An Organoiron Approach towards the Enantioselective Synthesis of Hippeastrine

By Sarah Roseanne Delf

Doctoral Thesis

Submitted posthumously in partial fulfillment of the requirement for the award of Doctor of Philosophy.

University of East Anglia

School of Chemistry
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Preface.

The research described in this thesis is, to the best of our knowledge, the original work of the author, S. R. Delf, except where due reference has been made.

December 2017

Abstract.

This thesis describes work towards an organoiron approach towards the enantioselective synthesis of the alkaloid hippeastrine, starting from enantiomerically defined arene *cis* diols that can be made by biodioxygenation. Literature reviews of biodioxygenation and the stereocontrolled applications of cationic electrophilic pentahapto cyclohexadienylium complexes, and the description of original work on biodioxygenation using *R eutropha*, and a series of new studies of complexation, activation, and nucleophile addition reactions using the organoiron approach are presented, supported by an Experimental Section to provide details of experimental procedures and compound characterisation.

Acknowledgements.

I am sure that if Sarah had had the opportunity, she would have made a warm acknowledgement to her family, friends, lab mates, and academic colleagues at UEA, to Dr Simon Lewis (University of Bath) for a crucial collaboration on the microbial biodixygenation of arenes that is described in Chapter 2, Dr David Hughes (UEA) for X-ray crystallography, and the EPSRC Mass Spectrometry Centre at the University of Wales, Swansea for chemical ionization and high resolution mass spectrometry. This thesis was assembled after Sarah's death from sections written by her during the final months of her period of registration for the degree of Doctor of Philosophy. Acknowledgement should be made for editorial work by many members of the Organic Chemistry research groups at UEA, and perhaps particularly to Dr Paulina Glowacka and Dr Francesca Kinsey who performed much of this compilation using files and spectroscopic data recovered from Sarah's personal laptop computer, which was kindly leant to us by her family after her death.

PhD supervisors normally work with their students during the preparation of a thesis, discussing the structure of the document, the best way to organise the material to be presented, and mentoring the style of writing and layout of Schemes and Figures, etc. In the case of this thesis, that process was only just beginning in the Autumn of 2015, and was cut short. We have left the wording of the main sections of the thesis without significant revision, but the final task of interpreting for the internal and external examiners the contribution to new knowledge that had been achieved in the doctoral research fell to me as Sarah's PhD supervisor. In performing this task, I based this final commentary on the detailed 'Experimental Section' (Chapter 4) which was available at the time of Sarah's death. The research described here is Sarah's intellectual contribution to the field, not mine, though as is the case with PhD project, as a PhD supervisor and research group leader, I have throughout the doctoral research period played the normal mentor's role.

Editorial note.

Sections of text added by me to make this thesis ready for consideration by the examiners are distinguished from the original text of the author by the use of the Arial font.

Dr G. R. Stephenson,
December 2017

Contents.

Chapter 1

Introduction

The chemical element iron, Fe, is by mass the most common element on Earth. It forms a great amount of both the Earth's outer and inner core and has been known in its pure form for at least five thousand years. Both animals and humans are immensely dependant upon iron. Animals utilise it during the process of photosynthesis and humans possess Fe in the haemoglobin molecules in the blood to allow the transport of oxygen to tissues throughout the body. The first ever catalysis reaction performed by Nature billions of years ago in an anaerobic environment is believed to include protein containing iron-sulphur (Fe-S) clusters.

Alkaloids

The name 'alkaloids' was coined by the German chemist Carl Friedrich Wilhelm Meißner in 1819 and loosely translates as 'the ashes of plants'.[1] Alkaloids have been used by humans since ancient times for both therapeutic and recreational purposes, however, it was not until 1804 that the first known alkaloid, morphine, was isolated from the opium poppy (*Papaver somniferum*).[2] Numerous other alkaloids were discovered shortly after this, including quinine **1** (1820) which is a successful antimalarial agent, caffeine **2** (1820), coniine **3** (1827), nicotine **4** (1828) and cocaine **5** (1860) a potent local aesthetic.[3] Their structures are shown in Figure 1.

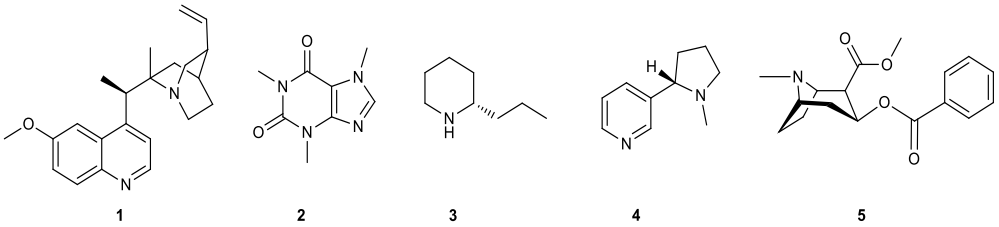


Figure 1: Chemical structures of the alkaloids quinine, caffeine, coniine, nicotine and cocaine consecutively.

Their function in plants is not yet understood, however it has been suggested that they could potentially be waste products of metabolic processes or serve specific biological functions. In some plant species the concentration of alkaloids are noted to increase before seed formation and reduce following the ripening stage, suggesting that alkaloids play a key role in this process.[4] It has also been proposed that these compounds may prevent the plant from being damaged or destroyed by various herbivorous mammals or insects. This could be due to their characteristic bitter taste and not their varying levels toxicity that effect animals and humans differently.[5,6]

Although there is no uniform classification of alkaloids, it is possible to vaguely describe this class of structures as naturally occurring chemical compounds that are characterised by the nitrogen atom in their heterocyclic ring.[7]

Amaryllidaceae Alkaloids

Our target molecule hippeastrine belongs to the alkaloid family amaryllidaceae that takes its name from the genus Amaryllis. This subgroup consists of roughly 75 genera and 1100 species that are extensively circulated in the tropics and warm climate regions of the world.[8] Plants from the amaryllidaceae family have been used for thousands of years in traditional herbal medicine. The Greek physician Hippocrates of Kos (ca. B.C. 460-370) pioneered the therapeutic applications of these alkaloids by using the oil from the *Narcissus poeticus L*. daffodil bulb in treatment for uterine tumors.[9]

Since the isolation of the first alkaloid lycorine, from *Amaryllidaceae lycoris* in 1877, more than 500 amaryllidaceae alkaloids have been isolated over the past three decades.[10] The enormous numbers of diverse amaryllidaceae alkaloids are classified into different groups mainly according to their structural features as displayed in *Figure 2*.

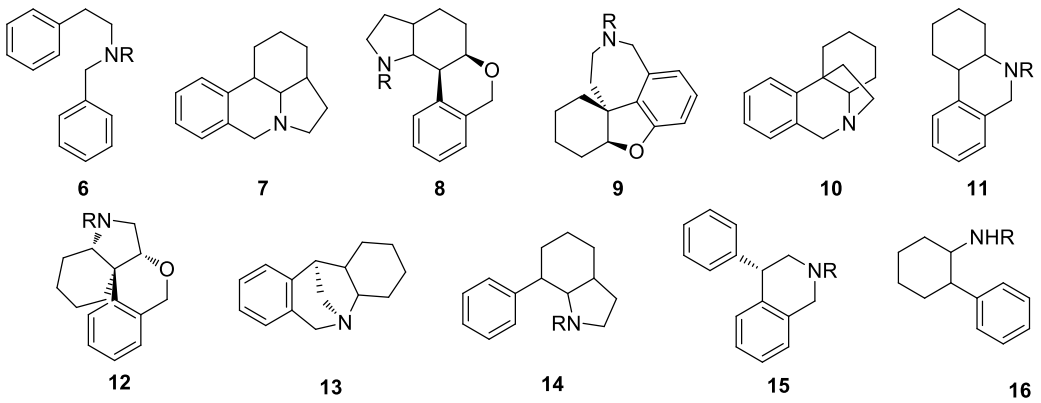
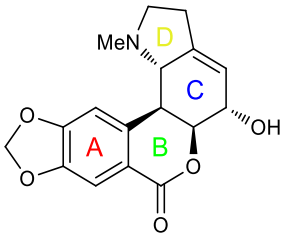


Figure 2: Basic skeletal structures representing the different subgroups of the amaryllidaceae alkaloids.

Biological research was carried out on this family of alkaloids as early as the 1960s, however since then very little development has been made towards their synthesis. The most significant study involved the compound galanthamine which is the only amaryllidaceae alkaloid to be approved as a prescription drug for the treatment of Alzheimer's disease.[11]

Hippeastrine

Our target molecule, hippeastrine, has a lycorenine type frame-work similar to that of molecule **8** shown in Figure 2. It shares common features with other alkaloids from its class. These include the aromatic **A** ring as well as the unsaturated six membered **C** ring. Hippeastrine possesses four stereogenic centres which pose a formidable synthetic challenge. The nitrogen in the 5 membered **D** ring is in a *cis* arrangement relative to the hydroxyl group whereas the two bonds connecting the **B** and **C** rings are *trans* as shown in *Figure 3*.

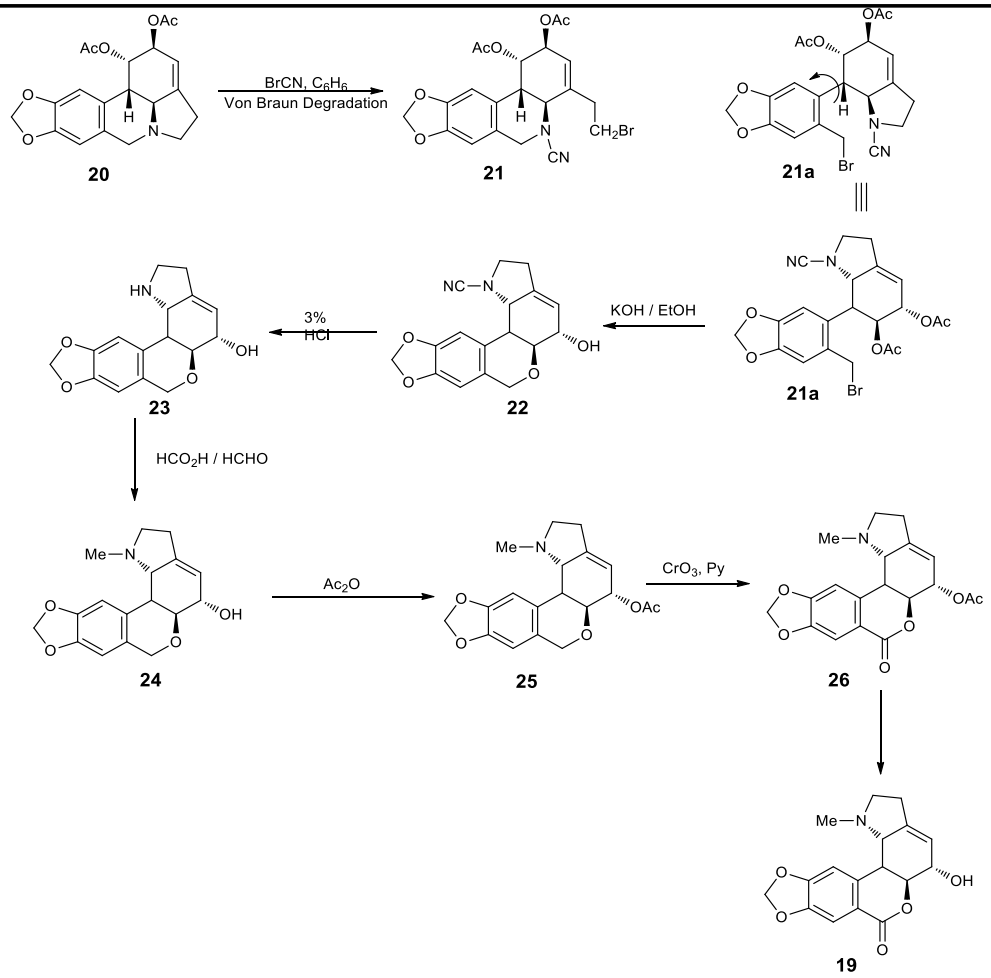


19

Figure 3: Target molecule hippeastrine.

Hippeastrine has been shown to exhibit anti-influenza behaviour as well as antimalarial activity.[12,13] Interestingly out of all the alkaloids tested, hippeastrine dimers expressed the highest anitimalarial activity.[14] The double bond present in the **C** ring and the free hydroxyl group proved to be crucial in the inhibitory process.

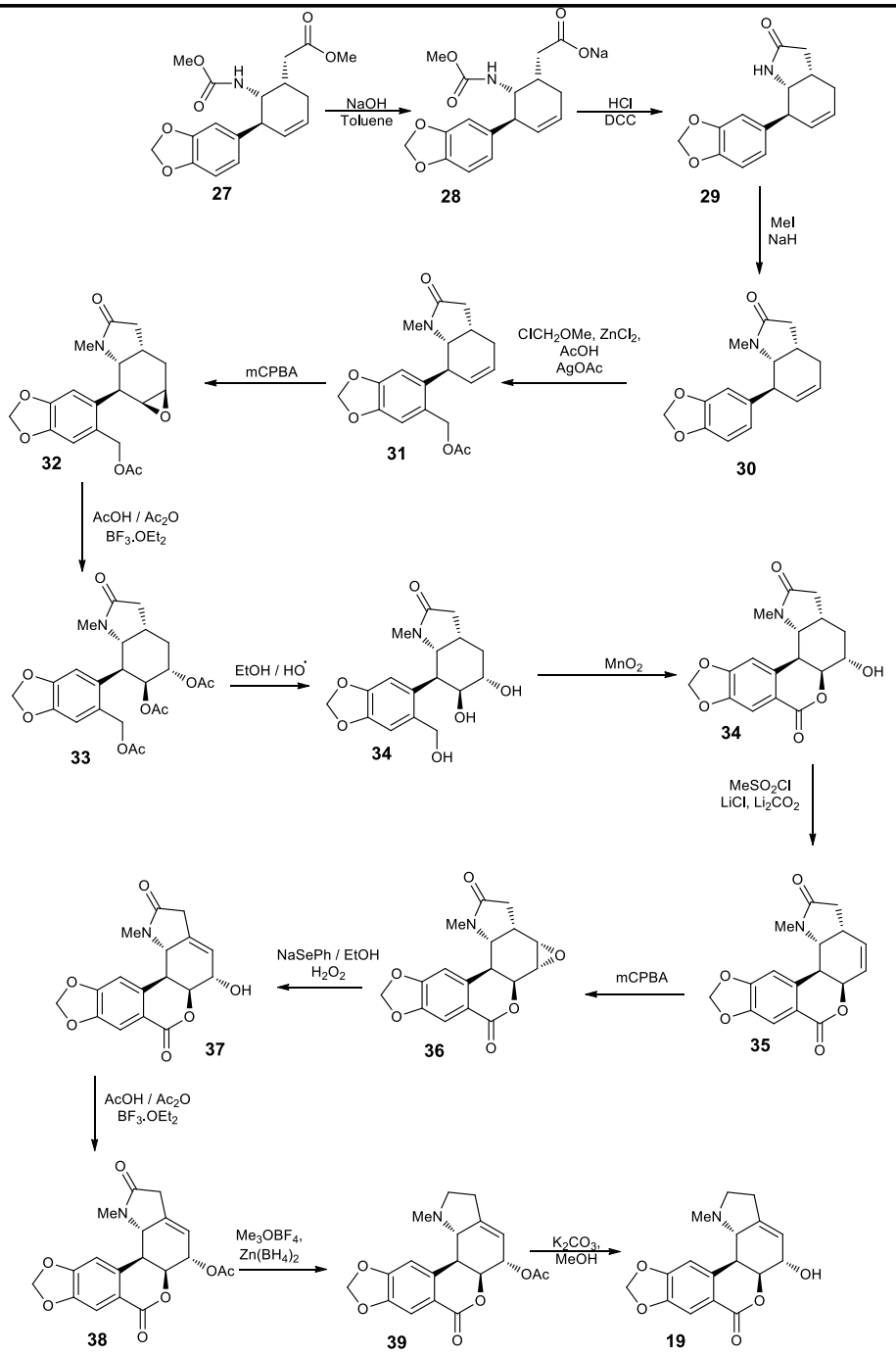
Hippeastrine was first synthesised by Kotera and co-workers in 1968.[15] The stereochemistry of the alkaloid starting material lycorine provided both the 1,2-regiochemistry of the bonds connecting the B and C rings and the stereo- and regiochemistry of the oxygen and nitrogen substituents of the C ring.



Scheme 1: First total synthesis of hippeastrine to be published by Kotera and co-workers in 1968.

A von Braun degradation of the cyclic amine generated the two cyanamide isomers. The major product was isolated and used for the rest of the synthesis. The rotation around this bond provided the basic skeletal structure of hippeastrine. After an Eshchwieler-Clarke methylation the remainder of the synthesis involved minor chemical modifications to generate hippeastrine. Removal of the acetyl protecting groups and selective oxidation of the benzyl alcohol produces the lactone **26** with substituents in the correct orientation for the final product.

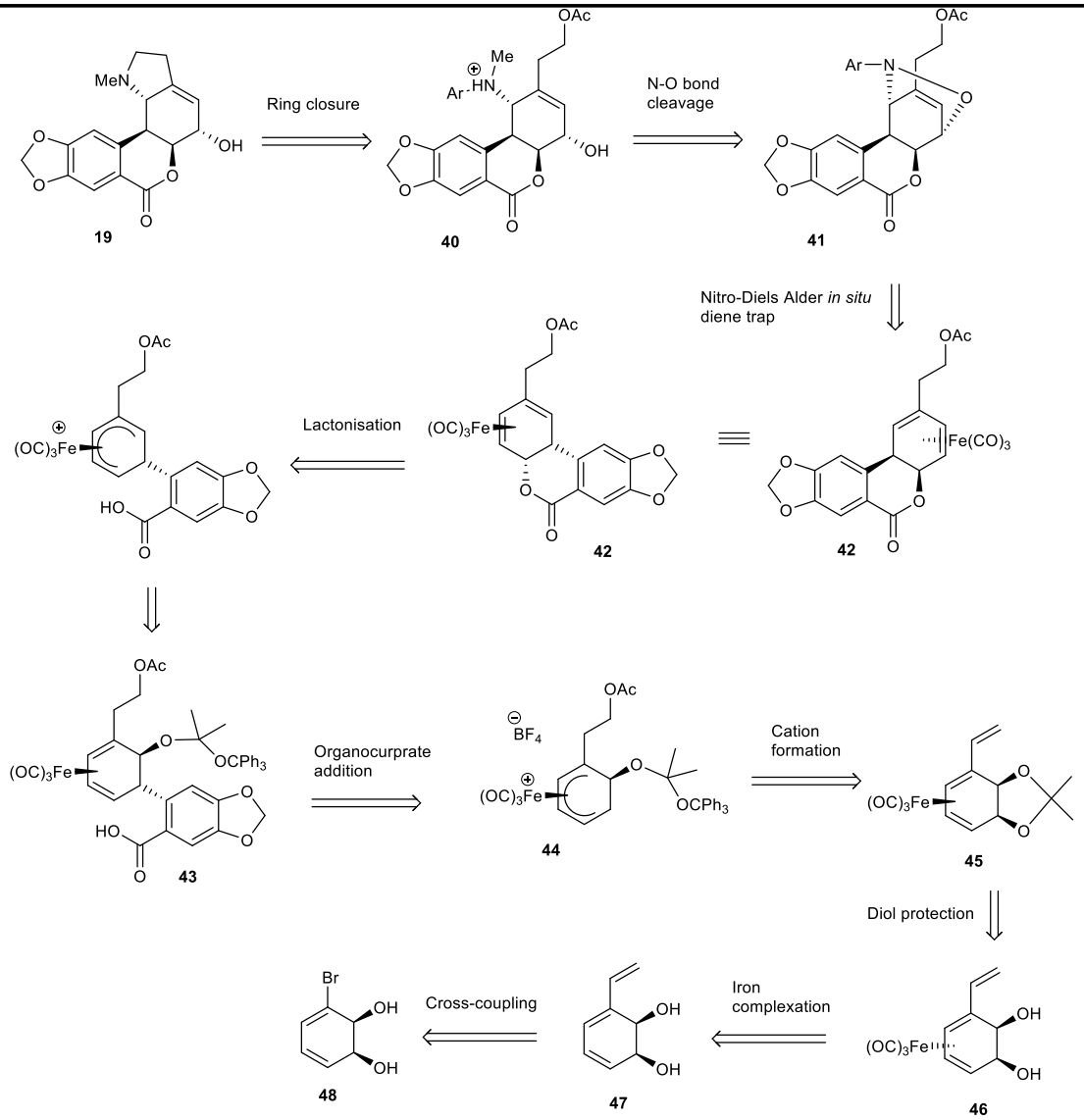
Katakawa and co-workers developed a slightly more complicated approach which involves the modification of urethane ester, a common starting material for other Amaryllidaceae alkaloids.[16] The orientation of the starting material is conserved throughout the synthesis. The starting material is treated with sodium hydroxide to produce the oxo-anion. Treatment with acid and DCC initiates the cyclisation of what eventually becomes the D ring of hippeastrine. The next reaction is a methylation of the cyclic amine followed by alkylation of the aryl ring. Epoxidation of the alkene gives the sole enantiomer **32**. Ring opening of the epoxide in the presence of an acetylating agent produces the triacetyl intermediate.



Scheme 2: Alternative total synthesis of the target molecule hippeastrine developed by Katakawa and co-workers in 1984.

General Synthetic Strategy

The aim of this PhD project was to build upon earlier research directed towards the synthesis of hippeastrine **19** that has previously been developed within the group. The model **ABC** ring system has been generated by employing organoiron technologies, Scheme 3.



Scheme 3: Retrosynthetic route towards the preparation of target molecule **19**.

Chapter 2

Microbial Biooxidation

First Synthetic Route

The approach towards the synthesis of the target molecule Hippeastrine **19** was started by performing a microbial biooxidation using a mutant strain *R. eutropha* B9 bacteria. The oxidation of benzene derivatives using a mutant strain of *Pseudomonas putida* bacteria was pioneered by Gibson.[17] The procedure has since been successfully scaled up providing a commercial source of optically active starting materials for the synthesis of a number of natural and unnatural products.[18]

This chapter begins with a short review of the microbial biodioxygenation of arenes and continues in the 'Results and Discussion' section by describing original research performed in collaboration with Dr Simon Lewis (University of Bath). Previous work in the Stephenson group at UEA had concentrated on the use of *Pseudomonas putida* as a means of access to enantiopure tricarbonyliron complexes of 1,2-dihydroxycyclohexadienes. Although based on well established principles from the Meyers group at Harvard and the Lewis groups at Bath, when Sarah brought these procedures to Norwich, a substantial effort was needed to adapt the *R. eutropha* methods for use under UEA's safety protocols. Although described quite briefly in the thesis, the new information presented in Graphs 1-7 contributes to the understanding of the *R. eutropha* biodoxygenation procedure, and its first use in the Stephenson research group. It represents only a small part of the extensive series of experiments using *R. eutropha* performed by Sarah during her doctoral work.

Arene *cis*-dihydroxylation

It has been found that aromatic hydrocarbons can be utilized as the sole carbon source by certain bacteria under aerobic conditions. Biodegradation is initiated by bacterial Rieske non-heme iron dioxygenases (RO) with molecular oxygen, yielding the corresponding *cis*-diols, which are subsequently oxidized by catechol dioxygenases. Therefore organisms expressing Rieske dioxygenases can play an important role in bioremediation of serious environmental pollutants.[19,20,21] The most studied dioxygenases are toluene dioxygenase (TDO), benzene dioxygenase (BDO), naphthalene 1,2-dioxygenase (NDO), phthalate dioxygenase (PDO), anthranilate 1,2-dioxygenase (ADO), and benzoate 1,2-dioxygenase (BZDO).[22]

Non-enzymatic approaches to arene dihydroxylation

1,2-*Syn* diols are very common motifs in natural products and important intermediates in organic synthesis. Arene dioxygenases are selective towards a small range of aromatic hydrocarbons, which is the major problem in their applicability. Biotransformations are often problematic to control with low accessibility to the microorganisms and low selectivity throughout substrates. In response to these issues, several research groups have addressed the problem of an alternative method of arene dihydroxylation able to mimic natural enzymes. In 2009, Que *and co-workers* have reported the first non-heme iron complex that catalyses the *cis*-dihydroxylation of naphthalene.[23] Napthalene was oxidised in the presence of the catalyst and hydrogen peroxide in acetontirile, albeit the yield was very low. ^{18}O labelling studies

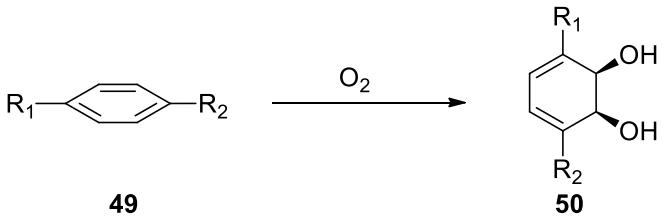
have shown that the water-assisted mechanism is highly possible with initial formation of low spin Fe(III)-OOH species, further cleaved by water to the reactive *cis*-HO-Fe(V)=O oxidant responsible for *cis*-dihydroxylation of naphthalene.[23] Motherwell *et al.* have also looked at alternative dihydroxylations of aromatic compounds.[24]

Degradation of sodium benzoate

Many microorganisms can utilize aromatic compounds as a source of carbon. The microbial degradation of aromatic compounds has tremendous practical significance. The aromatic ring structure is degraded and the products are converted into compounds that can enter central metabolic pathways to provide a carbon source and energy. Most soil bacteria can further degrade the *cis*-diol products of arene dioxygenases with dihydrodiol dehydrogenases to yield ring opened products.[25,26] The β-ketoadipate pathway is widely spread among taxonomically diverse bacteria and fungi. It plays an important role in the degradation of environmental pollutants and naturally occurring aromatic compounds, for example compounds derived from lignins.[27] and homoprotocatechates.[28]

Boyd's model

Boyd *et al.* have derived a very useful method to predict the outcome of dihydroxylation of mono- and 1,4-disubstituted benzene substrates and in most cases the obtained product is an enantiometrically pure *cis*-2,3-diol **50**.[29]



49 **50**

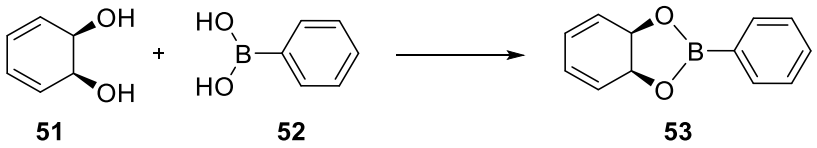
Scheme 4: Boyd's model for predicting the regio- and stereochemical outcome of microbial oxidation of monocyclic aromatics.

In monosubstitued arenes (R_2 = H), good facial selectivity for the dioxygenase-mediated dihydroxylation is observed, with *e.e.* ≈ 100%, since all RL substituents were significantly larger than a hydrogen atom. The notable exception, where a significant decrease in the *e.e.* value was observed, was for fluorobenzene.

Isolation of *cis*-dihydrodiols

Almost all *cis*-dihydroxydiols are highly water soluble and naturally unstable. This means that the isolation process of microbial biooxidation products can pose significant problems. In

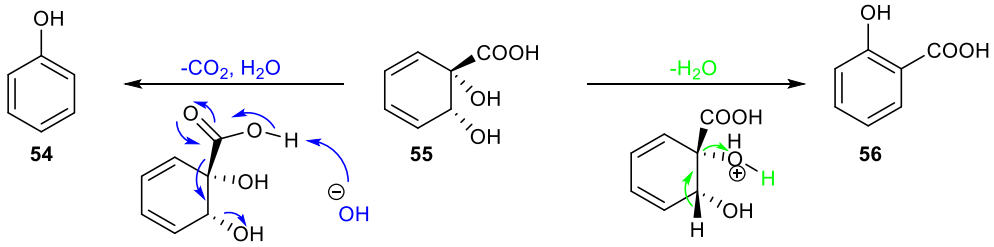
general, the *cis*-dihydroxydiols are extracted numerous times with ethyl acetate before being concentrated and stored at –78 °C. If traces of phenols or acids are present, catalytic rearomatisation can occur.



Scheme 5: Formation of phenylboronate complex **53**.

One approach to long-term storage was the formation of insoluble phenylboronate complexes. Herbert *et al.* discovered the method of formation of these complexes, and after recrystallization, how readily they can be hydrolysed and reused.[30]

Some methods of purification of dihydroxylation products required use of charcoal or zeolite and after binding DHCD successively passing through the column an aqueous solution to remove water soluble components (DNA, proteins) followed by methanol.[31] It must be kept in mind that **55** itself is unstable upon prolonged exposure to air and moisture at room temperature, which leads to rearomatisation products phenol **54** and salicylic acid **56**.



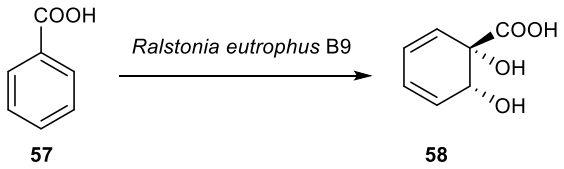
Scheme 6: Degradation of *cis*-3,5-cyclohexadiene-1,2-diol, the oxidation product from benzoic acid, to phenol and salicyclic acid.

In this chapter, the production of microbial diols from aromatic precursors by different types of dioxygenases is described, including mechanistic investigations of bio-oxidation process. Information has been added about their applications in syntheses of several natural products and polymers. More work must be done in order to recover microbial oxidation products, and on strain development to access new enantiomerically pure building blocks on industrial scales.

Results and Discussion

Preparation of my (1S,2R)-1,2-dihydroxycyclohexa-3,5-diene-1-carboxylic acid starting material

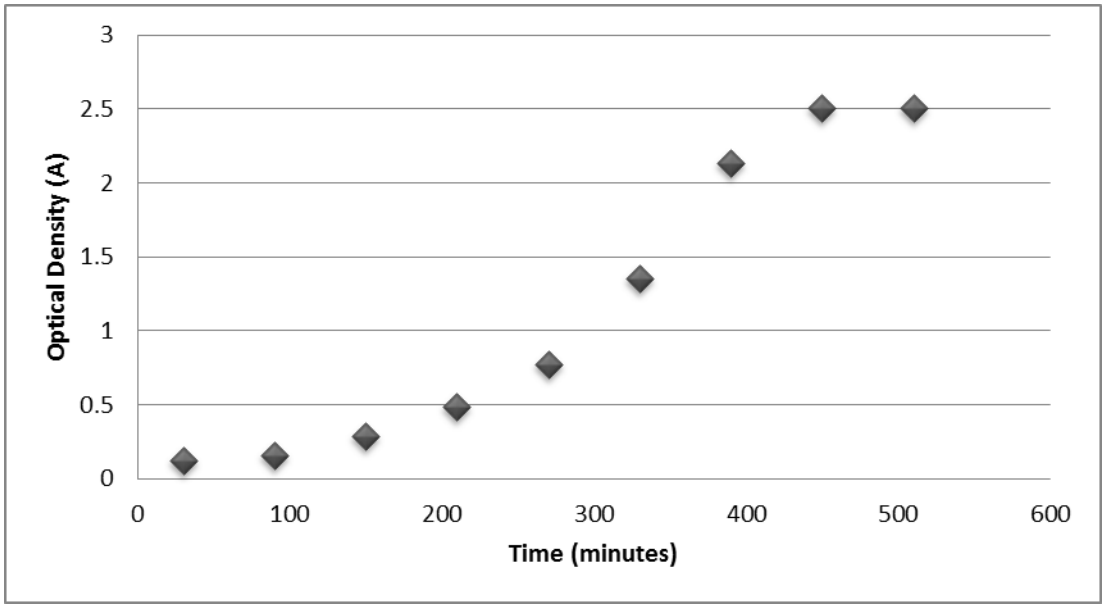
The first synthetic route was attempted initially by performing a microbial biooxidation using the microorganism *Ralstonia eutrophus* B9. The cellular dihydroxylation of commercially available sodium benzoate was carried out using a modified procedure published by Myers' group.[32]



Scheme 7*:* Microbial biooxidation to form (1*S*,2*R*)-1,2-dihydroxycyclohexa-3,5-diene-1-carboxylic acid starting material.

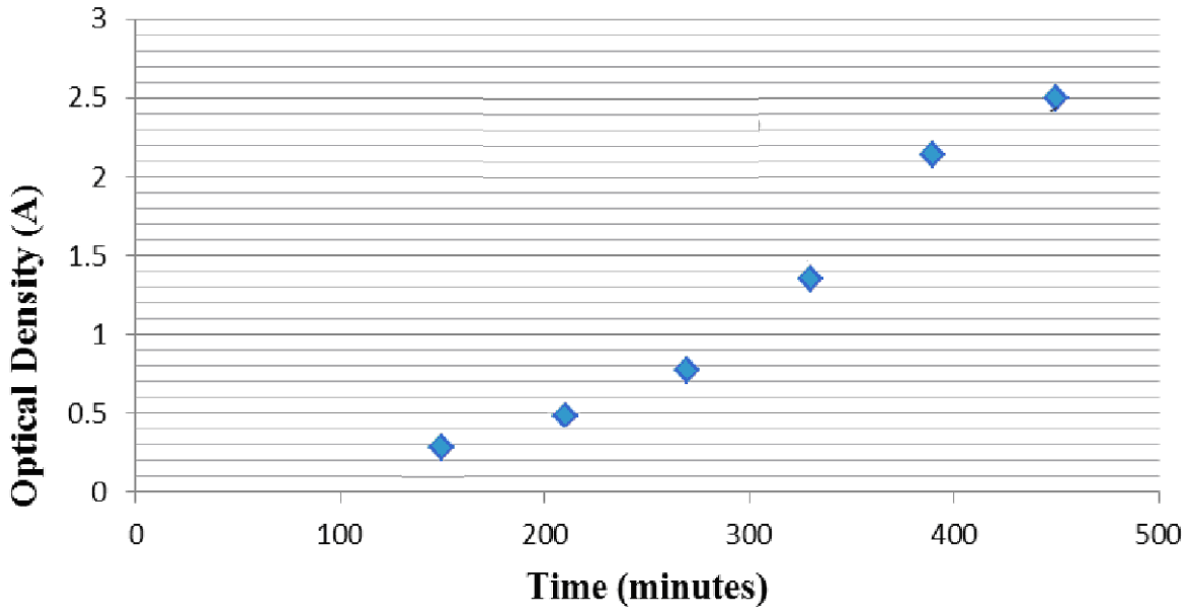
The effect of lysogeny broth medium, LB, on the growth of *R. Eutropha* cells compared to that of Hutner's mineral base medium, HMB, was explored. LB media is known to be an especially nutritionally rich media and is primarily used for the growth of bacteria. In contrast to the densely carbon saturated LB medium, HMB medium is nutritionally less rich and has been specifically designed to starve the microorganisms from any carbon sources. This is theoretically more likely to encourage the microorganisms to dihydroxylate the substrates which are introduced.

Graph 1: Growth curve for microbial *R. Eutropha* cells grown in LB medium only.



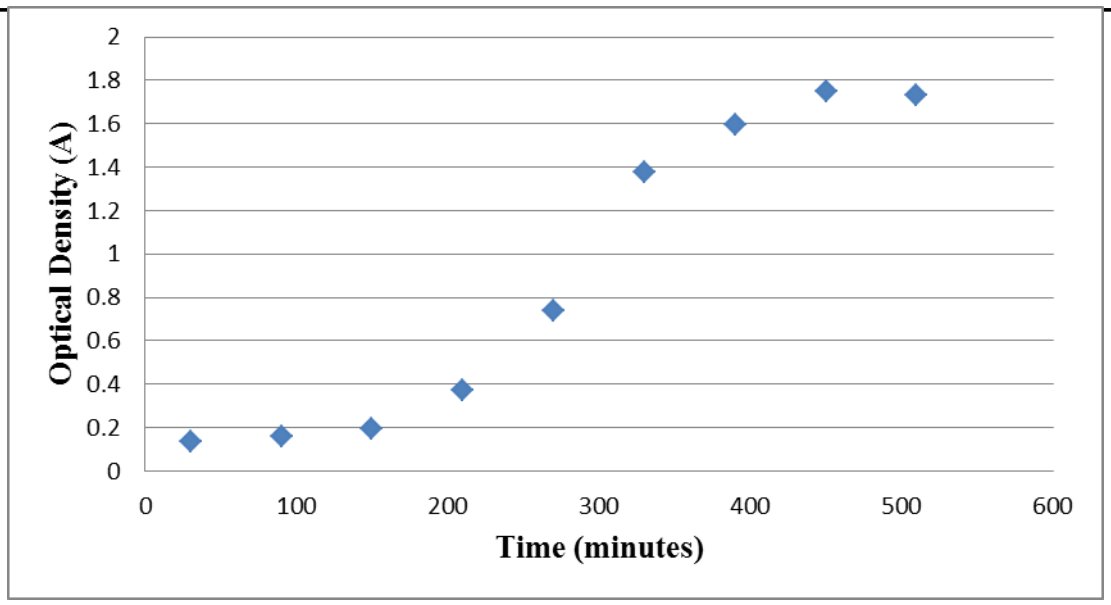
The growth curve for the *R. Eutropha* cells (Graph 1) implies that the cells reached their optimum growth in just over 8 hours, however, the machine used could only record a maximum optical density of 2.5. The samples will be diluted next time to measure a more accurate growth curve and record the true population maximum. There is a high population recorded as indicated by the optical density of greater than 2.5.

Graph 2: Stationary phase for *R. Eutropha* cells grown in LB media only.



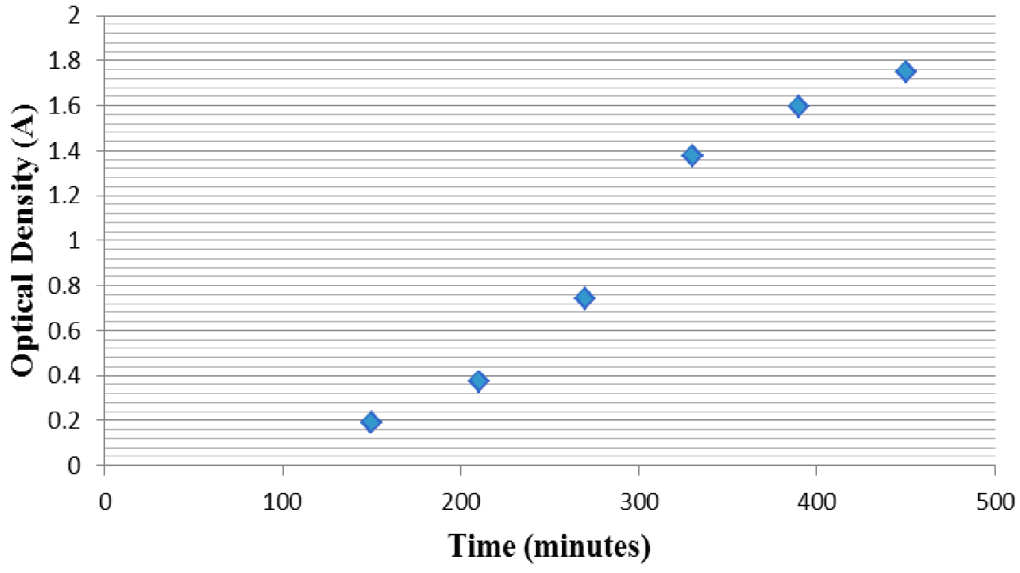
The carbon rich medium LB has been shown (Graph 2) to increase the period of growth as well as the growth population for the *R. Eutropha* microorganisms. The opposite is true for the carbon deficient medium HMB.

Graph 3: Growth curve for *R.eutrophua* cells grown in LB medium initially followed by HMB medium.

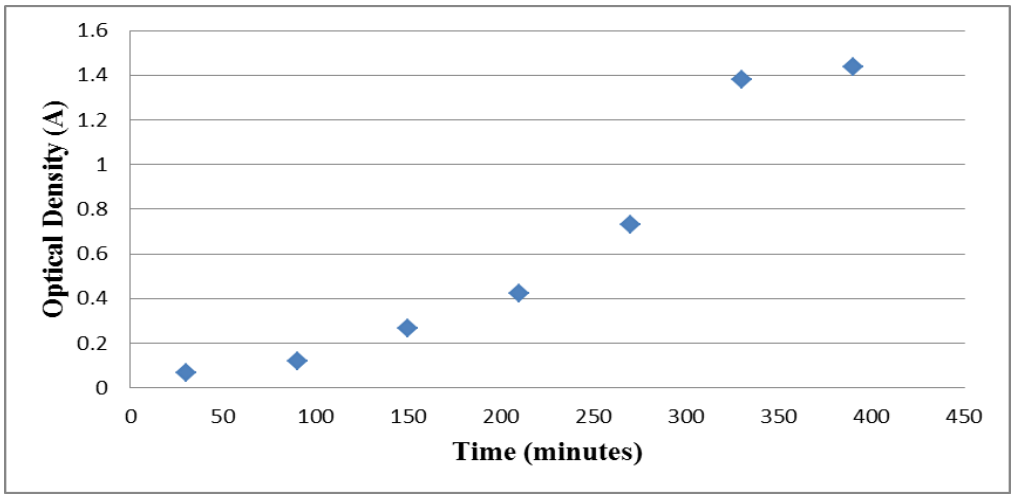


The maximum population was shown (Graph 3) to be reached in 7 hours for the growth of *R. eutropha* cells in LB medium followed by HMB. After induction of cells grown up in LB medium into Sample 2 HMB media the optical density appeared to peak around 1.748 and aqueous sodium succinate solution (0.06 mL of a 1.5 M stock solution) was added to maintain a high population overnight. This reflects the influence of the low carbon source medium that the cells have been grown up in. Both the growth peak and the period of how long the cells grew up and reached optimum population before decreasing were shorter compared to the growth in LB medium alone.

Graph 4: Stationary phase for *R. Eutropha* cells grown in LB medium initially followed by HMB medium.

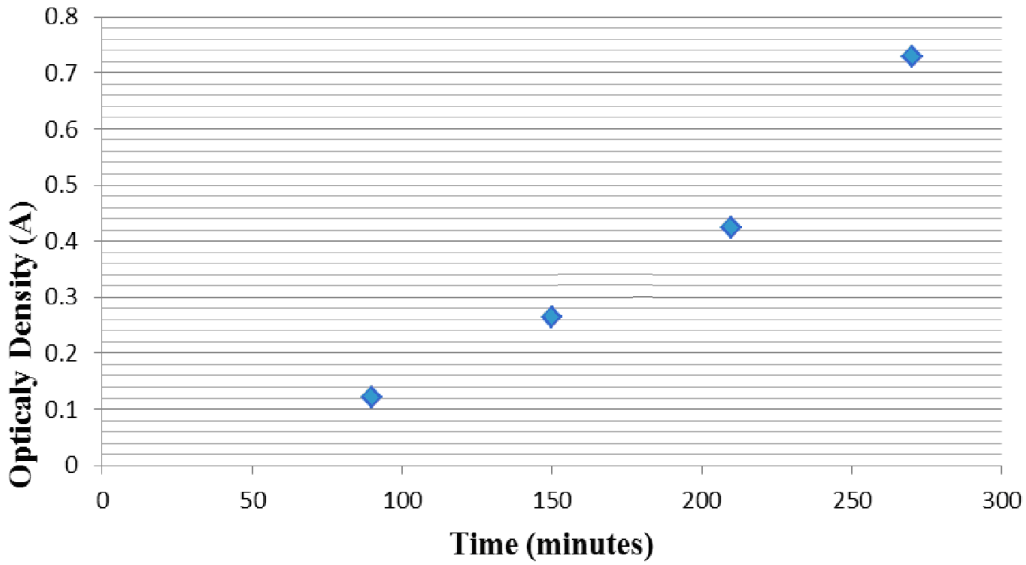


Graph 5: Growth curve for *R. Eutropha* cells grown in Hutner's mineral base only.

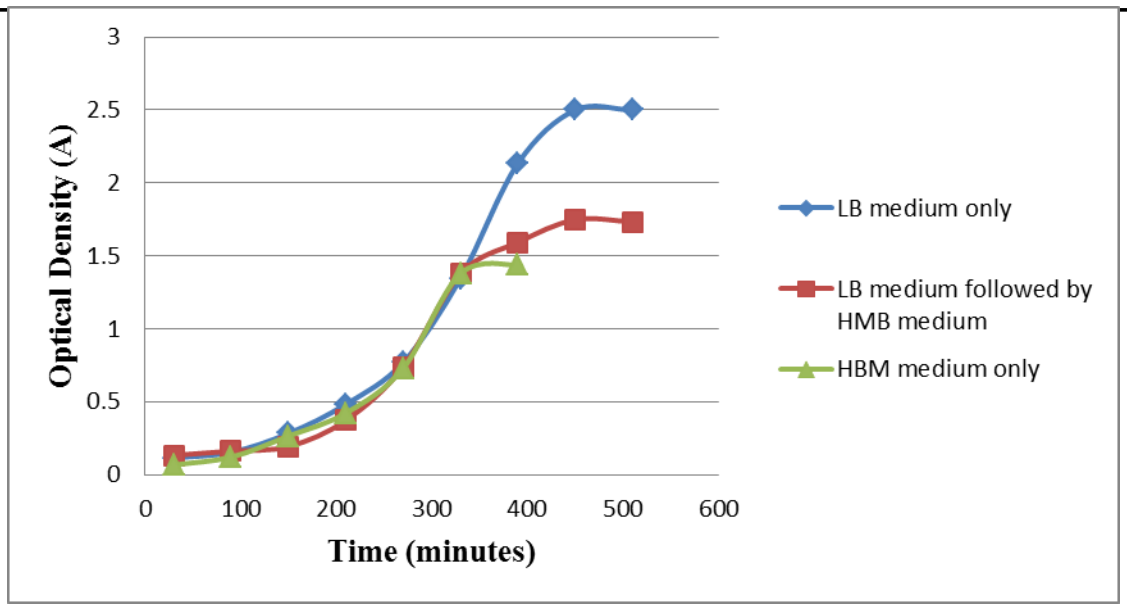


The HMB was the quickest medium in reaching the maximum levels of growth in just over 5 hours (Graph 5). The medium provided insufficient nutrition for the cells to grow to a large population and maintain this population for a large period of time.

Graph 6: Stationary phase for *R. Eutropha* cells grown in Hutner's mineral base only.



Graph 7: Graph showing the difference in growth for *R. Eutropha* cells in LB and HMB medium.



The difference in the time taken to reach the maximum cell population and to maintain this population is clearly represented in Graph 7. The growth rate, as indicated by the gradient of the stationary phase graphs, remained fairly constant throughout. This suggests that the microorganisms were growing at a similar rate in each medium, however, insufficient carbon sources in HMB medium caused the population to peak at a smaller value compared to that of the carbon rich LB medium.

The substrate aqueous sodium benzoate (1 M stock solution) was added to cells grown up in LB medium in the same way as in HMB, however, no product could be isolated at the end of the work up. This implies that the microorganisms were in too rich a carbon medium, so that they did not dihydroxylate the sodium benzoate that was added hourly but instead fed off the LB medium.

The reaction was shown to go to completion as the product could be deduced from the ^{1}H NMR spectra taken. The peaks in the NMR spectrum have chemical shifts δ = 4.89, 5.78, 5.82, 5.95 and 6.14 ppm which indicate the hydrogen atoms at the positions 5, 4, 1, 3 and 2 on the compound respectively. The hydrogen atoms in the carboxyl and hydroxyl groups were not visible due to the fast exchange of these protons with protons in the solvent. Peaks around the values δ = 6.7, 6.9 and 7.11 indicate the by-product salicylic acid. Also, peaks around the value δ = 8.1 suggest the presence of the aromatic starting material benzoic acid. The salicylic acid was not successfully removed by dichloromethane extraction. Also, after discussions with Simon Lewis, it was proposed that a higher yield of the diol acid **58** was made than indicated. This is due to the fact that the compound itself is highly insoluble and

the solvent used to take the NMR spectrum dissolved a large amount of the starting material and by-product, but only a small amount of the diol acid **58**. *R. eutropha* was shown to be a good model microorganism for biotransformation due to its genetic manoeuverability, biosafety and high tolerance to chemical toxicity in biotechnological processes. It should be noted that isolation of the (1*S*,2*R*)-diol starting material proved troublesome and yields tended to fluctuate depending on the scale used (see Table 1).

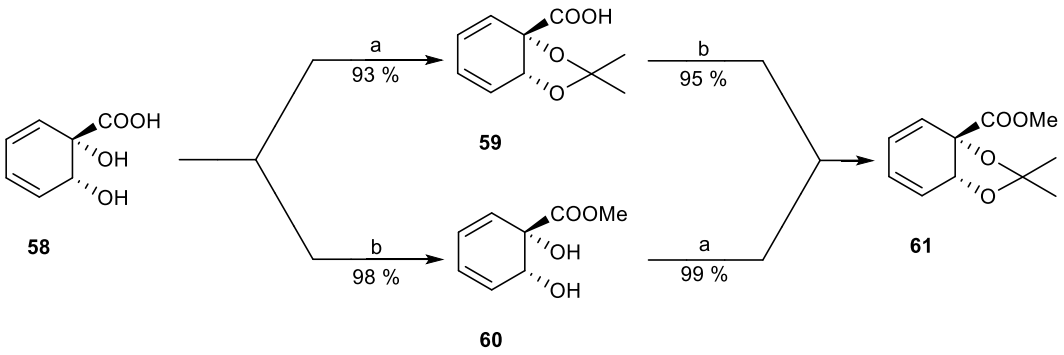
Table 1: Percentage yields from the dihydroxylation of sodium benzoate.

Entry	Scale of biotransformation / L	Percentage Yield of isolated compound 58 / %
1	0.25	89
2	0.50	91
3	0.75	
4	1	
5	2	
6	4	
7	6	

The polar functional groups present in diol **58** made purification by silica chromatography difficult. Due to the instability of this compound when exposed to air and how readily it forms the rearomatisation products phenol and salicylic acid, it was decided that it was it was best to carry out protection early on in the synthesis.

Diol protection

Once the *cis*-diol was in hand, the protected acetonide **61** could be prepared in two steps as illustrated in Scheme 8.



Scheme 8: Synthesis of protected acetonide **61**.

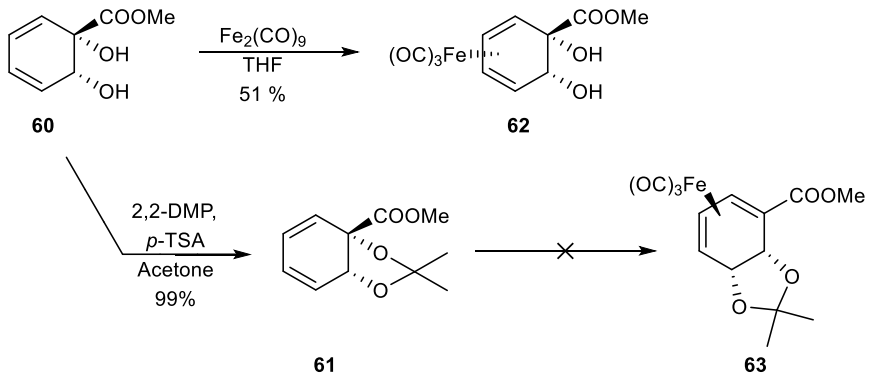
Reagents and conditions: (a) *p*TSA (cat.), DMP, acetone, rt, 2 h; (b) $TMSCHN_2$, rt, Benzene-MeOH(1:1), rt, 1 h, 100%.

Esterification of the microbial starting material to the desired methyl ester was performed using (trimethylsilyl)diazomethane in a solvent system of benzene / methanol (1:1). It was possible to isolate the desired product in near quantitative yields following purification by column chromatography. The use of TMS-diazomethane was preferred to that of diazomethane due to the high explosive nature of the latter, However, both are equally toxic.

The diol protection was carried out by the standard literature procedure published by Jenkins *et al.* involving the treatment of 1,2-*cis* diol with a catalytic quantity of *p*-toluenesulfonic acid and 2,2-dimethoxypropane in dry acetone.[33] It was observed that the route involving the direct conversion to the corresponding methyl ether **60** before exposure to catalytic *p*-toluenesulfonic acid and 2,2-dimethoxy propane in dry acetone gave us slightly increased yields than when the order of addition of the substrates was reversed.

Iron Complexation

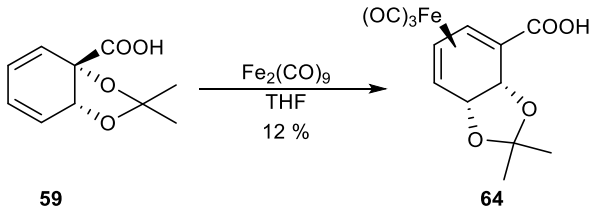
To carry out the iron complexation experiments, the procedures published by the Lewis group were followed using commercially available $Fe_2(CO)_9$.[34]



Scheme 9: Iron complexation of protected diols.

Treatment of methyl ester diol **60** with $Fe_2(CO)_9$ in dry THF whilst stirring at room temperature under a nitrogen atmosphere for 7 days provided (−)-(3*S*)-tricarbonyl[η^4-(1*S*,2*S*)-methyl 1,2-dihydroxycyclohexa-3,5-dienecarboxylate]iron **62** in 51 % yield. The carbonyliron moiety was shown to attach to the same face as the hydroxyl groups, presenting us with the desired stereochemistry. However, when iron complexation was attempted on the methyl ester acetonide **61**, unfortunately it was observed that a complex mixture was produced and it was not possible to isolate the target compound from the desired

rearrangement. After useful discussions with Simon Lewis in Bath, his procedure for the iron complexation of the carboxylic acid acetonide **59** was followed to produce (−)-(3*R*)-tricarbonyl[η^4-(1*S*,2*R*)-1,2-isopropylidenedioxycyclohexa-3,5-dienecarboxylic acid]iron(0) **64** in a yield of 12 %.

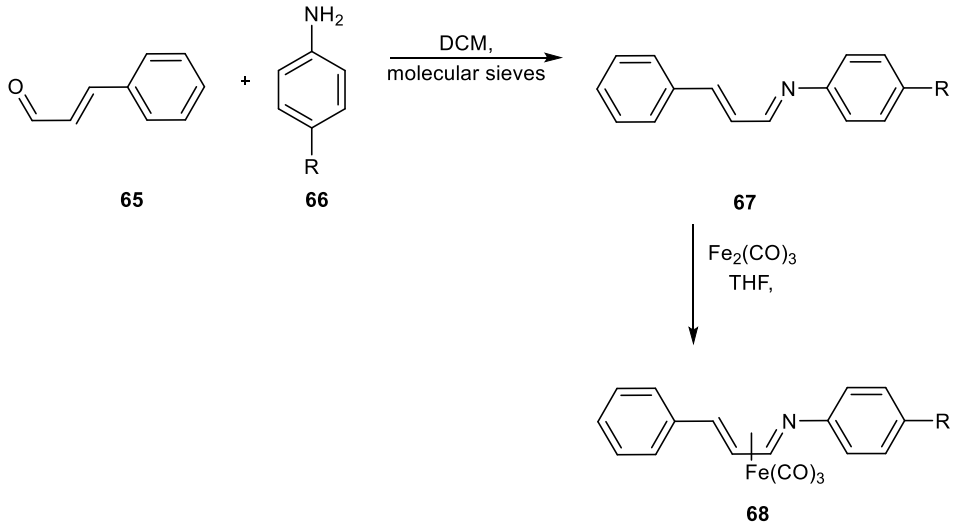


Scheme 10: Formation of the rearranged carboxylic iron complex.

Unfortunately, attempts to esterify the rearranged iron complex **64** using the same conditions as before [TMS-diazomethane in a solvent system of benzene / methanol (1:1)] proved unsuccessful.

Ligand transfer reagents

As this was still relatively early on in the synthetic route, so the possibility of increasing iron complexation yields by using ligand exchange reagents was explored. Following the work published by Knolker *et al.* , the diene ligands were synthesised from an equimolar reaction mixture of suitable amine and *trans*-cinnamaldehyde **67** in the presence of dry dichloromethane with molecular sieves.[35] The products were isolated in good yields (Table 2).



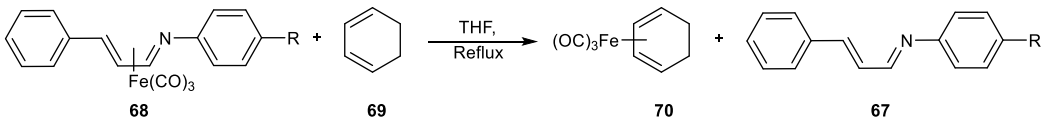
Scheme 11: Preparation of ligand exchange iron complexes.

(a: R = H; b: R = OMe)

Table 2: Percentage yields from Scheme 11.

Entry	R	Yields for compounds 67a, 67b / %	Yields for compounds 68a, 68b / %
1	H	89	91
2	OMe	91	97

These two ligand exchange complexes **67** were used in the next step by addition of 1,3-cyclohexadiene **69** and heating at reflux in dry THF. The reaction mixture was heated for 1.5 hours before being quenched. The advantage of this reaction is that the azabuta-1,3-diene **68**, Scheme 12 can be recovered and reused to prepare further ligand exchange complexes. The results for this reaction are shown in Table 3.



68 **69** **70** **67**

Scheme 12: Reaction involving ligand exchange iron complex **70**.

Table 3: Percentage yields from Scheme 12.

Entry	R	Yields for compound 70 / %
1	H	45
2	OMe	65

As was reported by Pearson group, the yield was increasingly improved in comparison with previous methods but it was not possible to obtain the same yield as in the literature. When this method was attempted with carboxylic acetonide **58**, no formation of the desired compound was observed. Application of this method on the methyl ester **61** again proved unsuccessful.

Chapter 3

Organoiron Approach

The organoiron strategy for stereocontrolled organic synthesis, which was referred to briefly in Chapters 1 and 2, is now reviewed in detail at the start of Chapter 3. The 'Experimental Section' (Chapter 4) gives details of the reactions performed by Sarah in her work towards the application of the organoiron approach towards the enantioselective synthesis of hippeastrine. Three important model studies were completed, and the original synthetic proposal discussed by Sarah in Chapter 1 (Scheme 3) and a later alternative synthetic approach (now summarised in Scheme 25) were validated in this stage of the research, and twenty four new compounds were fully characterised.

Introduction

The ionic compound potassium trichloroethyleneplatinate(II) was the first complex ever to be published and was synthesised by the Danish organic chemist William Christopher Zeise in 1827.[36] It was subsequently discovered that many metals such as palladium, chromium, magnesium and rhodium, are able to form complexes. It was this finding as well as the accidental discovery of ferrocene in 1951 that provided the impulse for rapid developments in the organometallic chemistry field in recent decades.[37] The concept of back-bonding was introduced and there became a greater understanding of metal-olefin complexes. These organoiron complexes are of great use in synthetic organic chemistry. The main focus for this project is centred on organoiron complexes, in particular tricarbonyliron complexes. These compounds are highly valued for their stability and their ability to bind to complex organic ligands.[38] Pearson stated that the ability of iron to form stable complexes with a wide range of ligands made it perhaps the most valuable metal in the periodic table.[39]

Preparation of η^4-Tricarbonyliron Complexes

Traditionally, the preparation of tricarbonyliron-diene complexes involves the direct complexation of dienes with a carbonyliron compound. Common reagents that are utilised during this process are iron pentacarbonyl $Fe(CO)_5$ **72**, diironnonacarbonyl $Fe_2(CO)_9$ **72**, and dodecacarbonyltriiron $Fe_3(CO)_{12}$ **73**.

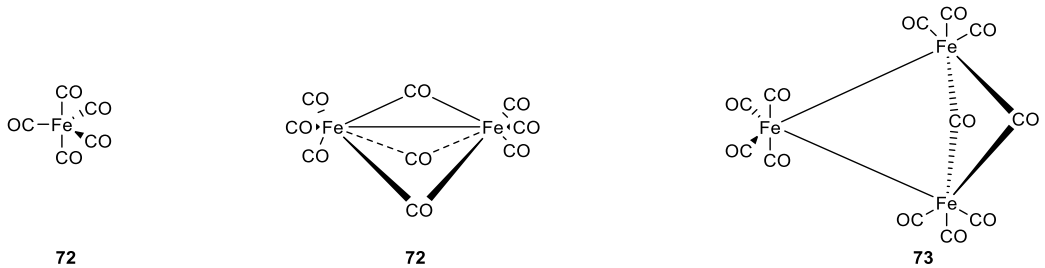


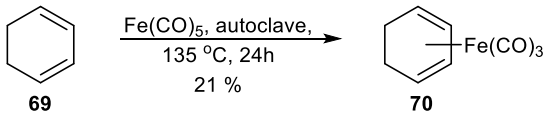
Figure 4: Common reagents used for the synthesis of tricarbonyliron complexes.

Iron pentacarbonyl **72** was discovered independently by Monde and Bertholet as a musty smelling yellow liquid.[40,41] The preparation involved a direct reaction of finely divided iron and carbon monoxide. Reactions utilising $Fe(CO)_5$ proceed by first forming the 16 electron species $Fe(CO)_4$. These are carried out by heat, light or sonication. The more reactive solid

diironnonacarbonyl **72** is prepared by photolysis of $Fe(CO)_5$ in acetic acid using a medium pressure mercury lamp to provide the product in the form of golden flakes. The final common reagent used, dodecacarbonyltriiron **73**, is a result of the thermal decomposition of $Fe_2(CO)_9$.

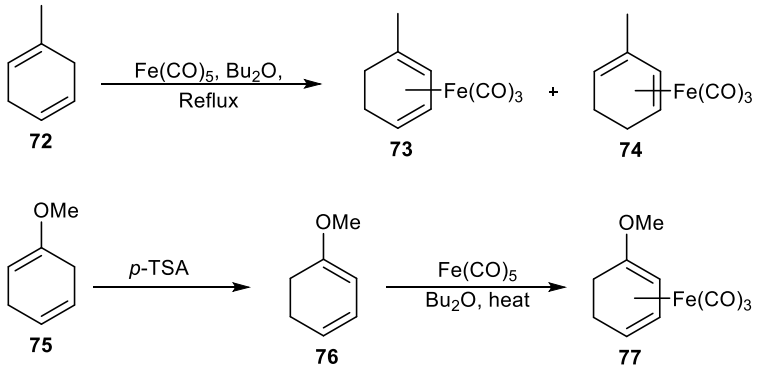
Synthesis of η^4-Tricarbonyliron Complexes

Organoiron complexation was first developed in 1930 when Reihlen and co-workers synthesised the acyclic (η^4-buta-1,3-diene)tricarbonyliron(0) complex.[42] This complexation method proceeded by the loss of a molecule of carbon monoxide which resulted in the initial generation of the 16 electron species $Fe(CO)_4$. This co-ordinatively unsaturated species then reacted with one of the double bonds of a diene moiety to form a more stable 18 electron complex species. When another carbonyl unit was lost, a 16 electron species was created and complexation to the second double bond occurred resulting in the formation of the η^4-complex.



Scheme 14: Hallam and Pauson synthesis of (η^4-cyclohexa-1,3-diene)tricarbonyl complex.

Having pioneered the synthesis of tricarbonyliron complexes, it appears that Reihlen did not fully appreciate the significance of his discovery, or its contribution to organometallic chemistry. His report made no impact and no further papers were published in this field until 1958 when the cyclic iron complex variant was described by Hallam and Pauson, Scheme 14.[43] This methodology was expanded upon by Arnet and Pettit who discovered that non-conjugated 1,4-dienes such as compound **72** were capable of reacting with pentacarbonyliron to from conjugated tricarbonyliron complexes.[44]

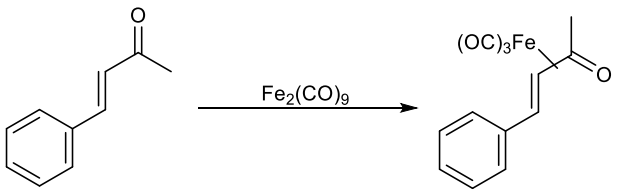


Scheme 15: Complexation of dihydrotoluene.

This reaction allowed a vast array of substituted 1,4-cyclohexadiene ligands to be complexed. These ligands were easily synthesised by Birch reduction to provided a variety of substituted 1,4-cyclohexadiene ligands from their corresponding aromatic precursors.[45,46] The iron complexation of substituted cyclohexadienes such as dihydrotoluene **72** often gives rise to isomeric products (**73** and **74**) with roughly a 1:1 ratio as shown in Scheme 15. When the system is preconjugated as in the case for dihydroanisole **75** using a catalytic quantity of p-TSA then only one isomer is observed during the complexation process **77**.

Tricarbonyliron transfer reagents

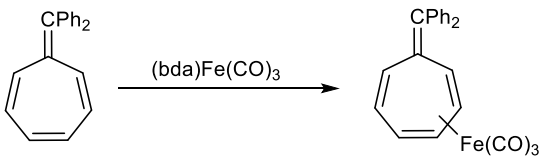
Compound **79** was first synthesised by Weiss *et al*. in 1964 and was later employed by Lewis and co-workers as a transfer reagent in 1972.[47,48] Complexation of benzylideneacetone **78** and $Fe_2(CO)_9$ provided the ligand transfer reagent (bda)$Fe(CO)_3$ as shown in Scheme 16.



78 **79**

Scheme 16: Preparation of the transfer reagent **79**.

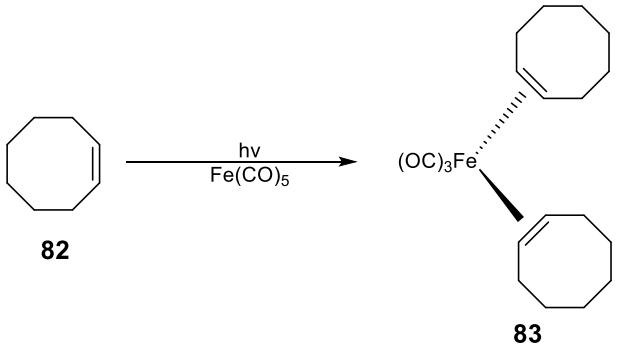
Ligand **79** was found to be sensitive to both heat and UV light so that the usual complexation reagents $Fe(CO)_5$ and $Fe_3(CO)_{12}$ were unusable. Furthermore, when iron complexation was attempted on the free ligand using $Fe_2(CO)_9$, an unstable hexacarbonyldiiron complex was isolated.[49] To overcome these drawbacks, the (bda)$Fe(CO)_3$ transfer ligand was used as a potential source of the tricarbonyliron moiety in the complexation of 8,8-diphenylheptafulvene **80** to yield the iron complexed derivative **81**. Whilst managing to complex the ligand, one disadvantage associated with this particular transfer reagent is that it is only successful in complexing conjugated dienes.[50]



80 **81**

Scheme 17: Synthesis of iron complex **81** using ligand transfer reagent (bda)$Fe(CO)_3$.

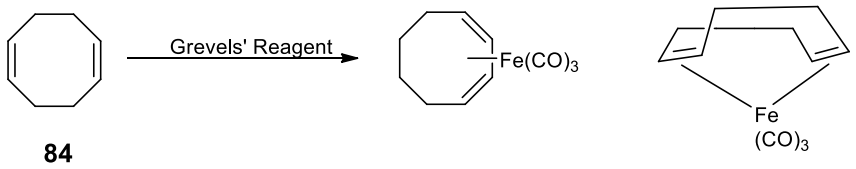
In 1984, Grevels synthesised the bis(η^2-cis-cyclooctene)tricarbonyliron complex **83** which was formed during a photolytic reaction of pentacarbonyliron and cis-cyclooctene **82** shown in Scheme 18.[51]



82 **83**

Scheme 18: Synthesis of Grevels' reagent **83** by a photolytic reaction of *cis*-cyclooctene with $Fe(CO)_5$.

This became a commonly used transfer reagent due to the extremely mild reaction conditions that were required and its ability to complex non-conjugated dienes. When Grevels' reagent **83** was reacted with *cis*-cycloocta-1,5-diene **84** two products were observed. Double bond migration allowed the formation of *cis*-cycloocta-1,5-diene **85** as the major product followed by (η^4-cycloocta-1,5-diene)tricarbonyliron **86** as the minor product.



84 **85** **86**

Scheme 19: Reaction of Grevels' reagent **83** with non-conjugated cycloocta-1,5-diene **84**.

Chiral enantiopure (η^4-1-aza-1,3-butadiene)tricarbonyl complexes are known to act as asymmetric catalysts and can deliver enantiopure tricarbonyliron complexes. Knölker *et al*. published the asymmetric complexation of prochiral ligands with chiral camphor derivatives of 1-azabutadienes.[52]

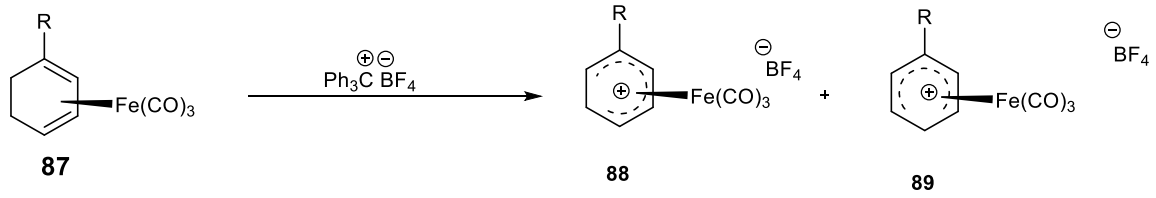
Cationic Tricarbonyliron Complexes

These relatively stable yellow crystalline solids are usually obtained as tetrafluoroborate or hexafluorophosphate salts. They exhibit two strong infrared absorptions at approximately 2130 and 2050 cm^{-1}. The shift in absorbance for these cations when compared to their neutral tricarbonyliron complexes is due to the delocalised positive charge from the dienyl group to the metal. This results in the carbonyl groups resonating at a higher frequency.

Fisher and Fisher reported the first formation of a cationic tricarbonyliron complex in 1960 using a hydride abstraction procedure with the reagent trityl tetrafluoroborate.[53] These

compounds became highly valued as useful electrophiles. Various alternative methods are available to produce η^5-cyclohexadienyliron tricarbonyl intermediates. The most utilised approach involves the direct hydride abstraction of the corresponding neutral complex with trityl hexafluorophosphate or trityl tetrafluoroborate in dichloromethane.[54,55,56,57]

The regioselectivity of these cation complexes can be controlled to some extent by manipulating the functional group of the 2-subsituted cyclohexadiene. If an electron donating methoxy functional group is present then the reaction will be favoured towards producing isomer **88**. When an electron withdrawing group such as a methyl ester is attached, cationic isomer **89** will be formed as the major product as shown in Scheme 20.[58]

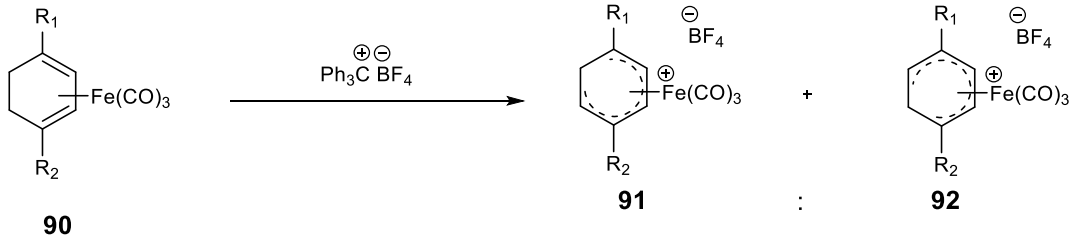


Scheme 20: Hydride abstraction using reagent trityl hexafluorophosphate to achieve cationic intermediates.

Table 4 Hydride abstraction of compound **88** and **89**.

Entry	R^2	Ratio 88:89
1	OMe	94:6
2	Me	60:40
3	COOMe	20:80

Unsymmetrically disubstituted diene complexes are shown to be controlled by the steric effects of the substituent as well as the electronic influence of the substituents on the diene. Electron withdrawing groups favour 'ortho' hydride abstraction whilst electron withdrawing groups direct towards the 'meta' position.



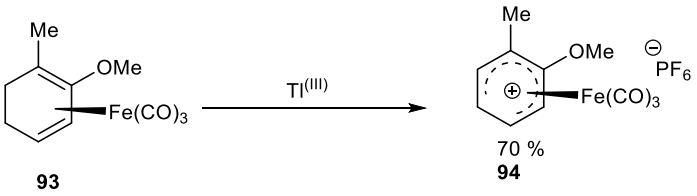
Scheme 21: Hydride abstraction when diene **90** is unsymmetrically disubstituted.

Table 5 Hydride abstraction compound **91** and **92** when diene is unsymmetrically disubstituted.

Entry	R^1	R^2	Ratio 91:92
1	OMe	H	80:20
2	COOMe	H	95:5
3	OMe	Me	5:95

The steric demand is equivalent at either end of the diene when R^2 = Me. This results in regiocontrol being switched to the other isomer so that the mechanism is under electronic control.

From a synthetic chemist's point of view this lack of regioselectivity is extremely troublesome. However, hydride abstraction is not the only method of salt formation. The steric effects of the neutral iron complex can also influence the outcome of the hydride abstraction reaction. Substituents that are present at the C-5 position and are orientated anti to the iron group have been reported to hinder any cationic reaction from taking place.[10] Thus in the case of compound **93**, it is believed that the methyl group '*exo*- to' the tricarbonyliron moiety hinders attack.

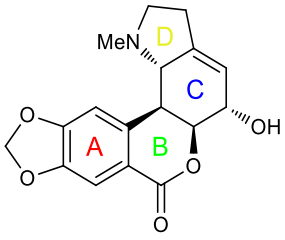


Scheme 22: Hydride abstraction reached by oxidation method.

Stephenson *et al.* looked at alternative oxidation methods to overcome this problem of steric inhibition of hydride abstraction. Complementary results were observed by using the more selective thallium trifluoroacetate in place of the bulky triphenylcarbenium cation.[59] Preparation of η^5-cyclohexadienyl salts can be achieved by acid induced protonation and hydrogen transfer from the ring to the side chain. Birch and coworkers first reported the preparation of η^5-cationic complexes by acid catalysed demethoxylation.[60]

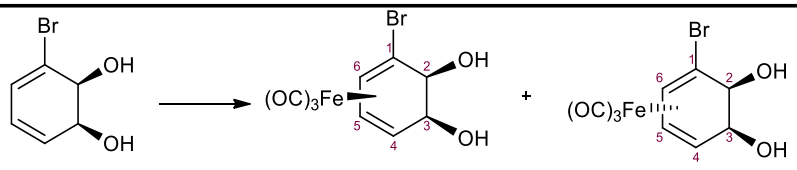
Results and Discussion

Model studies for the hippeastrine C ring



19

At this stage in the project, because of problems with the scale-up of the *R. eutropha* biodioxygenation, commercially available *cis*-(1*S*,2*S*)-1,2-dihydroxy-3-bromocyclohexa-3,5-diene was converted into the diastereomeric tricarbonyliron complexes **48a** and **48b** and the diastereoisomer **48a** was converted into the acetal **96b**.



48a **48b**

The stereochemistry of the diastereoisomer **48a** was confirmed by X-ray crystallography (see Figure 1 and Appendix 1).

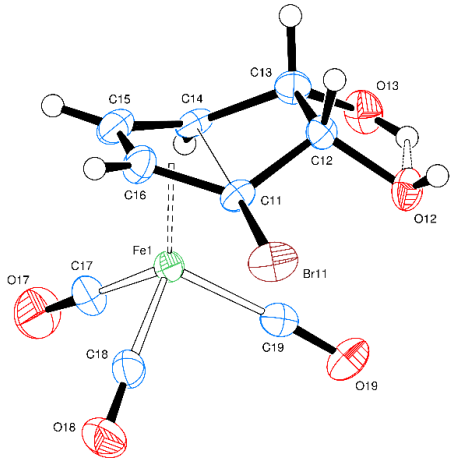


Figure 1

Complex **96b** was also characterised by X-ray crystallography (see Figure 2 and Scheme 23).

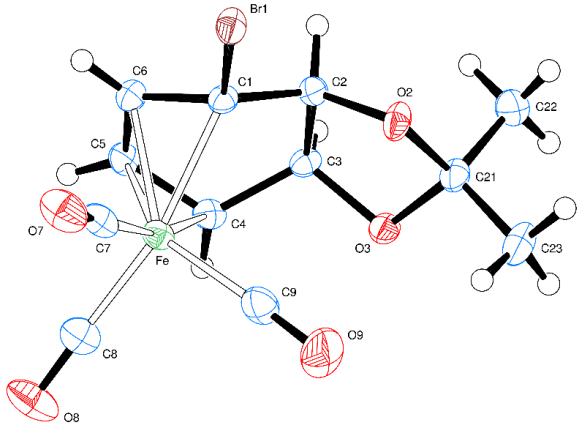
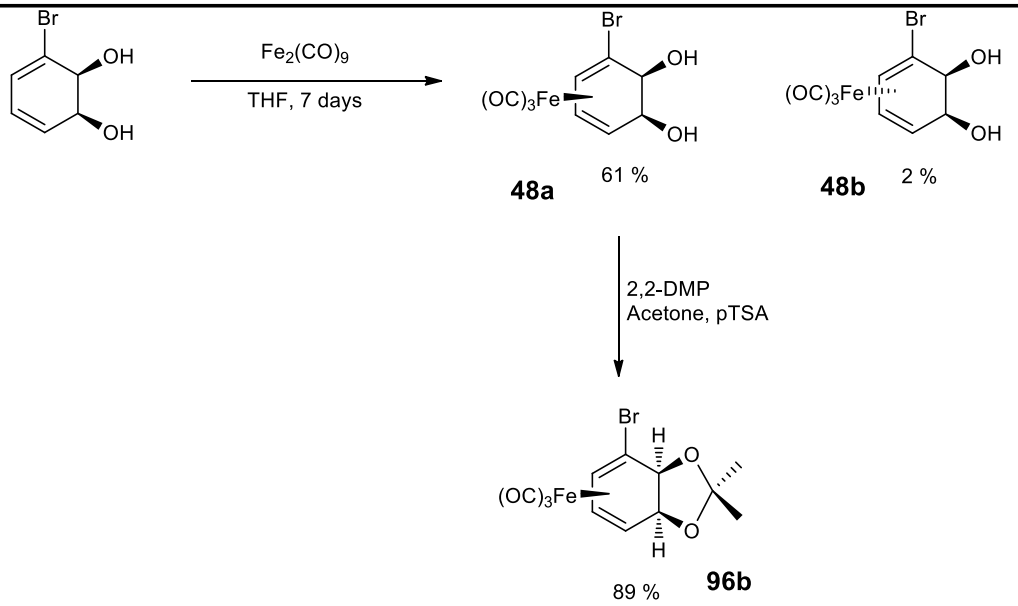
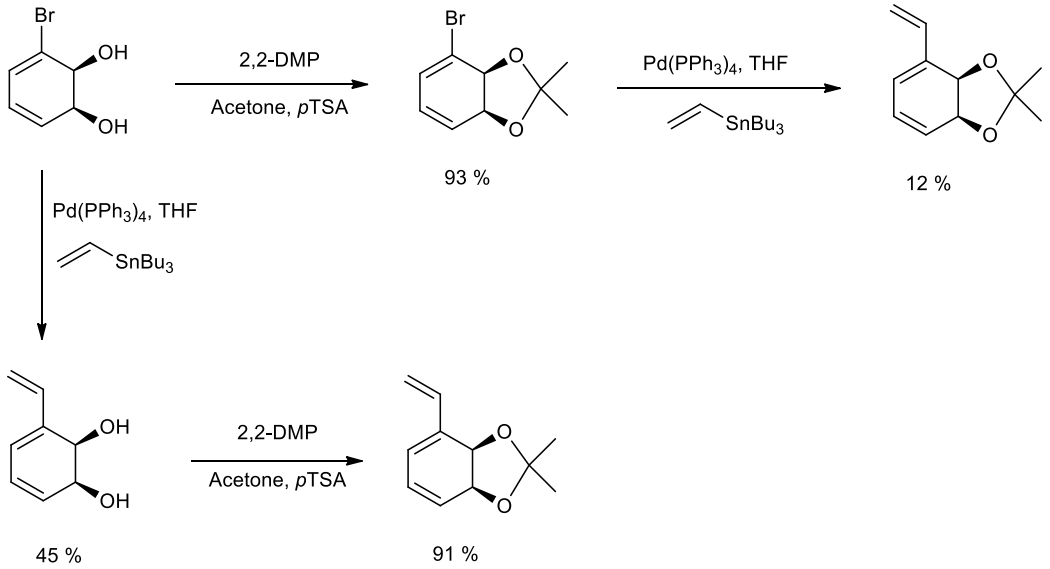


Figure 2



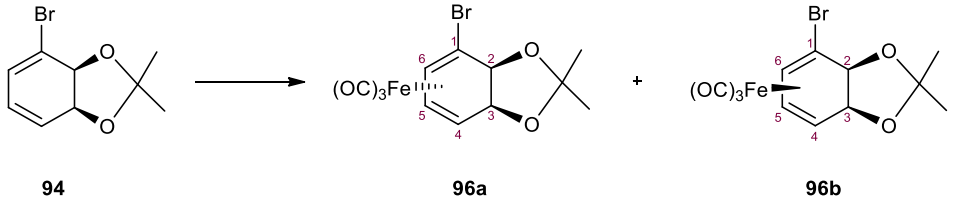
Scheme 23:

The second synthetic route began by the diol protection of the 1,2-*cis* bromo diol starting material (see Scheme 24).

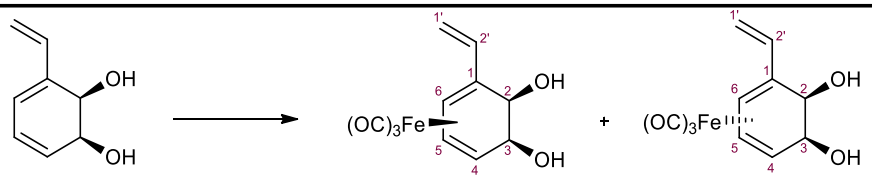


Scheme 24:

The protected derivative **94** was converted into the diastereomeric tricarbonyliron complexes **96a** and **96b**.

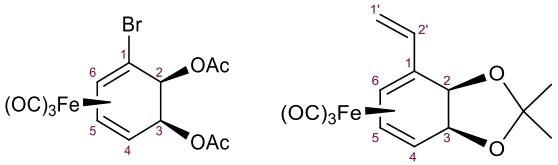


The diastereomers **96a** and **96b** were obtained in a similar way.



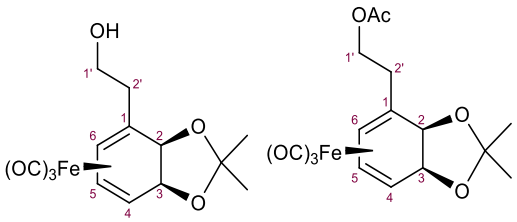
97a **97b**

The diacetate **98** was obtained from complex **48a** and the acetal **45** was obtained from **97a** in an 86% yield.



98 **45**

Successful access to complex **45** successfully completed the first three steps of the synthetic route proposed in Chapter 1 (Scheme 3). The access to the fully-functionalised cyclohexadienyliron complex **44** from **45** could be approached by hydroboration followed by acetylation and a novel extension of our earlier use of triphenylcarbenium ion reagents to form tricarbonyl(η^5-cyclohexadienyl)iron salts by deoxygenation of tricarbonyliron complexes originating from 1,2-dihydroxycyclohexadienes. Complex **45** was converted into alcohol **100** by hydroboration (96% yield) and the product was acetylated to afford the ester **104** in an 83% yield.



100 **101**

The successful formation of **101** provided the crucial starting material needed to explore the novel chemistry needed to form the key electrophilic intermediate **44**.

Eight new compounds were fully characterised in the course of this section of the research.

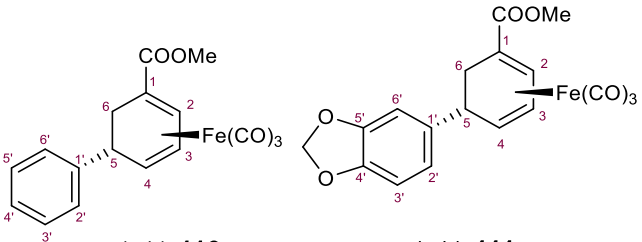
Model studies for the installation of the hippeastrine A ring

A variation of the retrosynthesis discussed in Chapter 1 was also under consideration at this time as a fall-back in case the novel conversion of **101** into **44** proved difficult or lacked regioselectivity. In this alternative, it was planned to use an ester in place of the two-carbon side-chain in **44**, and extend the side-chain after the arylation or lactonisation steps.

An organocuprate reagent had been successfully employed in Astley's model study[61] and so was selected as the nucleophile for this approach. In order to gain access to the organocuprate, piperonal was treated with bromine in acetic acid as described by Meyers and co-workers to give 6-bromo-benzo[1,3]dioxazole-carboxaldehyde in a 39 % yield.[62] The product, which was isolated as white needles, had a melting point consistent with the literature value of 131-132 °C as well as corresponding ^{1}H and ^{13}C NMR data. This material was reduced to 6-bromo-3,4-methylenedioxybenzyl alcohol using sodium borohydride. Again, the product was isolated as white needles in a 75 % yield, with a melting point and NMR data consistent with that reported. Additionally, infrared spectrometry showed the

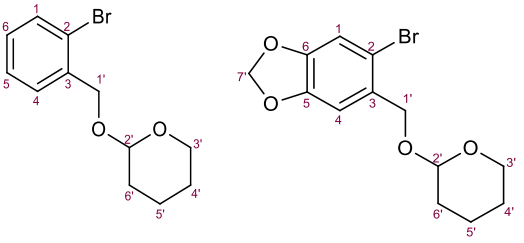
carbonyl peak at 1614 cm^{-1} of the aldehyde **102** had been replaced by a broad alcohol absorption at 3150 cm^{-1}.

Esters at C1 are known to direct nucleophiles to the far end of an η^5-dienyl complex, but unlike the intended use of organocuprate chemistry to form **43** from **44**, which was well precedented in our earlier studies that had been performed in a readily accessible model series lacking the C-6 oxygenation required for the lactonisation procedure that would access **42**, with the electron-withdrawing ester in place, the cyclohexadienyliron complex would be a far more reactive electrophile. It was necessary to check the applicability of our organocuprate chemistry for this purpose. Although phenyllithium is commercially available, to ensure exact comparability with later examples, the first examination of arylcuprate addition to the carbomethoxy-substituted tricarbonyl(η^5-cyclohexadienyl)iron complex was performed using an organocuprate reagent made from bromobenzene. The product **110** was obtained in a 72% yield.

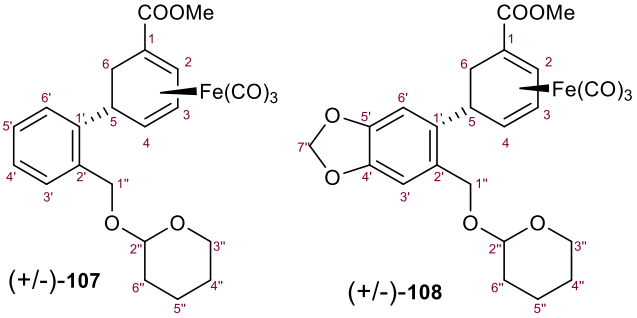


(+/-)-**110** (+/-)-**111**

A preliminary experiment was also performed to explore the inclusion of the required methylenedioxy group in the nucleophile. The product **111**, identified by comparison of its NMR spectra with those of complex **110**, was obtained in low yield (39%), and since better results were obtained with the more advanced methylendioxy-containing nucleophile derived from **105**, further work on the simple model series of aryl bromides was abandoned. The protected aryl bromides **106** and **105** were prepared and evaluated as the source of organocopper-based nucleophiles in a series of trial reactions again using tricarbonyl(η^5-carboxylic acid methyl ester)iron(1+) hexafluorophosphate(1–) as the electrophile.

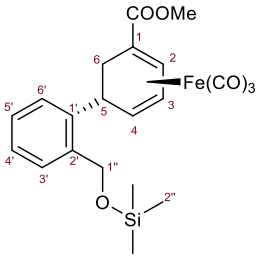


106 **105**



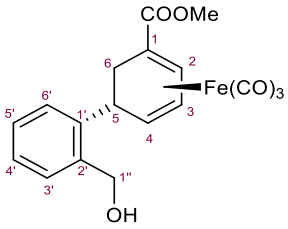
(+/-)-**107** (+/-)-**108**

The organocuprate addition again proceeded better in the absence of the methylenedioxy group. Complex **107** was obtained in 86% yield, compared to only 63% for **108**. The complex **114** was obtained in a 75% yield using the silyloxy-protected analogue of **106**.

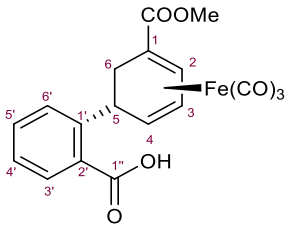


(+/-)-**114**

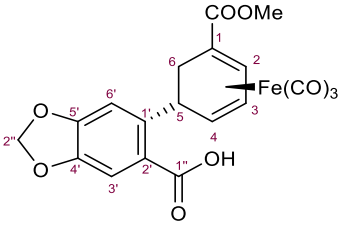
Complexes **109** and **112** were obtained in a similar way using 2-bromobenzyl alcohol or 2-bromobenzoic acid and two equivalents of butyllithium. The yields were lower (41% for **109** and 36% for **112**) and dropped to 24% for the methylenedioxy-substituted example **113**.



(+/-)-**109**



(+/-)-**112**



(+/-)-**113**

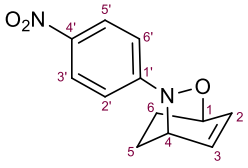
At this stage in the work, the best source of the organocuprate reagent was identified as **105**.

The successful formation of **113** established that the alternative synthetic route would be viable if acetalisation of complex **62** (see Chapter 2, Scheme 9; an alternative to the illustrated formation of **61** prior to complexation) and salt formation using Me_3OBF_4 in place of Ph_3CBF_4 could be developed to provide the $OCMe_2OMe$ analogue of the *cis*-diol to displace complexation to the ester-substituted face of the $OCMe_2OCPh_3$ ether **44** (see Chapter 1, Scheme 3). Whereas the intended formation of **44** from **43** was based on the expectation that the bulky Ph_3CBF_4 reagent would react at the less hindered of the two oxygen atoms of the acetal (steric control) the alternative using Me_3OBF_4 should proceed more readily at the more congested of the two oxygen atoms of the acetal to be formed from **62**.

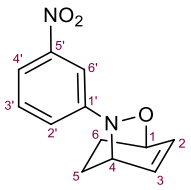
Ten new compounds were fully characterised in the course of this section of the research.

Model studies for C-ring functionalisation to prepare for the creation of ring D

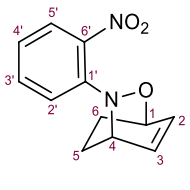
The final stages of the intended route to hippeastine would employ our *in situ* decomplexation heterocycloaddition method with advanced products obtained from reaction of the fully-functionalised arylcuprate reagents and enantiopure electrophiles from the biodioxygenation studies described in Chapter 2. In particular, we needed to extend the range of arylnitroso reagents to examples where subsequent removal of the arene (which is not present in hippeastrine) after installation of the *N*-Me group. To prepare for this, Sarah extended our experience of the required nitroso chemistry preparing the cycloadducts **118**-**121** in 92%, 94%, 92%, and 98% yields, respectively.



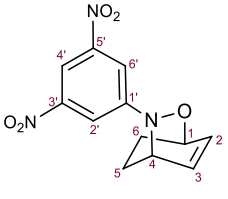
118



120

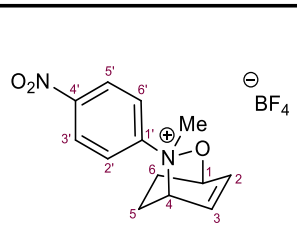


121

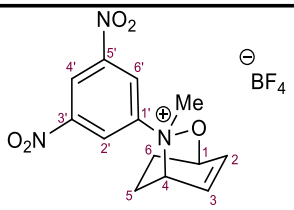


119

In this model series, an initial study of the *N*-methylation reaction gave **124** in 48% and **126** in 65% yield. Compound **126** was identified by comparison of its 1H NMR data with that of compound **124**, its molecular weight was confirmed by high resolution mass spectrometry.

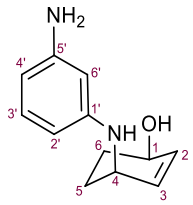


124



126

The successful formation of **124** prepares the way for a dearylation strategy in reduction of the N-O bridge introduced by the nitrosocycloaddition and reduction of the nitro group would form a para-diamino substitution pattern on the arene. Oxidation to the diimine equivalent of a quinone and hydrolysis should then detach the arene and hydrolyse the acetate to prepare for a Mitsunobu-type cyclisation to form ring D. In a trail experiment, the required reduction of **120** gave an uncharacterised product which by HRMS showed a molecular ion consistent with the desired formation of **123**.



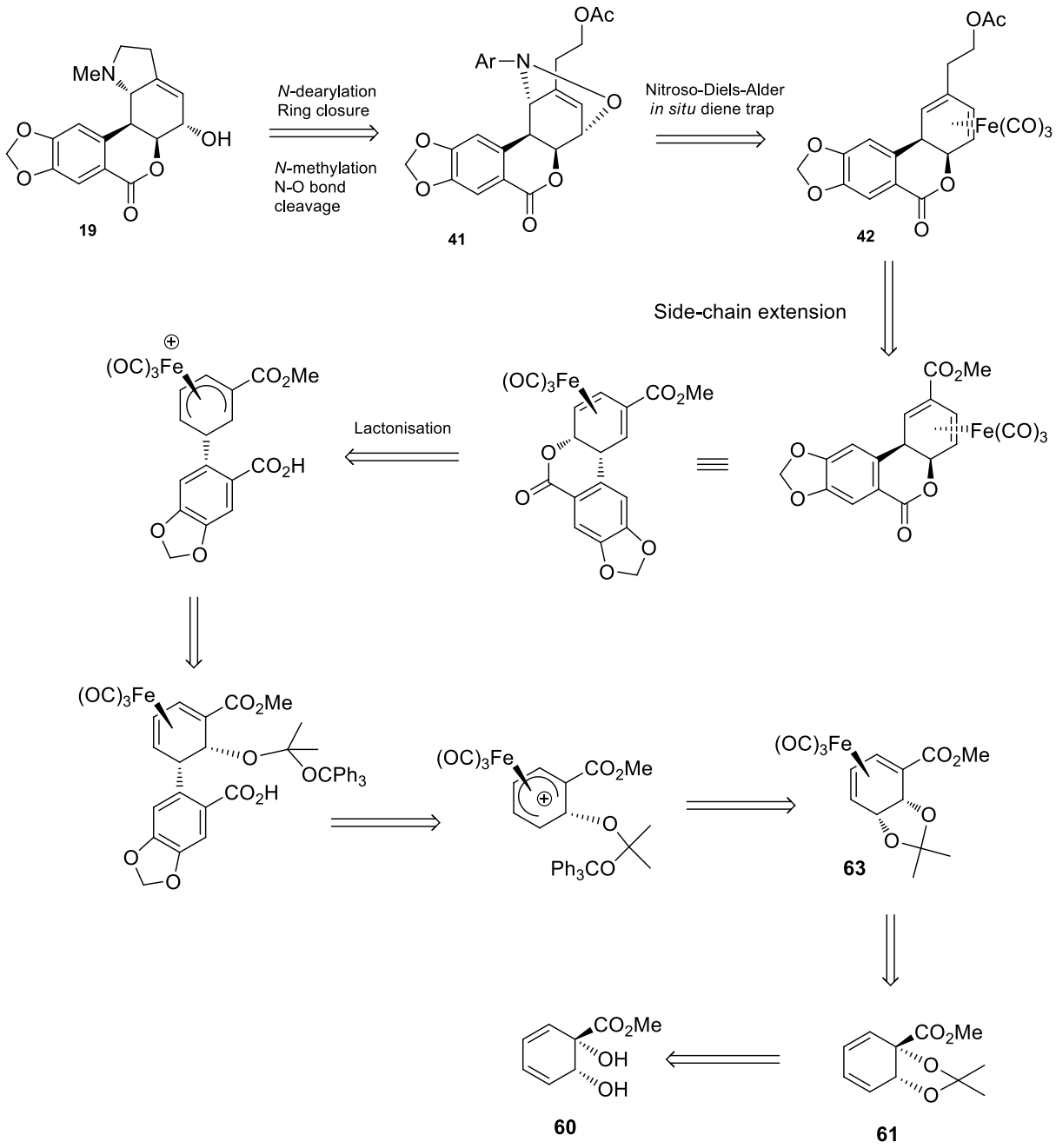
123

Rather than optimise this reaction, it had been intended to concentrate of the comparable reduction of **124** which has the *N*-Me group already in place.

Similar reduction of **126** should again eventually lead to the formation of an amino-substituted p-quinone from which the aryl group should also be able to be detached by hydrolysis under acidic conditions (conjugate addition of water to the quinone, protonation of the nitrogen atom and cleavage of the N-O bond).

The model studies for the functionalisation of ring C to prepare for the formation of the D ring, established by the formation of 124 and 126, that the cycloaddition and methylation steps were high-yielding.

Six new compounds were fully characterised in the course of this section of the research.



Scheme 25: Alternative retrosynthetic analysis adapted from a group meeting talk by Sarah in February 2016

In conclusion, the reactions and compound characterisation data presented in the Experimental Section of the thesis establish the viability of the organoiron approach to hippeastrine discussed by Sarah in Chapter 1 (see Scheme 3) and an alternative fall-back approach which is now summarised in Scheme 25. The doctoral studies presented in this thesis constitute a new and substantial conceptual advance in the understanding of the biodioxygenation/organoiron approach to the enantioselective synthesis of the alkaloid hippeastrine.

Future Work

Work still to be done includes the study the regiochemistry of the conversion of **101** into **44**, the acetalisation of **62** and formation of the $OCMe_2OMe$ analogue of the $OCMe_2OCPh_3$ ether **44**, the arylation of the $OCMe_2OMe$ analogue of the $OCMe_2OCPh_3$ ether **44**, and the extenion of the side-chain and formation of the lactone **42**. The use of nitroarylniroso reagents to trap the diene liberated by the decomplexation of **42** would also need to be investigated, after which the *N*-methylation, reduction of the N-O bridge and nitro groups, and the closure of ring D could be tested.

Chapter 4

Experimental Section

General Experimental Procedures

Where mentioned, water and brine refer to deionised water and a saturated aqueous solution of sodium chloride, respectively. Reaction temperatures of –100 °C, –78 °C and 0 °C correspond to the use of [nitrogen / diethyl ether], [dry ice / acetone] and [ice / water] baths, respectively. All non-aqueous reactions were carried out under an oxygen-free atmosphere using either nitrogen or argon and flame-dried glassware.

Purification of Reagents and Solvents

When mentioned as distilled, the following solvents were freshly refluxed under a nitrogen atmosphere over sodium and benzophenone ketyl before distillation; THF, Et_2O and DME. Dichloromethane, acetonitrile and methanol were distilled over calcium hydride. Toluene was distilled over sodium. Acetone was freshly distilled before the reaction over potassium carbonate.

Commercially available MCPBA (35 g) was dissolved in diethyl ether (250 mL) and washed with an aqueous solution of NaOH (410 mL, 0.1 M). The ether layer was dried over $MgSO_4$ and carefully evaporated (**CAUTION! Potential explosive**) under reduced pressure to yield pure MCBA (17 g).

Commercially available *cis*-(1*S*-2*S*)-3-bromo-3,5-cyclohexadiene-1,2-diol was purchased from Sigma Aldrich 0.2 g/mL in 0.1 M phosphate buffer, 96 %. To recover the pure product from the suspension the solid was filtered and rinsed with a few millilitres of base-washed ethyl acetate (using Na_2CO_3). The solid was collected and further product was extracted from the aqueous layer using equal volumes of base-washed ethyl acetate. The organic layer was dried over $MgSO_4$ and the solvent was removed using rotary evaporation (**temperature not to exceed 37 °C**). Pure crystals could be stored at –78 °C. The suspension of the product in phosphate buffer solution is stable at 0 °C.

Analysis of Compounds

Flash column chromatography was carried out using Davisil LC60A 40-63 micron silica (amorphous silicon dioxide). Thin layer chromatography was carried out using commercially available Macherey-Nagel pre-coated TLC sheets (ALUGRAM® SIL G/UV254 silica plates). Proton and carbon NMR spectra were recorded on a Varian UNITYplus 400 MHz spectrometer with a 5 mm Inverse detect broad band z-gradient probe, a Bruker Avance III nanobay 400 MHz spectrometer with a 5 mm broad band observe BBFOplus probe fitted

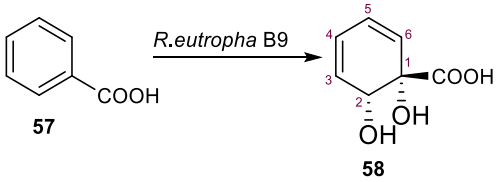
with an actively shielded z-gradient coil and Bruker Avance III 500 MHz spectrometer with a 5 mm broad band observe BBFOplus smart probeTM fitted with an actively shielded z-gradient coil (500 MHz). NMR signals were measured using the residual non-deuteriated NMR solvent signal as a reference, see Table below.

Table 1: Residual peak values for different deuterated NMR solvents used.

	$CDCl_3$	**CD_3CN**	**CD_3OD**	**D_2O**	**$(CD_3)_2SO$**	**$(CD_3)_2CO$**
^{1}H NMR	7.26 ppm	1.94 ppm	3.31 ppm	4.79 ppm	2.50 ppm	2.05 ppm
^{13}C NMR	77.16 ppm	1.32 ppm 118.26 ppm	49.00 ppm	-	39.52 ppm	29.84 ppm 206.26 ppm

Melting points were measured on a Buchi melting point B-545 apparatus. Infra-red spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR spectrometer. The specific rotations were measured on an ADP 440 polarimeter from Bellingham + Stanley, and were measured in DCM at 10 mg mL^{-1} unless otherwise stated. Chemical ionisation and high resolution mass spectra were measured at the EPSRC Mass Spectrometry Centre at the University of Wales, Swansea.

Cellular dihydroxylation of sodium benzoate using LB medium for initial growth followed by Hutner's Mineral Base medium to produce (1*S*,2*R*)-1,2-dihydroxycyclohexa-3,5-diene-1-carboxylic acid **58**



57 **58**

Chemical Formula: $C_7H_8O_4$

Molecular Weight: 156.1370

Preparation of Lysogeny Broth media (1 L)

To a 2 L Erlenmeyer flask tyrptone (10 g), yeast extract (5 g) and sodium chloride (10 g) were added in sequence. The solids were suspended in 800 mL of distilled water and a magnetic stirrer bar was added to aid dissolving. After a period of 5 minutes further deionised

water was added using a measuring cylinder to make a total of 1 L. A foam bung was placed in the neck of the flask and aluminium foil was wrapped around it to secure it in place. Autoclave tape was added to indicate complete sterilisation. The flask was then placed in the autoclave machine at 121 ^{o}C. After cooling to room temperature the LB media was ready for use.

Preparation of Hutner's Mineral Base Medium

Hutner's Metals 44 solution was prepared as follows for use in Hutner's Mineral Base Medium: Concentrated sulfuric acid (100 μL) was added to nanopure water (50 mL) in a 250 mL Erlenmeyer flask. Solid EDTA (0.50 g), zinc sulfate heptahydrate (2.20 g), iron(II) sulfate heptahydrate (1.0 g), copper(II) sulfate (0.39 g), cobalt(II) nitrate hexahydrate (0.05 g) and sodium tetraborate decahydrate (36 mg) were then added in sequence followed by 50 mL of nanopure water.

Solid potassium hydroxide (0.4 g) was dissolved in deionised water (500 mL) in a 2 L Erlenmeyer flask. To this flask the following were added sequentially; nitrilotriacetic acid (200 mg), magnesium sulfate (283 mg), calcium chloride dehydrate (67 mg), ammonium molybdate (0.2 mg), iron(II) sulphate (2.0 mg), Hutner's Metals 44 solution (1 mL), ammonium sulfate (1.0 g), potassium dihydrogen phosphate (2.72 g) and sodium monohydrogen phosphate heptahydrate (5.36 g). The solution was diluted to a total volume of 1 L and the pH was adjusted to 6.77 with concentrated hydrochloric acid. The medium was sterilized by heating in an autoclave and allowed to reach room temperature before use.

Cellular dihydroxylation of sodium benzoate

A sterile pipette tip was streaked across the surface of a frozen glycerol stock solution of the microorganism *R. Eutropha* to produce small shards (ca. 10 mg). The frozen shards were streaked across the surface of a sterile petri dish containing LB agar medium and stored at a constant temperature of 37 ^{o}C overnight. A sterile stick was used to collect a single colony of the freshly grown cells and was placed in a sterile 125 mL Erlenmeyer flask containing HMB (25 mL) and aqueous sodium succinate solution (140 μL of a 1.5 M stock solution). The flask was aerated at 250 rpm for a period of 2 days a constant temperature of 30 ^{o}C.

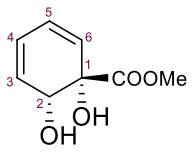
An aliquot (10 mL) of the resultant white heterogeneous solution was transferred using a sterile pipette to a mammalian cell growth jar containing HMB (6 L) and aqueous sodium succinate solution (20 mL of a 1.5 M stock solution). The jar was warmed on a hot plate to an

internal temperature of 30 °C and cotton filtered air was sparged through the medium. After 2 days the white, heterogeneous solution was treated with aqueous sodium benzoate solution (18 mL of a 1.0 M stock solution) and aqueous sodium succinate solution (10 mL of a 1.5 M stock solution). The resulting mixture was aerated vigorously for 6 hours at an internal temperature of 30 °C.

After induction, sufficient aqueous sodium benzoate solution (24 to 48 mL of a 1.0 M stock solution, depending on the rate of consumption) was added hourly to maintain a concentration of 10-20 mM (determined by UV absorbance at 225 nm). Aqueous sodium succinate solution (10 mL of a 1.5 M solution) was added every fourth hour. These additions proceeded over a period of 18 hours. The solution was then aerated overnight at an internal temperature of 30 °C to ensure complete conversion.

The fermentation broth was centrifuged at 6000 rpm (Sorvall GS-3 rotor, model SLA-3000) for 30 minutes to remove cellular material. The supernatant was concentrated to a volume of 400 mL using a rotary evaporator (bath temperature <45°C). The concentrate was cooled to 0 °C and then acidified to pH 3.0 using concentrated aqueous hydrochloric acid. The acidified aqueous solution was extracted repeatedly with ethyl acetate (8 x 250 mL, 4 x 100 mL, 8 x 50 mL). The ethyl acetate extracts were dried over sodium sulfate before concentration using a rotary evaporator (bath temperature <45 °C), providing a pale yellow solid residue. Trituration of the residue with dichloromethane (2 x 400 mL) followed by drying *in vacuo* afforded the impure title compound as a pale yellow powder (2.5 g). Further trituration with dichloromethane was required to remove both the starting material and the bi-product salicylic acid produced, affording the title compound as a pure white solid (11.2 g, 12 %); $\mathbf{[\alpha]_D^{25}}$ –109 (*c* 0.5, EtOH), Lit $[\alpha]_D^{25}$ –123.8 (c 1.78, H_2O*);* $\mathbf{\delta_H}$ (500 MHz, MeOD) 6.1 (1H, dd, *J* = 9.6, 5.0, H^5), 5.97-5.88 (1H, br m, H^2), 5.80 (2H, d, *J* = 10.4, $H^{3/4}$), 4.85 (1H, s, H^6) ppm; $\mathbf{\delta_C}$ (500 MHz, MeOD) 178.1, 133.6, 127.3, 127.2, 123.6, 75.5, 72.5 ppm.
Data in agreement with that previously reported by Myers and Siegel.[63]

Methyl (1*S*,2*R*)-1,2-dihydroxycyclohexa-3,5-diene-1-carboxylate **60**.



60

Chemical Formula: $C_8H_{10}O_4$

Molecular Weight: 170.1626

A solution of (trimethylsilyl)diazomethane 2.0 M in hexane (4.5 mL, 28.1 mmol, 5.7 eq) was added dropwise using a syringe over the period of 30 minutes to a stirred solution of (1*S*,2*R*)-1,2-dihydroxycyclohexa-3,5-diene-1-carboxylic acid (0.76 g, 4.9 mmol, 1 eq) in benzene/methanol (1:1, 100 mL) until the effervescence ceased and a yellow colour persisted. The reaction mixture was then stirred for 2 hours under a nitrogen atmosphere at room temperature before being concentrated under reduced pressure. The residue was purified by column chromatography using a solvent system of hexane / ethyl acetate [2:1] to provide the title compound as a pale yellow oil (1.18 g, 98 %); $\mathbf{R_f}$ 0.67 hexane / ethyl acetate [2:1]; $\mathbf{[\alpha]_D^{23}}$ +68 (*c* 1.6, $CHCl_3$), lit $[\alpha]_D^{25}$ +71.3 (c 1.6, $CHCl_3$); $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 6.17 – 6.12 (m, 1H, H^2), 5.96 (dddd, 1H, *J* = 9.6, 5.3, 2.8, 1.1 Hz, H^3), 5.85 – 5.80 (m, 1H, H^4), 5.77 (ddd, 1H, *J* = 9.5, 2.0, 1.1 Hz, H^5), 4.85 (s, 1H, C1-OH), 3.88 (s, 3H, -Me) ppm; $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 175.7, 132.1, 127.0, 124.8, 122.9, 74.0, 71.0, 53.8 ppm; $\boldsymbol{\nu_{max}}$ (film) 3444, 2967, 1738, 1439, 1407, 1260, 1083, 1043 cm^{-1}.

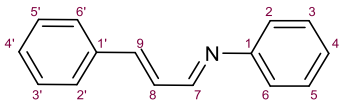
Data in agreement with that previously reported.[64]

General Procedure 1

Preparation of 1-azabuta-1,3-diene derivatives:

Trans-cinnaldehyde (82.8 mmol, 1 eq) and suitable amine (82.8 mmol, 1 eq) were added to a flask containing dry dichloromethane (120 mL) and molecules sieves. The reaction mixture was left overnight. The solvent was removed by rotary evaporation and the remaining solid was dried *in vacuo*.

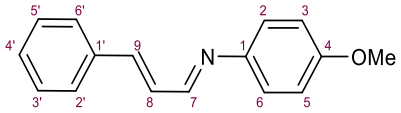
1,4-Diphenyl-1-azabuta-1,3-diene **67a**.



67a

In accordance with **General Procedure 1**, employing aniline (4.90 mL, 53.7 mmol) in dichloromethane (65 mL) with *trans*-cinnamaldehyde (6.76 mL, 53.7 mmol) to provide the title compound as pale yellow needles (10.26 g, 92 %); **Mp.** 103-105 °C. *(lit.*[65] *107°C)*; **δ_H** (300 MHz, $CDCl_3$) 8.19 (dd, *J* = 7.1, 1.2 Hz, 1H, H^7), 7.52 – 7.43 (m, 2H, $H^{8/9}$), 7.40 – 7.26 (m, 5H, Ar-H), 7.20 – 7.03 (m, 5H, Ar-H) ppm; **δ_C** (300 MHz, $CDCl_3$) 161.78, 151.83, 144.17, 135.71, 129.73, 129.30, 129.05, 128.71, 127.63, 126.25, 121.05 ppm.
Data in agreement with that previously reported.[65]

1-(4-Methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene **67b**.



67b

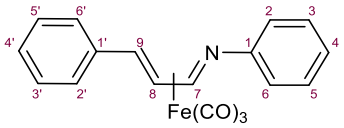
In accordance with **General Procedure 1**, employing *p*-anisidine (6.78 mL, 58.9 mmol) in dichloromethane (70 mL) with *trans*-cinnamaldehyde (7.41 mL, 58.9 mmol) provided the title compound as yellow-green crystals (13.4 g, 96 %); **Mp.** 118-120 °C. *(lit. 122°C*[65]*)*; **δ_H** (300 MHz, $CDCl_3$) 8.31 – 8.28 (m, 1H, H^7), 7.57 – 7.50 (m, 2H, $H^{2'/6'}$), 7.42 – 7.32 (m, 3H, $H^{3'/4'/5'}$), 7.23 – 7.19 (m, 2H, $H^{2/6}$), 7.12 (d, *J* = 4.6 Hz, 2H, $H^{8/9}$), 6.94 – 6.91 (m, 2H, $H^{3/5}$), 3.83 (s, 3H, -OMe) ppm; **δ_C** (300 MHz, $CDCl_3$) 159.65, 158.54, 144.67, 143.16, 135.90, 129.51, 129.02, 128.90, 127.52, 122.35, 114.55, 55.60 ppm.
Data in agreement with that previously reported.[65]

General Procedure 2

Iron complexation of dienes using $Fe_2(CO)_9$ in THF

To a flask containing diene (2.104 mmol, 1 eq) and nonacarbonyldiiron (2.272 mmol, 1.08 eq) was added freshly distilled THF (30 mL). The slurry was stirred at room temperature for 7 days under a nitrogen atmosphere, before being filtered through a plug of celite and concentrated under reduced pressure. **(Care! Toxic pentacarbonyliron distilled over at this point!)** The oil residue was purified by column chromatography to provide the title compound.

Tricarbonyl[(1-4-η)-1,4-diphenyl-1-azabuta-1,3-diene]iron(0) complex **68a**.

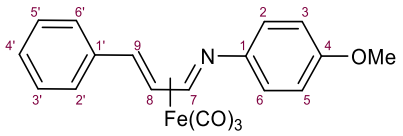


68a

In accordance with **General Procedure 2**, employing 1,4-diphenyl-1-azabuta-1,3-diene (8.71 g, 42.1 mmol) in tetrahydrofuran (550 mL) with diironnonacarbonyl (16.5 g, 45.4 mmol) and purification using column chromatography with a solvent system of diethyl ether / hexane [1:10] provided the title compound as yellow crystals (10.9 g, 75 %); $\mathbf{R_f}$ 0.74 hexane / ethyl acetate [3:1]; δ_H (300 MHz, $CDCl_3$) 7.58 – 6.70 (m, 11H, Ar-H), 5.80 (s, 1H, H^8), 3.47 (s, 1H, H^9) ppm; $\boldsymbol{\delta_C}$ (300 MHz, $CDCl_3$) 162.3, 153.4,; 138.8, 129.0, 128.8, 126.9, 126.7, 122.5, 122.1, 104.2, 75.5, 62.2 ppm; $\boldsymbol{\nu_{max}}$ (film) 2051 (C≡O symmetric), 1980 (C≡O asymmetric) cm^{-1}.

Data in agreement with that previously reported.[65]

Tricarbonyl[(1-4-η)-1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene]iron(0) complex **68b**.

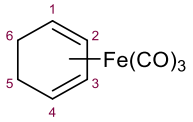


68b

In accordance with **General Procedure 2**, employing 1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene (6.48 g, 27.3 mmol) in tetrahydrofuran (300 mL) with diironnonacarbonyl (10.7 g, 29.5 mol) and purification using column chromatography with a solvent system of diethyl ether / hexane [1:9] provided the title compound as red crystals (8.92 g, 87 %); $\mathbf{R_f}$ 0.74 hexane / ethyl acetate [3:1]; **Mp.** 138-142 ºC. *(lit. 139 °C)*; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 7.49 – 6.59 (m, 5 H, Ar-H), 5.61 (s, 1H, H8), 3.69 (s, 3H, -OMe), 3.32 (s, 1H, H^9) ppm; $\boldsymbol{\delta_C}$ (500 MHz, $CDCl_3$) 155.5, 146.7, 139.1, 129.1, 128.9, 127.5, 127.0, 126.7, 122.7, 122.4, 114.6, 114.4, 104.4, 74.1, 62.0, 55.6 ppm; $\boldsymbol{\nu_{max}}$ (film) 2049 (C≡O symmetric), 1987 (C≡O asymmetric) cm^{-1}.

Data in agreement with that previously reported.[65]

Tricarbonyl(η^4-cyclohexa-1,3-diene)iron(0) **70**.



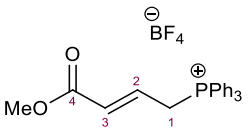
70

Cyclohexa-1,3-diene (0.831 mL, 0.00873 mol) in dry THF (11.9 mL) was added to a solution of the azadiene complex (0.47 g, 0.00125 mol) in dry THF (10 mL). The reaction mixture was stirred at reflux for 2 hours. The mixture was cooled to room temperature before almost all of the solvent was evaporated *in vacuo*. **(Care! Toxic pentacarbonyliron distilled over at this point!)** The residue was purified using column chromatography with a solvent system of hexane / diethyl ether [9:1] to afford the title compound as a yellow oil.

(1.22 g, 78 %); $\boldsymbol{\delta_H}$ (300 MHz, $CDCl_3$) 5.33 – 5.23 (m, 2H, $H^{2/3}$), 3.34 – 3.08 (m, 2H, $H^{1/4}$), 1.90 – 1.43 (m, 4H, $H^{5/6}$) ppm; $\boldsymbol{\delta_C}$ (75 MHz, $CDCl_3$) 212.1, 85.2, 63.4, 23.5 ppm; $\boldsymbol{\nu_{max}}$ (film) 2059 (C≡O symmetric) ,1981 (C≡O asymmetric) cm^{-1}.

Data in agreement with that previously reported.[66]

(3-Methoxycarbonylallyl)triphenylphosphonium bromide

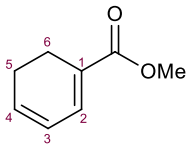


Chemical Formula: $C_{23}H_{22}BrO_2P$

Molecular Weight: 441.2973

To a solution of triphenylphosphine (32 g, 0.12 mol) dissolved in toluene (200 mL), was added 4-bromo-but-2-enoic acid methyl ester (17.1 mL, 0.12 mol) dropwise over a period of 15 minutes. The reaction mixture was stirred at ambient temperature for the period of 2 days. The precipitate was removed by suction filtration, washed with toluene (100 mL) followed by diethyl ether (100 mL) before being dried under vacuum to afford the title compound as a colourless powder (56.4 g, 99%); $\mathbf{R_f}$ 0.74 hexane / ethyl acetate [3:1]; $\boldsymbol{\delta_H}$ (300 MHz, $CDCl_3$) 7.85-7.75 (m, 10 H), 7.68 – 7.65 (m, 5H), 6.70 (dtd, *J* = 13.9, 7.6, 6.4 Hz, 1H), 6.42 (dd, *J* = 15.5, 4.9 Hz, 1H), 5.19 (ddd, *J* = 16.4, 7.6, 1.0 Hz, 2H), 3.62 (s, 3H) ppm.
Data in agreement with that previously reported by Olsson and Graden.[67]

Cyclohexa-1,3-dienecarboxylic acid methyl ester



Chemical Formula: $C_8H_{10}O_2$

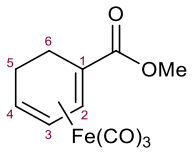
Molecular Weight: 138.1638

Saturated sodium bicarbonate (800 mL) was added in two portions to a solution of (3-methoxycarbonylallyl)triphenylphosphonium bromide (56.5 g, 0.128 mol) dissolved in dichloromethane (1.0 L). Acrolein (8.8 mL, 0.128 mmol) was then added dropwise over a period of 15 minutes. The reaction mixture was stirred at room temperature for a period of 3 days. The two phases were separated and the organic phase was concentrated by rotary evaporation. The residue was purified using column chromatography with a solvent system of dichloromethane to afford the title compound as a colourless oil (15.3 g, 87%); $\mathbf{R_f}$ = 0.75 (CH_2Cl_2); $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 6.99 (d, *J* = 5.4 Hz, 1H, H^2), 6.17 – 6.11 (m, 1 H, H^3), 6.05

(ddt, *J* = 9.3, 5.4, 1.8 Hz, 1H, H^4), 3.75 (s, 3 H, -OMe), 2.50 – 2.41 (m, 2 H, H^6), 2.30-2.22 (m, 2 H, H^5) ppm; δ_C (75 MHz, $CDCl_3$) 168.1, 133.6, 133.4, 127.2, 124.1, 51.7, 23.0, 20.9 ppm; ν_{max} (film) 1722 (COOMe) cm^{-1}.

Data in agreement with that previously reported by Olsson and Graden.[67]

Tricarbonyl(η^4-cyclohexa-1,3-dienecarboxylic acid methyl ester)iron(0)



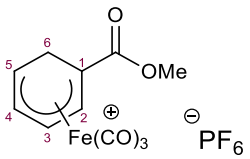
Chemical Formula: $C_{11}H_{10}FeO_5$

Molecular Weight: 278.0391

In accordance with **general procedure 2**, employing cyclohexa-1,3-dienecarboxylic acid methyl ester (0.50 g, 3.64 mmol) in THF (3 mL) with diironnonacarbonyl (3.05 g, 8.38 mmol) and purification using column chromatography with a stepwise gradient of petroleum ether / ethyl acetate [80:20], followed by petroleum ether / ethyl acetate / acetic acid [79:20:1] to afford the title compound as yellow crystals (0.65 g, 65 %); R_f 0.74 hexane / ethyl acetate [3:1]; δ_H (300 MHz, $CDCl_3$) 6.04 (s, 1H, H^2), 5.36 (s, 1H, H^3), 3.70 (s, 3H, -OMe), 3.37 (s, 1H, H^4), 2.29 – 1.33 (m, 4H, $H^{5/6}$). ppm; δ_C (300 MHz, $CDCl_3$) 210.3, 172.7, 88.6, 85.3, 64.8, 63.3, 51.7, 25.3, 23.0 ppm; ν_{max} (film) 2056 (C≡O symmetric), 1982 (C≡O asymmetric), 1715 (COOMe) cm^{-1}.

Data in agreement with that previously reported.[42]

Tricarbonyl(η^5-carboxylic acid methyl ester)iron(1+) hexafluorophosphate(1−)



Chemical Formula: $C_{11}H_9F_6FeO_5P$
Molecular Weight: 422.00

Chemical Formula:

Molecular Weight:

Triphenylcarbenium hexafluorophosphate (12.71 g, 0.032 mol) was dissolved in a minimum volume of dichloromethane (40 mL) under a nitrogen atmosphere. The tricarbonyl(cyclohexa-1,3-dienecarboxylic acid methyl ester) iron (6.5 g, 0.023 mol) was also dissolved in dichloromethane (15 mL) under nitrogen atmosphere and was added dropwise to the triphenylcarbenium hexafluorosphosphate solution. The resulting dark mixture was stirred overnight at room temperature and was slowly added to diethyl ether (165 mL). A bright yellow precipitate formed which was collected and washed with diethyl ether and dried under vacuum to afford the title compound as a yellow solid (7.06 g, 72%).

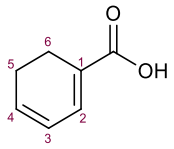
δ_H (300 MHz, $CDCl_3$) 6.56 (d, *J* = 5.1 Hz, 1H), 5.89 (s, 1H), 4.7 (t, *J*= 6.3 Hz, 1H), 3.82 (s, 3H), 3.28 (dd, *J*= 15.5, 6.4 Hz, 1H), 1.91 (d, *J* =15.6 Hz, 1H);

δ_C (75 MHz, $CDCl_3$) 117.93, 104.71, 102. 53, 90.79, 71.63, 53.94, 23.92;

ν_{max} (film) 2125, 2084, 1724, 1445, 1288, 1267, 1109 cm^{-1}.

Data in agreement with that previously reported.[42]

Cyclohexa-1,3-dienecarboxylic acid



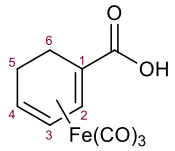
Chemical Formula: $C_7H_8O_2$

Molecular Weight: 124.1372

To a solution of cyclohexa-1,3-dienecarboxylic acid methyl ester (2.04 g, 14.5 mmol) in MeOH (20 mL), NaOH (aq) was added in two portions (1 M, 2x20 mL). After stirring for 3 h, the aqueous phase was washed once with petroleum ether (25 mL), acidified with concentrated aqueous HCl, and extracted with dichloromethane (5 x 50 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by column chromatography using a solvent system of petroleum ether / ethyl acetate / acetic acid [79:20:1] to afford the title compound as colourless crystals (1.05 g, 59 %); **R_f** 0.74 hexane / ethyl acetate [3:1]; **δ_H** (300 MHz, $CDCl_3$) 7.14 (d, *J* = 5.4 Hz, 1H, H^2), 6.27 – 6.16 (m, 1H, H^3), 6.09 (ddt, *J* = 9.3, 5.4, 1.9 Hz, 1H, H^4), 2.52 – 2.40 (m, 2H, H^6), 2.37 – 2.25 (m, 2H, H^5) ppm; **δ_C** (300 MHz, $CDCl_3$) 173.0, 135.7, 134.9, 126.5, 124.1, 23.0, 20.4 ppm;

Data in agreement with that previously reported.[68]

Tricarbonyl(η^4-cyclohexa-1,3-dienecarboxylic acid)iron(0)

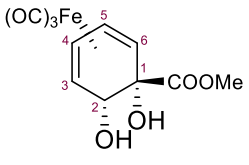


Chemical Formula: $C_{10}H_8FeO_5$

Molecular Weight: 264.0125

In accordance with **general procedure 2**, employing cyclohexa-1,3-dienecarboxylic acid (1.48 g, 11.9 mmol) in THF (15 mL) with diironnonacarbonyl (10 g, 27.5 mmol) and purification using column chromatography using a solvent system of petroleum ether / ethyl acetate / acetic acid [59:40:1]. The yellow solution was again evaporated onto silica gel and purified by column chromatography using a stepwise gradient of petroleum ether / ethyl acetate [95:5], petroleum ether / ethyl acetate [80:20], and petroleum ether / ethyl acetate / acetic acid [79:20:1] yielding the title compound as yellow crystals (2.5 g, 79 %); $\mathbf{R_f}$ 0.74 hexane / ethyl acetate [3:1]; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 6.07 (s, 1H, H^2), 5.39 (s, 1H, H^3), 3.42 (s, 1H, H^4), 2.33 – 2.07 (m, 1H, H^5), 2.06 – 1.86 (m, 1H, H^5), 1.80 – 1.55 (m, 1H, H^6), 1.52 – 1.32 (5-*H*, m, 1H, H^6) ppm; $\boldsymbol{\delta_C}$ (500 MHz, $CDCl_3$) 178.1, 93.2, 89.4, 69.7, 68.1, 28.9, 26.4 ppm; $\boldsymbol{\nu_{max}}$ (film) 2055 (C≡O symmetric), 1980 (C≡O asymmetric), 1660 (C=O) cm^{-1};
Data in agreement with that previously reported.[68]

(−)-(3*S*)-Tricarbonyl[η^4-(1*S*,2*S*)-methyl 1,2-dihydroxycyclohexa-3,5-dienecarboxylate]-iron(0) **62**.



62

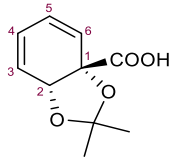
In accordance with the **General Procedure 2**, employing methyl (1*S*,2*R*)-1,2-dihydroxycyclohexa-3,5-diene-1-carboxylate **60** (0.358 g, 2.104 mmol, 1 eq),

nonacarbonyldiiron (0.827 g, 2.272 mmol, 1.08 eq.) and purification by column chromatography using a solvent system of hexane / ethyl acetate [60:40] to provide the title compound as a yellow crystalline solid (0.334 g, 51 %); **Mp** 134-137 °C, *(lit[69] Mp 130 – 132 °C)*; **R_f** 0.34 hexane / ethyl acetate [60:40]; **$[\alpha]_D^{25}$** –177 (*c* 0.1, CH_2Cl_2), *lit* $[\alpha]_D^{25}$ *–190 (c 0.1, CH_2Cl_2)*; **δ_H** (500 MHz, $CDCl_3$) 5.39 (d, 1H, *J* = 5.3 Hz, H^4), 5.36 (d, 1H, *J* = 5.0 Hz, H^3), 3.89 (s, 2H, H6, C1-OH), 3.75 (s, 3H, -Me), 3.22 (d, 1H, *J* = 5.9 Hz, H5), 3.18 (d, 1H, *J* = 5.1 Hz, C2-OH), 2.84 (d, 1H, *J* = 5.9 Hz, H2) ppm; **δ_C** (126 MHz, $CDCl_3$) 210.3 (3 x Fe(CO)), 175.1 (C=O), 84.7 (C3), 84.4 (C4), 77.5, (C1), 72.2 (C6), 67.6 (C5), 64.6 (C2), 53.6 (OMe) ppm; **ν_{max}** (film) 3418, 3002, 2955, 2053 (Fe(CO)), 1983 (Fe(CO)), 1732 (CO), 1436, 1379, 1246, 1174, 1136, 1065, 1014, 981, 940, 911, 869, 831, 794, 732 cm^{-1}.
Data in agreement with that previously reported.[69]

General Procedure 3

Diol protection using 2,2-dimethoxypropane
To a solution the diol (7.677 mmol, 1 eq) and *para*-toluenesulfonic acid (0.252 mmol, 0.03 eq) in acetone (50 mL), was added 2,2-dimethoxypropane (48.365 mmol, 6.3 eq). The reaction mixture was stirred under an atmosphere of argon at room temperature for 2 hours before the addition of brine (15 mL). The reaction mixture was then extracted with ethyl acetate (3 × 40 mL). The organic phases were combined and dried over magnesium sulphate. The filtrate was concentrated under reduced pressure and purified by column chromatography.

(1*S*,2*R*)-1,2-*O*-isopropylidene-1,2-dihydroxycyclohexa-3,5-diene carboxylic acid **59**.



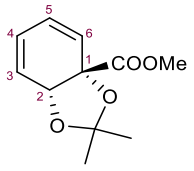
59

In accordance with the **General Procedure 3**, employing (1*S*,2*R*)-1,2-dihydroxycyclohexa-3,5-diene-1-carboxylic acid (0.785 g, 5.028 mmol, 1.00 eq), *p*-TSA (0.026 g, 0.151 mmol, 0.03 eq) in acetone (35 mL), with 2,2-DMP (3.881 mL, 31.676 mmol, 6.30 eq) and purification by column chromatography using a solvent system of dichloromethane / methanol [95:5] provided the title compound as a colourless oil (0.921 g, 93 %); **δ_H** (500

MHz, $CDCl_3$) 6.17-6.11 (m, 2H), 6.04-5.99 (m, 1H), 5.84-5.80 (m, 1H), 4.96-4.94 (m, 1H), 1.48 (s, 3H, -Me), 1.42 (s, 3H, -Me); δ_C (500 MHz, $CDCl_3$) 176.5, 124.8, 124.6, 124.2, 123.9, 107.7, 79.4, 73.0, 27.0, 25.4; ν_{max} (film) 3490, 1735, 1384, 1213, 1166 cm^{-1}.

Data in agreement with that previously reported.[70]

(1*S*,2*R*)-Methyl 1,2-*O*-isopropylidene-1,2-dihydroxycyclohexa-3,5-dienecarboxylate **61**.



61

Method A

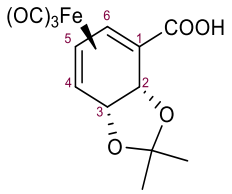
To a stirred solution of (1*S*,2*R*)-1,2-*O*-isopropylidene-1,2-dihydroxycyclohexa-3,5-diene carboxylic acid (0.457 g, 2.927 mmol, 1 eq) in a solvent system of benzene / methanol (1:1, 145 mL), at room temperature was added dropwise TMS-diazomethane (3.17 mL, 2.0 M in hexanes) until the yellow colour persisted and effervescence ceased. The solution was stirred at room temperature under a nitrogen atmosphere for 1 hour before being concentrated under reduced pressure and dried *in vacuo*. The title compound was provided as a yellow oil, sufficiently pure to be used without purification (0.584 g, 95 %); δ_H (500 MHz, $CDCl_3$) 6.12-6.05 (m, 2H), 6.03-5.97 (m, 1H), 5.82-5.77 (m, 1H), 4.95 (d, 1H, J = 4.4 Hz), 3.77 (s, 3H, -OMe), 1.42 (s, 3H, Me), 1.39 (s, 3H, Me) ppm; δ_C (126 MHz, $CDCl_3$) 172.3, 124.8, 124.6, 124.1, 124.0, 106.9, 79.5, 72.8, 53.0, 27.0, 25.3 ppm; ν_{max} (film) 3041, 2977, 2956, 2924, 1750, 1735, 1453, 1432, 1384, 1368, 1251, 1214, 1166, 1081, 1044, 885, 805, 710 cm^{-1}.

Method B

In accordance with **General Procedure 3**, employing methyl (1*S*,2*R*)-1,2-dihydroxycyclohexa-3,5-diene-1-carboxylate (0.263 g, 1.546 mmol, 1 eq), *p*-TSA (7.98 mg, 0.046 mmol, 0.03 eq) in acetone (25 mL), with 2,2-DMP (1.193 mL, 9.740 mmol, 6.30 eq). The title compound was provided as a yellow oil, sufficiently pure to be used without purification (0.323 g, 99 %).

Data in agreement with that previously reported.[71]

(−)-(3*R*)-Tricarbonyl[(η^4-(1*S*,2*R*) 1,2-isopropylidenedioxycyclohexa-3,5-dienecarboxylic acid]iron(0) **64**.

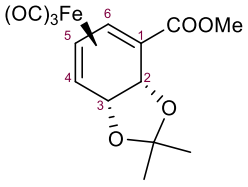


64

In accordance with **General Procedure 2**, employing (1*S*,2*R*)-1,2-*O*-isopropylidene-1,2-dihydroxycyclohexa-3,5-diene carboxylic acid (658 mg, 3.36 mmol, 1 eq), nonacarbonyldiiron (1.39 g, 3.36 mmol, 1 eq) and purification by column chromatography using a solvent system of hexane / ethyl acetate [10:90] to provide the title compound as a light yellow oil (136 mg, 12 %); $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 6.38 (d, *J* = 2.9 Hz, 1H), 5.73 (t, *J* = 5.1 Hz, 1H), 5.09 (d, *J* = 8.2 Hz, 1H), 4.73 (dd, *J* = 8.3, 3.5 Hz, 1H), 3.19 – 3.15 (m, 1H), 1.36 (s, 3H), 1.24 (s, 3H) ppm; $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 178.5, 176.2, 151.2, 148.6, 115.0, 87.0, 57.1, 27.1, 25.5 ppm; $\boldsymbol{\nu_{max}}$ (film) 2993, 2941, 2065, 1996, 1681, 1464, 1408, 1381, 1283 cm^{-1}.

Data in agreement with that previously reported.[72]

(−)-(3*R*)-Tricarbonyl[η^4-(1*S*,2*R*) 1,2-isopropylidenedioxycyclohexa-3,5-dienemethyl ester]iron(0) **63**.



63

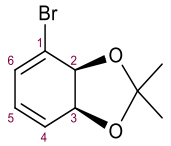
To a solution of (−)-(3*R*)-tricarbonyl[η^4-(1*S*,2*R*) 1,2-isopropylidenedioxy cyclohexa-3,5-dienecarboxylic acid]iron(0) (1.08 g, 3.23 mmol, 1 eq) benzene/MeOH (1:1) was added 100 mL, flushed with nitrogen, and (trimethylsilyl)-diazomethane was added dropwise via syringe over 15 min until effervescence ceased and a yellow colour persisted (~ 6.5 mL). The reaction mixture was stirred for 2 h and then concentrated under reduced pressure, dried in vacuo to give brown oil crude esters (221 mg) further purified by column chromatography

[10:90 EtOAc-petroleum ether] to provide the title compound as a yellow oil (190 mg, 17%): **R_f** 0.39 ethyl acetate / hexane [10 : 90]; **$[\alpha]_D^{25}$** +73 (*c* 0.1, CH_2Cl_2), *(lit $[\alpha]_D^{25}$ +80 (c 0.1, CH_2Cl_2)*;

δ_H (500 MHz, $CDCl_3$) 5.70-5.62 (m, 2H), 5.16 (d, 1H, *J* = 4.3 Hz), 3.85 (s, 3H,), 3.20-3.12 (m, 1H), 3.07 (ddd, 1H, *J* = 5.2, 4.0, 2.4 Hz), 1.41 (s, 3H,), 1.20-1.18 (m, 3H,); **δ_C** (126 MHz, $CDCl_3$) 117.1, 107.0, 87.2, 86.0, 80.0, 72.9, 57.6, 55.8, 53.0, 28.2, 27.3; **ν_{max}** (film) 2989, 2954, 2252, 2059, 1978, 1710, 1460, 1436, 1380, 1372, 1278, 1244, 1204, 1161 cm^{-1}.

Data in agreement with that previously reported.[72]

(3a*S*,7a*R*)-4-Bromo-3a,7a-dihydro-2,2-dimethyl-1,3-benzodioxole **94**.



94

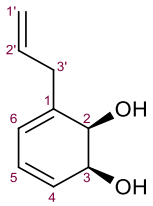
Chemical Formula: $C_9H_{11}BrO_2$

Molecular Weight: 231.0864

In accordance with **General Procedure 3** employing *cis*-(1*S*,2*S*)-1,2-dihydroxy-3-bromocyclohexa-3,5-diene (0.65 g, 3.403 mmol), *p*-TSA (0.016 g, 0.102 mmol) in acetone (45 mL) with 2,2-DMP (2.63 mL, 21.4 mmol) provided the title compound as a colourless oil (0.72 g, 92 %); **δ_H** (500 MHz, $CDCl_3$) 6.34 (d, 1H, *J* = 6.1 Hz), 5.96 (d, 1H, *J* = 9.4 Hz), 5.87 (ddd, 1H, *J* = 9.4, 6.0, 1.7 Hz), 4.73 (d, 2H, *J* = 8.7 Hz), 1.43 (d, 6H, *J* = 7.0 Hz) ppm; **δ_C** (126 MHz, $CDCl_3$) 125.9, 124.7, 124.5, 124.2, 106.3, 76.0, 72.6, 26.8, 25.1 ppm; **ν_{max}** (film) 3050, 2988, 2934, 2895, 1651, 1582, 1455, 1373, 1211, 1158, 1062, 1035, 997, 872, 726, 655, 632 cm^{-1}.

Data in agreement with that previously reported.[73]

Cis-(1*S*,2*R*)-1,2-dihydroxy-3-allylcyclohexa-3,5-diene **95**.



95

Chemical Formula: $C_9H_{12}O_2$

Molecular Weight: 152.1904

Method A

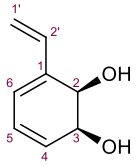
To a solution of *cis*-(1*S*,2*S*)-1,2-dihydroxy-3-bromocyclohexa-3,5-diene (70 mg, 0.37 mmol) and tetrakis(triphenylphosphine)palladium(0) (63 mg, 0.055 mmol) in anhydrous THF (15 mL) was added allyltributyltin (0.12 mL, 0.40 mmol). The mixture was refluxed for 8 hours under a nitrogen atmosphere. Removal of the solvent and purification by column chromatography using a solvent system of hexane / ethyl acetate [40:60] to provide the title compound as a low-melting unstable solid (11.2 mg, 20%); $\mathbf{R_f}$ 0.44 hexane / ethyl acetate [40:60]; $\mathbf{[\alpha]_D^{22}}$ + 11 (*c* 0.5, MeOH), (lit $[\alpha]_D^{25}$ + 16 (c 0.5, MeOH*)*; $\mathbf{\delta_H}$ (500 MHz, $CDCl_3$) 5.97 – 5.72 (m, 4H, $H^{2'/4/5/6}$), 5.16 – 5.08 (m, 2H, $H^{1'}$), 4.31 (s, 1H, H^2), 4.05 (s, 1H, H^3), 2.99 (d, 2H, J = 6.7 Hz, $H^{3'}$), 2.25 (s, 1H, -OH), 2.07 (s, 1H, -OH); $\mathbf{\delta_C}$ (126 MHz, $CDCl_3$) 140.2, 135.7, 128.1, 124.9, 120.4, 117.1, 70.2, 69.2, 38.2; $\mathbf{\nu_{max}}$ (film) 3338, 3084, 3051, 2982, 2924, 2858, 1643, 1595, 1432, 1410, 1264, 1162, 1103, 1081, 1001, 921, 855, 815, 739 cm^{-1}.

Method B

To a solution of *cis*-(1*S*,2*S*)-1,2-dihydroxy-3-bromocyclohexa-3,5-diene (70 mg, 0.37 mmol) and tetrakis(triphenylphosphine)palladium(0) (63 mg, 0.055 mmol) in anhydrous THF (2 mL) was added allyltributyltin (0.12 mL, 0.40 mmol). The mixture was irradiated in a microwave at 100 °C and 200 W for 6 minutes in a sealed tube under a nitrogen atmosphere. Removal of the solvent and purification by flash chromatography on silica gel (6:4, EtOAc: hexanes) gave *cis*-(1*S*,2*R*)-1,2-dihydroxy-3-allylcyclohexa-3,5-diene (**2a**) as a low-melting unstable solid (23.6 mg, 42%).

Data in agreement with that previously reported.[74]

Cis-(1*S*,2*R*)-1,2-dihydroxy-3-vinylcyclohexa-3,5-diene **47**.



47

Chemical Formula: $C_8H_{10}O_2$

Molecular Weight: 138.1638

Method A

To a solution of *cis*-(1*S*,2*S*)-1,2-dihydroxy-3-bromocyclohexa-3,5-diene (70 mg, 0.37 mmol) and tetrakis(triphenylphosphine)palladium (0) (63 mg, 0.055 mmol) in anhydrous THF (15 mL) was added vinyltributyltin (0.12 mL, 0.40 mmol). The mixture was refluxed for 8 hours under a nitrogen atmosphere. Removal of the solvent and purification by column chromatography using a solvent system of hexane / ethyl acetate [20:80] to provide the title compound as a pale yellow oil (11.2 mg, 20%); **R_f** 0.58 hexane / ethyl acetate [20:80]; **Mp.:** 58-60 °C, (*lit., 54-55 °C);* **$[\alpha]_D^{23}$** +119 (*c* 0.5, MeOH), (lit $[\alpha]_D^{25}$ +126 (c 0.5, MeOH); **δ_H (500 MHz, $CDCl_3$)** 6.41 (dd, 1H, *J* = 17.6, 10.9 Hz, $H^{2'}$), 6.04 – 5.93 (m, 2H, $H^{4/5}$), 5.90 – 5.83 (m, 1H, H^6), 5.51 (d, 1H, *J* = 17.6 Hz, $H^{1'}$), 5.26 -5.18 (m, 1H, $H^{1'}$), 4.50 (s, 1H, H^3), 4.38 (s, 1H, H^2), 2.67 (d, 1H, *J* = 6.0 Hz, OH), 1.75 (s, 1H, OH) ppm; **δ_C (500 MHz, $CDCl_3$)** 136.1, 132.8, 125.1, 124.0, 116.0, 114.5, 71.0, 65.9 ppm; **ν_{max} (film)** 3338, 3084, 3052, 2982, 2924, 2858, 1643, 1596, 1432, 1410, 1264, 1162, 1103, 1082, 1001, 921, 855, 815, 739 cm^{-1}.

Method B

To a solution of *cis*-(1*S*,2*S*)-1,2-dihydroxy-3-bromocyclohexa-3,5-diene (70 mg, 0.37 mmol) and tetrakis(triphenylphosphine)palladium (0) (63 mg, 0.055 mmol) in anhydrous THF (2 mL) was added allyltributyltin (0.12 mL, 0.40 mmol). The mixture was irradiated in a microwave at 100 °C and 200 W for 6 minutes in a sealed tube under a nitrogen atmosphere. Removal of the solvent and purification by flash chromatography on silica gel (6:4, EtOAc: hexanes) gave *cis*-(1*S*,2*R*)-1,2-dihydroxy-3-allylcyclohexa-3,5-diene as a low-melting unstable solid (23.6 mg, 42%).

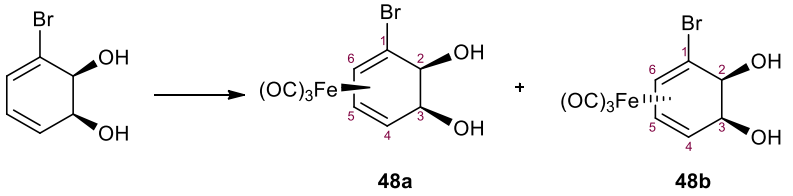
Method C

To a solution of *cis*-(1*S*,2*S*)-1,2-dihydroxy-3-iodocyclohexa-3,5-diene (0.5 g, 2.1 mmol), palladium(II) acetate (0.047 g, 10 mol%) and triphenylphosphine (0.11 g, 20 mol%) in

anhydrous THF (40 cm^3) was added vinyltributyltin (0.73 g, 2.3 mmol). The mixture was stirred at room temperature for 16 h under an atmosphere of nitrogen. The THF was removed under reduced pressure and the residue was stirred overnight at room temperature with saturated aqueous potassium fluoride (15 cm^3) and ethyl acetate (100 cm^3). The organic layer was separated and the aqueous phase re-extracted with ethyl acetate. The combined extracts were dried (anhydrous magnesium sulfate) and concentrated under reduced pressure to yield the crude product which on purification by flash chromatography (80% ethyl acetate–hexane) gave *cis*-(1*S*,2*R*)-1,2-dihydroxy-3-vinylcyclohexa-3,5-diene as a pale yellow solid (0.076 g, 26%).

Data in agreement with that previously reported.[74]

(3*S*)-Tricarbonyl(3-bromo-(1*S*,2*S*)-3,5-cyclohexadiene-1,2-diol)iron(0) **48a**.



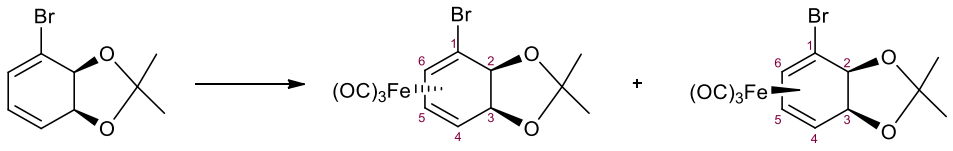
48a **48b**

Chemical Formula: $C_9H_7BrFeO_5$

Molecular Weight: 330.8979

In accordance with **General Procedure 2**, employing *cis*-(1*S*,2*S*)-1,2-dihydroxy-3-bromocyclohexa-3,5-diene (658 mg, 3.36 mmol, 1 eq), nonacarbonyldiiron (1.39 g, 3.78 mmol, 1 eq) and purification by column chromatography using a solvent system of hexane / ethyl acetate [90:10] to provide the title compound as a yellow liquid (0.689 g, 62 %); $\mathbf{R_f}$ 0.39 hexane / ethyl acetate [90:10]; $\mathbf{[\alpha]_D^{22.2}}$ +53.8 (0.003, CH_2Cl_2); $\mathbf{\delta_H}$ (500 MHz, $CDCl_3$); 5.67 (dd, 1H, *J* = 4.4, 1.3 Hz), 5.14 (dd, 1H, *J* = 6.1, 4.6 Hz), 3.95 – 3.89 (m, 1H), 3.86 (s, 1H), 3.11 (ddd, 2H, *J* = 12.8, 6.7, 2.6 Hz), 2.99 (d, 1H, *J* = 3.8 Hz) ppm; $\mathbf{\delta_C}$ (126 MHz, $CDCl_3$); 87.5, 81.2, 79.3, 73.4, 68.3, 66.1 ppm; $\mathbf{\nu_{max}}$ (film) 3347, 3072, 3014, 2924, 2891, 2855, 2058, 1989, 1683, 1602, 1391, 1345, 1277, 1217, 1139, 1079, 1065, 1026, 973, 921, 884, 846, 812, 751, 633, 612 cm^{-1}; **HRMS** (ESI): *m/z* $[M - 2H + H]^+$ calculated for $C_9H_5BrFeO_5H$: 326.8789; observed: 326.8786.

(4*R*)-Tricarbonyl[(3a*S*,7a*R*)-4-bromo-3a,7a-dihydro-2,2-dimethyl-1,3-benzodioxole]iron(0) **96a** and (4*S*)-tricarbonyl[(3a*S*,7a*R*)-4-bromo-3a,7a-dihydro-2,2-dimethyl-1,3-benzodioxole]-iron(0) **96b**.



94 **96a** **96b**

In accordance with **General Procedure 2**, employing (3a*S*,7a*R*)-4-bromo-3a,7a-dihydro-2,2-dimethyl-1,3-benzodioxole (658 mg, 3.36 mmol, 1 eq), nonacarbonyldiiron (1.39 g, 3.78 mmol, 1 eq) and purification by column chromatography using a solvent system of hexane / ethyl acetate [90:10] to provide the title compound as a yellow crystalline solid (0.462 g, 62 %);

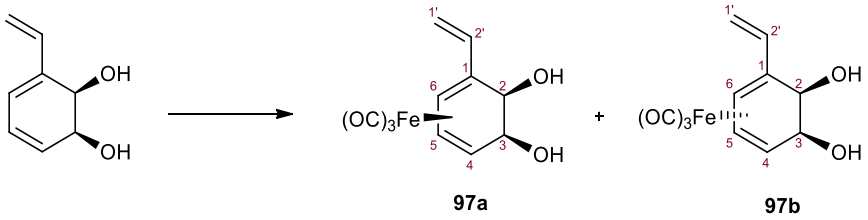
Compound 96a

δ_H (500 MHz, $CDCl_3$) 5.95 (d, 1H, *J* = 3.7 Hz), 5.47 (t, 1H, *J* = 4.9 Hz), 4.83 (d, 1H, *J* = 8.4 Hz), 4.66 (dd, 1H, *J* = 7.9, 3.3 Hz), 2.86 (s, 1H), 1.40 (s, 3H), 1.22 (s, 3H); **δ_C** (126 MHz, $CDCl_3$) 115.4, 89.8, 85.1, 83.3, 77.33, 69.6, 53.9, 27.2, 25.5; **ν_{max}** (film) 3065, 2989, 2935, 2917, 2872, 2061, 1989, 1455, 1438, 1381, 1373, 1323, 1284, 1247, 1206, 1160, 1094, 1044, 1034, 1016, 989, 966, 951, 915, 877, 861, 809 cm^{-1}; **HRMS** (ESI): *m/z* $[M + H]^+$ calculated for $C_{12}H_{11}BrFeO_5H$: 368.9259; observed: 368.9253.

Compound 96b

δ_H (500 MHz, $CDCl_3$) 5.60 (d, 1H, *J* = 3.8 Hz), 5.11 (dd, 1H, *J* = 6.1, 4.6), 4.18 (d, 1H, *J* = 6.0 Hz), 4.03 (dd, 1H, *J* = 5.8, 1.9 Hz), 3.16 (d, 1H, *J* = 6.3 Hz), 1.65 (s, 3H), 1.28 (s, 3H); **δ_C** (126 MHz, $CDCl_3$) 209.4, 108.5, 87.3, 81.1, 81.0, 75.7, 74.1, 62.4, 24.2, 24.0; **ν_{max}** (film) 3022, 2987, 2945, 2871, 2062, 1998, 1461, 1421, 1385, 1376, 1354, 1318, 1282, 1248, 1206, 1162, 1133, 1064, 1047, 979, 922, 871, 846, 812 cm^{-1}; **HRMS** (ESI): *m/z* $[M + NH_4]^+$ calculated for $C_{12}H_{11}BrFeO_5NH_4$: 385.9524; observed: 385.9520.

(3*R*)-Tricarbonyl[(1*R*,2*S*)-1,2-dihydroxy-3-vinylcyclohexa-3,5-diene]iron(0) **97b**.



Chemical Formula: $C_{11}H_{10}FeO_5$

Molecular Weight: 278.0391

In accordance with **General Procedure 2**, employing *cis*-(1*S*,2*R*)-1,2-dihydroxy-3-vinylcyclohexa-3,5-diene (0.25 g, 0.91 mmol), *p*-TSA (0.005 g, 0.028 mmol). in acetone (45 mL), with 2,2-DMP (0.7 mL, 5.8 mmol) and purification by column chromatography using a solvent system of hexane / ethyl acetate [1:1] to provide the title compound as a yellow oil (0.67 g, 86%);

Compound 97b

R_f 0.43 hexane / ethyl acetate [1:1]; **$[\alpha]_D^{23.9}$** −56.8 (0.01, CH_2Cl_2); **δ_H** (500 MHz, $CDCl_3$) 6.22 (dd, 1H, *J* = 17.3, 11.3 Hz), 5.51 (s, 1H), 5.39 – 5.26 (m, 2H), 5.12 (d, 1H, *J* = 11.1 Hz), 3.94 (s, 1H), 3.80 (s, 1H), 3.10 (s, 1H), 2.85 (s, 1H), 2.66 (s, 1H); **δ_C** (126 MHz, $CDCl_3$) 211.0, 138.1, 113.0, 84.5, 80.9, 69.0, 65.5, 29.8, 14.2; **ν_{max}** (film) 3357, 2925, 2856, 2047, 1975, 1715, 1619, 1543, 1396, 1269, 1227, 1176, 1127, 1064, 1030, 1010, 973, 908, 836 cm^{-1}; **HRMS** (ESI): *m/z* $[M - H]^+$ calculated for $C_{11}H_9FeO_5$: 274.9841; observed: 274.9843.

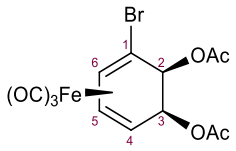
General Procedure 4

Acetylation of diols using pyridine and acetic anhydride

To a stirred solution of diol (27 mmol, 1 eq) in pyridine (10 mL) was added acetic anhydride (81 mmol, 3 eq) at 0 °C. The reaction mixture was stirred at 0 °C for 6 hours before the addition of ice cold water (50 mL) followed by extraction using diethyl ether (3 x 50 mL). The combined organic extracts were washed with an aqueous solution of $NaHCO_3$ (3 x 15

mL) and then dried over $MgSO_4$. Removal of the solvent under reduced pressure provided the title compound.

(3*S*)-Tricarbonyl[(1*S*,2*S*)-3-bromocyclohexa-3,5-diene-1,2-diyl diacetate]iron(0) **98**.



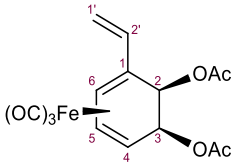
98

Chemical Formula: $C_{13}H_{11}BrFeO7$

Molecular Weight: 414.9712

In accordance with **General Procedure 4** employing (3*S*)-tricarbonyl(3-bromo-(1*S*,2*S*)-3,5-cyclohexadiene-1,2-diol)iron(0) (0.12 g, 0.359 mmol) in pyridine (0.13 mL) with acetic anhydride (0.10 mL, 1.07 mmol) provided the title compound as a yellow oil (0.084 g, 60%); $\mathbf{R_f}$ 0.67 hexane / ethyl acetate [4:1], $\mathbf{\delta_H}$ (500 MHz, $CDCl_3$) 5.75 (s, 1H), 5.18 (d, *J* = 44.1 Hz, 2H), 4.87 (s, 1H), 2.94 (s, 1H), 2.13 (s, 3H), 2.07 (s, 3H). $\mathbf{\delta_C}$ (126 MHz, $CDCl_3$) 211.3, 169.7, 87.9, 81.2, 74.1, 72.1, 70.2, 60.6, 20.7, 20.5. **HRMS** (ESI): *m/z* $[M + NH_4]^+$ calculated for $C_{13}H_{11}BrFeO_7NH_4$: 431.9378; observed: 431.9377.

(3*S*)-Tricarbonyl[(1*S*,2*S*)-3-vinylcyclohexa-3,5-diene-1,2-diyl diacetate]iron(0) **99**.



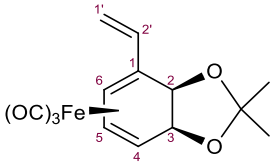
99

Chemical Formula: $C_{15}H_{14}FeO7$

Molecular Weight: 362.1150

In accordance with **General Procedure 4** employing diol (0.1531 g, 0.55064 mmol) in pyridine (0.787 mL) with acetic anhydride (0.517 mL, 1.07 mmol) provided the title compound as a yellow oil; $\mathbf{R_f}$ 0.67 hexane / ethyl acetate [4:1], **HRMS** (ESI): *m/z* $[M + H]^+$ calculated for $C_{15}H_{14}FeO_7NH_4$: 380.0427; observed: 380.0429.

(4*S*)-Tricarbonyl[(3a*S*,7a*R*)-2,2-dimethyl-4-vinyl-3a,7a-dihydrobenzo[1,3]dioxole]iron(0) **45**.



45

Chemical Formula: $C_{14}H_{14}FeO_5$

Molecular Weight: 318.1030

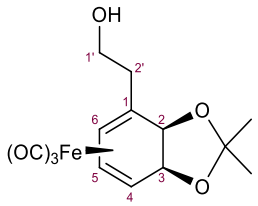
In accordance with **General Procedure 2** employing tricarbonyl[*cis*-(1*S*,2*R*)-1,2-dihydroxy-3-vinylcyclohexa-3,5-diene]iron (0.208 g, 0.747 mmol), para-toluenesulfonic acid (0.004 g, 0.022 mmol). In acetone (45 mL), with 2,2-dimethoxypropane (2.6 mL, 21.3 mmol) provided the title compound as a colourless oil (0.67 g, 86 %); $\mathbf{R_f}$ 0.74 hexane / ethyl acetate [3:1]; $\mathbf{[\alpha]_D^{23.9}}$ –4.8 (0.01, CH_2Cl_2); $\mathbf{\delta_H}$ (500 MHz, $CDCl_3$) 5.99 (dd, 1H, *J* = 17.6, 11.1 Hz), 5.48 (dd, 1H, *J* = 17.6, 1.2 Hz), 5.35 (d, 1H, *J* = 4.2 Hz), 5.20 (dd, 1H, *J* = 6.7, 4.3 Hz), 5.07 (dd, 1H, *J* = 11.1, 1.1 Hz), 4.11 (dd, 1H, *J* = 6.3, 2.4 Hz), 4.04 (d, 1H, *J* = 6.3 Hz), 3.21 (ddd, 1H, *J* = 6.7, 2.4, 1.3 Hz), 1.63 (s, 3H), 1.28 (s, 3H) ppm;

$\mathbf{\delta_C}$ (126 MHz, $CDCl_3$) 210.9, 139.0, 113.8, 108.2, 85.2, 80.7, 79.7, 76.2, 75.4, 63.0, 24.3, 24.1 ppm; $\mathbf{\nu_{max}}$ (film) 2984, 2928, 2856, 2051, 1989, 1972, 1727, 1620, 1462, 1384, 1375, 1345, 1321, 1289, 1252, 1206, 1162, 1045, 1017, 993, 970, 901, 893, 850, 817 cm^{-1}; **HRMS** (ESI): *m/z* $[M - H]^+$ calculated for $C_{14}H_{14}FeO_5H$: 319.0263; observed: 319.0269.

General Procedure 5: Hydroboration of alkenes using BH_3 – THF system followed by oxidation

To a flame dried flask containing alkene (30 mmol) was added a solution of BH_3 in THF (10 mL, 10mmol) dropwise under a nitrogen atmosphere over a period of 2 hours at 0 ^oC. The reaction mixture was then diluted with THF (3 mL) before an aqueous solution of sodium hydroxide (1 mL, 3 mmol, 3 M) was added followed by the dropwise addition of hydrogen peroxide (1 mL, 30 % aqueous solution). The reaction mixture was stirred at 0 ^oC for 4 hours before being saturated with potassium carbonate and the two phases separated. The aqueous phase was extracted with diethyl ether (3 x 20 mL) and the organic layers were combined before being washed with brine (15 mL) and dried over magnesium sulphate. The solvent was evaporated under reduced pressure and the residue was purified using column chromatography.

(4*S*)-Tricarbonyl{2-[(3a*S*,7a*R*)-2,2-dimethyl-3a,7a-dihydrobenzo[1,3]dioxol-4-yl]ethanol}iron(0) **100**.



100

Chemical Formula: $C_{14}H_{16}FeO_6$

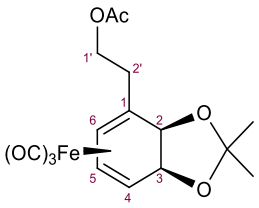
Molecular Weight: 336.1210

In accordance with **General Procedure 5** employing the iron complex (0.3764 g, 1.1832 mmol) with BH_3 in THF (0.39 mL, 0.3944 mmol), sodium hydroxide (0.05 mL, 0.039 mmol, 3M) and (hydrogen peroxide (0.05 mL, 0.039 mmol 30 % aqueous solution) to provide the title compound as a yellow oil (0.382 g, 96 %), $\mathbf{R_f}$ 0.74 hexane / ethyl acetate [3:1]; $\mathbf{\delta_H}$ (400 MHz, $CDCl_3$) 5.20 (d, *J* = 3.9 Hz, 1H, H^6), 5.15 (ddd, *J* = 6.5, 4.2, 0.5 Hz, 1H, H^5), 4.12 (dd, *J* = 6.0, 2.4 Hz, 1H, H^4), 3.93 (d, *J* = 6.3 Hz, 1H, $H^{2'}$), 3.81 (s, 2H, $H^{1'}$), 3.14 (ddd, *J* = 6.6, 2.6, 1.4 Hz, 1H, $H^{2'}$), 2.25 – 2.16 (m, 1H, H^2), 2.11 – 1.99 (m, 1H, H^3), 1.62 (s, 3H, -Me), 1.27 (s, 3H, -Me) ppm; $\mathbf{\delta_C}$ (101 MHz, $CDCl_3$) 211.0, 108.1, 88.8, 82.3, 80.2, 75.5, 63.6, 62.3, 41.3, 29.8, 24.3, 23.9 ppm; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has bot been added posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M + Na]^+$ calculated for $C_{14}H_{16}FeO_6Na$: 359.0189; observed: 359.0190.

General Procedure 6: Acetylation of alcohols using acetic anhydride

To a solution of alcohol (2 mmol, 1 eq) in dichloromethane (5 mL) was added acetic anhydride (1 mL) and $BF_3.OEt_2$ (0.5 mL). The mixture was stirred for 5 minutes before ice cold water (5 mL) was added. The reaction mixture was stirred for a further 15 minutes and extracted with dichloromethane (3 x 10 mL). The combined organic extracts were washed with water (3 x 15 mL), 10% aqueous $NaHCO_3$ (3 x 15 mL) and water (3 x 15 mL) before being dried over magnesium sulphate and evaporated *in vacuo* to provide the title compound.

(4*S*)-Tricarbonyl{2-[(3a*S*,7a*R*)-2,2-dimethyl-3a,7a-dihydrobenzo[1,3]dioxol-4-yl]ethyl acetate}iron(0) **101**.



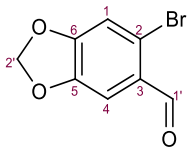
101

Chemical Formula: $C_{16}H_{18}FeO_7$

Molecular Weight: 378.1580

In accordance with **General Procedure 6**, employing the iron complex (0.0317 g, 0.0943 mmol) with Ac_2O (0.047 mL) and $BF_3.OEt_2$ (0.023 mL) to provide the title compound as a yellow oil (0.0295 g, 83 %); $\mathbf{R_f}$ 0.74 hexane / ethyl acetate [3:1]; **HRMS** (ESI): *m/z* [M + NH_4]$^+$ calculated for $C_{16}H_{18}FeO_7NH_4$: 396.0740; observed: 396.0740.

6-Bromo-benzo[1,3]dioxazole-5-carboxaldehyde **102**.



102

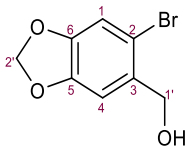
Chemical Formula: $C_8H_5BrO_3$

Molecular Weight: 229.0275

A solution of piperonal (55 g, 0.37 mol) in glacial acetic acid (50 mL) was treated with bromine (20 mL). The mixture was stirred under an atmosphere of nitrogen for 20 hours before being poured onto ice cold water (150 mL) and allowed to warm gradually to room temperature. The resultant orange powder was collected by suction filtration and washed with an aqueous solution of sodium metabisulfate (5 % w/v). The white filter cake was rinsed first with water and air dried before being recrystallized from aqueous ethanol (95 % 800 mL) to provide the title compound as white needles (33 g, 39 %); **Mp** 133-134 ^oC, *(lit Mp 131-*

132 °C); **δ_H** (500 MHz, $CDCl_3$) 10.16 (s, 1H), 7.34 (s, 1H), 7.04 (s, 1H), 6.07 (s, 2H) ppm; **δ_C** (126 MHz, $CDCl_3$) 190.5, 153.5, 148.3, 128.2, 113.4, 108.3, 102.9 ppm; **ν_{max}** (film) 2922, 2866 (b, s, alkyl), 1773, 1675 (s, m, C=O), 1615, 1597 (s, aromatic), 1493 (s, alkyl), 1413, 1392 (m, C-C), 1348, 1260, 1215, 1113 (s, C-O-C), 1032, 979, 924, 889, 855, 837 cm^{-1}.
Data in agreement with that previously reported.[75]

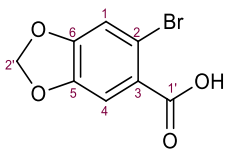
6-Bromo-3,4-methylenedioxybenzyl alcohol



Chemical Formula: $C_8H_7BrO_3$
Molecular Weight: 231.0434

A solution of 6-bromo-benzo[1,3]dioxazole-5-carboxaldehyde (26.8 g, 0.12 mol) in THF was treated with small portions of sodium borohydride (12.5 g, 0.33 mol), and the mixture was stirred under an atmosphere of nitrogen for approximately 20 hours. The reaction was poured onto ice water: 2M hydrochloric acid (1:1, 50 mL) and extracted with dichloromethane. The organic layers were combined, dried with sodium sulfate, concentrated to 50 mL and recrystallized by the slow addition of petroleum ether to give the title compound as fine white needles (20.3 g, 73 %); **Mp** 90-92 °C, *(lit Mp 92 °C)*; **δ_H** (500 MHz, $CDCl_3$) 6.96 (s, 1H, H^4), 6.93 (s, 1H, H^1), 5.96 (s, 2H, $H^{2'}$), 4.59 (s, 2H, $H^{1'}$), 2.47 (s, 1H, OH) ppm; **δ_C** (126 MHz, $CDCl_3$) 147.8, 147.6, 133.2, 113.0, 112.7, 109.1, 101.9, 64.9 ppm; **ν_{max}** (film) 3269 (b, w, O-H), 2908, 2853 (s, s, alkyl), 1501 (s, w, aromatic), 1481, 1455 (s, s, alkyl), 1412, 1392 (s, w, C-C), 1345, 1294, 1246, 1163, 1106, 1084 (s, m, C-O-C), 965, 928, 878, 858, 845, 830 cm^{-1}.

6-Bromo-1,3-benzodioxole-5-carboxylic acid **104**.



104

Chemical Formula: $C_8H_5BrO_4$
Molecular Weight: 245.0269

A solution of t-BuOH (51 mL) in water (128 mL) was added to 6-bromo piperonal (5.0 g, 0.021 mol). The resultant mixture was stirred and heated at reflux (85 °C). Only when the

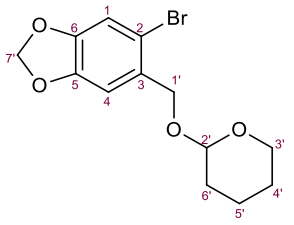
solution achieved a temperature of 85 °C could a solution of potassium permanganate (3.34 g, 0.021 mol) in distilled water (65 mL) be added dropwise over a period of 45 minutes. The brown suspension was left to reflux overnight. 10 % NaOH (25 mL) was added to the warm mixture before being filtered. The filtrate was extracted with EtOAc (3 x 25 mL) and the aqueous layer was acidified with concentrated HCl to precipitate out the product as a white solid (0.004 mol, 18%).

δ_H (500 MHz, DMSO) 13.14 (s, 1H, -OH), 7.31 (s, 1H, H^1), 7.28 (s, 1H, H^4), 6.14 (s, 2H, $H^{2'}$) ppm; **δ_C** (126 MHz, DMSO) 166.4, 150.4, 147.0, 126.0, 113.7, 112.9, 110.2, 102.8 ppm; **ν_{max}** (film) 2978, 2913, 2795, 2701, 2595, 1703, 1678, 1622, 1505, 1452, 1413, 1377, 1355, 1278, 1252, 1149, 1112, 1094, 1040, 955, 926, 878, 856, 845 cm^{-1}.

General Procedure 7: Alcohol protection using 3,4-dihydro-2H-pyran

A solution of your chosen bromo alcohol compound (0.133 mol, 1 eq) in dichloromethane (200 mL) was treated with a catalytic amount of pyridinium toluene-*p*-sulfonate (0.013 mol, 0.1 eq) and 3,4-dihydro-2*H*-pyran (0.267 mol, 2 eq) and the mixture was stirred under an atmosphere of nitrogen for approximately 20 hours. The reaction mixture was washed with water (2 x 50 mL), brine (50 mL) and the organic layer was separated and dried with sodium sulfate. Evaporation in vacuo provided the expected compound.

5-Bromo-6-(tetrahydro-pyran-2-yl-oxymethyl)benzo[1,3]dioxazole **105**.



105

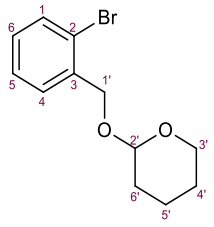
Chemical Formula: $C_{13}H_{15}BrO_4$

Molecular Weight: 315.1598

In accordance with **General Procedure 7**, employing 6-bromo-3,4-methylenedioxybenzyl alcohol (20.0 g, 0.133 mmol) in dichloromethane (200 mL) with pyridinium toluene-*p*-sulfonate (3.3 g, 0.013 mol) and 3,4-dihydro-2*H*-pyran (25 mL, 0.267 mol) to provide the title compound as a colourless crystalline solid (23.5 g, 86 %); **δ_H** (500 MHz, $CDCl_3$) 7.00 (d, 2H, *J* = 5.5 Hz), 5.96 (s, 2H), 4.76 – 4.70 (m, 2H), 4.49 (d, 1H, *J* = 12.8 Hz), 3.95 – 3.88 (m, 1H), 3.60 – 3.53 (m, 1H), 1.90 – 1.55 (m, 6H) ppm; **δ_C** (126 MHz, $CDCl_3$) 147.7, 147.5, 131.2, 113.3, 112.7, 109.4, 101.8, 98.4, 68.6, 62.3, 30.7, 25.6, 19.5 ppm;

ν_{max} (film) 2942, 1623, 1504, 1480, 1415, 1390, 1354, 1323, 1246, 1201, 1183, 1154, 1036 cm^{-1}; **HRMS** (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_{15}BrO_4Na$: 337.0046; observed: 337.0035.

2-(2-Bromo-benzyloxy)-tetrahydropyran **106**.



106

Chemical Formula: $C_{12}H_{15}BrO_2$

Molecular Weight: 271.1503

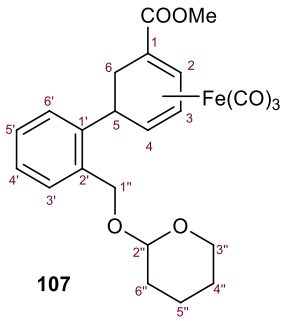
In accordance with **General Procedure 7**, employing 2-bromobenzyl alcohol (10.0 g, 0.05 mol) in dichloromethane (75 mL) with pyridinium toluene-*p*-sulfonate (1.30 g, 0.005 mol) and 3,4-dihydro-2*H*-pyran (9.7 mL, 0.11 mol) to provide the title compound as a colourless crystalline solid (23.5 g, 86 %). δ_H (500 MHz, $CDCl_3$) 7.52 (d, 2H, *J* = 7.8 Hz), 7.30 (t, 1H, *J* = 7.5 Hz), 7.12 (t, 1H, *J* = 7.6 Hz), 4.83 (d, 1H, *J* = 13.3 Hz), 4.78 (t, 1H, *J* = 3.3 Hz), 4.58 (d, 1H, *J* = 13.3 Hz), 3.97 – 3.87 (m, 1H), 3.57 (dd, 1H, *J* = 9.9, 4.6 Hz), 1.97 – 1.54 (m, 6H) ppm; δ_C 126 MHz, $CDCl_3$) 137.9, 132.5, 129.1, 128.8, 122.8, 98.4, 68.6, 62.2, 30.6, 25.5, 19.4 ppm; ν_{max} (film) 3068, 2942, 2870, 2851, 1569, 1468, 1455, 1441, 1386, 1349, 1323, 1271, 1261, 1201, 1184, 1155, 1132, 1078, 1069, 1036, 1024, 973, 907, 870, 816 cm^{-1}.
Data in agreement with that previously reported.[76]

General Procedure 8: Organocuprate addition of bromine derivative to iron cation

Using flame dried glassware, a solution of bromine derivative (2.19 mmol, 1 eq) in dry THF (10 mL) was cooled to –78 ^oC under an argon atmosphere. A solution of n-butyllithium in hexanes (2.19 mmol, 1 eq) was added dropwise over a period of 5 minutes. The reaction mixture generally turns yellow at this point and was stirred for 2 hours at –78 ^oC before being warmed to –30 ^oC. Either Cu(I)Br or Cu(I)CN (1.10 mmol, 0.5 eq) was added in one portion and the reaction mixture was recooled to –78 ^oC for 10 min before the addition of tricarbonyliron cation (0.55 mmol, 0.25 eq). The resulting suspension was allowed to warm to room temperature and monitored by IR for the appearance of the neutral tricarbonyliron

bands at approximately 1970 and 2050 cm^{-1} and the disappearance of the cationic tricarbonyliron bands at approximately 2050 and 2150 cm^{-1}. Once the reaction was deemed complete the reaction mixture was then treated with either a saturated solution of ammonium chloride (10 mL) or 2M hydrochloric acid (10mL). The aqueous layer was separated and extracted with diethyl ether (3 x 10 mL), before the organic layers were combined and dried over $MgSO_4$. Evaporation under reduced pressure **(Care! Toxic pentacarbonyliron distilled over at this point!)** gave a dark brown oil which was purified by column chromatography.

Tricarbonyl{methyl 2'-[tetrahydro-2H-pyran-2-yloxy)methyl}-1,2-dihydro-[1,1'-biphenyl]-3-carboxylate)iron(0) **107**.



107

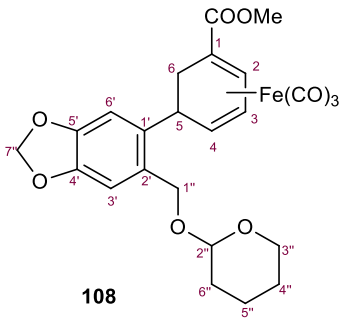
Chemical Formula: $C_{23}H_{24}FeO_7$

Molecular Weight: 468.2830

In accordance with **General Procedure 8**, employing 2-(2-bromo-benzyloxy)-tetrahydropyran (0.125 g, 0.461 mmol), in THF (2.1 mL) treated with nBuLi (0.04 mL, 0.461 mmol, 2.5 M in hexanes), Cu(I)CN (0.021 g, 0.230 mmol) and tricarbonyl(η^5-carboxylic acid methyl ester)iron(1+) hexafluorophosphate(1–) (0.049 g, 0.115 mmol) and purification using column chromatography with a solvent system of hexane / diethyl ether [90:10] to achieve the title compound as a yellow oil (0.186 g, 86 %); $\mathbf{R_f}$ 0.54 hexane / ethyl acetate [90:10]; $\mathbf{[\alpha]_D^{21.6}}$ +32.0 (*c* 0.003, CH_2Cl_2); $\mathbf{\delta_H}$ (500 MHz, $CDCl_3$) 6.27 (s, 2H), 5.49 (s, 2H), 4.78 (d, *J* = 11.1 Hz, 3H), 4.48 (d, *J* = 11.3 Hz, 1H), 4.38 (d, *J* = 11.4 Hz, 1H), 3.96 – 3.89 (m, 3H), 3.72 (s, 4H), 3.41 (d, *J* = 13.3 Hz, 2H), 2.87 – 2.79 (m, 2H), 2.17 (s, 2H), 1.85 (s, 3H), 1.76 (s, 3H) ppm; $\mathbf{\delta_C}$ (126 MHz, $CDCl_3$) δ 210.2, 172.5, 145.5, 135.3, 130.1, 128.8, 126.4, 98.5, 94.8, 89.2, 84.8, 68.0, 63.4, 63.1, 62.3, 51.8, 40.5, 32.5, 30.7, 25.6, 19.4 ppm; $\mathbf{\nu_{max}}$ (film) 2948, 2873, 2052, 1978, 1709, 1488, 1435, 1386, 1350, 1271, 1246, 1201, 1153, 1119, 1079, 1024, 973, 906, 870, 816 cm^{-1}; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added

posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M + H]^+$ calculated for $C_{23}H_{24}FeO_7H$: 467.0991; observed: 467.0980.

Tricarbonyl{methyl 5-[6-(tetrahydro-2H-pyran-2-yloxy)methyl] benzo[d][1,3]dioxol-5-yl)cyclohexa-1,3-dienecarboxylate}iron(0) **108**.



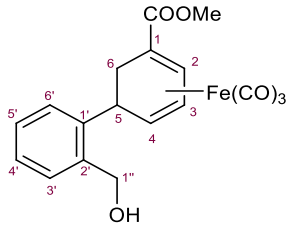
108

Chemical Formula: $C_{24}H_{24}FeO_9$

Molecular Weight: 512.2870

In accordance with **General Procedure 8**, employing 5-bromo-6-(tetrahydro-pyran-2-yl-oxymethyl)benzo[1,3]dioxazole (0.342 g, 1.085 mmol), in THF (5.0 mL) treated with nBuLi (0.1 mL, 1.085 mmol, 2.5 M in hexanes), Cu(I)CN (0.049 g, 0.543 mmol) and tricarbonyl(η^5-carboxylic acid methyl ester)iron(1+) hexafluorophosphate(1–) (0.114 g, 0.271 mmol) and purification using column chromatography with a solvent system of hexane / diethyl ether [60:10] to achieve the title compound as a yellow oil (0.349 g, 63 %); $\mathbf{R_f}$ 0.38 hexane / diethyl ether [60:10]; $\mathbf{\delta_H}$ **(500 MHz, $CDCl_3$)** 6.74 (d, *J* = 1.6 Hz, 1H), 6.62 (d, *J* = 9.6 Hz, 1H), 6.26 (t, *J* = 3.6 Hz, 1H), 5.90 (dt, *J* = 2.4, 1.4 Hz, 2H), 5.48 (ddd, *J* = 9.4, 6.3, 4.4 Hz, 1H), 4.73 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.32 (dd, *J* = 47.6, 11.3 Hz, 1H), 4.02 – 3.79 (m, 2H), 3.71 (d, *J* = 1.5 Hz, 3H), 3.60 (ddd, *J* = 15.6, 10.5, 4.7 Hz, 1H), 3.40 – 3.30 (m, 1H), 2.86 – 2.72 (m, 1H), 1.84 (ddd, *J* = 10.9, 10.3, 6.9 Hz, 1H), 1.75 (tdd, *J* = 13.1, 6.2, 3.3 Hz, 1H), 1.71 – 1.47 (m, 6H) ppm; $\mathbf{\delta_C}$ **(126 MHz, $CDCl_3$)** δ 215.6, 147.9, 145.8, 139.3, 128.6, 110.2, 106.6, 101.2, 98.3, 89.0, 84.7, 68.3, 67.9, 63.1, 62.4, 51.8, 40.4, 32.3, 30.8, 29.9, 25.6, 19.5 ppm; $\mathbf{\nu_{max}}$ **(film)** 2948, 2874, 2052, 1979, 1708, 1505, 1487, 1466, 1436, 1372, 1344, 1323, 1270, 1246, 1200, 1118, 1092, 1079, 1038, 1024, 971, 934, 906, 869, 815, 734 cm^{-1}; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M + NH_4]^+$ calculated for $C_{24}H_{24}FeO_9NH_4$: 530.1108; observed: 530.1105.

Tricarbonyl[methyl 2'-(hydroxymethyl)-1,2-dihydro-(1,1'-biphenyl)-3-carboxylate]iron(0) **109**.



109

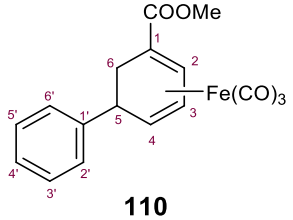
Chemical Formula: $C_{18}H_{16}FeO_6$

Molecular Weight: 384.1650

In accordance with **General Procedure 8**, employing 2-bromobenzyl alcohol (0.172 g, 0.919 mmol), in THF (4.2 mL) treated with nBuLi (0.170 mL, 1.839 mmol, 2.5 M in hexanes), Cu(I)CN (0.041 g, 0.459 mmol) and tricarbonyl(η^5 -carboxylic acid methyl ester)iron(1+) hexafluorophosphate(1–) (0.097 g, 0.229 mmol) and purification using column chromatography with a solvent system of hexane / diethyl ether [40:10] to achieve the title compound as a yellow oil (0.146 g, 41 %); $\mathbf{R_f}$ 0.51 hexane / diethyl ether [40:10];

$\boldsymbol{\nu_{max}}$ (film) 3326, 3065, 3030, 2952, 2872, 2054, 1984, 1707, 1689, 1603, 1579, 1496, 1454, 1436, 1380, 1275, 1247, 1209, 1194, 1149, 1092, 1045, 1023 cm^{-1}; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M + H]^+$ calculated for $C_{18}H_{16}FeO_6H$: 385.0369; observed: 385.0365.

Tricarbonyl[methyl 1,2-dihydro-(1,1'-biphenyl)-3-carboxylate]iron(0) **110**.



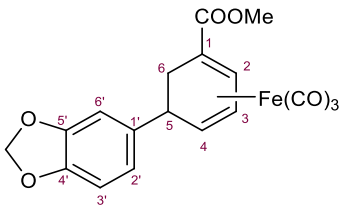
110

Chemical Formula: $C_{17}H_{14}FeO_5$

Molecular Weight: 354.1351

In accordance with **General Procedure 8**, employing bromobenzene (0.153 g, 0.974 mmol), in THF (4.4 mL) treated with nBuLi (0.09 mL, 0.974 mmol, 2.5 M in hexanes), Cu(I)CN (0.044 g, 0.487 mmol) and tricarbonyl(η^5-carboxylic acid methyl ester)iron(1+) hexafluorophosphate(1–) (0.103 g, 0.244 mmol) and purification using column chromatography with a solvent system of hexane / ethyl acetate [90:10] to achieve the title compound as a yellow oil (0.249 g, 72 %); **R_f** 0.42 hexane / ethyl acetate [90:10]; **δ_H (500 MHz, $CDCl_3$)** δ 6.96 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 8.5 Hz, 2H), 6.25 (d, *J* = 4.1 Hz, 1H), 5.46 (dd, *J* = 6.3, 4.5 Hz, 1H), 5.03 (s, 1H), 3.71 (s, 3H, -Me), 3.44 (dt, *J* = 11.4, 3.7 Hz, 1H), 3.33 – 3.28 (m, 1H), 2.78 (dd, *J* = 15.4, 11.5 Hz, 1H), 1.45 (dd, *J* = 15.4, 4.0 Hz, 1H); **δ_C (126 MHz, $CDCl_3$)** 210.2, 172.7, 154.3, 138.3, 128.1, 115.5, 89.1, 84.5, 68.2, 62.9, 51.9, 45.1, 32.6, 29.8, 22.8, 14.3 ppm; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added posthumously by the supervisor) **HRMS (ESI):** *m/z* $[M + H]^+$ calculated for $C_{17}H_{14}FeO_6H$: 371.0209; observed: 371.0213.

Tricarbonyl[methyl 5-(benzo[d][1,3]dioxol-5-yl)cyclohexa-1,3-dienecarboxylate]iron(0) **111**.



111

Chemical Formula: $C_{18}H_{14}FeO_7$

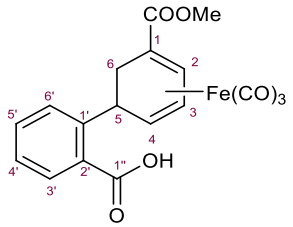
Molecular Weight: 398.1446

In accordance with **General Procedure 8**, employing 5-bromo-1,3-benzodioxole (0.326 g, 1.622 mmol), in THF (7.4 mL) treated with nBuLi (0.15 mL, 0.1.622 mmol, 2.5 M in hexanes), Cu(I)CN (0.073 g, 0.811 mmol) and tricarbonyl(η^5-carboxylic acid methyl ester)iron(1+) hexafluorophosphate(1–) (0.171 g, 0.405 mmol) and purification using column chromatography with a solvent system of hexane / ethyl acetate [90:10] to achieve the title compound as a yellow oil (0.253 g, 39 %); **R_f** 0.61 hexane / ethyl acetate [90:10]; **δ_H (500**

MHz, $CDCl_3$) 6.67 (d, *J* = 7.8 Hz, 1H), 6.56 (d, *J* = 9.6 Hz, 2H), 6.24 (d, *J* = 3.8 Hz, 1H), 5.90 (s, 2H), 5.51 – 5.43 (m, 1H), 3.71 (s, 3H), 3.47 – 3.39 (m, 1H), 3.28 (d, *J* = 5.1 Hz, 1H), 2.77 (dd, *J* = 15.3, 11.6 Hz, 1H), 1.44 (dd, *J* = 15.5, 3.7 Hz, 1H) ppm; **δ_C (126 MHz, $CDCl_3$)** 210.1, 172.4, 147.9, 146.2, 140.1, 120.1, 108.2, 107.1, 101.1, 89.1, 84.4, 67.8, 62.9, 51.8, 45.6, 32.5 ppm; **ν_{max} (film)** 3000, 2953, 2903, 2778, 2054, 1981, 1708, 1609, 1504, 1485, 1439, 1367, 1273, 1246, 1234, 1195, 1148, 1121, 1040, 979, 935, 913, 862, 812 cm^{-1}.

Provisionally identified on the basis of the spectroscopic data presented above (a sample of Sarah's lab book compound SD207 still needs to be identified for HRMS).

Tricarbonyl[3'-(methoxycarbonyl)-1',2'-dihydro-(1,1'-biphenyl)-2-carboxylic acid]iron(0) **112**.



112

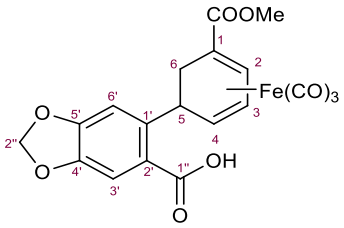
Chemical Formula: $C_{18}H_{14}FeO_7$

Molecular Weight: 398.1480

In accordance with **General Procedure 8**, employing 2-bromobenzoic acid (0.273 g, 1.358 mmol), in THF (6.2 mL) treated with nBuLi (0.251 mL, 2.716 mmol, 2.5 M in hexanes), Cu(I)CN (0.061 g, 0.679 mmol) and tricarbonyl(η^5-carboxylic acid methyl ester)iron(1+) hexafluorophosphate(1–) (0.143 g, 0.340 mmol) and purification using column chromatography with a solvent system of hexane / ethyl acetate [1:1] to achieve the title compound as a yellow oil (0.197 g, 36 %); **R_f** 0.73 hexane / ethyl acetate [1:1]; **$[\alpha]_D^{21.7}$** +13.6 (*c* 0.02, CH_2Cl_2); **δ_H** (500 MHz, $CDCl_3$) 6.67 (d, 1H, *J* = 7.8 Hz), 6.56 (d, 2H, *J* = 9.4 Hz), 6.24 (d, 1H, *J* = 4.1 Hz), 5.90 (s, 2H), 5.46 (dd, 1H, *J* = 6.3, 4.5 Hz), 3.71 (s, 3H, -Me), 3.42 (dt, 1H, *J* = 11.4, 3.7 Hz), 3.28 (ddd, 1H, *J* = 6.2, 3.3, 1.1, Hz), 2.77 (dd, 1H, *J* = 15.4, 11.5 Hz), 1.44 (dd, 1H, *J* = 15.5, 4.0 Hz) ppm; **δ_C** (126 MHz, $CDCl_3$) 210.0, 172.4, 147.9, 146.2, 140.1, 120.1, 108.2, 107.1, 101.1, 89.1, 84.4, 67.8, 62.9, 51.8, 45.6, 32.5 ppm; **ν_{max}** (film) 3413, 2953, 2904, 2054, 1979, 1707, 1655, 1504, 1485, 1439, 1366, 1273, 1246, 1234, 1195, 1092, 1039, 935, 863, 811, 768, 655, 611 cm^{-1}; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been

added posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M + H]^+$ calculated for $C_{18}H_{14}FeO_7H$: 397.0208; observed: 397.0208.

Tricarbonyl[6-(5-(methoxycarbonyl)cyclohexa-2,4-dien-1-yl)benzo[d][1,3]dioxole-5-carboxylic acid]iron(0) **113**.



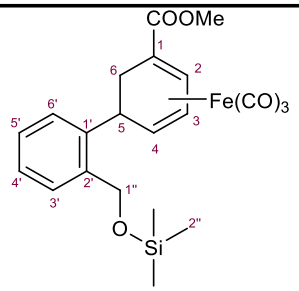
113

Chemical Formula: $C_{19}H_{14}FeO_9$

Molecular Weight: 442.1541

In accordance with **General Procedure 8**, employing 6-bromo-1,3-benzodioxole-5-carboxylic acid (0.195 g, 0.796 mmol), in THF (3.6 mL) treated with nBuLi (0.147 mL, 1.592 mmol, 2.5 M in hexanes), Cu(I)CN (0.036 g, 0.398 mmol) and tricarbonyl(η^5-carboxylic acid methyl ester)iron(1+) hexafluorophosphate(1–) (0.084 g, 0.199 mmol) and purification using column chromatography with a solvent system of hexane / ethyl acetate [3:1] to achieve the title compound as a yellow oil (0.086 g, 24 %); $\mathbf{R_f}$ 0.56 hexane / ethyl acetate [3:1]; $\boldsymbol{\nu_{max}}$ (film) 2953, 2054, 1982, 1705, 1683, 1621, 1594, 1506, 1487, 1447, 1256, 1094, 1062, 1040, 936 cm^{-1}; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M + NH_4]^+$ calculated for $C_{19}H_{14}FeO_9NH_4$: 460.0331; observed: 460.0332.

Tricarbonyl {methyl 2'-[(trimethylsilyloxy)methyl]-1,2-dihydro-(1,1'-biphenyl)-3-carboxylate}iron(0) **114**.



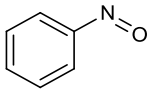
114

Chemical Formula: $C_{21}H_{24}FeO_6Si$

Molecular Weight: 456.3422

In accordance with **General Procedure 8**, employing (2-bromo-benzyloxy)trimethylsilane (0.381 g, 1.470 mmol), in THF (6.7 mL) treated with nBuLi (0.136 mL, 1.470 mmol, 2.5 M in hexanes), Cu(I)CN (0.066 g, 0.735 mmol) and tricarbonyl(η^5-carboxylic acid methyl ester)iron(1+) hexafluorophosphate(1–) (0.155 g, 0.367 mmol) and purification using column chromatography with a solvent system of hexane / diethyl ether [6:1] to achieve the title compound as a yellow oil (0.501 g, 75 %); $\mathbf{R_f}$ 0.55 hexane / diethyl ether [6:1]; $\mathbf{\delta_H}$ (500 MHz, $CDCl_3$) 7.50 (d, *J* = 7.3 Hz, 1H), 7.34 (dd, *J* = 4.8, 1.0 Hz, 2H), 6.24 (dd, *J* = 4.5, 0.9 Hz, 1H), 5.53 (ddd, *J* = 6.1, 4.6, 0.7 Hz, 1H), 4.55 (d, *J* = 11.2 Hz, 1H), 4.45 (d, *J* = 11.2 Hz, 1H), 4.17 (ddd, *J* = 6.4, 5.7, 2.9 Hz, 1H), 3.71 (s, 3H, -Me), 3.30 (ddd, *J* = 6.2, 3.6, 1.3 Hz, 1H), 2.76 (ddd, *J* = 15.2, 9.8, 0.9 Hz, 1H), 1.53 (dd, *J* = 15.3, 2.4 Hz, 2H), 0.32 (s, 9H, $H^{2''}$) ppm; $\mathbf{\delta_C}$ (126 MHz, $CDCl_3$) 210.5 (CO), 172.4, 143.5, 138.4, 134.8, 129.4, 128.7, 127.2, 90.3, 85.4, 71.5, 60.6, 58.4, 51.9, 30.3, 0.5 ($C^{2''}$) ppm; $\mathbf{\nu_{max}}$ (film) 2953, 2900, 2058, 1983, 1711, 1463, 1435, 1382, 1337, 1284, 1265, 1248, 1203, 1126, 1084, 1057, 986, 959, 931, 839 cm^{-1}; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M + Na]^+$ calculated for $C_{21}H_{24}FeO_6SiNa$: 479.0584; observed: 479.0588.

Nitrosobenzene **115**.



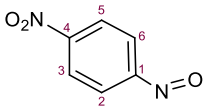
115

Chemical Formula: C_6H_5NO

Molecular Weight: 107.1100

Nitrobenzene (6.69 mL, 65.0 mmol) in a solution of ammonium chloride (4.02 g, 75.2 mmol, 1.2 eq) in water (134 mL) was treated with small additions of zinc powder (9.01 g, 138 mmol, 2.1 eq) over a 5 minute period while the temperature was increased to 45 ^{o}C. After addition the reaction mixture was heated to 65 ^{o}C for a period of 10 minutes before being cooled to 55 ^{o}C with the addition of ice. The reaction mixture was filtered and the solid that remained was washed with boiling water (30 mL) and treated with a solution of sulphuric acid (20.1 mL, 358 mmol, 5. 5 eq) in water (50 mL) whilst maintaining the temperature below 5 ^{o}C. An ice cold solution of sodium dichromate (4.48 g, 15.0 mmol, 0.23 eq) was added producing a fine dark brown powder that was isolated by filtration and steam distilled to produce the title compound as a cloudy green / yellow wax (2.09 g, 30 %). $\boldsymbol{\delta_H}$ (300 MHz, $CDCl_3$) 7.85 (2H, d, *J* 7.7, 2-H, 6-H), 7.66-7.64 (1H, m, 4-H), 7.56 (2H, dd, *J* 7.8, 7.7, 3-H, 5-H); $\boldsymbol{\delta_C}$ (300 MHz, $CDCl_3$) 166, 135.6, 129.4, 121.0; $\boldsymbol{\nu_{max}}$ (film) 3159, 2924, 2853 (s, s, alkyl), 1510 (s, w, aromatic N-O monomer), 1392 (s, m, alkyl), 1296 (s, m, aromatic N-O dimer), 1192 (s, w, C-N), 779, 762, 696 (s, aromatic) cm^{-1}.

1-nitro-4-nitrosobenzene **116**.



116

Chemical Formula: $C_6H_4N_2O_3$

Molecular Weight: 152.1076

A solution of potassium peroxymonosulfate (oxone) (30.74 g, 50 mmol) in water (125 mL) was added over a period of 20 minutes to a solution of 4-amino-1-nitrobenzene (3.45 g, 25 mmol) in water (125 mL) under argon. After stirring at room temperature for 2 hours, the solution was extracted with dichloromethane (3 x 200 mL). The combined organic extracts were washed with hydrochloric acid (100 mL, 1 M), aqueous saturated sodium hydrogen carbonate (100 mL), brine (50 mL), and water (50 mL). Drying over $MgSO_4$ and evaporation of the solvent *in vacuo* yielded the title compound as a yellow solid (3.65 g, 96 %). The compound was used immediately without further purification.

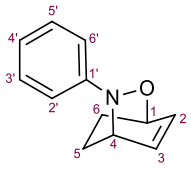
$\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 8.12 (2H, dd, *J* = 7.2, 2.2, $H^{3/5}$), 6.95 (2H, dd, *J* = 7.0, 2.2, $H^{2/6}$); $\boldsymbol{\delta_C}$ (500 MHz, $CDCl_3$) ppm; $\boldsymbol{\nu_{max}}$ (film) 1593, 1501, (s, m, aromatic), 1463, (s, m, C-N=O), 1443, 1377 (s, s, C-NO_2), 1260 (s, m, N-O), 732 (s, m, aromatic) cm^{-1}.

Data in agreement with that previously reported.[77]

General procedure 9: Hetero Diels-Alder cycloaddition

A solution of relevant nitroso compound (7.12 mmol, 1 eq) in a specified dry solvent (20 mL) was cooled to -78 ^{o}C before the dropwise addition of 1,3-cyclohexadiene (11.4 mmol, 1.6 eq) over the period of 10 minutes. The reaction was allowed to warm slowly to room temperature over 16 hours under an argon atmosphere before being evaporated *in vacuo* and purified by either column chromatography or recrystallization.

3-Phenyl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene **117**.



117

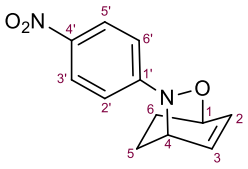
Chemical Formula: $C_{12}H_{13}NO$

Molecular Weight: 187.2377

In accordance with **General Procedure 9**, employing nitrosobenzene (0.76 g, 7.12 mmol) in diethyl ether (20 mL) with 1,3-cyclohexadiene (1.08 mL, 11.4 mmol) and purification by recrystallization from ethanol provided the title compound as a colourless crystalline solid (0.71 g, 53 %); **Mp.** 65-67 ^{o}C. (lit. mp 65-65.5 ^{o}C); $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 7.22 (t, *J* = 8.5, 2H, $H^{3'/5'}$), 7.02 (d, *J* = 8.5, 2H, $H^{2'/6'}$), 6.93 (t, *J* = 8.5 Hz, 1H, $H^{4'}$), 6.53 – 6.59 (m, 1H, H^{2}), 6.10 – 6.15 (m, 1H, H^{3}), 4.72 – 4.69 (m, 1H, H^{1}), 4.43 – 4.42 (m, 1H, H^{4}), 2.33 – 2.21 (m, 2H, $H^{5/6}$), 1.61 – 1.55 (m, 1H, H^{5}), 1.41 – 1.35 (m, 1H, H^{6}) ppm; $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 152.4 ($C^{1'}$), 131.6 (C^{2}), 130.0 (C^{3}), 128.4 ($C^{3'/5'}$), 122.0 ($C^{4'}$), 117.5 ($C^{2'/6'}$), 69.2 (C^{1}), 56.5 (C^{4}), 24.1 (C^{6}), 21.4 (C^{5}) ppm

Data in agreement with that previously reported[78]

3-(4-Nitrophenyl)-2-oxa-3-azabicyclo[2.2.2]oct-5-ene **118**.



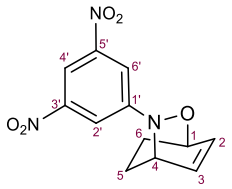
118

Chemical Formula: $C_{12}H_{12}N_2O_3$

Molecular Weight: 232.2353

In accordance with **General Procedure 9**, employing 1-nitro-4-nitrosobenzene (0.24 g, 1.58 mmol) in dichloromethane (5 mL) with 1,3-cyclohexadiene (0.24 mL, 2.52 mmol) and purification by column chromatography hexane / ethyl acetate [2:1] to provide the title compound as a yellow solid (0.18 g, 92 %); **Mp** 189-130 ^{o}C; $\mathbf{R_f}$ 0.61 hexane / ethyl acetate [2:1]; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 8.08 (d, 2H, *J* = 9.3 Hz, $H^{3'/5'}$), 7.02 (d, 2H, *J* = 9.3 Hz, $H^{2'/6'}$), 6.53 – 6.59 (m, 1H, H^2), 6.10 – 6.15 (m, 1H, H^3), 4.72 – 4.69 (m, 1H, H^1), 4.43 – 4.42 (m, 1H, H^4), 2.33 – 2.21 (m, 2H, $H^{5/6}$), 1.61 – 1.55 (m, 1H, H^5), 1.41 – 1.35 (m, 1H, H^6) ppm; $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 157.7 ($C^{1'}$), 141.5 ($C^{4'}$), 131.8 (C^2), 130.4 (C^3), 125.0 ($C^{3'/5'}$), 115.7 ($C^{2'/6'}$), 70.4 (C^1), 55.3 (C^4), 23.9 (C^6), 21.0 (C^5) ppm; $\boldsymbol{\nu_{max}}$ (film) 1652 (b, m, alkene), 1589 (b, s, aromatic), 1490 (b, m, C-NO_2), 1109 (s, s, C-O), 848 (s, w, aromatic), 712 (b, m, alkene) cm^{-1}; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M - H]^+$ calculated for $C_{12}H_{13}N_2O_3$: 233.0921; observed: 233.0917.

3-(3,5-Dinitrophenyl)-2-oxa-3-azabicyclo[2.2.2]oct-5-ene **119**.



119

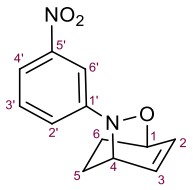
Chemical Formula: $C_{12}H_{11}N_3O_5$

Molecular Weight: 277.2328

In accordance with **General Procedure 9**, employing 1,3-dinitroso-benzene (0.34 g, 1.72 mmol) in dichloromethane (6 mL) with 1,3-cyclohexadiene (0.26 mL, 2.76 mmol) and purification by column chromatography hexane / ethyl acetate [80:20] to provide the title compound as a yellow oil (0.36 g, 98 %); $\mathbf{R_f}$ 0.66 hexane / ethyl acetate [8:2]; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 8.50 (t, 1H, *J* = 2.0 Hz), 8.09 (d, *J* = 2.0 Hz, 2H), 6.62 (ddd, *J* = 7.8, 5.9, 1.6 Hz, 1H), 6.24 (ddd, *J* = 8.1, 5.8, 1.3 Hz, 1H), 4.90 – 4.85 (m, 1H), 4.69 – 4.63 (m, 1H, H^4), 2.37 – 2.23 (m, 2H), 1.68 (m, 1H), 1.49 – 1.41 (m, 1H) ppm; $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 154.9 ($C^{1'}$), 149.0 ($C^{4'}$), 132.4 (C^2), 129.7 (C^3), 125.8 ($C^{3'}$), 123.1 ($C^{5'}$), 116.5 ($C^{2'}$), 111.0 ($C^{6'}$), 70.5 (C^1), 56.3 (C^4), 23.7 (C^6), 21.0 (C^5) ppm; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added

posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M + H]^+$ calculated for $C_{12}H_{12}N_3O_5$: 278.0771; observed: 278.0769.

3-(5-Nitrophenyl)-2-oxa-3-azabicyclo[2.2.2]oct-5-ene **120**.



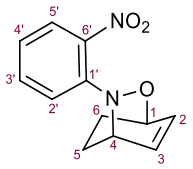
120

Chemical Formula: $C_{12}H_{12}N_2O_3$

Molecular Weight: 232.2353

In accordance with **General Procedure 9**, employing 1-nitro-3-nitrosobenzene (0.65 g, 4.27 mmol) in dichloromethane (12 mL) with 1,3-cyclohexadiene (0.65 mL, 6.84 mmol) and purification by column chromatography hexane / ethyl acetate [3:1] provided the title compound as an orange oil (0.47 g, 94 %); $\mathbf{R_f}$ 0.63 hexane / ethyl acetate [3:1]; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 7.83 (dd, *J* = 8.2, 1.5 Hz, 1H, $H^{4'}$), 7.41 (ddd, *J* = 8.6, 7.1, 1.5 Hz, 1H, $H^{3'}$), 7.35 (dd, *J* = 8.4, 1.4 Hz, 1H, $H^{2'}$), 7.12 (ddd, *J* = 8.6, 7.1, 1.5 Hz, 1H, $H^{6'}$), 6.73 (ddd, *J* = 7.9, 5.9, 1.7 Hz, 1H, H^2), 6.16 (ddd, *J* = 7.9, 5.9, 1.7 Hz, 1H, H^3), 4.78 – 4.75 (m, 1H, H^1), 4.45 – 4.42 (m, 1H, H^4), 2.43 – 2.38 (m, 1H, H^5), 2.29 – 2.34 (m, 1H, H^5), 1.58 – 1.48 (m, 1H, H^6), 1.48 – 1.36 (m, 1H, H^6) ppm; $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 146.2 ($C^{4'}$), 132.9 (C^2), 132.6 (C^3), 129.4 ($C^{5'}$), 125.2 ($C^{3'}$), 123.8 ($C^{6'}$), 123.5 ($C^{2'}$), 70.1 (C^1), 57.3 (C^4), 23.5 (C^6), 21.9 (C^5) ppm; $C^{1'}$ not detected but expected at around 154.9 ppm; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M + H]^+$ calculated for $C_{12}H_{13}N_2O_3$: 233.0921; observed: 233.0917.

3-(6-Nitrophenyl)-2-oxa-3-azabicyclo[2.2.2]oct-5-ene **121**.



121

Chemical Formula: $C_{12}H_{12}N_2O_3$

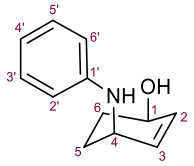
Molecular Weight: 232.2353

In accordance with **General Procedure 9**, employing 1-nitro-2-nitrosobenzene (0.37 g, 2.43 mmol) in dichloromethane (7 mL) with 1,3-cyclohexadiene (0.37 mL, 3.89 mmol) and purification by column chromatography hexane / ethyl acetate [2:1] provided the title compound as a yellow solid (0.360 g, 47.4 %); $\mathbf{R_f}$ 0.54 hexane / ethyl acetate [2:1], $\mathbf{\delta_H}$ (500 MHz, $CDCl_3$) 7.80 (t, *J* = 2.2 Hz, 1H, $H^{4'}$), 7.70 (ddd, *J* = 7.9, 2.2, 1.1 Hz, 1H, $H^{5'}$), 7.31 (t, *J* = 8.0 Hz, 1H, $H^{3'}$), 7.26 (ddd, *J* = 8.2, 2.2, 1.1 Hz, 1H, $H^{2'}$), 6.55 (ddd, *J* = 7.9, 5.9, 1.7 Hz, 1H, H^2), 6.12 (ddd, *J* = 8.1, 5.8, 1.4 Hz, 1H, H^3), 4.77 – 4.73 (m, 1H, H^1), 4.53 – 4.48 (m, 1H, H^4), 2.30 – 2.16 (m, 2H, $H^{5/6}$), 1.59 (tt, *J* = 11.6, 2.8 Hz, 1H, H^5), 1.42 – 1.31 (m, 1H, H^6) ppm; $\mathbf{\delta_C}$ (126 MHz, $CDCl_3$) 153.7 ($C^{1'}$), 148.7 ($C^{4'}$), 131.9 (C^2), 129.6 (C^3), 129.1 ($C^{5'}$), 123.0 ($C^{3'}$), 116.5 ($C^{6'}$), 112.0 ($C^{2'}$), 69.7 (C^1), 56.4 (C^4), 23.8 (C^6), 21.1 (C^5) ppm. (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M + H]^+$ calculated for $C_{12}H_{13}N_2O_3$: 233.0921; observed: 233.0918.

General procedure 10: N-O bond cleavage for cycloadducts

To a solution of nitro cyclo-adduct (1.23 mmol, 1.0 eq) in acetic acid (4.70 mL) at room temperature was added activated zinc powder (12.3 mmol, 10.0 eq). The reaction mixture was stirred for 16 hours at room temperature before being filtered. An aqueous solution of sodium hydroxide (2M, 25 mL) and diethyl ether (25 mL) was added to the filtrate. The organic layer was separated, dried with K_2CO_3 and evaporated *in vacuo* to produce a brown oil. Purification by column chromatography provided the title compound.

4-Phenylamino-cyclohex-2-enol 122.



122

Chemical Formula: $C_{12}H_{15}NO$

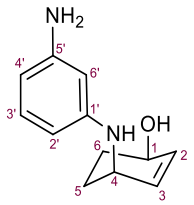
Molecular Weight: 189.2536

In accordance with **General Procedure 10**, employing 3-phenyl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (0.23 g, 1.23 mmol) in acetic acid (4.70 mL) with activated zinc powder (0.80 g, 12.3 mmol, 10.0 eq) provided the title compound as a light brown oil (0.11 g,

47 %); δ_H (300 MHz, $CDCl_3$) 7.11 (2H, t, *J* = 8.0, $H^{3'/5'}$), 6.64 (1H, t, *J* = 8.0, $H^{4'}$), 6.54 (2H, d, *J* = 8.0, $H^{2'/6'}$), 5.91 – 5.84 (2H, m, $H^{2/3}$), 4.11-4.10 (1H, m, H^1), 3.91 – 3.90 (1H, m, H^4), 1.80-1.67 (4H, m, $H^{5/6}$); δ_C (75 MHz, $CDCl_3$) 147.0, 132.3, 131.5, 129.5, 117.6, 113.3, 65.2, 47.8, 28.8, 24.8; ν_{max} (film) 3309 (b, s, O-H), 2896 (b, w, alkyl), 1639 (s, w, alkene), 1615 (s, w, aromatic), 1513 (s, w, N-H) cm^{-1}.

Data in agreement with that previously reported.[79]

5-Amino-4-phenylamino-cyclohex-2-enol **123**.



123

Chemical Formula: $C_{12}H_{16}N_2O$

Molecular Weight: 204.2730

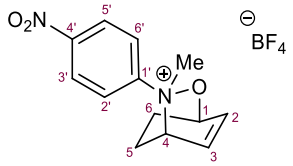
In accordance with **General Procedure 10**, employing 1-nitro-4-nitrosobenzene (0.23 g, 1.23 mmol) in acetic acid (4.70 mL) with activated zinc powder (0.80 g, 12.3 mmol, 10.0 eq) and purification by column chromatography [90:10 hexane-EtOAc] to yield the title compound as a dark brown oil (0.123 g, 49 %); **HRMS** (ESI): *m/z* $[C_{12}H_{15}N_2O]^+$ calculated for $C_{12}H_{15}N_2O$: 203.1179; observed: 203.1178.

We have not been able to find NMR or IR data for this compound, which is not discussed in the main text of the thesis but was included in the draft experimental section.

General procedure 11: Methylation of the nitrogen atom in cycloadducts using $AgBF_4$

A cloudy dark solution of cycloadduct (1.13 mmol, 1.0 eq) in CH_2Cl_2 (30 mL) was treated with $AgBF_4$ (1.24 mmol, 1.1 eq) followed by iodomethane (1.24 mmol, 1.1 eq). The reaction mixture was allowed to stir under an atmosphere of argon in the dark at room temperature for 2 hours. The yellow precipitate formed was collected by suction filtration and washed using acetone (30 mL). The combined filtrates were evaporated under reduced pressure to produce a brown oil. Dichloromethane (20 mL) was added to precipitate the salt which was filtered and dried in vacuo.

3-Methyl-3-(4-nitrophenyl)-2-oxa-3-azonia-bicyclo[2.2.2]oct-5-ene tetrafluoroborate **124**.



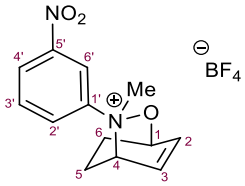
124

Chemical Formula: $C_{13}H_{15}BF_4N_2O_3$

Molecular Weight: 334.0782

In accordance with **General Procedure 11**, employing compound (1*R*,4*S*)-3-(4-nitrophenyl)-2-oxa-3-azabicyclo[2.2.2]oct-5-ene **118** (0.36 g, 1.55 mmol) in dichloromethane (20 mL) treated with silver tetrafluoroborate (0.36 g, 1.71 mmol) and iodomethane (0.11 mL, 1.71 mmol) and purification by precipitation using dichloromethane to yield the title compound as a light brown solid (0.25 g, 48 %); $\boldsymbol{\delta_H}$ (500 MHz, D_2O) 8.44 (d, *J* = 9.3 Hz, 2H, $H^{3'/5'}$), 7.92 (d, *J* = 9.3 Hz, 2H, $H^{2'/6'}$), 6.89 (ddd, *J* = 8.0, 6.2, 1.8, H^2), 6.36 (ddd, *J* = 8.0, 6.2, 1.8, H^3), 5.78 – 5.74 (m, 1H, H^1), 5.58 – 5.53 (m, 1H, H^4), 3.96 (s, 3H, -Me), 2.81 – 2.79 (m, 1H, H^5), 2.53 – 2.50 (m, 1H, H^6), 2.18 – 2.16 (m, 1H, H^5), 1.99 – 1.88 (m, H, H^6); $\boldsymbol{\delta_C}$ (500 MHz, $CDCl_3$); $\boldsymbol{\nu_{max}}$ (film) 2959 (s, m, alkyl), 1593 (s, m, aromatic), 1527 (s, NO_2), 1288, 1246, 1231 (s, m, N-O), 1053, 1015 (s, s, C-O), 854, 794 (s, m, aromatic), 730, 691 (s, s, alkene) cm^{-1}; (Editorial note: it is good practice to report both low and high resolution mass spectrometric data, but at the time of death low resolution data had not been added to the thesis draft; since this omission does not put the structure assignment at risk, the missing data has not been added posthumously by the supervisor) **HRMS** (ESI): *m/z* $[M]^+$ calculated for $C_{13}H_{15}N_2O_3$: 247.1077; observed: 247.1078.

Methyl-3-(3-nitrophenyl)-2-oxa-3-azonia-bicyclo[2.2.2]oct-5-ene tetrafluoroborate **125**.



125

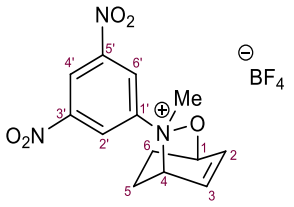
Chemical Formula: $C_{13}H_{15}BF_4N_2O_3$

Molecular Weight: 334.0782

HRMS (ESI): *m/z* $[M - BF_4]^+$ calculated for $C_{13}H_{15}N_2O_3$: 247.1077; observed: 247.1081.

We have not been able to find NMR or IR data for this compound, which is not discussed in the main text of the thesis but was included in the draft experimental section.

Methyl-3-(3,5-dinitrophenyl)-2-oxa-3-azonia-bicyclo[2.2.2]oct-5-ene tetra fluoroborate **126**.



126

Chemical Formula: $C_{13}H_{14}BF_4N_3O_5$

Molecular Weight: 379.0752

In accordance with **General Procedure 11**, employing compound (1*R*,4*S*)-3-(3,5-dinitrophenyl)-2-oxa-3-azabicyclo[2.2.2]oct-5-ene (0.418 g, 1.51 mmol) in dichloromethane (40 mL) treated with silver tetrafluoroborate (0.35 g, 1.66 mmol) and iodomethane (0.11 mL, 1.66 mmol) and purification by precipitation using dichloromethane to yield the title compound as a light brown solid (0.372 g, 65%); $\boldsymbol{\delta_H}$ (500 MHz, $(CD_3)_2CO$) 8.42 (t, *J* = 2.0 Hz, 1H, $H^{4'}$), 8.20 (d, *J* = 2.0 Hz, 2H, $H^{2'/6'}$), 5.94 (ddd, *J* = Hz, 1H, H^2), 5.87 (ddd, *J* = Hz, 1H, H^3), 4.57 (m, 1H, H^1), 4.30 – 4.24 (m, 1H, H^4), 3.38 (s, 3H, -Me), 2.22 – 2.17 (m, 1H, H^5), 2.16 – 2.10 (m, 1H, H^6), 1.77 – 1.69 (m, 1H, H^5), 1.61 – 1.51 (m, 1H, H^6) ppm; **HRMS** (ESI): *m/z* $[M - BF_4]^+$ calculated for $C_{13}H_{14}N_3O5$: 292.0928; observed: 292.0928.

Provisionally identified on the basis of the spectroscopic and mass spectrometric data presented above (a sample of Sarah's lab book compound SD285 still needs to be identified for ^{13}C NMR spectroscopy).

Appendix 1

Crystal Data of New Compounds 46b and 48a

Diastereoisomer **46b**

Crystal data and structure refinement for $(CO)_3$ Fe (C_6H_5-Br,O_2CMe_2)

Identification code	sarahd1
Elemental formula	C12 H11 Br Fe O5
Formula weight	370.97
Crystal system, space group	orthorhombic, P 2_1 2_1 2_1
Unit cell dimensions	a = 8.2371(2) Å α = 90 ° b = 12.0857(3) Å β = 90 ° c = 13.4968(3) Å γ = 90 °
Volume	1343.62(6) Å^3
Z, Calculated density	4, 1.834 Mg/m^3
F(000)	736
Absorption coefficient	4.108 mm^{-1}
Temperature	140(1) K
Wavelength	0.71073 Å
Crystal colour, shape	colourless prism
Crystal size	0.30 x 0.18 x 0.17 mm

Crystal mounting: on a glass fibre, in oil, fixed in cold N_2 stream

On the diffractometer:

Theta range for data collection	2.993 to 29.997 °
Limiting indices	-11<=h<=11, -17<=k<=17, -18<=l<=18
Completeness to theta = 25.242	99.8 %

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.60960
Reflections collected (not including absences)	27241
No. of unique reflections	3916 [R(int) for equivalents = 0.041]
No. of 'observed' reflections ($I > 2\sigma_I$)	3648
Structure determined by:	direct methods, in SHELXS
Refinement:	Full-matrix least-squares on F^2, in SHELXL
Data / restraints / parameters	3916 / 0 / 216
Goodness-of-fit on F^2	1.042
Final R indices ('observed' data)	R_1 = 0.022, wR_2 = 0.046
Final R indices (all data)	R_1 = 0.025, wR_2 = 0.047
Reflections weighted: $w = [\sigma^2(Fo^2)+(0.0247P)^2+0.0650P]^{-1}$ where $P=(Fo^2+2Fc^2)/3$	
Absolute structure parameter	-0.011(4)
Extinction coefficient	n/a
Largest diff. peak and hole	0.35 and -0.20 e.Å^{-3}
Location of largest difference peak	close to bromine atom

Table 1. Atomic coordinates (x 10^5) and equivalent isotropic displacement parameters (Å^2 x 10^4). U(eq) is defined as one third of the trace of the orthogonalized Uij tensor. E.s.ds are in parentheses.

	x	y	z	U(eq)
C(1)	16760(30)	49960(20)	44957(18)	174(5)
C(2)	18670(30)	38030(20)	41873(19)	194(5)
C(3)	29130(30)	31960(20)	49639(19)	180(5)
C(4)	33510(30)	39480(20)	58146(18)	195(5)
C(5)	21190(30)	46450(20)	62103(19)	203(5)
C(6)	11960(30)	52120(20)	55010(20)	201(5)
O(2)	27530(20)	37033(16)	32863(13)	237(4)
O(3)	43250(20)	28576(15)	44180(13)	200(4)
C(21)	38040(30)	27670(20)	34110(20)	217(5)
C(22)	28910(40)	16910(30)	32400(30)	315(7)
C(23)	52340(40)	28920(30)	27230(20)	295(7)
Br(1)	6330(3)	58850(2)	35019(2)	236(1)
Fe	35982(4)	55926(3)	53332(3)	185(1)
C(7)	48770(30)	60040(20)	63630(20)	268(6)
O(7)	57040(30)	62620(20)	69947(16)	392(5)
C(8)	32230(30)	70100(30)	49980(20)	256(6)
O(8)	29810(30)	79037(19)	47724(19)	373(5)
C(9)	52000(40)	53090(30)	44700(20)	292(6)
O(9)	62440(30)	51740(20)	39350(20)	507(7)

Table 2. Molecular dimensions. Bond lengths are in Ångstroms, angles in degrees. E.s.ds are in parentheses.

(a) About the Fe atom

C(1)-Fe	2.075(2)	Fe-C(7)	1.813(3)
C(4)-Fe	2.101(3)	Fe-C(8)	1.798(3)
C(5)-Fe	2.049(3)	Fe-C(9)	1.793(3)
C(6)-Fe	2.044(3)		

C(9)-Fe-C(8)	98.36(14)	C(8)-Fe-C(1)	93.61(11)
C(9)-Fe-C(7)	97.06(13)	C(7)-Fe-C(1)	162.97(11)
C(8)-Fe-C(7)	91.78(13)	C(6)-Fe-C(1)	40.83(10)
C(9)-Fe-C(6)	137.84(12)	C(5)-Fe-C(1)	70.52(10)
C(8)-Fe-C(6)	94.35(12)	C(9)-Fe-C(4)	95.24(12)
C(7)-Fe-C(6)	122.62(12)	C(8)-Fe-C(4)	164.19(12)
C(9)-Fe-C(5)	134.91(13)	C(7)-Fe-C(4)	94.53(11)
C(8)-Fe-C(5)	125.13(12)	C(6)-Fe-C(4)	70.06(10)
C(7)-Fe-C(5)	93.22(11)	C(5)-Fe-C(4)	40.08(10)
C(6)-Fe-C(5)	40.04(11)	C(1)-Fe-C(4)	76.45(10)
C(9)-Fe-C(1)	98.12(12)		

(b) In the major ligand

C(1)-C(6)	1.437(3)	C(5)-C(6)	1.401(4)
C(1)-C(2)	1.508(4)	C(5)-H(5)	0.92(3)
C(1)-Br(1)	1.921(2)	C(6)-H(6)	0.91(3)
C(2)-O(2)	1.423(3)	O(2)-C(21)	1.435(3)
C(2)-C(3)	1.543(4)	O(3)-C(21)	1.430(3)
C(2)-H(2)	0.95(3)	C(21)-C(23)	1.507(4)
C(3)-O(3)	1.436(3)	C(21)-C(22)	1.520(4)
C(3)-C(4)	1.508(4)	C(22)-H(221)	0.91(3)
C(3)-H(3)	0.98(4)	C(22)-H(222)	1.01(4)
C(4)-C(5)	1.423(4)	C(22)-H(223)	0.90(4)
C(4)-H(4)	0.95(3)		

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      C(23)-H(231)
0.95(4)
      C(23)-H(232)
       C(6)-C(1)-C(2)
117.6(2)
      C(6)-C(1)-Br(1)
115.75(18)
      C(2)-C(1)-Br(1)
112.85(17)
      C(6)-C(1)-Fe
68.45(14)
      C(2)-C(1)-Fe
113.76(17)
      Br(1)-C(1)-Fe
121.81(13)
      O(2)-C(2)-C(1)
111.7(2)
      O(2)-C(2)-C(3)
104.7(2)
      C(1)-C(2)-C(3)
109.0(2)
      O(2)-C(2)-H(2)
112.6(16)
      C(1)-C(2)-H(2)
107.0(15)
      C(3)-C(2)-H(2)
111.9(16)
      O(3)-C(3)-C(4)
111.6(2)
      O(3)-C(3)-C(2)
103.85(19)
      C(4)-C(3)-C(2)
111.4(2)
      O(3)-C(3)-H(3)
107(2)
      C(4)-C(3)-H(3)
111(2)
      C(2)-C(3)-H(3)
112(2)
      C(5)-C(4)-C(3)
118.1(2)
      C(5)-C(4)-Fe
68.00(15)
      C(3)-C(4)-Fe
110.96(17)
      C(5)-C(4)-H(4)
116.2(18)
      C(3)-C(4)-H(4)
117.2(18)
      Fe-C(4)-H(4)
116.7(18)
      C(6)-C(5)-C(4)
114.8(2)
      C(6)-C(5)-Fe
69.80(15)
      C(4)-C(5)-Fe
71.92(15)
      C(6)-C(5)-H(5)
125.0(19)
0.89(3)
      C(23)-H(233)
0.94(4)
      C(4)-C(5)-H(5)
119.3(19)
      Fe-C(5)-H(5)
118.4(18)
      C(5)-C(6)-C(1)
114.0(2)
      C(5)-C(6)-Fe
70.16(15)
      C(1)-C(6)-Fe
70.72(14)
      C(5)-C(6)-H(6)
125.9(19)
      C(1)-C(6)-H(6)
119.6(19)
      Fe-C(6)-H(6)
121.7(18)
      C(2)-O(2)-C(21)
106.05(19)
      C(21)-O(3)-C(3)
105.47(19)
      O(3)-C(21)-O(2)
103.41(19)
      O(3)-C(21)-C(23)
110.1(2)
      O(2)-C(21)-C(23)
108.7(2)
      O(3)-C(21)-C(22)
111.0(2)
      O(2)-C(21)-C(22)
111.0(2)
      C(23)-C(21)-C(22)
112.3(2)
      C(21)-C(22)-H(221)
110(2)
      C(21)-C(22)-H(222)
113.1(19)
      H(221)-C(22)-H(222)
106(3)
      C(21)-C(22)-H(223)
107(2)
      H(221)-C(22)-H(223)
112(3)
      H(222)-C(22)-H(223)
110(3)
      C(21)-C(23)-H(231)
110(2)
      C(21)-C(23)-H(232)
110(2)
      H(231)-C(23)-H(232)
110(3)
      C(21)-C(23)-H(233)
110(3)
      H(231)-C(23)-H(233)
107(3)
      H(232)-C(23)-H(233)
110(3)
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(c) In the carbonyl ligands

C(7)-O(7)	1.135(3)
C(8)-O(8)	1.140(3)
C(9)-O(9)	1.135(4)
O(7)-C(7)-Fe	178.6(3)
O(8)-C(8)-Fe	179.0(3)
O(9)-C(9)-Fe	176.9(3)

Table 3. Anisotropic displacement parameters ($Å^2$ x 10^4) for the expression:
$\exp\{-2\pi^2(h^2a^{*2}U_{11} + \ldots + 2hka^*b^*U_{12})\}$
E.s.ds are in parentheses.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	161(11)	204(12)	158(11)	19(9)	-11(9)	28(9)
C(2)	178(12)	243(13)	161(11)	-25(10)	-6(9)	15(10)
C(3)	155(11)	209(13)	178(11)	27(10)	17(9)	8(10)
C(4)	190(12)	248(13)	148(10)	42(10)	-10(9)	-9(10)
C(5)	224(12)	244(14)	140(11)	10(9)	22(9)	-48(10)
C(6)	194(12)	218(12)	190(12)	-6(10)	26(9)	4(10)
O(2)	284(10)	285(10)	143(8)	-11(7)	9(7)	116(8)
O(3)	187(8)	243(9)	170(8)	4(7)	-14(7)	36(8)
C(21)	218(12)	255(13)	179(12)	-13(10)	-26(10)	85(10)
C(22)	275(15)	297(16)	372(17)	-112(13)	-39(13)	28(13)
C(23)	327(16)	323(17)	235(14)	18(12)	65(12)	130(13)
Br(1)	279.0(13)	274.8(13)	154.0(10)	-7.2(10)	-34.9(10)	102.8(11)
Fe	191(2)	216(2)	148(2)	16.1(14)	-9.6(13)	-28.1(14)
C(7)	290(13)	271(14)	242(13)	55(12)	-3(11)	-68(11)
O(7)	449(13)	450(13)	278(11)	76(10)	-138(10)	-188(12)
C(8)	271(14)	282(15)	216(12)	-4(11)	-51(10)	-57(11)
O(8)	440(13)	250(12)	430(13)	40(10)	-130(11)	-42(9)
C(9)	299(15)	294(15)	284(14)	-23(12)	29(12)	-109(12)
O(9)	419(14)	534(15)	569(16)	-152(13)	266(13)	-184(12)

Table 4. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3). All hydrogen atoms were located in difference maps and were refined freely.

	x	y	z	U(iso)
H(2)	800(30)	3500(20)	4142(19)	6(6)
H(3)	2390(40)	2520(30)	5210(30)	31(9)
H(4)	4140(40)	3690(20)	6270(20)	18(7)
H(5)	2100(40)	4780(20)	6880(20)	14(7)
H(6)	440(40)	5740(20)	5630(20)	22(8)
H(221)	3570(40)	1110(30)	3310(20)	31(9)
H(222)	1990(40)	1570(30)	3730(30)	32(9)
H(223)	2480(40)	1720(30)	2630(30)	32(9)
H(231)	5700(50)	3610(30)	2790(30)	46(11)
H(232)	5970(40)	2380(30)	2850(20)	22(8)
H(233)	4880(50)	2840(30)	2060(30)	51(12)

Table 5. Torsion angles, in degrees. E.s.ds are in parentheses.

C(6)-C(1)-C(2)-O(2)	-164.0(2)
Br(1)-C(1)-C(2)-O(2)	57.2(2)
Fe-C(1)-C(2)-O(2)	-86.9(2)
C(6)-C(1)-C(2)-C(3)	-48.8(3)
Br(1)-C(1)-C(2)-C(3)	172.42(16)
Fe-C(1)-C(2)-C(3)	28.3(2)
O(2)-C(2)-C(3)-O(3)	2.4(3)
C(1)-C(2)-C(3)-O(3)	-117.3(2)
O(2)-C(2)-C(3)-C(4)	122.7(2)
C(1)-C(2)-C(3)-C(4)	3.0(3)
O(3)-C(3)-C(4)-C(5)	158.9(2)
C(2)-C(3)-C(4)-C(5)	43.4(3)
O(3)-C(3)-C(4)-Fe	83.4(2)
C(2)-C(3)-C(4)-Fe	-32.2(2)
C(3)-C(4)-C(5)-C(6)	-46.3(3)
Fe-C(4)-C(5)-C(6)	56.5(2)
C(3)-C(4)-C(5)-Fe	-102.8(2)
C(4)-C(5)-C(6)-C(1)	-0.7(3)
Fe-C(5)-C(6)-C(1)	57.0(2)
C(4)-C(5)-C(6)-Fe	-57.7(2)
C(2)-C(1)-C(6)-C(5)	49.7(3)
Br(1)-C(1)-C(6)-C(5)	-172.70(19)
Fe-C(1)-C(6)-C(5)	-56.7(2)
C(2)-C(1)-C(6)-Fe	106.4(2)
Br(1)-C(1)-C(6)-Fe	-116.02(16)
C(1)-C(2)-O(2)-C(21)	139.8(2)
C(3)-C(2)-O(2)-C(21)	22.0(3)
C(4)-C(3)-O(3)-C(21)	-146.1(2)
C(2)-C(3)-O(3)-C(21)	-26.0(3)
C(3)-O(3)-C(21)-O(2)	40.3(2)
C(3)-O(3)-C(21)-C(23)	156.2(2)
C(3)-O(3)-C(21)-C(22)	-78.8(2)
C(2)-O(2)-C(21)-O(3)	-38.7(2)
C(2)-O(2)-C(21)-C(23)	-155.7(2)
C(2)-O(2)-C(21)-C(22)	80.3(3)

Crystal structure analysis of $(CO)_3Fe(C_6H_5\text{-}Br,O_2CMe_2)$

Crystal data: $C_{12}H_{11}BrFeO_5$, M = 370.97. Orthorhombic, space group $P2_12_12_1$ (no. 19), a = 8.2371(2), b = 12.0857(3), c = 13.4968(3) Å, V = 1343.62(6) $Å^3$. Z = 4, Dc = 1.834 g cm^{-3}, F(000) = 736, T = 140(1) K, μ(Mo-Kα) = 41.1 cm^{-1}, λ(Mo-Kα) = 0.71073 Å.

Crystals are colourless prisms. A fragment, *ca* 0.30 x 0.18 x 0.17 mm, was mounted in oil on a glass fibre and fixed in the cold nitrogen stream on an Oxford Diffraction Xcalibur-3/Sapphire3-CCD diffractometer, equipped with Mo-Kα radiation and graphite monochromator. Intensity data were measured by thin-slice ω- and φ-scans. Total no. of

reflections recorded, to θ_{max} = 30°, was 27241 of which 3916 were unique (Rint = 0.041); 3648 were 'observed' with $I > 2\sigma_I$.

Data were processed using the CrysAlisPro-CCD and -RED (1) programs. The structure was determined by the direct methods routines in the SHELXS program (2A) and refined by full-matrix least-squares methods, on F^2's, in SHELXL (2B). The non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were located in a difference map and were refined freely. At the conclusion of the refinement, wR_2 = 0.047 and R_1 = 0.025 (2B) for all 3916 reflections weighted $w = [\sigma^2(F_o^2) + (0.0247P)^2 + 0.0650P]^{-1}$ with $P = (F_o^2 + 2F_c^2)/3$; for the 'observed' data only, R_1 = 0.022.

In the final difference map, the highest peak (*ca* 0.35 eÅ^{-3}) was close to the bromine atom.

Scattering factors for neutral atoms were taken from reference (3). Computer programs used in this analysis have been noted above, and were run through WinGX (4) on a Dell Optiplex 755 PC at the University of East Anglia.

References

- Programs CrysAlisPro, Oxford Diffraction Ltd., Abingdon, UK (2010).
- G. M. Sheldrick, SHELX-97 – Programs for crystal structure determination (SHELXS) and refinement (SHELXL), *Acta Cryst.* (2008) A**64**, 112-122.
- *'International Tables for X-ray Crystallography'*, Kluwer Academic Publishers, Dordrecht (1992). Vol. C, pp. 500, 219 and 193.
- L. J. Farrugia, (2012) *J. Appl. Cryst.* **45**, 849–854.

Notes on the structure

The iron atom is seven-coordinate with a piano-stool pattern, with the three carbonyl ligands forming the legs and four of the conjugated carbon atoms of the six-membered ring forming the seat. The iron atom is displaced 1.619(2) Å from the mean-plane of the four carbon atoms C(1,4,5,6).

The six-carbon ring has a boat shape; the adjoining C_3O_2 five-membered ring has an envelope shape with C(21) as the out-of-plane flap atom.

The refinement showed clearly that the conformation shown in the figures is the correct absolute structure; this is the only conformation found in the crystal selected.

Figure 1. View of a molecule of $(CO)_3Fe(C_6H_5\text{-}Br,O_2CMe_2)$, indicating the atom numbering scheme. Thermal ellipsoids are drawn at the 50% probability level.

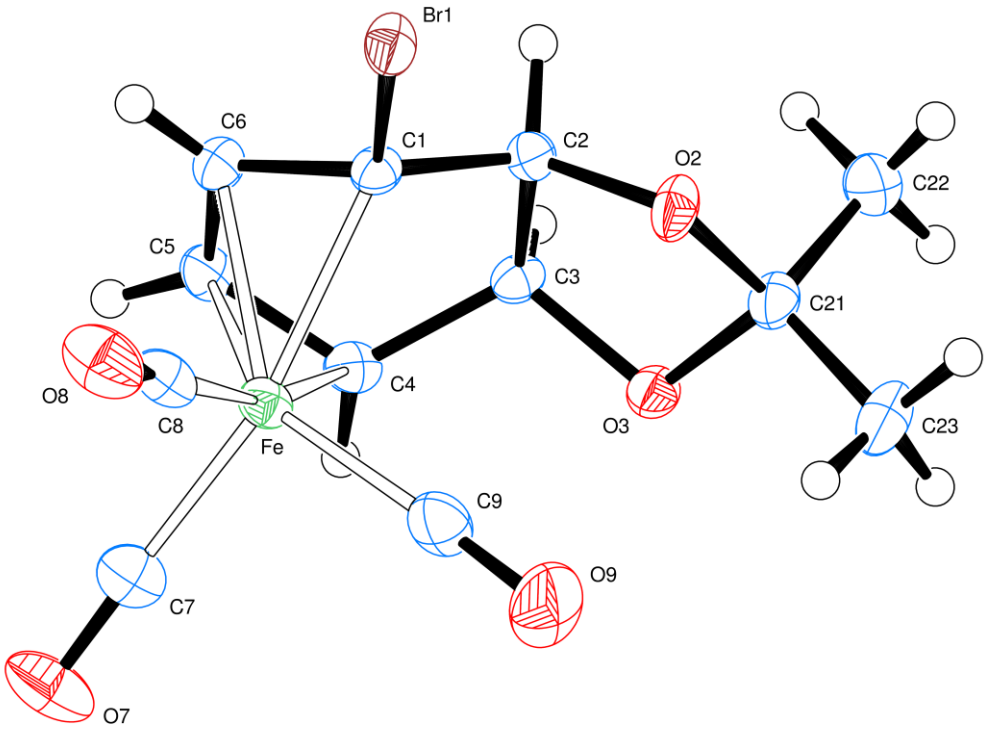


Figure 2. An alternative view, showing the boat-shaped six-membered ring and the envelope-shaped five-membered ring.

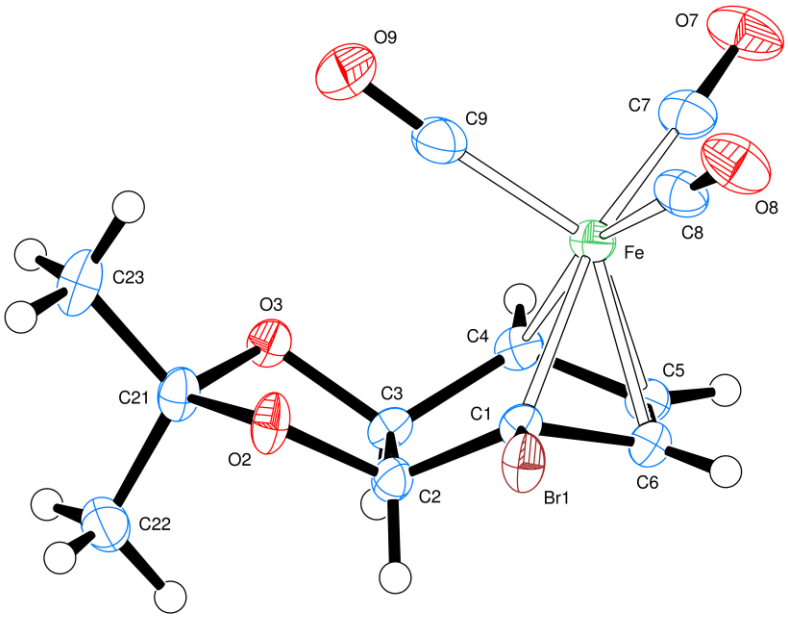
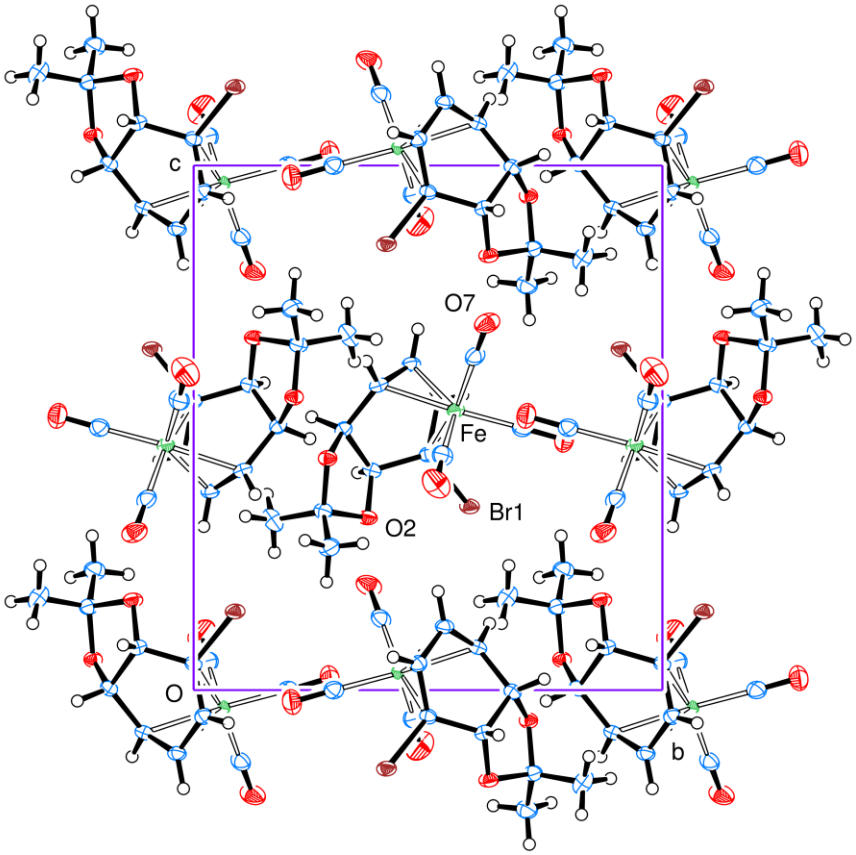


Figure 3. Packing view, down the *a* axis.



Diastereoisomer **48a**

Crystal data and structure refinement for $Fe(CO)_3\{C_6H_3Br,(H,OH)_2$

Identification code	sarahd2
Elemental formula	C9 H7 Br Fe O5
Formula weight	330.91
Crystal system, space group	orthorhombic, P 2_1 2_1 2_1
Unit cell dimensions	a = 9.3950(2) Å α = 90 ° b = 9.4086(2) Å β = 90 ° c = 25.3122(8) Å γ = 90 °
Volume	2237.44(10) $Å^3$
Z, Calculated density	8, 1.965 Mg/m^3
F(000)	1296
Absorption coefficient	4.920 mm^{-1}
Temperature	140(1) K
Wavelength	0.71073 Å
Crystal colour, shape	colourless plate
Crystal size	0.28 x 0.13 x 0.045 mm

Crystal mounting: on a glass fibre, in oil, fixed in cold N_2 stream

On the diffractometer:

Theta range for data collection	3.168 to 29.999 °
Limiting indices	-13<=h<=13, -13<=k<=13, -35<=l<=35
Completeness to theta = 25.242	99.7 %

Absorption correction: Semi-empirical from equivalents

Max. and min. transmission: 1.00000 and 0.41453

Reflections collected (not including absences) 45883

No. of unique reflections: 6523 [R(int) for equivalents = 0.070]

No. of 'observed' reflections ($I > 2\sigma_I$) 5793

Structure determined by:	direct methods, in SHELXS
Refinement:	Full-matrix least-squares on F^2, in SHELXL
Data / restraints / parameters	6523 / 3 / 302
Goodness-of-fit on F^2	1.199
Final R indices ('observed' data)	R_1 = 0.054, wR_2 = 0.112
Final R indices (all data)	R_1 = 0.065, wR_2 = 0.115
Reflections weighted: $w = [\sigma^2(Fo^2)+(0.0350P)^2+7.3750P]^{-1}$ where $P=(Fo^2+2Fc^2)/3$	
Absolute structure parameter	-0.008(5)
Extinction coefficient	n/a
Largest diff. peak and hole	1.42 and -0.85 e.Å^{-3}
Location of largest difference peak	close to Br(21)

Table 1. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^4). U(eq) is defined as one third of the trace of the orthogonalized Uij tensor. E.s.ds are in parentheses.

	x	y	z	U(eq)
Fe(1)	9370.3(11)	7617.7(11)	895.1(4)	191(2)
C(11)	10503(8)	9117(7)	1328(3)	198(13)
Br(11)	10065.0(9)	11109.8(9)	1306.6(4)	325(2)
C(12)	10724(8)	8636(7)	1893(3)	195(14)
O(12)	9502(6)	8927(6)	2206(2)	269(11)
C(13)	10941(9)	6976(8)	1895(3)	233(15)
O(13)	9926(7)	6310(6)	2228(2)	302(13)
C(14)	10812(8)	6391(8)	1346(3)	217(15)
C(15)	11489(8)	7087(9)	914(3)	274(17)
C(16)	11345(9)	8580(9)	909(3)	258(16)
C(17)	8907(10)	6140(11)	486(3)	319(19)
O(17)	8629(8)	5188(8)	224(3)	500(20)
C(18)	8597(9)	8851(10)	447(3)	264(16)
O(18)	8049(8)	9633(8)	162(3)	406(16)
C(19)	7917(8)	7535(7)	1352(3)	222(14)
O(19)	6940(6)	7524(6)	1625(3)	315(13)
Fe(2)	4563.7(11)	2915.5(12)	1127.0(4)	212(2)
C(21)	6432(7)	2564(7)	1544(3)	191(14)
Br(21)	7804.4(8)	4028.5(8)	1686.7(3)	244(2)
C(22)	6194(8)	1644(8)	2024(3)	201(14)
O(22)	5761(6)	2496(6)	2461(2)	232(11)
C(23)	5050(9)	506(8)	1887(3)	236(15)
O(23)	3934(6)	549(7)	2270(2)	296(13)
C(24)	4481(9)	742(8)	1341(3)	271(16)
C(25)	5398(9)	998(10)	921(3)	304(17)
C(26)	6505(9)	1958(9)	1029(3)	264(17)
C(27)	3160(10)	2757(10)	651(4)	330(20)
O(27)	2257(8)	2623(9)	348(3)	510(20)
C(28)	5102(10)	4602(10)	859(4)	344(19)
O(28)	5429(8)	5686(8)	696(3)	520(20)
C(29)	3552(8)	3527(9)	1680(4)	269(17)
O(29)	2912(7)	3951(8)	2028(3)	434(16)

Table 2. Molecular dimensions. Bond lengths are in Ångstroms, angles in degrees. E.s.ds are in parentheses.

Fe(1)-C(18)	1.778(9)	Fe(2)-C(29)	1.788(9)
Fe(1)-C(17)	1.787(10)	Fe(2)-C(27)	1.793(9)
Fe(1)-C(19)	1.791(8)	Fe(2)-C(28)	1.798(9)
Fe(1)-C(15)	2.053(8)	Fe(2)-C(25)	2.035(9)
Fe(1)-C(16)	2.064(8)	Fe(2)-C(26)	2.050(8)
Fe(1)-C(11)	2.078(7)	Fe(2)-C(21)	2.075(7)
Fe(1)-C(14)	2.115(8)	Fe(2)-C(24)	2.117(8)
C(11)-C(16)	1.415(10)	C(21)-C(26)	1.424(10)
C(11)-C(12)	1.516(10)	C(21)-C(22)	1.509(10)
C(11)-Br(11)	1.920(7)	C(21)-Br(21)	1.921(7)
C(12)-O(12)	1.421(9)	C(22)-O(22)	1.424(9)
C(12)-C(13)	1.575(10)	C(22)-C(23)	1.557(10)
O(12)-H(12O)	0.80(3)	O(22)-H(22O)	0.81(3)
C(13)-O(13)	1.419(10)	C(23)-O(23)	1.429(10)
C(13)-C(14)	1.499(11)	C(23)-C(24)	1.497(11)
O(13)-H(13O)	0.81(3)	O(23)-H(23O)	0.820 (0)
C(14)-C(15)	1.424(12)	C(24)-C(25)	1.391(12)
C(15)-C(16)	1.411(11)	C(25)-C(26)	1.405(12)
C(17)-O(17)	1.145(11)	C(27)-O(27)	1.150(11)
C(18)-O(18)	1.152(10)	C(28)-O(28)	1.142(11)
C(19)-O(19)	1.149(10)	C(29)-O(29)	1.138(11)
C(18)-Fe(1)-C(17)	92.2(4)	C(19)-Fe(1)-C(15)	135.5(4)
C(18)-Fe(1)-C(19)	97.4(4)	C(18)-Fe(1)-C(16)	95.3(4)
C(17)-Fe(1)-C(19)	98.9(4)	C(17)-Fe(1)-C(16)	124.7(4)
C(18)-Fe(1)-C(15)	124.8(4)	C(19)-Fe(1)-C(16)	133.9(3)
C(17)-Fe(1)-C(15)	93.5(4)	C(15)-Fe(1)-C(16)	40.1(3)

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      C(18)-Fe(1)-C(11)
95.9(3)
      C(17)-Fe(1)-C(11)
163.3(4)
      C(19)-Fe(1)-C(11)
94.6(3)
      C(15)-Fe(1)-C(11)
69.9(3)
      C(16)-Fe(1)-C(11)
40.0(3)
      C(18)-Fe(1)-C(14)
164.3(4)
      C(17)-Fe(1)-C(14)
92.5(4)
      C(19)-Fe(1)-C(14)
96.7(3)
      C(15)-Fe(1)-C(14)
39.9(3)
      C(16)-Fe(1)-C(14)
69.8(3)
      C(11)-Fe(1)-C(14)
76.0(3)
      C(16)-C(11)-C(12)
121.6(7)
      C(16)-C(11)-Br(11)
116.6(6)
      C(12)-C(11)-Br(11)
110.3(5)
      C(16)-C(11)-Fe(1)
69.5(4)
      C(12)-C(11)-Fe(1)
111.4(5)
      Br(11)-C(11)-Fe(1)
122.6(4)
      O(12)-C(12)-C(11)
111.0(6)
      O(12)-C(12)-C(13)
107.1(6)
      C(11)-C(12)-C(13)
108.4(6)
      C(12)-O(12)-H(12O)
101(6)
      O(13)-C(13)-C(14)
109.6(6)
      O(13)-C(13)-C(12)
110.6(6)
      C(14)-C(13)-C(12)
110.6(6)
      C(29)-Fe(2)-C(27)
99.4(4)
      C(29)-Fe(2)-C(28)
99.3(4)
      C(27)-Fe(2)-C(28)
91.5(4)
      C(29)-Fe(2)-C(25)
133.7(4)
      C(27)-Fe(2)-C(25)
92.1(4)
      C(28)-Fe(2)-C(25)
125.2(4)
      C(29)-Fe(2)-C(26)
135.2(3)
      C(27)-Fe(2)-C(26)
122.5(4)
      C(28)-Fe(2)-C(26)
95.3(4)
      C(25)-Fe(2)-C(26)
40.2(3)
      C(29)-Fe(2)-C(21)
95.9(3)
      C(27)-Fe(2)-C(21)
162.0(4)
      C(28)-Fe(2)-C(21)
95.4(3)
      C(25)-Fe(2)-C(21)
70.3(3)
      C(26)-Fe(2)-C(21)
40.4(3)
      C(29)-Fe(2)-C(24)
95.2(3)
      C(27)-Fe(2)-C(24)
93.7(4)
      C(28)-Fe(2)-C(24)
163.6(4)
      C(25)-Fe(2)-C(24)
39.1(3)
      C(26)-Fe(2)-C(24)
68.9(3)
      C(21)-Fe(2)-C(24)
75.3(3)
      C(26)-C(21)-C(22)
121.0(7)
      C(26)-C(21)-Br(21)
115.2(6)
      C(22)-C(21)-Br(21)
111.1(5)
      C(26)-C(21)-Fe(2)
68.8(4)
      C(22)-C(21)-Fe(2)
112.1(5)
      Br(21)-C(21)-Fe(2)
123.3(4)
      O(22)-C(22)-C(21)
110.2(6)
      O(22)-C(22)-C(23)
111.3(6)
      C(21)-C(22)-C(23)
108.5(6)
      C(22)-O(22)-H(22O)
110(7)
      O(23)-C(23)-C(24)
111.1(7)
      O(23)-C(23)-C(22)
109.6(6)
      C(24)-C(23)-C(22)
110.5(6)
      C(13)-O(13)-H(13O)
104(7)
      C(15)-C(14)-C(13)
120.4(7)
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C(15)-C(14)-Fe(1) 67.7(4)
C(13)-C(14)-Fe(1) 110.5(5)
C(16)-C(15)-C(14) 115.0(7)
C(16)-C(15)-Fe(1) 70.4(5)
C(14)-C(15)-Fe(1) 72.4(4)
C(15)-C(16)-C(11) 113.7(7)
C(15)-C(16)-Fe(1) 69.5(5)
C(11)-C(16)-Fe(1) 70.6(4)
O(17)-C(17)-Fe(1) 179.1(9)
O(18)-C(18)-Fe(1) 177.5(8)
O(19)-C(19)-Fe(1) 176.1(7)
C(23)-O(23)-H(23O) 109.5
C(25)-C(24)-C(23) 120.7(8)
C(25)-C(24)-Fe(2) 67.3(5)
C(23)-C(24)-Fe(2) 111.5(5)
C(24)-C(25)-C(26) 114.9(7)
C(24)-C(25)-Fe(2) 73.7(5)
C(26)-C(25)-Fe(2) 70.4(5)
C(25)-C(26)-C(21) 113.6(7)
C(25)-C(26)-Fe(2) 69.3(5)
C(21)-C(26)-Fe(2) 70.8(4)
O(27)-C(27)-Fe(2) 178.4(9)
O(28)-C(28)-Fe(2) 178.7(11)
O(29)-C(29)-Fe(2) 178.3(8)

Table 3. Anisotropic displacement parameters ($Å^2$ x 10^3) for the expression:

$$\exp\{-2\pi^2(h^2a^{*2}U_{11} + \ldots + 2hka^*b^*U_{12})\}$$

E.s.ds are in parentheses.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Fe(1)	19.4(5)	19.7(5)	18.2(5)	-1.9(4)	-0.5(4)	0.1(4)
C(11)	16(3)	16(3)	27(4)	-2(3)	1(3)	-2(3)
Br(11)	31.1(4)	18.5(3)	47.8(5)	4.8(3)	-2.8(4)	-2.3(3)
C(12)	22(4)	16(3)	21(3)	-5(3)	-1(3)	-2(3)
O(12)	31(3)	25(3)	24(3)	-9(2)	5(2)	-3(3)
C(13)	24(4)	21(4)	26(4)	2(3)	-1(3)	1(3)
O(13)	41(3)	22(3)	27(3)	6(2)	2(3)	1(3)
C(14)	14(3)	19(3)	33(4)	-4(3)	0(3)	3(2)
C(15)	20(4)	29(4)	34(4)	-7(4)	2(3)	2(3)
C(16)	25(4)	27(4)	25(4)	3(3)	7(3)	1(3)
C(17)	34(5)	41(5)	20(4)	-1(4)	-2(3)	1(4)
O(17)	49(4)	51(5)	50(5)	-29(4)	-6(4)	-1(4)
C(18)	30(4)	28(4)	22(4)	-3(3)	0(3)	1(4)
O(18)	46(4)	45(4)	31(3)	5(3)	-9(3)	11(3)
C(19)	25(4)	14(3)	28(4)	-5(3)	-6(3)	-1(3)
O(19)	27(3)	23(3)	44(3)	-1(3)	9(3)	1(2)
Fe(2)	17.5(5)	22.3(5)	23.7(5)	3.9(4)	-3.5(4)	-3.5(4)
C(21)	17(3)	15(3)	26(4)	-2(3)	-2(3)	-1(3)
Br(21)	23.1(3)	17.9(3)	32.2(4)	-1.0(3)	-2.1(3)	-5.8(3)
C(22)	17(3)	18(3)	25(4)	-2(3)	-3(3)	-1(3)
O(22)	26(3)	20(3)	24(3)	-3(2)	3(2)	-2(2)
C(23)	24(4)	14(3)	33(4)	-1(3)	-1(3)	-1(3)
O(23)	28(3)	27(3)	33(3)	9(2)	5(2)	-7(2)
C(24)	29(4)	23(4)	30(4)	-4(3)	-5(3)	0(3)
C(25)	37(4)	29(4)	26(4)	-8(3)	-4(3)	-5(4)
C(26)	27(4)	30(4)	22(4)	-3(3)	0(3)	2(3)
C(27)	29(4)	34(5)	37(5)	11(4)	-4(4)	-7(4)
O(27)	48(4)	57(5)	50(4)	20(4)	-27(4)	-22(4)
C(28)	30(4)	36(4)	37(5)	12(4)	-14(4)	-11(4)
O(28)	43(4)	42(4)	71(5)	28(4)	-19(4)	-19(3)
C(29)	22(4)	25(4)	34(4)	6(3)	-3(4)	3(3)
O(29)	32(3)	47(4)	50(4)	6(4)	10(3)	16(3)

Table 4. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3). Three of the hydroxyl hydrogen atoms were located in difference maps and were refined with O-H distance constraints. All remaining hydrogen atoms were included in idealised positions with U(iso)'s set at 1.2*U(eq) or, for the methyl group hydrogen atoms, 1.5*U(eq) of the parent carbon atoms.

	x	y	z	U(iso)
H(12)	11561	9107	2044	23
H(13)	11896	6765	2029	28
H(14)	10287	5568	1287	26
H(15)	11990	6595	655	33
H(16)	11763	9157	654	31
H(22)	7087	1163	2114	24
H(23)	5497	-434	1900	28
H(23O)	4055	-85	2488	44
H(24)	3504	717	1283	33
H(25)	5287	567	593	36
H(26)	7219	2177	788	32
H(12O)	9760(90)	9620(60)	2360(30)	20(20)
H(13O)	9540(90)	6970(70)	2380(30)	30(30)
H(22O)	4950(50)	2290(100)	2550(40)	30(30)

Table 5. Torsion angles, in degrees. E.s.ds are in parentheses.

C(16)-C(11)-C(12)-O(12) -160.5(7)	C(26)-C(21)-C(22)-O(22) -163.5(7)
Br(11)-C(11)-C(12)-O(12) 57.6(7)	Br(21)-C(21)-C(22)-O(22) 56.6(7)
Fe(1)-C(11)-C(12)-O(12) -82.0(6)	Fe(2)-C(21)-C(22)-O(22) -85.7(6)
C(16)-C(11)-C(12)-C(13) -43.1(9)	C(26)-C(21)-C(22)-C(23) -41.4(9)
Br(11)-C(11)-C(12)-C(13) 174.9(5)	Br(21)-C(21)-C(22)-C(23) 178.7(5)
Fe(1)-C(11)-C(12)-C(13) 35.3(7)	Fe(2)-C(21)-C(22)-C(23) 36.4(7)
O(12)-C(12)-C(13)-O(13) -3.7(8)	O(22)-C(22)-C(23)-O(23) -5.3(8)
C(11)-C(12)-C(13)-O(13) -123.5(7)	C(21)-C(22)-C(23)-O(23) -126.6(6)
O(12)-C(12)-C(13)-C(14) 117.9(7)	O(22)-C(22)-C(23)-C(24) 117.5(7)
C(11)-C(12)-C(13)-C(14) -1.9(9)	C(21)-C(22)-C(23)-C(24) -3.9(9)
O(13)-C(13)-C(14)-C(15) 166.5(7)	O(23)-C(23)-C(24)-C(25) 168.3(7)
C(12)-C(13)-C(14)-C(15) 44.2(10)	C(22)-C(23)-C(24)-C(25) 46.4(10)
O(13)-C(13)-C(14)-Fe(1) 90.9(6)	O(23)-C(23)-C(24)-Fe(2) 92.7(7)
C(12)-C(13)-C(14)-Fe(1) -31.3(8)	C(22)-C(23)-C(24)-Fe(2) -29.1(8)
C(13)-C(14)-C(15)-C(16) -44.0(11)	C(23)-C(24)-C(25)-C(26) -43.7(11)
Fe(1)-C(14)-C(15)-C(16) 57.5(7)	Fe(2)-C(24)-C(25)-C(26) 58.6(7)
C(13)-C(14)-C(15)-Fe(1) -101.5(7)	C(23)-C(24)-C(25)-Fe(2) -102.3(7)
C(14)-C(15)-C(16)-C(11) -2.1(11)	C(24)-C(25)-C(26)-C(21) -3.7(11)
Fe(1)-C(15)-C(16)-C(11) 56.5(6)	Fe(2)-C(25)-C(26)-C(21) 56.7(6)
C(14)-C(15)-C(16)-Fe(1) -58.6(6)	C(24)-C(25)-C(26)-Fe(2) -60.4(7)
C(12)-C(11)-C(16)-C(15) 47.2(11)	C(22)-C(21)-C(26)-C(25) 47.8(10)
Br(11)-C(11)-C(16)-C(15) -173.1(6)	Br(21)-C(21)-C(26)-C(25) -173.8(6)
Fe(1)-C(11)-C(16)-C(15) -55.9(7)	Fe(2)-C(21)-C(26)-C(25) -55.9(6)
C(12)-C(11)-C(16)-Fe(1) 103.2(7)	C(22)-C(21)-C(26)-Fe(2) 103.7(7)
Br(11)-C(11)-C(16)-Fe(1) -117.1(5)	Br(21)-C(21)-C(26)-Fe(2) -117.9(5)

Table 6. Hydrogen bonds, in Ångstroms and degrees.

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(13)-H(13)...O(22)#1	0.98	2.64	3.535(10)	151.5
C(14)-H(14)...Br(21)	0.93	2.93	3.697(7)	141.2
C(23)-H(23)...O(19)#2	0.98	2.45	3.386(10)	159.2
O(22)-H(22O)...O(23)	0.81(3)	2.02(8)	2.557(8)	123(8)
O(12)-H(12O)...O(13)#1	0.80(3)	1.92(3)	2.715(8)	171(9)
O(13)-H(13O)...O(12)	0.81(3)	1.89(7)	2.494(8)	130(9)
O(23)-H(23O)...Br(21)#3	0.82	2.85	3.419(6)	128.4
O(23)-H(23O)...O(22)#3	0.82	2.29	2.966(8)	140.7

Symmetry transformations used to generate equivalent atoms:
#1 : 2-x, y+1/2, 1/2-z #2 : x, y-1, z #3 : 1-x, y-1/2, 1/2-z

Crystal structure analysis of Fe $(CO)_3$ $\{C_6H_3$-Br,$(H,OH)_2$

Crystal data: $C_9H_7FeO_5$, M = 330.91. Orthorhombic, space group $P2_12_12_1$ (no. 19), a = 9.3950(2), b = 9.4086(2), c = 25.3122(8) Å, V = 2237.44(10) $Å^3$. Z = 8, Dc = 1.965 g cm^{-3}, F(000) = 1296, T = 140(1) K, μ(Mo-Kα) = 49.2 cm^{-1}, λ(Mo-Kα) = 0.71073 Å.

Crystals are colourless plates. A single crystal, *ca* 0.045 x 0.13 x 0.28 mm, was mounted on a glass fibre and fixed in the cold nitrogen stream on an Oxford Diffraction Xcalibur-3/Sapphire3-CCD diffractometer, equipped with Mo-Kα radiation and graphite monochromator. Intensity data were measured by thin-slice ω- and φ-scans. Total no. of reflections recorded, to θ_{max} = 30°, was 45883 of which 6523 were unique (Rint = 0.070); 5793 were 'observed' with $I > 2\sigma_I$.

Data were processed using the CrysAlisPro-CCD and -RED (1) programs. The structure was determined by the direct methods routines in the SHELXS program (2A) and refined by full-matrix least-squares methods, on F^2's, in SHELXL (2B). The non-hydrogen atoms were refined with anisotropic thermal parameters. Three of the hydroxyl hydrogen atoms were located in difference maps; the location of the fourth was estimated, and all four were refined with O-H distance constraints. The remaining hydrogen atoms were included in idealised positions and their Uiso values were set to ride on the Ueq values of the parent carbon atoms. At the conclusion of the refinement, wR_2 = 0.115 and R_1 = 0.065 (2B) for all 6523 reflections weighted $w = [\sigma^2(F_o^2) + (0.0350P)^2 + 7.375P]^{-1}$ with $P = (F_o^2 + 2F_c^2)/3$; for the 'observed' data only, R_1 = 0.054.

In the final difference map, the highest peaks (to *ca* 1.4 eÅ^{-3}) were close to the bromine atoms.

Scattering factors for neutral atoms were taken from reference (3). Computer programs used in this analysis have been noted above, and were run through WinGX (4) on a Dell Optiplex 755 PC at the University of East Anglia.

References

- Programs CrysAlisPro, Oxford Diffraction Ltd., Abingdon, UK (2010).
- G. M. Sheldrick, SHELX-97 – Programs for crystal structure determination (SHELXS) and refinement (SHELXL), *Acta Cryst.* (2008) A**64**, 112-122 and (2015) E**71**, 3-8.
- *'International Tables for X-ray Crystallography'*, Kluwer Academic Publishers, Dordrecht (1992). Vol. C, pp. 500, 219 and 193.
- L. J. Farrugia, (2012) *J. Appl. Cryst.* **45**, 849–854.

Notes on the structure

There are two independent, but essentially identical, molecules in the crystal, Figures 1 and 2. The six-membered rings are boat-shaped, with the conjugated section, C1-4 in each molecule coordinating an iron atom, and the other half supporting two hydroxyl groups, both in axial sites, directed to the same side of the ring as the iron atom. The conformations about the C2-C3 bonds in each molecule are eclipsed and the hydroxyl hydrogen atoms of O(13) and O(22) form intramolecular hydrogen bonds with the neighbouring oxygen atoms. The hydrogen atoms on O(12) and O(23) form hydrogen bonds that link molecules in chains along the *b* axis, Figure 3; the O(12)-H(12o)…O(13') is a well-defined hydrogen bond, whereas H(23o) appears to form a bifurcated link to O(22) and Br(21) in the next molecule.

The iron atoms have a three-legged stool coordination pattern, with the plane of the C1,4-6 atoms forming the seat and three carbonyl ligands as the legs. The orientation of the legs is such that there is pseudo-mirror symmetry in the molecule with the mirror plane passing through the iron atom, the carbonyl ligand of O9 and the mid-points of the C5-C6 and C2-C3 bonds, Figure 4. The molecules differ principally in the orientations of the hydroxyl hydrogen atoms: in the molecule of Fe(1), the intramolecular hydrogen bond is from the O3 to O2 atom whereas in the molecule of Fe(2), the bond is from O2 to O3.

Figure 1. View of the two independent molecules of $Fe(CO)_3\{C_6H_3\text{-}Br,(H,OH)_2$, showing their different orientations in the crystal. The atom numbering scheme is indicated. Thermal ellipsoids are drawn at the 50% probability level.

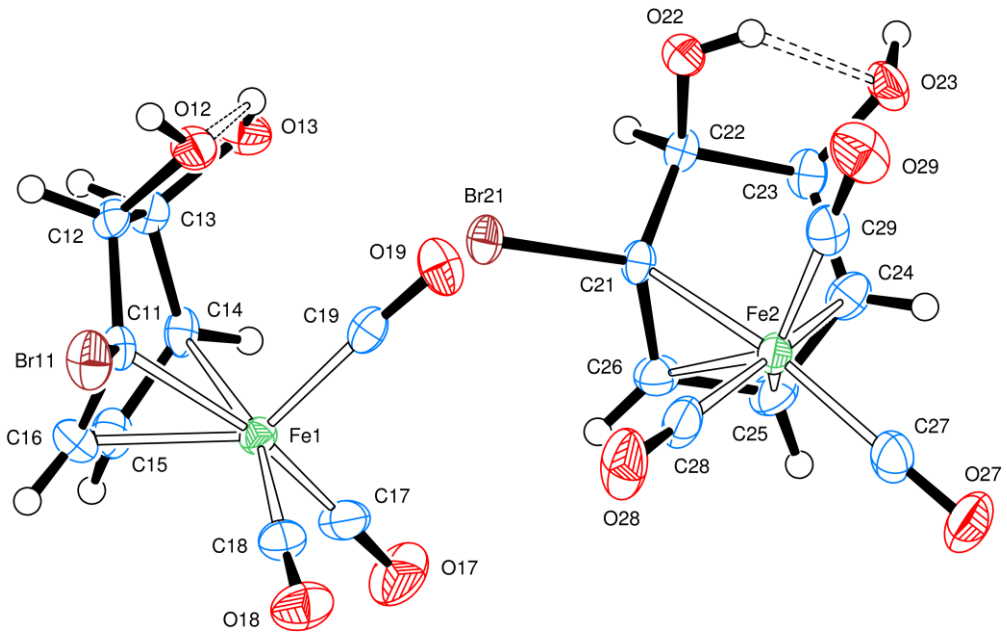
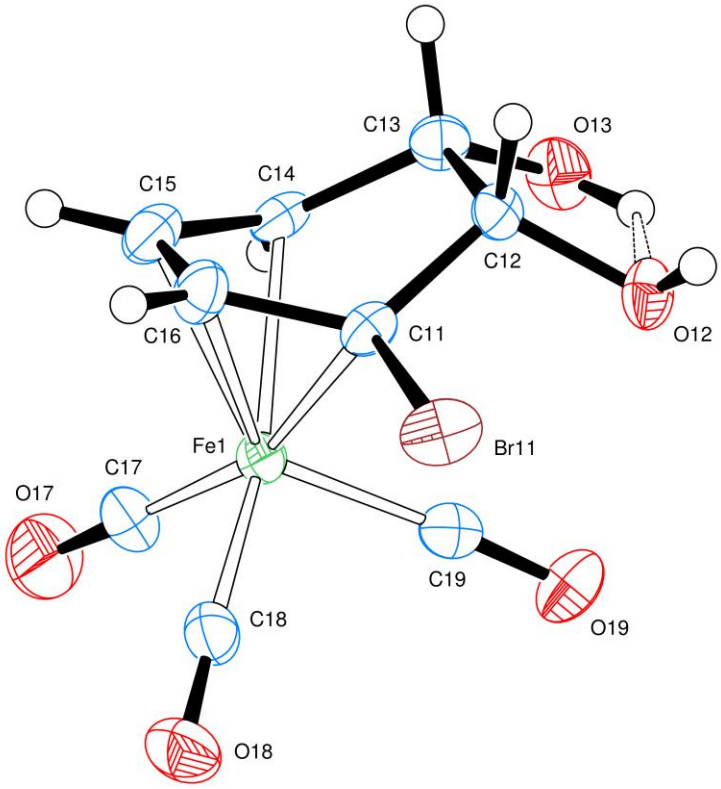


Figure 2. Views of the two independent molecules, showing their similarities.



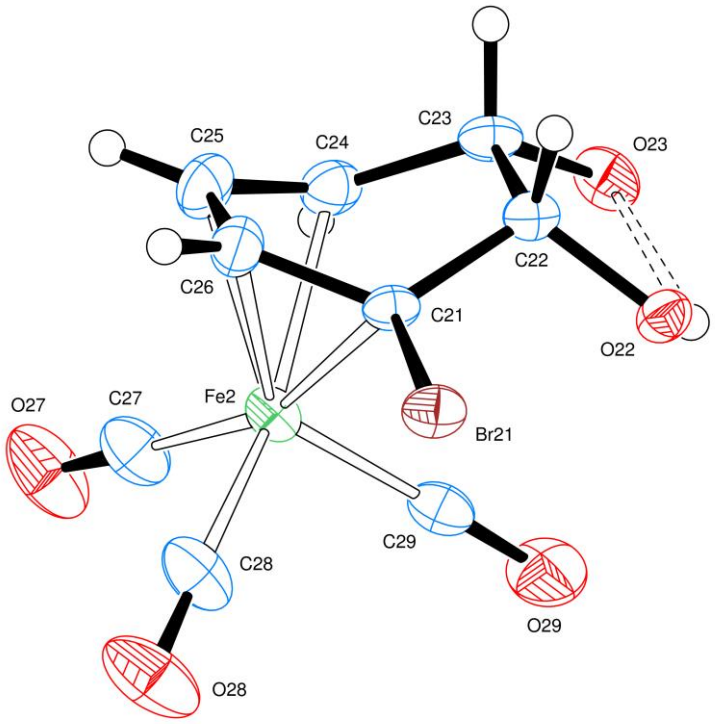


Figure 3. Packing of the molecules, viewed along the *a* axis. The molecules are linked, through hydrogen bonds, in chains parallel to the *b* axis.

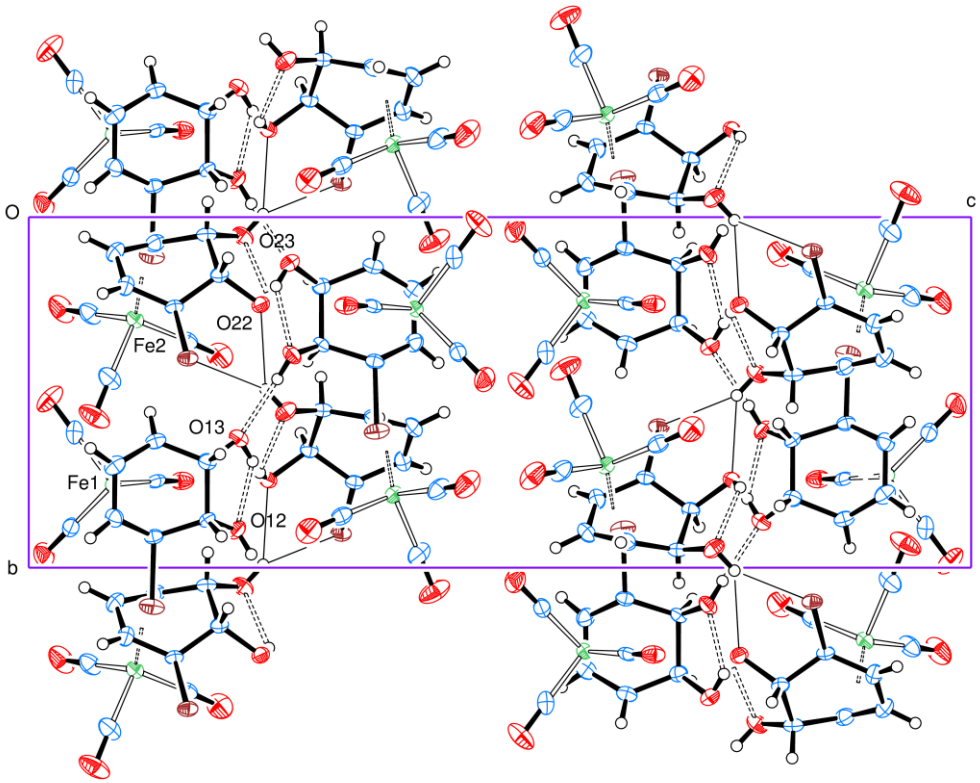
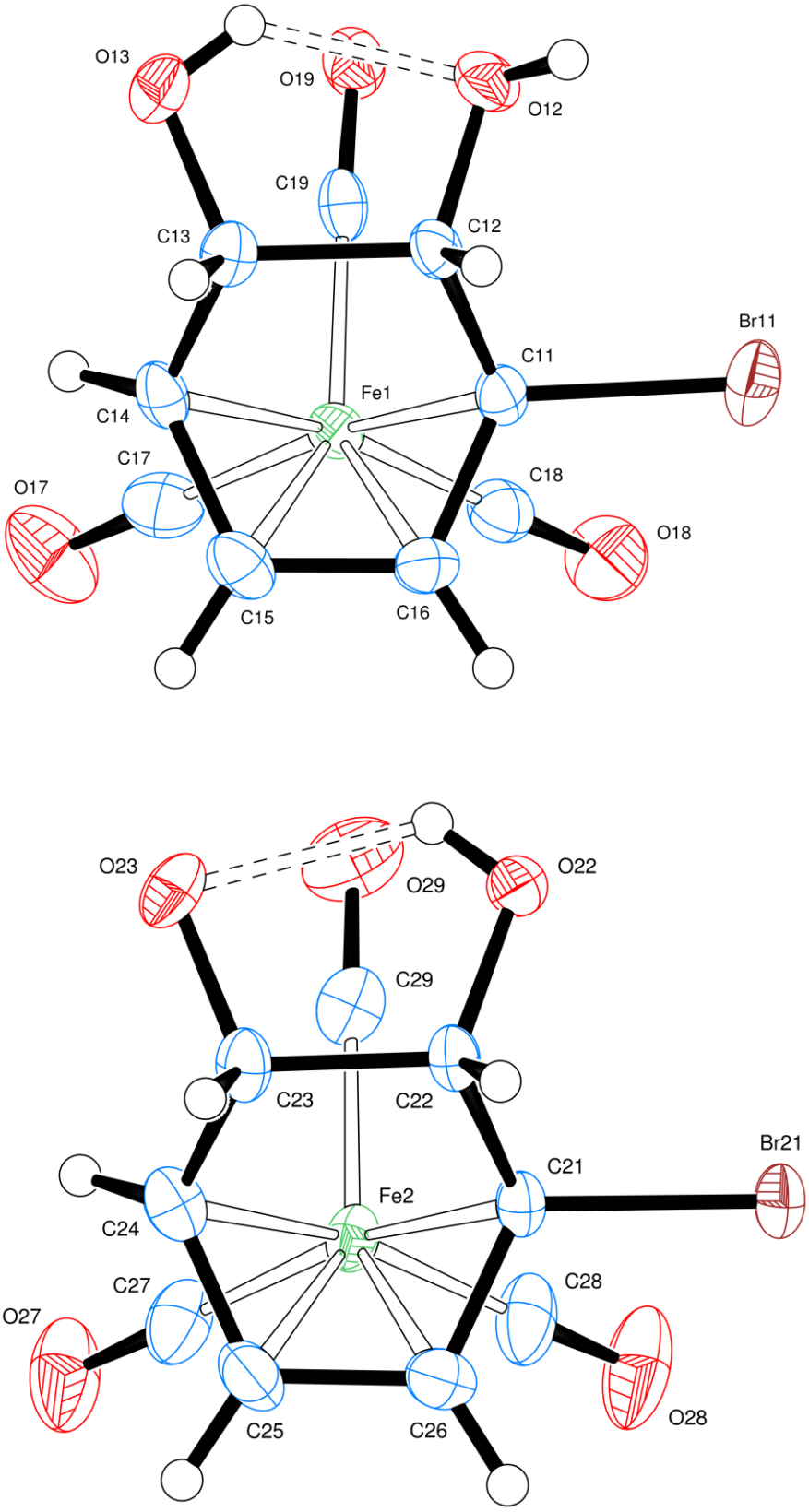


Figure 4. The two molecules viewed on to the mean-plane of the four coordinating atoms, C1,4-6 in each molecule.

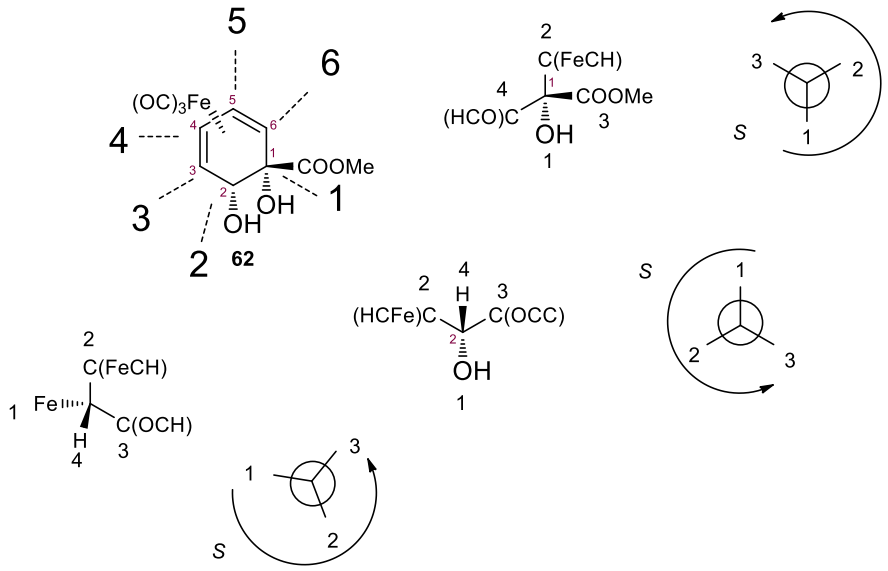


Appendix 2

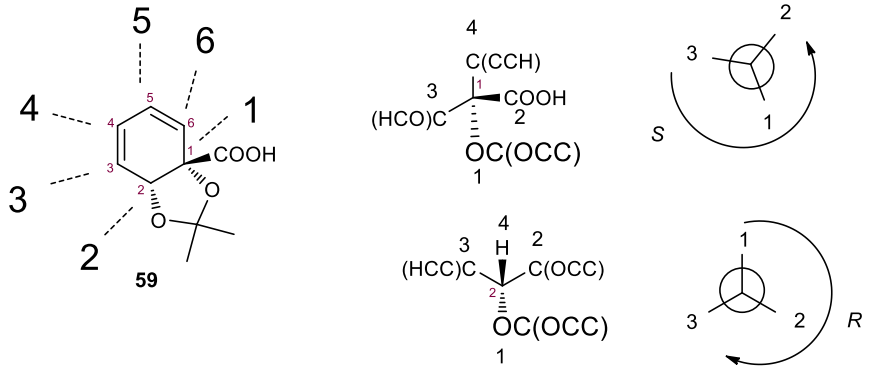
Assignment of Absolute Configurations

The method Sarah used in her thesis to assign (R) and (S) labels was based on earlier papers by Stephenson, perhaps most significantly, on his definitive 1994 publication relating the configurations of tricarbonyliron complexes to the signs of $\Delta\varepsilon$ in the bands of their circular dichroism spectra. She was aware of other assignment systems for planar chirality. Which method to use in the final version of the thesis would have been discussed before submission, but there is an argument in the interests of clarity for allowing the present method to be retained in the thesis to make the comparison with other P. putida derived enantiopure complexes more straight-forward.

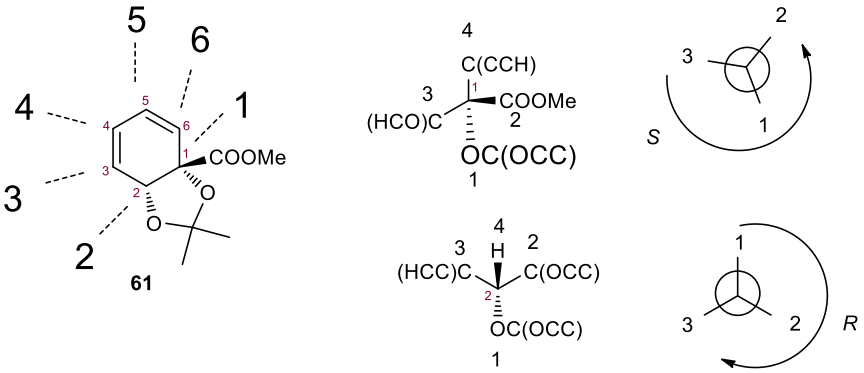
(−)-(3*S*)-Tricarbonyl[η^4-(1*S*,2*S*)-methyl 1,2-dihydroxycyclohexa-3,5-dienecarboxylate]-iron(0) **62**.



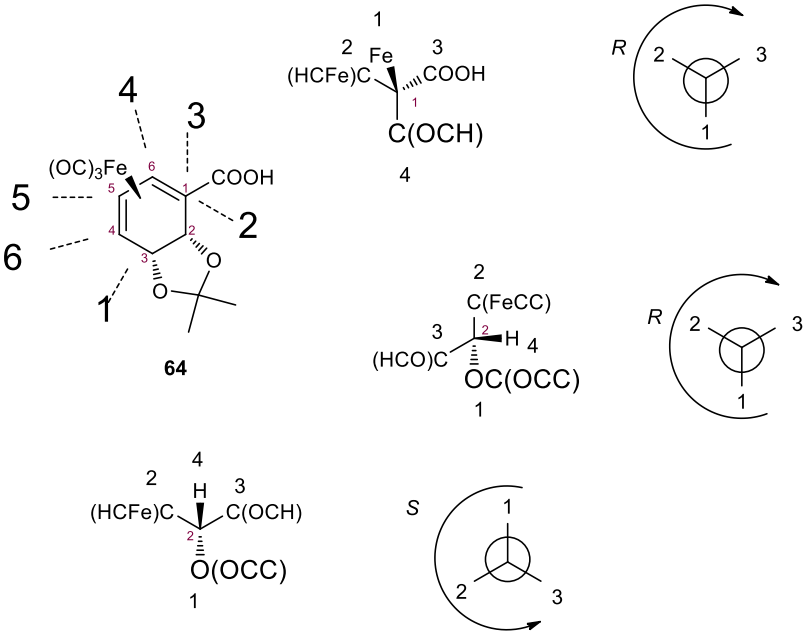
(1*S*,2*R*)-1,2-*O*-isopropylidenedioxycyclohexa-3,5-diene carboxylic acid **59**.



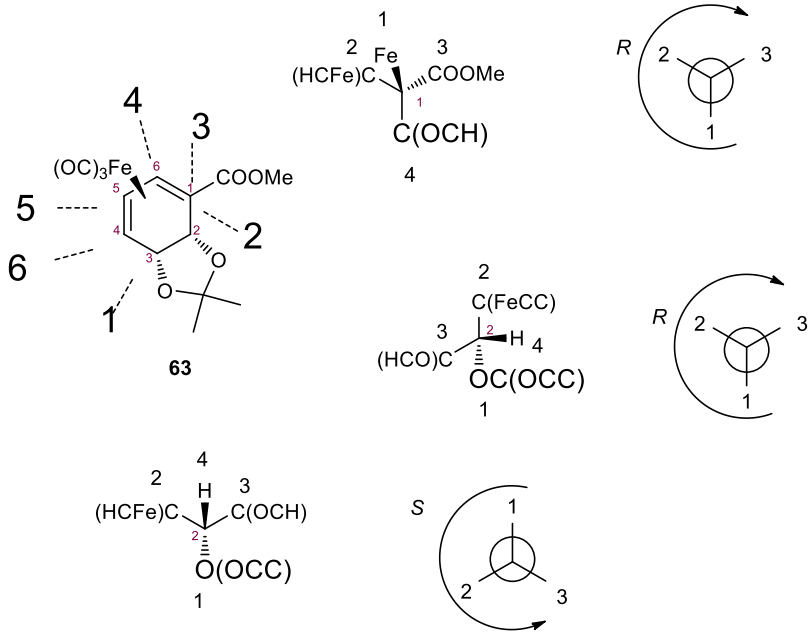
(1*S*,2*R*)-methyl 1,2-*O*-isopropylidenedioxycyclohexa-3,5-dienecarboxylate **61**.



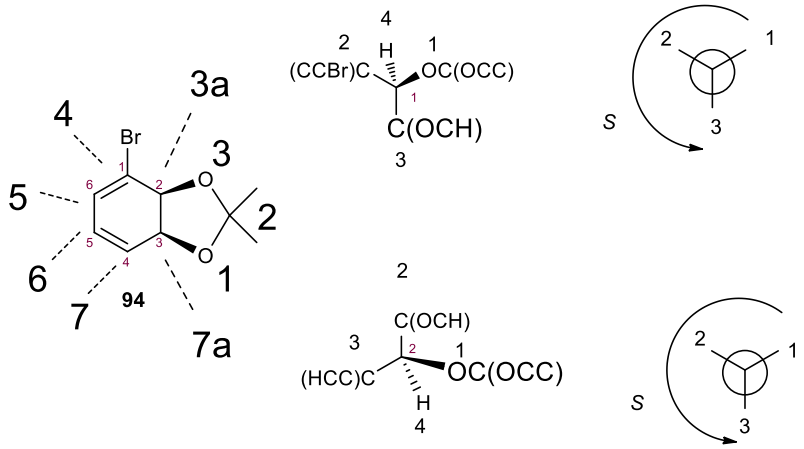
(−)-(3*R*)-Tricarbonyl[(η^4-(1*S*,2*R*) 1,2-isopropylidenedioxycyclohexa-3,5-dienecarboxylic acid]iron(0) **64**.



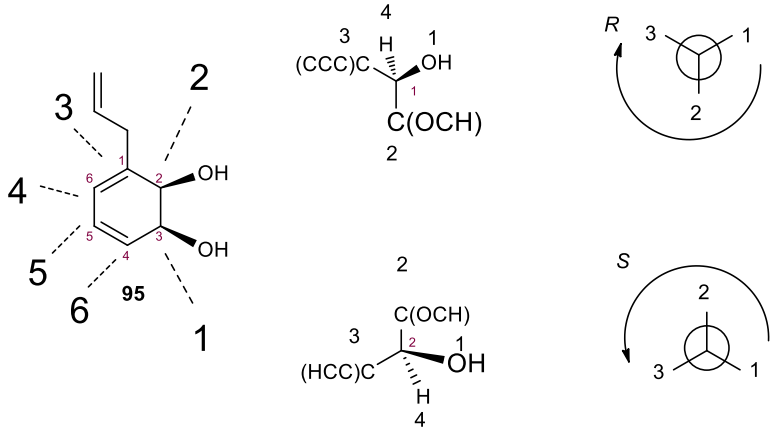
(−)-(3*R*)-Tricarbonyl[η^4-(1*S*,2*R*)-1,2-isopropylidenedioxycyclohexa-3,5-dienecarboxylic acid methyl ester]iron(0) **63**.



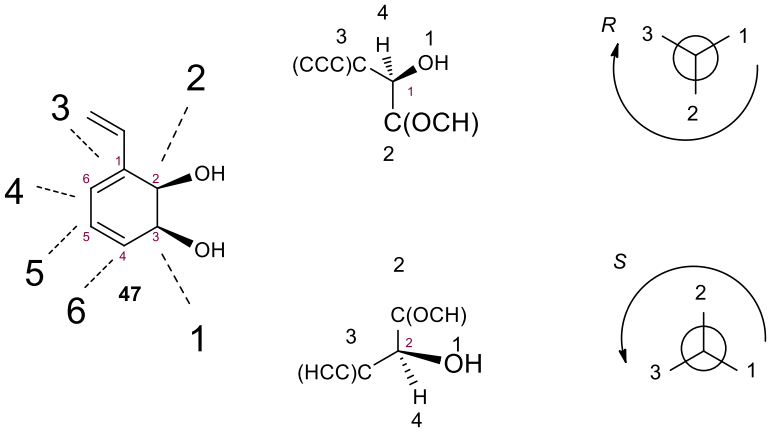
(3a*S*,7a*S*)-4-Bromo-3a,7a-dihydro-2,2-dimethyl-1,3-benzodioxole **94**.



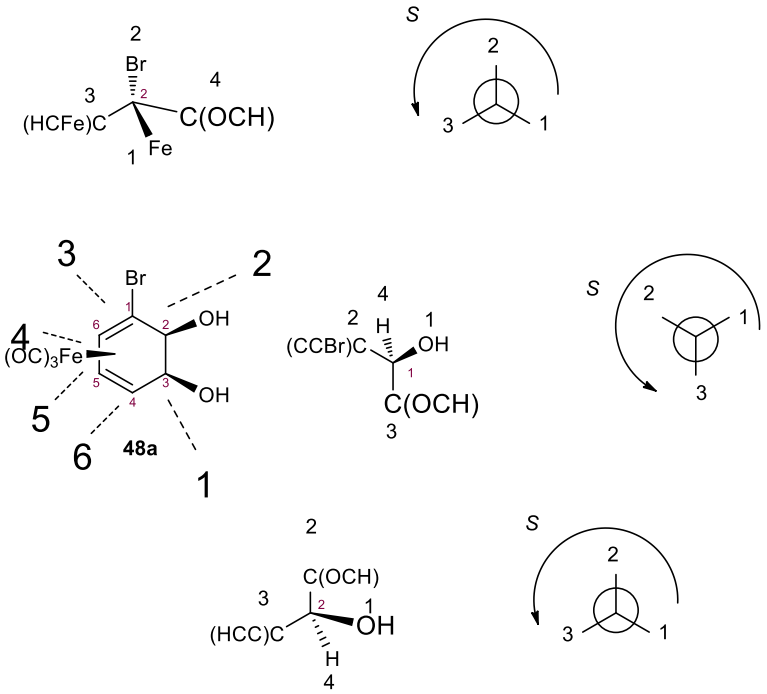
Cis-(1*S*,2*R*)-1,2-dihydroxy-3-allylcyclohexa-3,5-diene **95**.



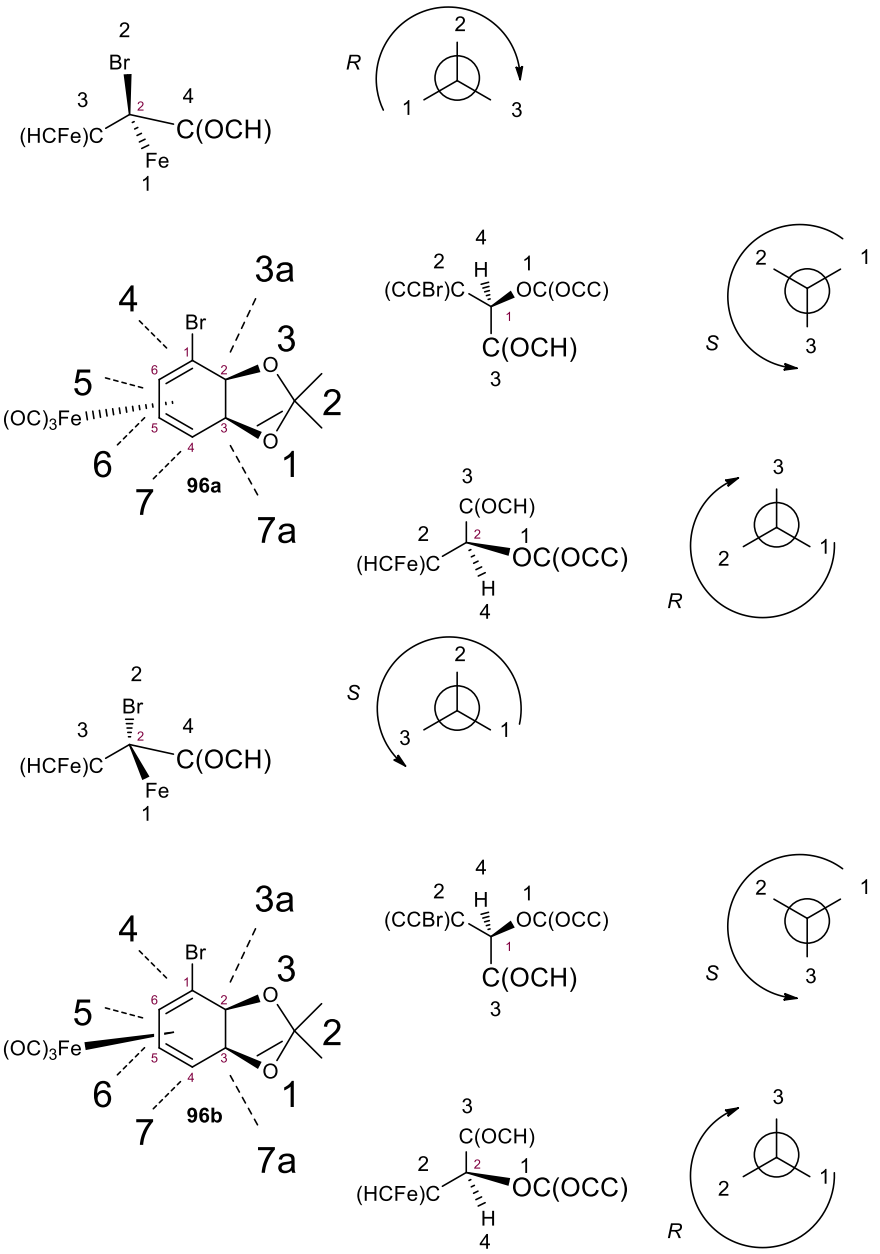
*Cis-(*1*S*,2*R*)-1,2-dihydroxy-3-vinylcyclohexa-3,5-diene **47**.



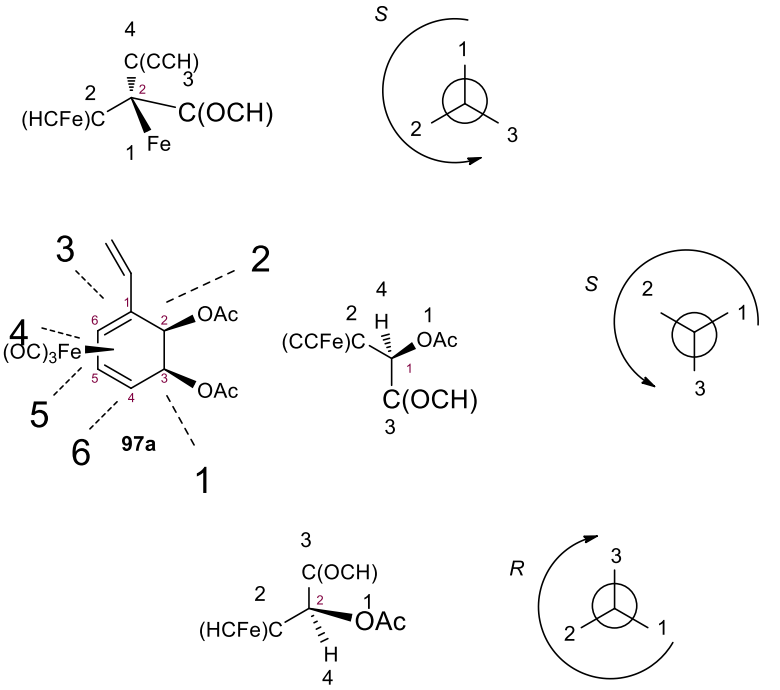
(3*S*)-Tricarbonyl(3-bromo-(1*S*,2*S*)-3,5-cyclohexadiene-1,2-diol)iron(0) **48a**.



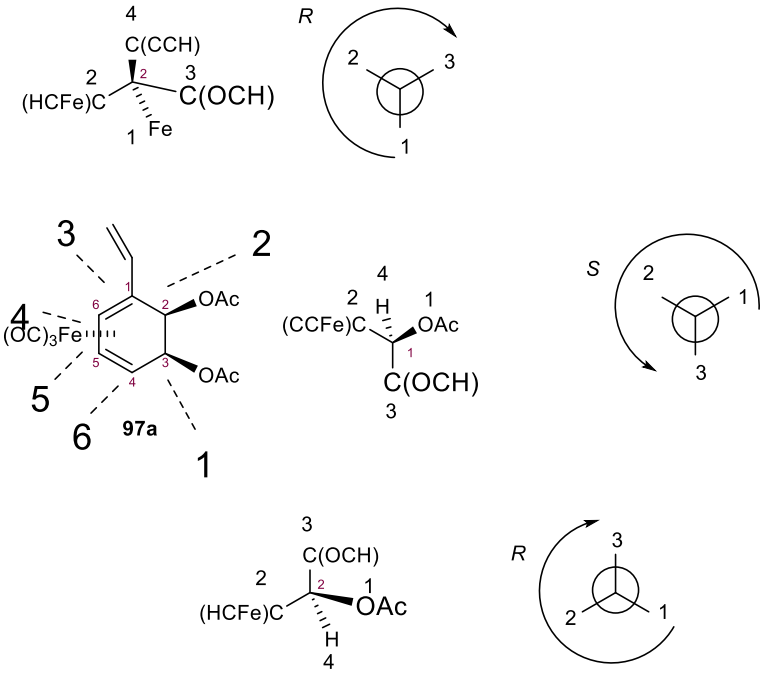
(4*R*)-Tricarbonyl[(3a*S*,7a*R*)-4-bromo-3a,7a-dihydro-2,2-dimethyl-1,3-benzodioxole]iron(0) **96a** and (4*S*)-Tricarbonyl[(3a*S*,7a*R*)-4-bromo-3a,7a-dihydro-2,2-dimethyl-1,3-benzodioxole]-iron(0) **96b**.



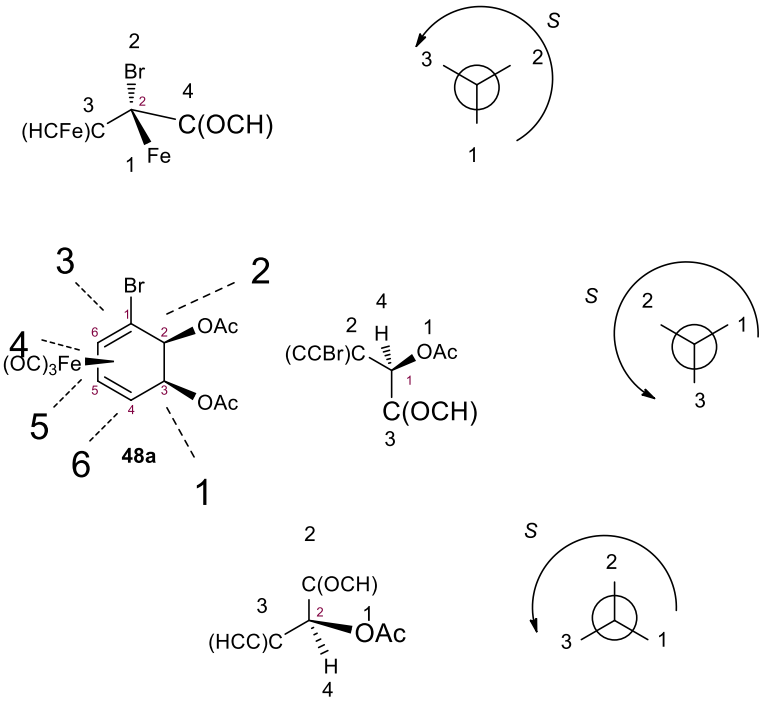
(3*S*)-Tricarbonyl[(1*R*,2*S*)-1,2-dihydroxy-3-vinylcyclohexa-3,5-diene diacetate]iron(0) **97a**.



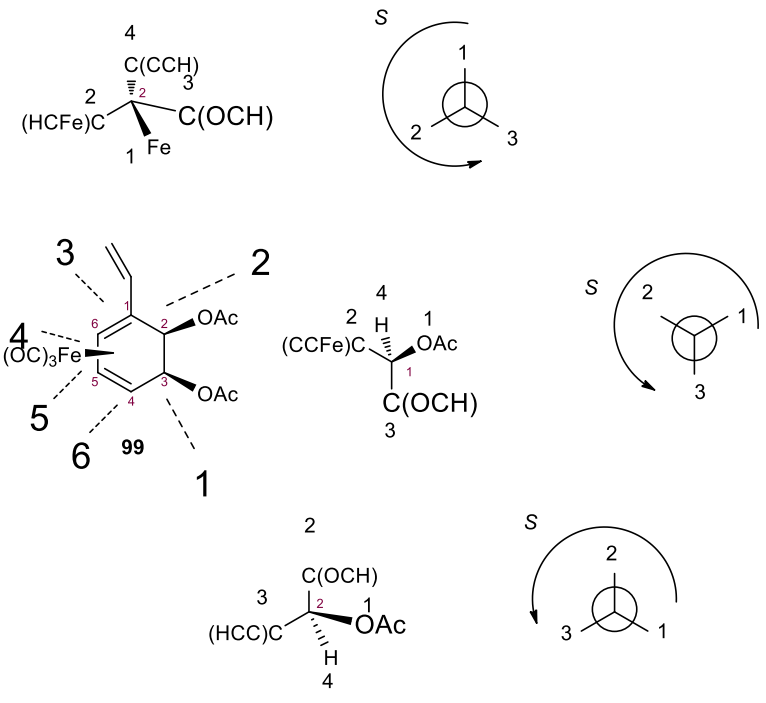
(3*R*)-Tricarbonyl[(1*R*,2*S*)-1,2-dihydroxy-3-vinylcyclohexa-3,5-diene diacetate]iron(0) **97b**.



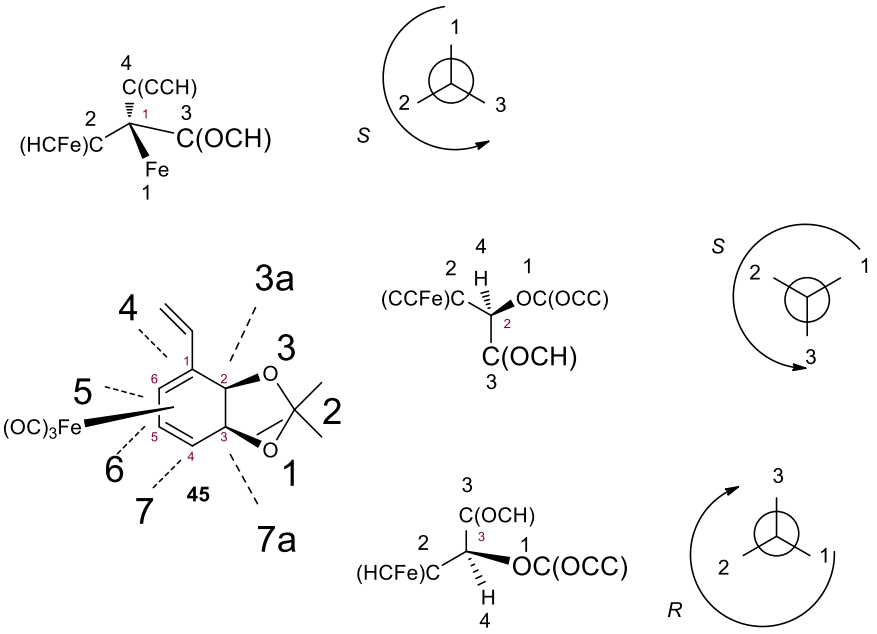
(3*S*)-Tricarbonyl[(1*S*,2*S*)-3-bromocyclohexa-3,5-diene-1,2-diyl diacetate]iron(0) **98**.



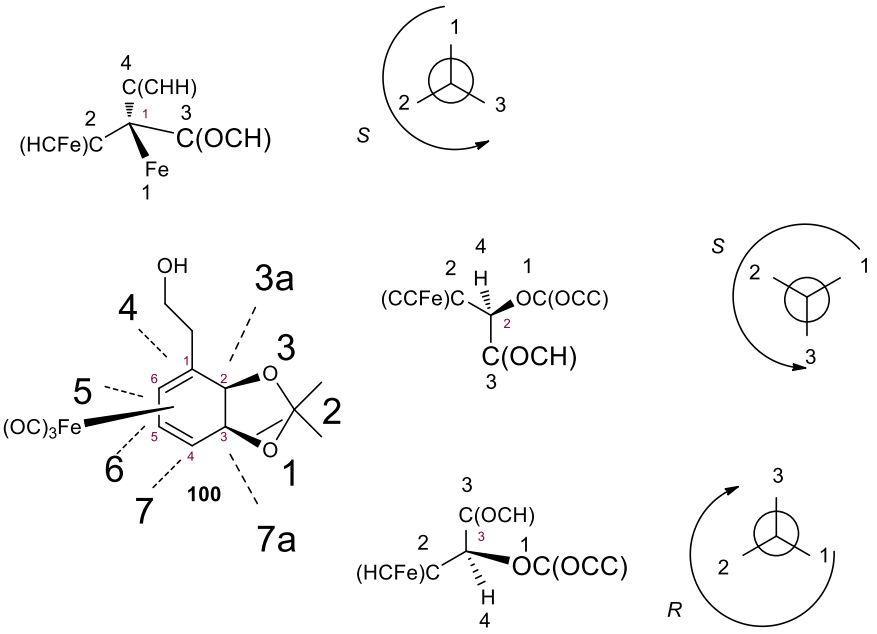
(3*S*)-Tricarbonyl[(1*S*,2*S*)-3-vinylcyclohexa-3,5-diene-1,2-diyl diacetate]iron(0) **99**.



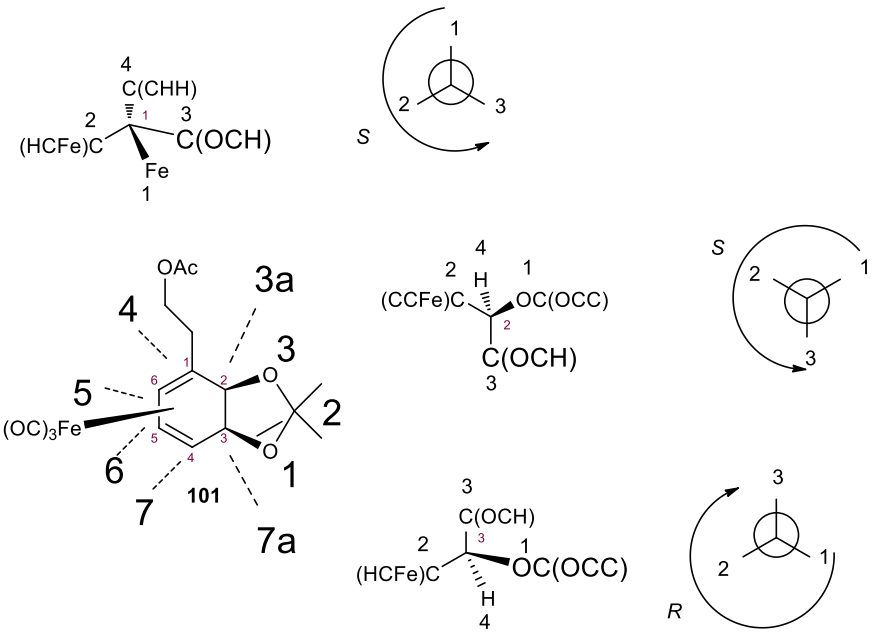
(4*S*)-Tricarbonyl[(3a*S*,7a*R*)-2,2-dimethyl-4-vinyl-3a,7a-dihydrobenzo[1,3]dioxole]iron(0) **45**.



(4*S*)-Tricarbonyl{2-[(3a*S*,7a*R*)-2,2-dimethyl-3a,7a-dihydrobenzo[1,3]dioxol-4-yl]-ethanol}iron(0) **100**.



(4*S*)-Tricarbonyl{2-[(3a*S*,7a*R*)-2,2-dimethyl-3a,7a-dihydrobenzo[1,3]dioxol-4-yl]ethyl acetate}iron(0) **101**.



Chemical Formula: $C_{16}H_{18}FeO_7$

Molecular Weight: 378.1580

References

[1] W. Meissner; "Über Pflanzenalkalien: II. Über ein neues Pflanzenalkali (Alkaloid)" (On plant alkalis: II. On a new plant alkali (alkaloid)); *Journal für Chemie und Physik*, **1819**, *25*, 379 - 381.

[2] A. Luch; Molecular, clinical and environmental toxicology; *Springer*; **2009**, 20.

[3] M. Hesse; *J. Nat. Prod.*, **2003**, *66*, 901-902.

[4] *G. Safronich; The chemical analysis of medicinal plants*, **1983,** 122-123.

[5] D. F. Rhoades, Evolution of Plant Chemical Defense against Herbivores". **1979** In G. A. Rosenthal and D. H. Janzen, *Herbivores: Their Interaction with Secondary Plant Metabolites*, New York, **1979**, 41.

[6] E. Fattorusso and O. Taglialatela-Scafati, *Modern Alkaloids: Structure, Isolation, Synthesis and Biology*, *Wiley-VCH, **2008,** 53.*

[7] H. Manfred, *Alkaloids: Nature's Curse or Blessing, **2002**, 1.*

[8] Z. Jin, *Nat. Prod. Rep.*, **2013**, *30*, 849-868.

[9] A. Kornienko and A. Evidente, *Chem. Rev.*, **2008**, *108*, 1982-2014.

[10] Y. Nakagawa, S. Uyeo and H. Yajima, *Chemistry and Industry (London)*, **1956**, 1238-1239.

[11] H. Maomao, Q. Chunrong, G. Oude, H. Xianming and H. Xuechuan Hong, *RSC Adv.*, **2015**, 5, 16562.

[12] J. He, W. B. Qi, L. Wang, J. Tian, P. R. Jiao, G. Q. Liu, W. C. Ye and M. Liao, *Influenza Other Respir. Viruses*, **2013**, 7, 922-93.

[13] S.-D. Huang, Y. Zhang, H.-P. He, S.-F. Li, G.-H. Tang, D.-Z. Chen, M.-M. Cao, Y.-T. Di and X.-J. Hao, *Chin. J. Nat. Med*., **2013**, 11, 406-410.

[14] J. C. Cedron, D. Gutierrez, N. Flores, A. G. Ravelo and A. Estevez-Braun, *Eur. J. Med. Chem.*, **2013**, 63, 722-730.

[15] K. Kotera, Y. Hamada and R. Nakane, *Tetrahedron*, **1968**, 24, 759.

[16] J. Katakawa, H. Meguri , and H. Irie, *Hetreocycles*, **1984**, 22, 2213-2216.

[17] D. T. Gibson, J. R. Koch, and R. E. Kallio, *Biochemistry*, **1968**, 7, 2653-2662.

[18] R. E. Parales, S. M. Resnick, C.-L. Yu, D. R. Boyd, N. D. Sharma, and D. T. Gibson, *J. Bacteriol.*, **2000**, 19, 5495-5504.

[19] D. T. Gibson and R. E. Parales, *Curr. Opin. Biotech*., **2000**, 11, 236-243.

[20] B. Keenan and T. Wood, *Appl. Microbiol. Biotechnol.*, **2006**, 73, 827-838.

[21] K. Furukawa, *Curr. Opin. Biotech*., **2000**, 11, 244-249.

[22] J. R. Mason, and R. Cammack, *Ann. Rev. Microbiol.,* 1992, 46, 277-305.

[23] Y. Feng, C.-Y. Ke, G. Xue, and L. Que, *Chem.Commun*., **2009**, 50-52.

[24] W. B. Motherwell and A. S. Williams, *Angew. Chem. Intl. Edn*., **1995**, 34, 2031-2033.

[25] J. B. Broderick, *Essays Biochem.* **1999**, 34, 173-189.

[26] S. Fetzner, *Appl. Environ. Microbiol*., **2012**, 78, 2505-2514.

[27] C. S. Harwood, and R. Parales, *Ann. Rev. Microbiol*., **1996**, 50, 553-90.

[28] M. M. Mbughuni, M. Chakrabarti, J. A. Hayden, K. K. Meier, J. J. Dalluge, M. P. Hendrich, E. Munck and J. D. Lipscomb, *Biochemistry,* **2011**, 50, 10262-10274.

[29] D. R. Boyd, N. D. Sharma, M. V. Hand, M. R. Groocock, N. A. Kerley, H. Dalton, J. Chima and G. N. J. Sheldrake, *Chem. Soc., Chem. Commun*., **1993**, 974-976.

[30] G.-Q. Chen, *Microbiology Monographs,* **2010**, *14*, 427-446.

[31] B. Günzel, C. H. Berke, S. Ernst, J. Weitkamp and W.-D. Deckwer, *Chem. Ing. Tech*., **1990**, 62, 748-750.

[32] A. G. Myers, D. R. Siegel, D. J. Buzard and M. G. Charest, *Org. Lett.,* **2001**, *3*, 2923-2926.

[33] G. N. Jenkins, D. W. Ribbons, D. A. Widdowson, A. M. Z. Slawin and D. J. Williams, *J. Chem. Soc., Perkin Trans. 1,* **1995**, 2647-2655.

[34] J. A. Griffen, A. M. Le Coz, G. Kociok-Köhn, M. A. Khan, A. J. W. Stewart, and S. E. Lewis, *Org. Biomol. Chem*., **2011**, 9, 3920.

[35] H-J. Knolker, G. Baum, N. Foitzik, H. Goesmann, P. Gonser, P. G. Jones and H. Rottele, *Eur. J. Inorg. Chem.*, **1998**, 993-1007.

[36] W. C. Zeise, *Annalen der Physik und Chemie*, **1831**, 21, 497.

[37] T. J. Kealy and P. L. Pauson, *Nature*, **1951**, 168, 1039.

[38] B. Plietker (Ed) *Iron catalysis in Organic Chemistry*. Wiley-VCH, Weinheim, **2008**.

[39] A. J. Pearson, *Iron Compounds in Organic Synthesis*, Academic Press, London, **1994**.

[40] L. Monde and F. Quincke, *J. Chem. Soc*., **1891**, 59, 604.

[41] M. Bertholet, *C. R. Hebd. Seances Acad. Sci.,* **1891**, 112, 1343.

[42] H. Reihlen, A. Gruhl, G. von-Hessling and O. Pfengle, *Liebigs Ann. Chem.,* **1930**, 482, 161.

[43] B. F. Hallam and P. L. Pauson, *J. Chem. Soc.,* **1958**, 642.

[44] J. E. Arnett, R. Pettit, *J. Am. Chem. Soc.,* **1961**, 83, 2985.

[45] A. J. Birch, P. E. Cross, J. Lewis, D. A. White and S. B. Wild, *J. Chem. Soc.,* **1968**, 332-340.

[46] A. J. Birch and D. H. Williamson, *J. Chem. Soc., Perkin Trans. 1,* **1973**, 1892-1900.

[47] K. Stark, J. E. Lancaster, H. D. Murdoch and E. Z. Wiess, *Naturforsch.*, **1964**, 19b, 284.

[48] J. A. S. Howell, B. F. G. Johnson, P. L. Josty and J. Lewis, *J. Organometallic Chem.*, **1972**, 39, 329.

[49] J. A. S. Howell, B. F. G. Johnson, P. L. Josty and J. Lewis, *J. Organometallic Chem.*, **1972**, 39, 329.

[50] M. Brookhart and G. O. Nelson, *J. Organometallic Chem.*, **1979**, 164, 193.

[51] H. Fleckner, F. W. Grevels and D. Hess, *J. Am. Chem. Soc.*, **1984**, 106, 2027.

[52] H.-J. Knölker and H. Hermann, *Angew. Chem. Int. Ed. Engl.*, **1996**, 35, 341-344.

[53] E. O. Fischer and R. D. Fischer, *Angew. Chem.*, **1960**, 72, 919-919.

[54] A. J. Birch, K. B. Chamberlain, M. A. Haas and D. J. Thompson, *J. Chem. Soc., Perkin Trans. 1,* **1973**, 1882-1891.

[55] A. J. Pearson and R. J. J. Shively, *Organometallics,* **1994**, 25, 578-584.

[56] M. Leivers, I. Tam, K. Groves, D. Leung, Y. Xie and R. Breslow, *Org. Lett.,* **2003**, 5, 3407-3409.

[57] R. E. Ireland, G. G. Brown, R. H. Stanford and T. C. McKenzie, *J. Org.Chem.*, **1974**, 39, 51-59.

[58] O. Eisenstein, W. M. Butler and A. J. Pearson, *Organometallics,* **1984**, 3, 1150-1157.

[59] G. R. Stephenson and R. P. Alexander, *J. Chem. Soc., Dalton Trans.*, **1987**, 885.

[60] A. J. Birch, B. Chauncy, L. F. Kelly and D. J. Thompson, *J. Organomet. Chem.*, **1985**, 286, C37.

[61] S. T. Astley and G. R. Stephenson, *J. Chem. Soc., Perkin Trans. 1*, **1993**, 1953-1955.

[62] A. I. Meyers, J. R. Flisak and R. A. Aitken, *J. Am. Chem. Soc.*, **1987**, 109, 5446.

[63] A. G. Myers, D. R. Siegel, D. J. Buzard and M. G. Charest, *Org. Lett.*, **2001**, 3, 2923-2926.

[64] F. Fabris, J. Collins, B. Sullivan, H, Leisch and T. Hudlicky, *Org. Biomol. Chem.*, **2009**, 9, 2619-2627.

[65] H.-J. Knölker, G. Baum, N. Foitzik, H. Goesmann, P. Gonser, P. G. Jones and H. Rottele, *Eur. J. Inorg. Chem.*, **1998**, 993-1007.

[66] A. J. Birch, P. E. Cross, J. Lewis, D. A. White and S. B. Wild, *J. Chem. Soc. (A),* **1968**, 332-340.

[67] T. Olsson, H. Graden, J. Hallberg and N. Kann, *J. Comb. Chem.*, **2004**, *6*, 783-788.

[68] B. M. R. Bandara, A. J. Birch, W. D. Raverty, *J. Chem. Soc., Perkin Trans. 1*, **1982**, 1763-1769.

[69] M. A. Khan, M. F. Manhon, A. J. W. Stewart and S. E. Lewis, *Organometallics*, **2010**, 29, 199–204.

[70] M. J. Palframan, G. Kociok-Köhn and S. E. Lewis, *Org. Lett.*, **2011**, 13, 3150-3153.

[71] G. N. Jenkins, D. W. Ribbons, D. A. Widdowson, A. M. Z. Slawin and D. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, **1995**, 2647-2655.

[72] J. A. Griffen, A. M. Le Coz, G. Kociok-Köhn, M. A. Khan, A. J. W. Stewart and S. E. Lewis, *Org. Biomol. Chem.*, **2011**, 9, 3920.

[73] T. Hudlicky, J. D. Price and H. F. Olivo, *Synlett*, **1991**, 9, 645-646.

[74] D. R. Boyd, N. D. Sharma, B. Byrne, M. V. Hand, J. F. Malone, G. N. Sheldrake, J. Blacker and H. Dalton, *J. Chem. Soc., Perkin Trans. 1*, **1998**, 1935-1943.

[75] A. I. Meyers, J. R. Flisak and R. A. Aitken, *J. Am. Chem. Soc.*, **1987**, 109, 5446.

[76] M. F. Semmelhack and A. Zask, *J. Am. Chem. Soc.*, **1983**, (1983), 105, 2034-2043

[77] A. Defoin, *Synthesis*, 2004, 706-710.

[78] E. R. Møller and K. A. Jørgensen, *J. Org. Chem.*, **1996**, 61, 5770-5778.

[79] B. Yang, M. J. Miller, *Org. Lett.*, **2010**, 12, 392-395.