 (m, 1 H, CH-OMe), 3.25 (s, 3 H, CH$_3$O), 7.13 (m, 1 H, arom), 7.30 (m, 2 H, arom) 7.48 (m, 2 H, arom); $^{13}$C NMR 22.6 (t), 30.8 (t), 31.8 (q), 36.1 (t), 45.1 (t), 47.1 (d), 56.8 (q), 73.5 (d), 73.8 (s), 82.5 (d), 125.3 (2 x d), 126.0 (d), 127.9 (2 x d), 149.1 (s); HRMS m/z 264.17252 (calcd for C$_{16}$H$_{24}$O$_3$: 264.17254). The minor epimer: $^1$H NMR δ 1.57 (s, 3 H, CH$_3$), 1.95 (dd, $J = 14.7$ and 5.0 Hz, 1 H, CH$_2$CH), 2.35 (dd, $J = 14.7$ and 3.0 Hz, 1 H, CH$_2$CH), 2.77 (dt, $J = 10.0$ and 3.8 Hz, 1 H, CH-OMe), 3.09 (dt, $J = 10.1$ and 4.1 Hz, 1 H, CH-OH), 3.42 (s, 3 H, CH$_3$O), 7.22 (m, 1 H, arom), 7.33 (m, 2 H, arom), 7.51 (m, 2 H, arom); $^{13}$C NMR δ 20.3 (t), 29.7 (t), 31.6 (q), 35.3 (t), 45.4 (t), 47.5 (d), 57.2 (q), 73.7 (d), 73.9 (s), 83.6 (d), 125.8 (2 x d), 126.7 (d), 128.4 (2 x d), 149.4 (s); HRMS m/z 264.17252 (calcd for C$_{16}$H$_{24}$O$_3$: 264.17254).
To a stirred suspension of copper(I) iodide (141 mg; 0.75 mmol) in dry ether (5 mL) was added a 1.39M solution of methyllithium in ether (1.61 mL; 2.24 mmol) at -20 °C. The mixture was stirred at -20 °C for 10 min and then cooled to -78 °C. A solution of the organomercurial acetate 70 (300 mg; 0.75 mmol) in ether (1 mL) was added and the mixture was stirred at -78 °C for 10 min and then quenched by a dropwise addition of a solution of BF$_3$ • Et$_2$O (1 mL) in ether (10 mL) at -78 °C. The mixture was allowed to warm to rt and stirred at rt overnight. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel using first a petroleum ether-acetone mixture (95:5, then 90:10, and 80:20) to obtain 112 (48 mg; 35%), followed by 113 (26 mg; 26%), and 73 (29 mg; 19%). 112: $^1$H NMR δ 1.39 (s, 3 H, CH$_3$), 1.51 (s, 3 H, CH$_3$), 3.27 (dt, 1 H, $J$ = 7.6 and 3.8 Hz, 1 H, OMe), 3.51 (s, 3 H, CH$_3$O), 4.22 (m, $\omega/2$ = 8 Hz, 1 H, CH-O); $^{13}$C δ 19.4 (t), 38.3 (t), 29.0 (t), 29.7 (q), 31.0 (q), 43.1 (t), 46.6 (d), 56.8 (q), 76.8 (d), 79.5 (s), 81.1 (d).
(1'R*,2'R*,6'R*)-1-(2'-Hydroxy-6'-methoxy-cyclohexan-1'-yl)-2-methylprop-1-ene

Obtained from 70 in 26% yield along with the less polar 112 (35%) and more polar 73 (19%) using the procedure described for the preparation of 112. IR ν(OH) 3430 and 3650 cm⁻¹;

1H NMR δ 1.64 (s, 3 H, CH₃), 1.71 (s, 3 H, CH₃), 2.62 (m, W = 28 Hz, 1 H, CH-CH=C), 3.27 (s, 3 H, CH₃O), 3.27 (m, 1 H, -OCH₃), 3.89 (m, W/2 = 11 Hz, 1 H, CH-OH), 5.16 (br d, J = 9.1 Hz, 1 H, CH=C); ¹³C NMR δ 18.8 (q), 19.3 (t), 26.7 (q), 28.1 (t), 31.8 (t), 45.8 (d), 53.8 (q), 70.4 (d), 80.3 (d), 122.5 (d), 136.5 (s); HRMS (EI) m/z 184.1463 (calcd for C₁₁H₂₀O₃: 184.1463).

(E,1'R*,2'R*,6'R*)-1-(2'-Hydroxy-6'-methoxy-cyclohexan-1'-yl)-2,3,3-trimethylbut-1-ene (114).

To a stirred suspension of copper(I) iodide (141 mg; 0.75 mmol) in dry ether (5 mL) was added a 1.39M solution of methyl lithium in ether (1.61 mL; 2.24 mmol) at -20 °C. The mixture was stirred at -20 °C for 10 min and then cooled to -78 °C. A solution of the organomercurial pivalate 76 (331 mg; 0.75 mmol) in ether (1 mL) was added and the mixture was stirred at -78 °C for 10 min and then quenched by a dropwise addition of a solution of BF₃·Et₂O (1 mL) in ether (10 mL) at -78 °C. The mixture was allowed to warm to rt and
stirred at rt overnight. The product was extracted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel using first a petroleum ether-acetone mixture (95:5, then 90:10, and 80:20) to first obtain 114 (36 mg; 24%), followed by 78 (30 mg; 21%). 114: \( ^1H \) NMR \( \delta \) 1.08 (s, 9 H, t-Bu), 1.72 (s, 3 H, CH₃), 2.73 (m, \( W = 28 \) Hz, 1 H, CH-C=C), 3.34 (s, 3 H, CH₃O), 3.34 (m, 1 H, CH-OCH₃), 3.96 (m, \( W/2 = 13 \) Hz, 1 H, CHO), 5.30 (br d, \( J = 9.1 \) Hz, 1 H, CH=C); \( ^13C \) NMR \( \delta \) 13.8, 19.4, 28.1 (t-Bu), 31.7, 37.0, 45.5, 56.8, 70.1, 80.6, 118.4, 148.6; HRMS (El) m/z 226.19329 (calcd for C₁₄H₂₆O₂: 226.19328). NOE experiments (using the 1D ROESY technique):\(^72\) irradiation of t-Bu resulted in the increase of HC=C (16%) and Me-C=C (5%); irradiation of HC=C resulted in increase of t-Bu (1%); irradiation of CH-C=C resulted in the increase of CHO (7%); irradiation of CHO resulted in the increase of CH-CH=C (6%).

**Ethyl(1R*,2S*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cyclohexan-1-yl Carbonate (121).**

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\text{O} \\
\text{OEt} \\
\text{HgMe} \\
\text{OMe}
\end{array}
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To a stirred solution of 48 (200 mg; 0.56 mmol) in pyridine (5 mL) was added ethyl chloroformate (180 mg; 1.67 mmol) at 0 °C and the mixture was then stirred at rt overnight. The mixture was then poured onto ice and water and the product was extracted into ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel (20 g) first with petroleum ether to elute lipophilic impurities and then with a petroleum ether-dichloromethane mixture (3:1) to obtain the pure 121 (182 mg; 75%): IR \( \nu(C=O) \) 1735 cm\(^{-1}\); \( ^1H \) NMR \( \delta \) 0.25 (s 83% and d 17%, \( J_{HH\text{g}} = 105.0 \) Hz, 3 H, CH₃Hg), 0.90 (dd, \( J_{\text{gem}} = 13.2 \) Hz, \( J_{2-\text{H},7-\text{H}} = 8.7 \) Hz, 1 H, CH₂Hg), 1.02 (dd, \( J_{\text{gem}} = 13.2 \) Hz, \( J_{2-\text{H},7-\text{H}} = 5.9 \) Hz, 1 H, CH₂Hg), 1.33 (t, \( J = 7.1 \) Hz, 3 H, CH₃CH₂), 3.10 (dt, \( J = 9.8 \) and 4.0 Hz, 1 H, CHOCH₃).
103

3.37 (s, 3 H, CH₃O), 4.19 (q, J = 7.1 Hz, 2 H, CH₂CH₂O), 4.89 (m, W/2 = 9 Hz, 1 H, CH-O);
¹³C NMR δ 14.7 (q), 19.2 (q), 19.3 (t), 30.0 (t), 30.2 (t), 40.9 (t), 46.4 (d), 56.6 (q), 64.1 (t),
81.6 (d), 82.3 (d), 155.4 (s); MS (EI) m/z 432 (M⁺, 11). Anal. Calcd for C₁₂H₂₂O₄Hg: C,
33.45; H, 5.15. Found: C, 33.29; H, 5.30.

Phenyl(R⁺,2S⁺,3R⁻)-3-Methoxy-2-[(methylmercurio)methyl]-cyclohexan-1-yl
Carbonate (122).

To a stirred solution of 48 (200 mg; 0.56 mmol) in pyridine (5 mL) was added phenyl
chloroformate (337 mg; 1.67 mmol) at 0 °C and the mixture was then stirred at rt overnight.
The mixture was then poured onto ice and water and the product was extracted into ether and
the ethereal solution was worked up. The crude product was chromatographed on silica gel
(30 g) first with petroleum ether to elute lipophilic impurities and then with a petroleum
ether-dichloromethane mixture (3:1) to obtain the pure 122 (125 mg; 43%): mp 40-41 °C
(hexane); IR ν(C=O) 1752 cm⁻¹; ¹H NMR δ 0.27 (s (83%) and d (17%), J₃-Hg = 103.2 Hz, 3
H, CH₃Hg), 0.92 (dd, J₉,₁H-Hg = 13.1 Hz, J₃,₉-Hg = 9.1 Hz, 1 H, CH₂Hg), 1.02 (dd, J₉,₁H-Hg = 13.1
Hz, J₂-H,₇-H = 5.7 Hz, 1 H, CH₂Hg), 3.08 (dt, J = 9.8 and 4.0 Hz, 1 H, CH-OCH₃), 3.35 (s, 3
H, CH₃O), 4.98 (m, W/2 = 9 Hz, 1 H, CH-OCO), 7.17 (m, 3 H, arom), 7.36 (m, 2 H, arom);
¹³C NMR δ 19.3 (q), 19.7 (t), 30.1 (t), 30.2 (t), 40.9 (t), 46.4 (d), 56.7 (q), 82.2 (d), 83.0 (d),
121.5 (2 x d), 126.3 (d), 129.9 (2 x d), 151.7 (s), 153.9 (s); HRMS m/z 480.12244 (calcd for
H, 4.50.
(LR*,2S*,3R*)-3-Methoxy-2-[(methylmercurio)methyl]-cyclohexan-1-yl
(p-Nitrophenyl)carbonate (123).

To a stirred solution of 48 (200 mg; 0.56 mmol) in pyridine (5 mL) was added p-nitrophenyl chloroformate (262 mg; 1.67 mmol) at 0 °C and the mixture was then stirred at rt overnight. The mixture was then poured onto ice and water and the product was extracted into ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel (20 g) first with petroleum ether to elute lipophilic impurities and then with a petroleum ether-dichloromethane mixture (3:1) to obtain the pure 123 (164 mg; 61%): IR ν(νO 2) 1345 and 1525, ν(C=O) 1760 cm⁻¹; ¹H NMR δ 0.27 (s (83%) and d (17%), J_H,Me = 103.6 Hz, 3 H, CH₂Hg), 0.90 (dd, J_gem = 13.0 Hz, J₂-H,7-H = 9.2 Hz, 1 H, CH₂Hg), 1.03 (dd, J_gem = 13.0 Hz, J₂-H,7-H = 5.6 Hz, 1 H, CH₂Hg), 3.11 (dt, J = 9.8 and 4.0 Hz, 1 H, CH-OCH₃), 3.38 (s, 3 H, CH₃O), 5.02 (m, W/2 = 10 Hz, 1 H, CH-OCO), 7.39 (m, 2 H, arom), 8.27 (m, 2 H, arom); ¹³C NMR δ 18.9 (q), 19.6 (t), 29.9 (t), 30.1 (t), 40.9 (t), 46.3 (d), 56.7 (q), 82.1 (d), 84.2 (d), 122.2 (2 x d), 125.7 (2 x d), 145.6 (s), 152.6 (s), 156.1 (s); HRMS m/z 525.10752 (calcd for C₁₆H₂₁NO₆Hg: 525.10754).
(15\textsuperscript{R},2R\textsuperscript{a},6R\textsuperscript{a})-2-Methoxy-7-oxabicyclo[4.3.0]nonan-8-one (125). From 121:

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\text{O} \\
\text{OMe}
\end{array}
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Obtained as a minor product in a mixture with 73 (1:3), using procedure C.

From 37: Obtained by carbonylation of 37 in 60% yield using procedure D; IR \nu(C=O) 1772 cm\textsuperscript{-1}; \textsuperscript{1}H NMR \delta 1.04 (m, 1 H), 1.27-1.65 (m, 3 H), 2.00 (m, 2 H), 2.13 (m, 1 H), 2.47 (dd, 1 H, J = 16.5 and 7.8 Hz, CH\textsubscript{2}-CO\textsubscript{2}), 2.56 (dd, 1 H, J = 16.5 and 6.0 Hz, CH\textsubscript{2}-CO\textsubscript{2}), 2.93 (ddd, 1 H, J = 10.6, 9.1, and 3.8 Hz, CH-OCH\textsubscript{3}), 3.26 (s, 3 H, CH\textsubscript{3}O), 4.60 (dd, 1 H, J = 7.0 and 3.5 Hz, CH-OCO); \textsuperscript{13}C NMR \delta 18.5 (t), 27.6 (t), 27.8 (t), 36.1 (t), 42.3 (d), 57.0 (q), 79.7 (d), 80.5 (d), 177.5; HRMS \textit{m/z} (%) 170.09429 (M\textsuperscript{+} 14; calcd for C\textsubscript{9}H\textsubscript{14}O\textsubscript{3}: 170.09429). Anal. Calcd. for C\textsubscript{9}H\textsubscript{14}O\textsubscript{3}: C, 63.51; H, 8.29. Found: C, 63.37; H, 8.51.

(1R\textsuperscript{a},2S\textsuperscript{a},3R\textsuperscript{a})-2-[Chloromethyl]-3-methoxycycloheptan-1-yl Acetate (128)

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\begin{array}{c}
\text{OAc} \\
\text{OMe}
\end{array}
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To a stirred solution of acetate 76 (200mg, 0.48mmol) in dry ether was added MoCl\textsubscript{5} (131mg, 0.48 mmol). The reaction was stirred overnight, quenched with water and worked up. The crude product was purified by column chromatography, eluting with a petrol-acetone mixture ((95:5) to give pure 128 (61%) along with chloromercurio acetate 74a (14%). IR \nu(C=O)
1730 cm⁻¹; ¹H NMR δ 83.30 (m, 1H, CHOME), 3.35 (s, 3H, OCH₃), 3.62 (dd, J₁=10.8Hz, J₂=4.8Hz, 1H, CH₂Cl), 3.75 (dd, J₁=10.8Hz, J₂=4.8Hz, 1H, CH₂Cl), 5.39 (m, W/2 = 13Hz, 1H); ¹³C NMR δ 21.2 (q), 21.9 (t), 24.1 (t), 30.0 (t), 31.1 (t), 45.1 (t), 50.4 (d), 56.6 (q), 71.7 (d), 80.0 (d); MS m/z (El) 234 (M⁺, Cl³⁵ Int. 13%), 236 (M⁺, Cl³⁷ Int.4%).

[(Bromomercurio)methyl)cyclohexane (135).

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\text{HgBr}
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To the Grignard reagent generated from bromomethylcyclohexane 134 (5.0 g; 28 mmol) and magnesium turnings (750 g; 31 mmol) in THF (10 mL) was added a solution of mercury(II) bromide (8.9 g; 25 mmol) in THF (10 mL) and the reaction mixture was heated at 60 °C overnight. The mixture was quenched with water, decanted from the residual mercury, the decantate was diluted with ether and the resulting solution was washed with brine and water and dried with MgSO₄. The solvent was evaporated and the crude solid was crystallized from ethanol to afford 88 (4.5 g; 53%); mp 57-59 °C; ¹H NMR δ 0.87-1.33 (m, 5 H), 1.53-1.92 (m, 6 H), 2.13 (d, J = 5.7 Hz, 2 H, CH₂HgCl); ¹³C NMR δ 26.2 (t), 26.7 (t), 38.6 (d), 38.9 (t), 46.6 (t); HRMS (El) m/z 374.98834 (caled for C₇H¹₅Br⁻¹⁹⁹Hg: 374.98836).

[(Methylmercurio)methyl)cyclohexane (136):

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\text{HgMe}
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Obtained from 135 in 83% yield using procedure B; ¹H NMR δ 0.26 (s (83%) and d (17%), J = 95 Hz, 3 H, CH₃Hg), 0.86-1.08 (m, 2 H), 1.11 (d, J = 7.0 Hz, 2 H, CH₂Hg), 1.17-1.33 (m, 3
H), 1.66-1.90 (m, 5 H), 2.03-2.33 (m, 1 H); $^{13}$C NMR δ 24.4 (q), 26.7 (t), 27.2 (t), 39.1 (d), 39.1 (t), 52.5 (t); HRMS (EI) m/z 314.09582 (calcd for C$_8$H$_{16}$O$_2$: 314.09583).

2-Methylcyclohex-2-en-one (148).

To a stirred solution of 37 (400 mg; 1.1 mmol) in DME (10 mL) was added palladium(II) chloride (187 mg; 1.1 mmol) and lithium chloride (90 mg; 2.1 mmol) and the reaction mixture was stirred at rt for 48 h. The mixture was then diluted with ether and the ethereal solution was worked up. The crude product was chromatographed on silica gel (20 g) using a petroleum ether-ether mixture (9:1) to give pure 148 (50 mg; 43%): IR ν(C=O) 1655, ν(C=CH) 1680 cm$^{-1}$; $^1$H NMR δ 1.80 (br s, 3 H, CH$_3$), 2.16 (t, J = 6.6 Hz, 2 H), 2.34 (m, 2 H), 2.45 (t, J = 6.8 Hz, 2 H), 6.76 (m, W/2 = 9 Hz, 1 H, CH=CH); MS (EI) m/z (%) 111 (M+1, 45).

(1R*,2R*,2R*)-3-Methoxy-2-methylcyclohexan-1-one (149).

Obtained as a less polar byproduct from 40 in 10% yield along with 150 (59%) using procedure D. 149: IR ν(C=O) 1705 cm$^{-1}$; $^1$H NMR δ 1.09 (d, J = 7.2 Hz, 3 H, CH$_3$CH), 2.16 (t, J = 6.6 Hz, 2 H), 2.34 (m, 2 H), 2.45 (t, J = 6.8 Hz, 2 H), 6.76 (m, W/2 = 9 Hz, 1 H, CH=CH); MS (EI) m/z (%) 111 (M+1, 45).
(q), 82.7 (d), 215.2 (s).

\((1S^*,2R^*,7R^*)\)-2-Methoxy-8-oxabicyclo[5.3.0]decan-9-one (150).

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\begin{align*}
\text{OMe} \\
\end{align*}
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Obtained from 40 in 59% yield using procedure D; IR \(\nu(C=O)\) 1768 cm\(^{-1}\); \(^1\)H NMR 8 2.52 (d, \(J = 10.0\) Hz, 1 H), 2.75 (m, \(W = 37\) Hz, 2 H), 3.12 (br t, \(J \equiv 9\) Hz, 1 H, CH-\(OCH_3\)), 3.30 (s, 3 H, CH\(_2\)O), 4.62 (ddd, \(J = 8.0, 6.3, 3.4\) Hz, 1 H, CH-O); \(^{13}\)C NMR 8 25.0 (t), 27.3 (t), 31.6 (t), 32.4 (t), 34.1 (t), 44.9 (d), 56.9 (q), 82.4 (d), 83.7 (d), 176.9 (s); HRMS \(m/z\) 184.10996 (calcd for C\(_{10}\)H\(_{16}\)O\(_3\): 184.10994). Anal. Calcd for C\(_{10}\)H\(_{16}\)O\(_3\): C, 65.19; H, 8.75. Found: C, 65.40; H, 8.94.

\((1S^*,2R^*,5R^*)\)-2-Methoxy-6-oxabicyclo[3.3.0]octan-7-one (151).

\[
\begin{align*}
\text{OMe} \\
\end{align*}
\]

Obtained from 42 in 52% yield using procedure D; IR \(\nu(C=O)\) 1769 cm\(^{-1}\); \(^1\)H NMR 8 2.31 (m, \(W = 19\) Hz, 1 H), 2.87 (d, \(J = 12.0\) Hz, 1 H), 2.87 (m, 1 H), 3.27 (s, 3 H, CH\(_2\)O), 3.58 (m, \(W/2 = 8\) Hz, 1 H, CH-\(OCH_3\)), 5.07 (m, \(W = 9\) Hz, 1 H, CH-O); \(^{13}\)C NMR 8 28.4 (t), 31.1 (t), 33.7 (t), 44.8 (d), 56.7 (q), 85.8 (d), 88.6 (d), 177.4 (s); HRMS \(m/z\) 156.07864 (calcd for C\(_8\)H\(_{12}\)O\(_3\): 156.07865). Anal. Calcd. for C\(_8\)H\(_{12}\)O\(_3\): C, 61.52; H, 7.74. Found: C, 61.33; H, 7.89.
(1S*,2R*,6S*)-2-Methoxy-7-oxabicyclo[4.3.0]nonan-8-one (152).

Obtained from 55 in 58% yield using procedure D; IR ν(C=O) 1778 cm⁻¹; ¹H NMR δ 2.37 (dd, J = 16.3 and 12.9 Hz, 1 H, CH₃CO), 2.72 (dd, J = 16.3 and 6.6 Hz, 1 H, CH₂CO), 3.17 (dt, J 10.2 and 4.1 Hz, 1 H, CH-OCH₃), 3.35 (s, 3 H, CH₂O), 3.80 (dt, J = 11.0 and 3.8, 1 H, CH-O); ¹³C NMR δ 21.2 (t), 29.6 (t), 31.3 (t), 34.8 (t), 50.7 (d), 57.0 (q), 80.4 (d), 82.5 (d), 176.5 (s); HRMS m/z 170.09429 (calcd for C₉H₁₄O₃: 170.09427). Anal. Calcd for C₉H₁₄O₃: C, 63.51; H, 8.29. Found: C, 63.30; H, 8.34.

(1S*,2R*,5S*)-2-Methoxy-6-oxabicyclo[3.3.0]octan-7-one (153).

Obtained from 56 in 47% yield using procedure D; IR ν(C=O) 1780 cm⁻¹; ¹H NMR δ 2.41 (dd, J = 15.6 and 13.4 Hz, 1 H, CH₃CO), 2.74 (dd, J = 15.6 and 6.0 Hz, 1 H, CH₂CO), 3.30 (s, 3 H, CH₂O), 3.68 (dt, J = 9.1 and 5.0 Hz, 1 H, CHOCH₃), 3.84 (dt, J = 11.1 and 6.0 Hz, 1 H, CH-O); ¹³C NMR δ 26.8 (t), 31.6 (t), 36.0 (t), 53.4 (d), 57.6 (q), 78.0 (d), 82.6 (d), 178.9 (s); HRMS m/z 156.07864 (calcd for C₈H₁₂O₃: 156.07864). Anal. Calcd. for C₈H₁₂O₃: C, 61.52; H, 7.74. Found: C, 61.26; H, 7.72.
(1R*,2R*,6R*)-2-Methoxy-7-oxabicyclo[4.3.0]nonan-8-one (154).

![Chemical Structure](image)

 Obtained from 63 in 63% yield using procedure D; IR ν(C=O) 1776 cm⁻¹; ¹H NMR δ 2.34 (dd, J = 16.1 and 6.4 Hz, 1 H, CH₂CO), 2.63 (dd, J = 16.1 and 13.2 Hz, 1 H, CH₂CO), 3.33 (s, 3 H, CH₃O), 3.66 (m, W/2 = 7 Hz, 1 H, CH-OCH₃), 4.28 (dt, J = 11.1 and 3.8 Hz, 1 H, CH-O); ¹³C NMR δ 19.3 (t), 27.7 (t), 30.6 (t), 32.0 (t), 48.8 (d), 57.1 (q), 75.3 (d), 79.7 (d), 176.9 (s); HRMS m/z 170.09429 (calcd for C₉H₁₄O₃: 170.09428). Anal. Calcd. for C₉H₁₄O₃: C, 63.51; H, 8.29. Found: C, 63.28; H, 8.47.

(1R*,2R*,7R*)-2-Methoxy-8-oxabicyclo[5.3.0]decan-9-one (155).

![Chemical Structure](image)

 Obtained from 64 in 58% yield using procedure D; IR ν(C=O) 1765 cm⁻¹; ¹H NMR δ 2.44 (dd, J = 19.3 and 8.2 Hz, 1 H, CH₂CO), 2.91 (dd, J = 19.3 and 14.8 Hz, 1 H, CH₂CO), 3.33 (s, 3 H, CH₃O), 3.47 (m, W/2 = 12 Hz, 1 H, CH-OCH₃), 4.60 (dt, J = 10.0 and 4.5 Hz, 1 H, CH-O); ¹³C NMR δ 20.9 (t), 25.0 (t), 32.4 (t), 33.0 (2 x t), 47.2 (d), 57.2 (q), 75.1 (d), 79.8 (d), 177.2 (s); HRMS m/z 184.10994 (calcd for C₁₀H₁₆O₃: 184.10988). Anal. Calcd. for C₁₀H₁₆O₃: C, 65.19; H, 8.75. Found: C, 64.90; H, 8.94.
**(1R*,2R*,6S*)-2-Methoxy-7-oxabicyclo[4.3.0]nonan-8-one (156).**

![Methoxy-7-oxabicyclo[4.3.0]nonan-8-one](image)

Obtained from 69 (200 mg) in 58% yield using procedure D; IR v(C=O) 1770 cm\(^{-1}\); \(^1\)H NMR δ 2.38 (dd, J = 16.8 and 8.0 Hz, CH\(_2\)CO), 2.48 (dd, J = 16.8 and 6.8 Hz, 1 H, CH\(_2\)CO), 2.74 (m, W = 32 Hz, 1 H, CH\(_2\)CO), 3.27 (s, 3 H, CH\(_3\)O), 3.39 (m, W/2 = 19 Hz, 1 H, CH-OCH\(_3\)), 4.50 (dt, J = 11.7 and 6.1 Hz, 1 H, CHO); \(^13\)C NMR δ 15.8 (t), 25.2 (t), 27.8 (t), 31.1 (t), 39.0 (d), 56.5 (q), 76.7 (d), 78.4 (d), 177.3 (s); HRMS m/z 170.09427 (calcd for C\(_9\)H\(_{14}\)O\(_3\): 170.09429). Anal. Calcd for C\(_9\)H\(_{14}\)O\(_3\): C, 63.51; H, 8.29. Found: C, 63.30; H, 8.16.

**(1R*,2R*,3R*)-2-([Cobalttetraacarbonyl]mercurio)methyl-3-methoxycyclohexan-1-ol (159).**

![Cobalttetraacarbonylmercurio)methyl-3-methoxycyclohexan-1-ol](image)

To a stirred solution of Co\(_2\)(CO)\(_8\) (180 mg; 0.53 mmol) in THF (5 mL) was added a solution of the organomercurial 37 (200 mg; 0.53 mmol) in THF (2 mL) and the mixture was stirred at rt for 10 min under nitrogen. The solvent was then evaporated under reduced pressure, the residue was chromatographed on silica gel (20 g) with a petroleum ether-acetone mixture (95:5) to afford pure 159: IR v(CO) 1940, 2005, 2070 cm\(^{-1}\); \(^1\)H NMR δ 2.92 (m, W/2 = 25 Hz, 1 H, CH-OCH\(_3\)), 3.19 (br s, 3 H, CH\(_3\)O), 3.80 (m, W/2 = 20 Hz, 1 H, CHO); \(^13\)C NMR δ 19.2 (t), 30.1 (t), 33.4 (t), 46.6 (t), 47.9 (d), 56.8 (q), 72.6 (d), 81.1 (d); MS (EI) m/z 516 (M\(^{+}\)). Anal. Calcd for C\(_{12}\)H\(_{15}\)O\(_6\)CoHg: C, 27.99; H, 2.94. Found: C, 27.73; 2.79.
4-Chlorocycloheptene (164)

In a 10ml flask fitted with a condenser connected to a balloon containing carbon monoxide was stirred a solution of cyclopropane 34 (20 mg, 0.18 mmol), CuCl₂ (61 mg, 0.36 mmol) and (MeCN)₂PdCl₂ (4.6 mg, 0.018 mmol) in THF (4mL) at 60°C for 2 d. The reaction was then quenched with water, extracted with ether and worked up. The crude product was purified by chromatography on silica gel (15 g) eluting with petrol to give chloride 164 (15 mg, 63%). ¹H NMR 81.42 (m, 1H), 1.80 (m, 1H), 2.02 (m, 1H), 2.14 (m, 2H), 2.40 (m, 1H), 2.63 (m, 2H), 4.02 ((m W/2 = 20Hz, 1H, CHCl), 5.66 (m, W/2 = 20Hz, 1H, H=), 5.95 (m, W/2 = 20Hz, 1H, H=); ¹³C 827.0 (t), 28.5 (t), 39.0 (t), 43.1 (t), 60.0 (d), 127.3 (d), 135.4 (d).

The attempted Reaction of Thallium Methylating Reagents with Methylmercurio Acetate 70.

2 thallium reagents were used to attempt this reaction, TlMe₂ and TlMe₂MeLi, both of which were made from TlMe₂Cl.

Synthesis of TlMe₂Cl

TlI (5.0 g, 0.015 mol) and MeI (2.35 mL, 0.038 mol) were stirred in dry ether (5 mL) at room temperature. To this suspension was added MeLi (1.36M in diethyl ether); 21.3 mL, 0.029 mol dropwise over 3 hrs, to produce a nearly transparent brown solution. This was stirred overnight, protected from light by foil. The solution was then filtered, cooled to 0°C and acidified to 1-2 pH by the dropwise addition of 5% HCl. The white precipitate of TlMe₂Cl was removed by filtration, washed with water and dried.
Reaction of TlMe₃ with 70.

Me₂TlCl (40 mg, 0.15 mmol) was stirred in 5 mL of dry ether at room temperature. To this was added MeLi (1.36M in diethyl ether, 0.1 mL, 0.15 mmol) dropwise to produce a colourless solution of TlMe₃. The mercurial acetate 70 (50 mg, 0.12 mmol), in 0.5 mL of ether, was then added. No reaction was observed.

Reaction of TlMe₃, MeLi with 70.

TlMe₃ was formed as above, the solution was cooled to -50°C and another equivalent of MeLi added (0.1 mL). After stirring at this temperature for 1 hour the acetate 70 (50 mg, 0.12 mmol) in 0.5 mL of ether was added and the reaction maintained at -50°C. No reaction was observed.
References
References


(37) The acetal 82 exists as a 5:1 mixture of anomers in CDCl₃, with that having exo-OH being the main constituent, as revealed by NOE experiments. The NMR spectrum of this mixture further shows that, due to the conformational mobility of the 7-membered ring, the main anomer is formed by a 5:1 mixture of two stable conformers, while the minor one exists as a 1:1 mixture of conformers. The other lactols exhibit a similar pattern: thus, 83, 84 and 78 exist as 6:1, 8:1 and 5:1 anomic mixtures, respectively.


(42) Acetals R₂C(OR')₂ are known to exchange one of the alkoxy groups for an alkyl (R'') on reaction with R''CuBF₃ (Yamamoto reagent) to afford the corresponding


(46) In the 7-membered ring series, this reaction proved much less clean. Thus, 79 produced a mixture compounds, in which analogues of 110 (24%) and 111 (8%) could be identified by NMR spectroscopy. In principal, this sequence could also be carried out stepwise, starting with lactol 82.

(48) All spectra were recorded in diethyl ether at -40 °C in a 5mm NMR tube inside a 10mm NMR tube containing CDCl₃ for a deuterium lock.


(56) In the ¹H NMR spectra of BuLi, obtained for Et₂O solution, the methylene protons of PrCH₂Li and (PrCH₂)₂CuLi appear at -1.0 and 0.30 ppm, respectively: (a) Cheema, Z. K.; Gibson, G. W.; Eastman, J. F. J. Am. Chem. Soc. 1963, 85, 3517. (b) San Filippo, J. Inorg. Chem. 1978, 17, 275.


(60) As a rule, the Hg → Pd transmetallation works efficiently only at a primary carbon. When HgX is adjacent to a secondary or tertiary carbon, treatment with, e.g., PdCl₂ usually results in the exchange of the anions, rather than in transmetallation; Kocovsky, P. *Organometallics* 1993, 12, 1969. However, the analogous B → Zn transmetallation (at a primary carbon) appears to be high yielding: Klement, I.; Knochel, P. *Synlett* 1995, 1113. See also ref. 66.


(62) Low yields have usually been obtained for those carbonylations, which required the Hg → Pd transmetallation at an sp³ carbon: (a) Stille, J. K.; Wong, P. K. *J. Org. Chem.* 1975, 40, 335. (b) Kocovsky, P.; Pour, M. *J. Org. Chem.* 1990, 55, 5580. By contrast much better results have been obtained when the transmetallation occurred at an sp² carbon: (c) Walkup, R. D.; Park, G. *Tetrahedron Lett.* 1988, 29, 5505 and *ibid.* 1987, 28, 1023. See also (d) Lathbury, D.; Vernon, P.; Gallagher,

(65) In this instance the lactone 150 was accompanied by ca. 7% of 149.


(69) A 6-membered lactone can also be synthesised from the corresponding chloromercurio alcohol via this technology, see ref 29.


Appendix
Spectra

Fig. 1 - $^1$H NMR of MeLi at -40°C in Diethyl Ether
Fig. 2 - $^{13}$C NMR of MeLi at -40°C in Diethyl Ether
Fig. 3 - $^7$Li NMR of MeLi at -40°C in Diethyl Ether
Fig. 4 - $^1$H NMR of Me$_2$CuLi at -40°C in Diethyl Ether
Fig. 5 - $^{13}$C NMR of Me$_2$CuLi at -40°C in Diethyl Ether
Fig. 6 - Li NMR of Me$_2$CuLi at -40°C in Diethyl Ether
Fig. 7 - $^1$H NMR of Me$_3$CuLi$_2$ at -40°C in Diethyl Ether
Fig. 8 - $^{13}$C NMR of Me$_3$CuLi$_2$ at -40°C in Diethyl Ether
Fig. 9 - $^7$Li NMR of Me$_3$CuLi$_2$ at -40°C in Diethyl Ether
Fig. 10 - $^1$H NMR of 134 at -40°C in Diethyl Ether
Fig. 11 - $^{13}$C NMR of 134 at -40°C in Diethyl Ether
Fig. 12 - $^1$H NMR of Me$_3$CuLi$_2$ + 134 at -40°C in Diethyl Ether
Fig. 13 - $^{13}$C NMR of Me$_3$CuLi$_2$ + 134 at -40°C in Diethyl Ether
Fig. 14 - $^7$Li NMR of Me$_3$CuLi$_2$ + 134 at -40°C in Diethyl Ether

Publications

Cupration of Organomercurials: A Mild Method for the Intramolecular Addition of Organometallics to Ester Groups

A Selective Synthesis of Cis- and Trans-Fused Lactones via the Palladium(II)-Catalysed Carbonylation of Organomercurials

Selective Reduction of the Carbonyl Group in Organomercurials. A Facile Method for the Protection-Deprotection of the Mercurio Group and a new Route to Annulated Lactones.
FIG. 1 PROTON NMR OF MeLi
FIG. 2: CARBON NMR OF MeI
Fig. 7: Proton NMR of Me₃CuLi₂
Fig 8: Carbon NMR of Me₃CuLi₂
\[ R - \text{Hg} - \text{CH}_3 \]
Fig. 13 - Carbon NMR of RH2Me + Me3CuLi2
Cupration of Organomercurials: A Mild Method for the Intramolecular Addition of Organomercurials to Ester Groups

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Addition of Grignard and alkyl lithium reagents to carbonyl groups is one of the widely used applications of organomercurials in organic synthesis. However, its intramolecular version has never been fully developed, owing to the reactivity of the reagents required to generate the C-Hg or C-Li group in the molecule already containing an unprotected carbonyl function. Alternatively, involving less reactive organomercurial species (B, Si, Sn, Zn, Cr, and Ni) are confined to allylic, benzylic, or vinylic halides and enol triflates as precursors. Much more successful is the Sm(II) and Yb(II)-mediated cyclization of halo ketones and halo esters.1-8 We have recently shown that the intramolecular addition to an aldehyde group in 1 and 2 can be accomplished via activating the neighboring C-Hg moiety by organocuprates (Scheme 1). A Similarly, intramolecular addition across an activated double bond (1,4-addition) has also been observed.2 Herein, we describe related intramolecular additions to ester groups.

Scheme 1

Scheme 2

Scheme 3

Whereas esters react rapidly with Grignard and alkyl lithium reagents, they are essentially inert toward organocuprates. However, an intramolecular reaction of this type has rarely been attempted,3 presumably in view of the difficulties associated with generating a suitable precursor. Since the carbonyl-containing organomercurials can be prepared as stable compounds,4 we reasoned that they might serve as the starting materials of choice. Furthermore, it was of interest to explore whether the species resulting from their activation by treatment with organocuprates were prone to add intramolecularly to ester groups.

(1) Dedicated to Dr. Jiří Zavada on the occasion of his 60th birthday.
(2) University of Leicesters.
(3) Glaxo.
(4) Polarity


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the ester carbonyl as they are in the case of aldehydes (e.g., 1 and 2).

The model organometallics were prepared by mercury-Cl-mediated ring opening of cyclopropyl alcohols 4-6, which, in turn, were obtained via the stereoselective Simmons-Smith cyclopropanation of the corresponding allicylic alcohols. As expected, the reaction rate of the ring-opening is dependent on the nature of the mercury-mercury-mediated ring opening of cyclopropyl alcohols.

The six-membered ring acetate 11, obtained by acetylation of 10 (Ac2O, DMAP; 94%), was treated with an essentially quantitative conversion of 2 into 3 at -78 °C in 10 min.

The acyl migration can be rationalized as follows: the organometalic species 17, generated from 16a, reacted with MeLi to effect the desired metathesis of acetate 20a (41% and 22%); whereas MeCuONLi effected simple demethylation and chlorination; RCH2HgMe — RCH2HgCl (14%).

Communications


The reaction turned out to be very clean; only traces of unidentified byproducts were detected. Since MeLi itself gives a complex mixture of products, it is obvious that Cu plays a crucial role in the reaction, so that the reactivity must originate from MeCuLi (or a similar species) rather than from free MeLi.

The acyl migration can be rationalized as follows: the organometalloc species 17, generated from 16a, reacted via attack on the neighboring ester group and the corresponding intermediate 18 subsequently collapsed to 19a on aqueous workup. The benzoate 16b and pivalate 16c exhibited the same behavior, producing 19b (50%) and 19c (55%).

The acyl migration can be rationalized as follows: the organometalloc species 17, generated from 16a, reacted via attack on the neighboring ester group and the corresponding intermediate 18 subsequently collapsed to 19a on aqueous workup. The benzoate 16b and pivalate 16c exhibited the same behavior, producing 19b (50%) and 19c (55%).

The reaction of the seven-membered ring acetate 20a with MeCuLi gave rise to a mixture of acetate 21a (57%) and the hydrolysis product 22 (22%).

The reaction of the seven-membered ring acetate 20a with MeCuLi gave rise to a mixture of acetate 21a (57%) and the hydrolysis product 22 (22%).

Two mechanisms of the intramolecular addition can be envisaged: (a) second methylation of MeHg—CH2R to generate [MeHg—CH2R]2 and (b) transmetalation or formation of a cluster [MeCuLiHgR]3 as the reactive intermediate. More experiments will be needed to resolve this issue.

In summary, on treatment with MeCuLi, organometallics containing a suitably located ester group (16, 20, and 25) give the corresponding acetals (18, 21, and 25), respectively. This unique transformation represents a novel, mild way for intramolecular addition of organometallics across a carbonyl group.

Acknowledgment. We thank EPSRC and Glaxo for a CASE award to J.M.G. and Dr. Jim Srogl for stimulating discussions.

Supplementary Material Available: Experimental procedures and spectral and analytical data for the new compounds (9 pages).

(11) All yields refer to isolated preparative yields of the often dative compounds. The genuine yields (e.g., the "GC yields") were, most cases, much higher.

10a JO942041H

(13) All new compounds were characterized by spectral and analytical methods.
(14) Reinvestigation of the reaction of 2 with MeCuLi revealed that a large excess of this reagent has to be used with only 1 equiv of MeCuLi prepared from 1 equiv of Cul and 2 equiv of a freshly prepared MeLi in no reaction occurs. Furthermore, the reaction of 2 with 1 equiv of MeCuLi yielded an essentially quantitative conversion of 2 into 3 at -78 °C in 10 min.
(15) Prepared from the parent alcohol by acetylation with (PhCO)2O or Et2O (reflux), respectively, in the presence of 4-[(W)-dimethylamino]pyridine.
(16) The configuration at the anomic center has not been experimentally established. However, MM2 calculations suggest that the anomers with endo-OH (i.e., 21) are more stable.
(17) Lithium methyldiisopropylamide gave a similar mixture of 21a (41%) and 22 (22%), whereas MeCuCLi afforded simple demethylation. No reaction was observed with MeCuCl2 at low temperature (-78 °C), while a complex mixture resulted on heating to 9 °C. Finally, the reagent generated from Bu2CuLi turned out to be inert. Another possible approach would be the activation of the carbonyl by a strong Lewis acid, such as Me2AlCl.
(18) However, treatment of 20b with MeCuLi resulted only in the demethylation and chlorination: RCH2HgMe — RCH2HgCl (14%) + RCH2Cl (66%).
A Stereoselective Synthesis of cis- and trans-Fused Lactones via the Palladium(II)-Catalyzed Carbonylation of Organomercurials

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Abstract: Organomercurials 2a-c, obtained by the regioselective, Hg(II)-mediated cleavage of cyclopropyl alcohols 1a-c, are converted into the corresponding 5-membered cis-annulated lactones 3a-c via the Pd(II)-catalyzed carbonylation in the presence of p-benzoquinone. Isomeric, trans-fused lactones can be synthesized in a similar way (6 – 7). The carbonylation occurs under an atmospheric pressure of CO.

The five-membered lactone, annulated to another ring in a cis- or trans-fashion, is a typical structural motif encountered in a number of natural products. Whereas the stereoselective synthesis of cis-lactones is usually accomplished via halolactonization and related reactions, trans-isomers are more difficult to obtain. The frequent requirement for the presence of another substituent in a stereo-defined position may present additional synthetic problems. Herein, we wish to report on a versatile method for the stereoselective construction of either cis- or trans-annulated 5-membered lactones with three adjacent chiral centers on the parent ring.

Recently, we have reported on the stereoselective "corner" opening of cyclopropane rings with mercury(II) and thallium(III) reagents. Whereas the resulting organothallium species are unstable and immediately undergo subsequent in situ reactions, the corresponding organomercurials can be isolated and handled as stable compounds. Thus, the cis-cyclopropyl alcohols 1a-c, obtained via the stereoselective Simmons-Smith cyclopropanation of the corresponding allylic alcohols, are regioselectively opened with (CF₃CO)₂Hg in MeOH to give, after quenching with aq. NaCl, the organomercurials 2a-c as the sole (2a and 2b) or major (2c) products (Scheme 1).

Carbonylation of 2a under an atmosphere of carbon monoxide was first explored in the presence of stoichiometric quantities of palladium(II) salts, namely (Ac₂O)₂Pd, (CF₃CO₂)₂Pd, PdCl₂, (Ph₃P)₂PdCl₂, or (MeCN)₂PdCl₂. The latter complex was the most promising one, mediating an essentially quantitative conversion of 2a into the lactone 3a (rt, 24 h). It has, therefore, been selected for the development of a catalytic cycle.
Since Pd(II) is converted into Pd(0) in the carbonylation reaction, a successful catalytic cycle would require that an efficient oxidant be employed in a stoichiometric amount. Among mild oxidants that are known to serve this purpose, copper(II) salts seem to play a prominent role, as documented by their successful use in methoxycarbonylation reactions. However, after numerous experiments, we found p-benzoquinone to be superior to CuCl₂, (AcO)₂Cu, or Cu(NO₃)₂ with our system. Thus, on heating at 60 °C with (MeCN)₂PdCl₂ (10 mol%) and p-benzoquinone (2.0 equiv) in THF under an atmosphere of CO for 4 days, the organomercurial 2a has been almost quantitatively converted into the lactone 3a as an essentially pure product in 60% isolated yield. Similarly, organomercurials 2b and 2c showed practically quantitative conversions, affording the respective lactones 3b (59%) and 3c (52%).

The isomeric organomercurials required for the synthesis of trans-fused lactones were prepared as follows. The cyclopropyl alcohol 1a was first protected by methylation (MeI, NaH, THF, 40 °C, 1 h) and the resulting methyl ether 4a (69%) was treated with (AcO)₂Hg in AcOH (60 °C, 2 h), followed by quenching with aq. NaCl (Scheme 2). The chloromercuri acetate 5a thus obtained was then hydrolyzed (NaOH, MeOH, rt) to furnish the chloromercurio alcohol 6a. Note that, in contrast to Scheme 1, where (CF₃CO)₂Hg in MeOH was used to introduce the MeO group, it was now the acetate anion that served as a nucleophile in the cyclopropane ring-opening; this reversal of reactivity enabled us to eventually prepare 6a with the desired trans-configuration. The seven-membered ring analogue 6b was prepared from 1b via 4b in a similar manner. The two organomercurials 6a and 6b have been converted into the trans-lactones 7a (63%) and 7b (58%), respectively, under the same conditions used for their cis counterparts. Thus, these experiments have demonstrated that even the trans-fused lactones can be synthesized using this methodology.
In summary: We have developed an efficient method for the annulation of 5-membered lactone rings, in which three consecutive chiral centers are introduced. The method relies on the cleavage of an annulated cyclopropane ring with Hg(II) (1 → 2 and 4 → 5), followed by the Pd(II)-catalyzed carbonylation (2 → 3 and 6 → 7), and works with comparable efficiency for the construction of either cis- or trans-fused lactone rings (5 or 7). The choice of the Hg(II) reagent, in conjunction with selective protection, controls the final stereochemistry of the lactone annulation.

Acknowledgment. We thank the EPSRC and Glaxo for a CASE award to J.M.G.

References and Notes

7. We have also shown that the organomercurials can be transmetalated with Cd and Pd.
12. All new compounds were characterized by spectral and analytical methods.


15. All yields refer to isolated (preparative) yields of the often volatile compounds. The genuine yields (e.g., the "GC yields") were, in most cases, much higher.

16. **Typical experiment:** In a 10 mL flask, fitted with a condenser connected to a balloon containing carbon monoxide, was stirred a solution of the organomercurial 2a (200 mg; 0.52 mmol), p-benzoquinone (113 mg; 1.0 mmol), and (CH$_3$CN)$_2$PdCl$_2$ (13 mg; 0.052 mmol) in THE (3 mL) at 60 °C for 4 days. The reaction was then quenched with sodium dithionite, the product was taken up into ether, and the ethereal solution was successively washed with water, 5% aqueous HCl (3x), water, 5% aqueous KHCO$_3$ (3x), and water, and dried with Na$_2$SO$_4$. The solvent was evaporated and the residue was chromatographed on silica gel (21 g) with a petroleum ether-acetone mixture (98:2) to give the pure lactone 3a (54 mg; 60%): $^1$H NMR S 1.04 (m, 1 H), 1.27-1.65 (m, 3 H), 2.00 (m, 2 H), 2.13 (m, 1 H), 2.47 (dd, 1 H, J = 15.5 and 7.8 Hz, CH$_2$CO$_2$), 2.56 (dd, 1 H, J = 17.5 and 6.0 Hz, CH$_2$'-CO$_2$), 2.93 (dd, 1 H, J = 10.6, 9.1, and 3.8 Hz, CH-OCH$_3$), 3.26 (s, 3 H, CH$_3$O), 4.60 (dd, 1 H, J = 7.0 and 3.5 Hz, CH-OCO); $^13$C NMR S 18.5 (t), 27.6 (t), 27.8 (t), 36.1 (t), 42.3 (d), 57.0 (q), 79.7 (d), 80.5 (d), 177.5; IR v 1772 cm$^{-1}$; HRMS m/z (%) 170 (M$^+$, 14).

17. Note, that the less reactive (AcO)$_2$Hg required higher temperature than did the more electrophilic (CF$_3$CO)$_2$Hg.

18. 7a: IR v(C=O) 1777 cm$^{-1}$; $^{13}$C NMR S 176.9 ppm.

19. The five-membered derivative 1c gives a 2:1 mixture of regioisomers on the cyclopropane cleavage. Therefore, it was omitted in the trans series.

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Selective Reduction of the Carbonyl Group in Organomercurials. A Facile Method for the Protection-Deprotection of the Mercurio Group and a New Route to Annulated Lactones

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Abstract: Reduction of the carbonyl group in organomercurials can be carried out with retention of the mercury, provided it is protected by methylation. Thus, the bromomercurio aldehyde 6 is first methylated by MeCu to give 11, whose reduction with NaBH₄, LiAlH₃(t-BuO)₃, L-Selectride®, or superhydride® affords the alcohol 12. Mercury is then deprotected by treatment with HgBr₂ (12 → 13). The resulting alcohol 13 undergoes the palladium(II)-catalyzed carbonylation to produce the corresponding lactone 15. Five- and six-membered lactones are readily accessible via this methodology.

Organomercurials are frequently encountered intermediates in organic synthesis.¹ The usual role of mercury is to serve as a vehicle introducing a desired substituent. In most cases, after having served its purpose, mercury is removed by reduction.¹² This scenario is exemplified by the well known xymercuration of olefinic double bonds¹ and by cyclopropane cleavage.³¬⁵ However, this is not the most economic strategy because, in general, stoichiometric processes, employing either expensive or toxic metals, should capitalize on the presence of the metal in the molecule by engaging it in more than one productive step.

As part of a program aimed at the more atom-economic utilization of organomercurials, we have recently shown that the C-HgX group can serve as a store of the carbon-metal bond. The mercurio group would be activated later in the synthetic scheme, eventually effecting, e.g., an intramolecular addition across a C=O or an activated C=C bond.⁴¬⁶

Organomercurials are relatively stable and easy-to-handle,¹ so that the R-HgX group (X = halogen) can be expected to survive a number of operations in a multiple-step sequence, before actually being activated and used. However, these compounds can easily be reduced even with relatively mild reducing agents,¹ which considerably limits the scope of this methodology. In order to avoid the latter law, we have developed a protocol that involves protection of the mercurio group from reduction and its subsequent deprotection.
We have shown earlier that, on reaction with MeCu, halomercurials (e.g., R-HgCl) undergo an instantaneous, high yielding methylation on mercury. We now wish to report that the resulting methylmercurio derivatives R-HgMe are stable to a number of hydride reagents and that the halomercurio functionality can then be regenerated by treatment with HgX₂.

To develop this method, we have utilized two model compounds: the chloromercurio alcohol 4 and the steroidal aldehyde 6. The former compound was prepared from the cyclopropyl alcohol 1 via a sequence involving protection of the OH group by Mel/NaH methylation (1 → 2; 69%), cyclopropane ring opening with (AcO)₂Hg (2 → 3; 74%), and saponification (3 → 4; 98%). The aldehyde 6 has been readily obtained from the cyclopropyl derivative 5 (which, in turn, was prepared in four steps from cholesterol) via the mercury(II)-mediated rearrangement.

The chloromercurio alcohol 4 was first methylated with MeCu (generated in situ from equimolar amounts of MeLi and Cul) to afford the methylmercurio derivative 7. The latter compound was then oxidized with pyridinium chlorochromate (PCC) and the resulting ketone 8 stereoselectively reduced with NaBH₄ to give the inverted alcohol 9 as the major product (16:1). Finally, the chloromercurio grouping was regenerated by treatment with HgCl₂ (9 → 10).

Similarly, methylation of the steroidal aldehyde with MeCu (6 → 11), followed by the NaBH₄ reduction, gave the alcohol 12. Treatment of the latter product with HgBr₂ furnished the bromomercurio alcohol 13. A brief screening showed that the reduction (11 → 12) can also be carried with LiAlH₄(r-BuO)₃, L-Selectride®, or superhydride® in high yields. By contrast, treatment with LiAlH₄ led to the reduction of both functional groups.
On heating at 60 °C with \((\text{MeCN})_2\text{PdCl}_2\) (10 mol%) and 2 equivs of \(p\)-benzoquinone (\(p\)-BQ) in THF under an atmosphere of CO for 4 days,\(^{13}\) the chloromercurio alcohol 10 has been almost quantitatively consumed, giving almost exclusively the five-membered lactone 14, which was isolated as a pure compound in 58% yield.\(^{14}\) On the other hand, the organomercurial 13 exhibited high conversion to the corresponding lactone only when the reaction was carried out with a stoichiometric amount of Pd\(^{2+}\) (still in the presence of \(p\)-BQ which, apparently, serves as a ligand\(^{15}\)). The six-membered lactone 15 (55%)\(^{16}\) thus formed, was accompanied by the tetrahydrofuran derivative 16 (11%)\(^{17}\). The catalytic version (8 mol% of Pd\(^{2+}\), 60 °C, 7 days) gave rise to a mixture of 15 (14%) and 16 (44%), with the latter product dominating. These results indicate that the lactonization will be less successful if a competing pathway, such as a 5(0)''-exo-tet cyclization,\(^{18}\) is available. By contrast, synthesis of 5-membered lactones does not seem to suffer from that kind of competition, for the only available 4-(O)''-exo-tet cyclization is much less likely.

\[
\text{OMe} \quad \text{CO, } p\text{-BQ} \quad \text{(MeCN)}_2\text{PdCl}_2 \\
\text{THF, 60 °C} \\
\text{(58%)}
\]

\[
\begin{align*}
10 & \quad \text{HgCl} \\
\text{OH} & \quad \text{OMe} \\
\text{MeCN} & \quad \text{CO, } p\text{-BQ} \\
\text{THF, 60 °C} & \quad (58\%)
\end{align*}
\]

\[
\begin{align*}
13 & \quad \text{BrHg} \\
\text{HO} & \quad \text{CO, } p\text{-BQ} \\
\text{MeCN} & \quad \text{THF, 60 °C} \\
\text{(58 - 66%)}
\end{align*}
\]

\[
\begin{align*}
10 & \quad \text{HgCl} \\
\text{OH} & \quad \text{OMe} \\
\text{MeCN} & \quad \text{CO, } p\text{-BQ} \\
\text{THF, 60 °C} & \quad (58\%)
\end{align*}
\]

\[
\begin{align*}
13 & \quad \text{BrHg} \\
\text{HO} & \quad \text{CO, } p\text{-BQ} \\
\text{MeCN} & \quad \text{THF, 60 °C} \\
\text{(58 - 66%)}
\end{align*}
\]

In conclusion: We have developed a protocol for the protection/deprotection of the organomercurials, namely via the methylation-demethylation. The protected organomercurials are stable to a number of hydride reagents, enabling a selective reduction of an aldehyde or ketone group, present in the molecule. The resulting halomercurio alcohols readily afford either 5- or 6-membered lactones on the Pd(II)-catalyzed carbonylation. This protocol represents a novel approach to the synthesis of lactones and supplements those in existence.\(^{19}\)

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References and Notes

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2. Trumpe et al. (2001) have shown that the hydride reduction, via addition to a double bond, seems to be the only notable exception: Giese, B. Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds; Pergamon: Oxford, 1986.


5. Organomercurials can be transmetalated with Cu^2+ and Pd^2+.


8. All new compounds gave satisfactory spectral and analytical data. All yields refer to isolated (preparative) yields.


10. The diagnostic feature for the MeHg group is a singlet (83%) and a doublet (17%) of the methyl group in the ^1H NMR spectrum, which appear at 0.22 ppm; the doublet (J = 102 Hz) corresponds to the coupling with the less abundant ^203Hg isotope.

11. The reduction turned out to be stereoselective, as revealed by using LiAl^3H(r-BuO)₃, which gave mainly the alcohol i. The configuration at the new center of chirality (i.e. C-6) has been established via converting the latter alcohol into the rigid tetrahydrofuran derivative iii; the NOE technique has been used to unequivocally assign the signals to the respective protons of the CH₂-O-CH₂ group in the unlabeled analogue 16 [δ 3.41 (d, J = 9.1 Hz, 6α-H), 3.47 (dd, J = 40 and 8.8 Hz, J = 4.8 Hz, 4α-H), 3.95 (t, J = 9.0 Hz, 4α-H), 4.00 (d, J = 9.1 Hz, 6α-H) ppm]. An almost identical stereoselectivity has been observed for super deuteride® (87:13). Reduction of the deuterated aldehyde with LiAlH(r-BuO)₃ gave a complementary result.

12. IR ν(C=O) 1770 cm⁻¹; NMR 5 177.3 ppm. Grennberg, H.; Gogoll, A.; Backvall, J.-E. Organometallics 1993, 12, 1790.

13: IR ν(C=O) 1740 cm⁻¹; NMR 5 174.3 ppm.

14: IR ν(C=O) 1770 cm⁻¹; ¹³C NMR 5 177.3 ppm.

15: IR ν(C=O) 1740 cm⁻¹; ¹³C NMR 5 174.3 ppm.

16 arises from an intramolecular substitution reaction that dominates in the absence of CO.
