2007

Novel catalysis by metalloporphyrins

Harun M. Mbuvi

Iowa State University

Follow this and additional works at: https://lib.dr.iastate.edu/rtd

Part of the Inorganic Chemistry Commons

Recommended Citation

https://lib.dr.iastate.edu/rtd/15909

This Dissertation is brought to you for free and open access by the Iowa State University Capstones, Theses and Dissertations at Iowa State University Digital Repository. It has been accepted for inclusion in Retrospective Theses and Dissertations by an authorized administrator of Iowa State University Digital Repository. For more information, please contact digirep@iastate.edu.
Novel catalysis by metalloporphyrins

by

Harun M. Mbuvi

A dissertation submitted to the graduate faculty
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

Major: Inorganic Chemistry

Program of Study Committee:
L. Keith Woo, Major Professor
Robert J. Angelici,
John G. Verkade
William S. Jenks
Aaron Sadow

Iowa State University

Ames, Iowa

2007
### TABLE OF CONTENTS

**LIST OF ABBREVIATIONS**

Abstract

**GENERAL INTRODUCTION**

Dissertation Organization 1
Porphyrins 1
Metalloporphyrins as Catalysts 2

**CHAPTER 1. USE OF DIAZO REAGENTS AS CARBENE SOURCE IN CYCLOPROPANATION, N-H AND C-H INSERTION REACTIONS USING VARIOUS METAL COMPLEXES AS CATALYSTS**

Introduction 3
Types of Diazoo Reagents Used as Carbenes Sources 4
Cyclopropanation Reactions Using Diazoo Reagents 7
N-H Insertion Reactions Using Diazoo Reagents 9
Intramolecular Carbenoid C-H Activation 9
Intermolecular C-H Activation Reactions 12
References 13

**CHAPTER 2: IRON PORPHYRIN CATALYZED N-H INSERTION REACTIONS WITH ETHYL DIAZOACETATE**

Abstract 17
Introduction 18
Results and Discussion 19
Mechanistic Considerations 27
Conclusion 34
Experimental Procedures 34
Acknowledgement 44
References 44

**CHAPTER 3: CATALYTIC C-H INSERTIONS USING SILVER(II), COPPER(II) AND IRON(III) PORPHYRIN COMPLEXES**

Abstract 47
Introduction 48
Results and Discussions 49
Diazomalonate Reactions 49
Substituted methyl 2-phenylacetates 54
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>µmol</td>
<td>micromole</td>
</tr>
<tr>
<td>¹³C NMR</td>
<td>carbon-13 nuclear magnetic resonance</td>
</tr>
<tr>
<td>¹H NMR</td>
<td>proton nuclear magnetic resonance</td>
</tr>
<tr>
<td>BF₄⁻</td>
<td>anion of tetrafluoroborate</td>
</tr>
<tr>
<td>CHT</td>
<td>1,3,5-cycloheptatriene</td>
</tr>
<tr>
<td>Cp</td>
<td>anion of cyclopentadienyl</td>
</tr>
<tr>
<td>DEF</td>
<td>diethyl fumarate</td>
</tr>
<tr>
<td>DEM</td>
<td>diethyl maleate</td>
</tr>
<tr>
<td>DMM</td>
<td>dimethyl diazomalonate</td>
</tr>
<tr>
<td>DOSP</td>
<td>N-(4-dodecylphenylsulfonyl)prolinate</td>
</tr>
<tr>
<td>EDA</td>
<td>ethyl diazoacetate</td>
</tr>
<tr>
<td>Fe(TPPF₂₀)Cl</td>
<td>chloro[meso-tetrakis(pentafluorophenyl)porphyrin]iron(III)</td>
</tr>
<tr>
<td>GC</td>
<td>gas chromatography</td>
</tr>
<tr>
<td>GC-MS</td>
<td>gas chromatography coupled with mass spectrometry</td>
</tr>
<tr>
<td>HRMS</td>
<td>high resolution mass spectrometry</td>
</tr>
<tr>
<td>m/z</td>
<td>mass/charge ratio</td>
</tr>
<tr>
<td>MeO</td>
<td>methoxy</td>
</tr>
<tr>
<td>MEOX</td>
<td>methyl 2-hydroxyoxazolidine-4-carboxylate anion</td>
</tr>
<tr>
<td>MEPY</td>
<td>methyl-2-oxopyrrolidin-5-carboxylate anion</td>
</tr>
<tr>
<td>mg</td>
<td>milligram</td>
</tr>
<tr>
<td>mL</td>
<td>milliliter</td>
</tr>
</tbody>
</table>
mmol  millimole
MPDA  methyl 2-phenyldiazoacetate
MPPIM  methyl 2-hydroxy-1-(2-phenylacetyl)imidazolidine-4-carboxylate anion
MS{EI}  mass spectrometry by electron impact
NBD  norbornadiene
OAc  acetate anion [CH₃CO₂⁻]
PNA  peptide nucleic acid
ppm  parts per million
saldach  diation of trans-1,2-bis(salicylidene)cyclohexanediamine
salen  dianion of bis(salicylidene)diamine
$t$-Bu  tert-butyl
THF  tetrahydrofuran
TMeO-PP  dianion of meso-tetra(p-methoxyphenyl)porphyrin
TMP  dianion of meso-tetramesitylporphyrin
tmtaa  dianion tetramethylidibenzotetraaza[14]annulene
TP$^{Br_3}$  Hydrotris(3,4,5-tribromo-1-pyrazolyl)borate
TPP  meso-tetraphenylporphyrinato dianion
TTP  meso-tetratolylporphyrinato dianion
Abstract. Metalloporphyrins have long been known to be effective catalysts for a variety of organic reactions. These include cyclopropanation, epoxidation, and aziridination of olefins. Iron porphyrins are also efficient catalysts for the olefination of aldehydes and ketones in the presence of triphenylphosphine. This suggested to us that iron porphyrins may have the potential to mediate a variety of other processes. The work described in this dissertation broadly extends the reactions catalyzed by iron(III) tetraphenylporphyrin chloride, Fe(TPP)Cl. We have found that Fe(TPP)Cl is an efficient catalyst for N-H insertion reactions, C-H activation and the Büchner reaction between diazo reagents and arenes. These studies have also led to the development of efficient syntheses of piperazinones and morpholinones.

N-H insertion reactions of a variety of aliphatic and aromatic amines were catalyzed by Fe(TPP)Cl using ethyldiazoacetate (EDA) as a carbene source with yields ranging from 68-97%. Primary amines were able to undergo a second insertion when another equivalent of EDA was added by slow addition. N-Heterocyclic compounds were poor substrates giving low yields or no N-H insertion products. Competition reactions and linear free energy relationships provided mechanistic insights for the insertion reaction.

An attempt to achieve C-H insertions using EDA and Fe(TPP)Cl led to formation of maleate and fumarate dimers. However, using Fe(III), Cu(II) and Ag(II) porphyrin complexes and carbenes transferred from methyl diazomalonate produced both benzylic and aromatic C-H insertions products
when toluene was used as substrate. Temperatures above 100 °C are required and yields greater than 70% can be achieved. C-H insertions reactions with cyclohexane and tetrahydrofuran occur at a lower temperature of 60 °C and yields above 60% have been achieved when using substituted methyl 2-phenyldiazoacetates as the carbene source. Hammett studies have provided evidence of an involvement of an electrophilic iron-carbene complex in the reaction mechanism. Initial rates of reactions were found to be first order with respect to the diazo indicating that the loss of N₂ and concomitant formation of metal carbene is the rate-determining step.

Büchner addition of carbenes formed from substituted methyl 2-phenyldiazoacetates to substituted benzenes to give equilibrating mixtures of cycloheptatriene-norcaradiene valence isomers in yields over 70% have been achieved using Fe(TPP)Cl. Chlorobenzene gave a regioisomeric mixture of 7-carbomethoxy-2-chloro-7-phenylnorcaradiene/7-carbomethoxy-2-chloro-7-phenylcycloheptatriene and 7-carbomethoxy-3-chloro-7-phenylnorcaradiene/7-carbomethoxy-3-chloro-7-phenylcycloheptatriene when treated with methyl 2-phenyldiazoacetate. The dienes of the fluxional norcaradiene-cycloheptatriene systems were trapped with benzyne to give one stereoisomer of 3,3-disubstituted benzhomobarralenes. The cycloheptatriene-norcaradiene valence isomers quantitatively converted to ring-opened diaryl acetate products upon acidification in acetonitrile. A concerted mechanism is proposed for these iron porphyrin-catalyzed Büchner reactions.
Iron(III) tetraphenylporphyrin chloride, Fe(TPP)Cl, efficiently catalyzes O-H insertion reactions of both aliphatic and aromatic alcohols to give yields above 80% when methyl 2-phenyldiazoacetates were used as carbene sources. Unlike in the N-H insertion reactions, which are very rapid at room temperature, O-H insertions required heating in refluxing methylene chloride for about 8 hours using 1% catalyst. This catalyst also effectively catalyzes tandem N-H insertion/cyclization reactions when EDA is treated with ethylenediamine and ethanolamine to give 2-piperazinone and 2-morpholinone respectively. This reaction provides a new simple route for synthesizing these classes of important products.
GENERAL INTRODUCTION

Dissertation Organization

The first chapter of this dissertation is a literature review of various diazo reagents and their use in cyclopropanation and N-H and C-H insertion reactions using various catalysts. The second chapter is a paper that is in press in Organometallics, 2007. The remaining chapters are papers that are being prepared for submission to Organometallics. General conclusion follows the last chapter. The author performed the mechanistic studies in chapter two, constituting about 30% of the work. The remaining chapters describe work done entirely by the author.

Porphyrrins

A porphyrin is a heterocyclic macrocycle derived from four pyrrole subunits interconnected at their α carbon atoms via methine bridges (CH). The macrocycle is highly conjugated and consequently deeply colored, hence the name porphyrin, derived from the Greek word for purple. Many porphyrins occur in nature and in bio-inspired synthetic catalysts and devices.
Related to porphyrins are corrins, chlorins (2,3-dihydroporphyrin) and bacteriochlorophylls (2,3,12,13-tetrahydroporphyrin). All of them follow the Hückel 4n+2 rule and hence have aromatic properties. Porphyrins combine readily with metals to form tetrachelate complexes. Iron in hemes, magnesium in chlorophyll, zinc, copper, nickel, and cobalt-containing porphyrins are known, and many other metals porphyrins have been synthesized. A porphyrin in which no metal is inserted in its cavity is called a free base. Some iron-containing porphyrins (heme-containing proteins or hemoproteins) are found extensively in nature, e.g., hemoglobin. Hemoglobin iron is the actual binding site for dioxygen. This iron site can be preferentially bound by carbon monoxide leading to poisoning by asphyxiation. Some shellfish with green-colored blood have a copper-centered porphyrin. If one of the four pyrrole subunits is reduced to pyrroline, a chlorin is produced, which is the ring structure found in chlorophyll. If two of the four pyrrole subunits are reduced, then either a bacteriochlorin (as found in some photosynthetic bacteria) or an isobacteriochlorin is formed, depending on the relative positions of the reduced pyroles.

**Metalloporphyrins as Catalysts**

Metalloporphyrins have long been used as catalysts due to their robust nature and ability to impart unique stereoselectivity to the products. Manganese, iron and ruthenium porphyrins are extensively used as oxidation catalysts. Iron porphyrins have been found to be efficient catalyst for cyclopropanation and olefination of alkenes. The present work focuses on the use of iron porphyrins for N-H, C-H and O-H insertions reactions and cyclopropanation of arenes.
CHAPTER 1. USE OF DIAZO REAGENTS AS CARBENE SOURCES IN CYCLOPROPANATION, N-H AND C-H INSERTION REACTIONS USING VARIOUS METAL COMPLEXES AS CATALYSTS

Introduction

Hydrocarbons from oil and natural gas are the main feedstocks for the chemical industry. Therefore, direct and catalytic transformations of alkanes and arenes to various useful chemicals via C-H activation, especially of the least reactive alkanes, is of considerable interest to chemical industries and remain a challenge to chemists.\(^1\) Over the past 20+ years, there has been an intensive effort to achieve selective C-H bond activation by transition metal complexes.\(^1\) Although catalytic reactions involving oxidative addition to C-H bonds\(^2\) and electrophilic substitution\(^3\) of C-H bonds of alkanes by highly reactive metal complexes were initially thought to be promising approaches to C-H activation of alkanes in syntheses of carboxylic acid, amine, and alcohol derivatives, the difficulty associated with regeneration of the highly reactive complexes has complicated the efforts toward achieving a catalytic process.

An alternative strategy that has afforded great results in C-H activation is the development of metal-carbene-induced C-H insertion reactions.\(^4\) In metal-carbene-induced C-H activation, the metal atom typically does not interact directly with the alkane C-H bond.\(^4,5\) Thus, the mechanism of the carbene complex reaction is different from those of other C-H activation processes that involve metal/C-H interactions. Furthermore, transient metal-carbene complexes are conveniently formed from diazo compounds.\(^4,8\) The metal complex that initiates the reaction is readily regenerated, and so the chemistry is very amenable to involvement in catalytic processes.\(^4\) However, a
number of alternative reaction pathways are open to the carbene intermediates and therefore controlling this diverse reactivity has been the central requirement for the effective development of synthetically useful carbene-induced C-H activations.\textsuperscript{9-14}

The electrophilicity of the metal-carbene intermediate has been found to have a great influence on the chemo-, regio-, and stereoselectivity of the C-H activation reaction.\textsuperscript{15-19} This electrophilicity stems not only from the effect of the associated ligated metal complex\textsuperscript{17,18} but also from the substituents on the carbene carbon.\textsuperscript{20-24} The nature of the substituents attached to the carbonyl group and identity of the additional substituent at the carbene carbon can dramatically influence the stability of the carbene complex.

**Types of Diazoo Reagents Used as Carbenes Sources**

One common type of diazo compound contains a single electron-withdrawing substituent (Fig. 1).\textsuperscript{4,7} Nitrogen extrusion from these diazo compounds can be achieved with a variety of catalysts to generate a highly reactive carbene complex. A major problem that needs to be avoided with this class of carbenoid is the formation of carbene dimers. This type of diazo compound has been widely applied in intramolecular C-H activation reactions where the high reactivity can be offset by entropic factors.\textsuperscript{4,7} The most utilized examples of this class are alkyl diazoacetates. The carbene complexes obtained from diazoketones are usually more reactive than those obtained from diazoacetates, whereas those from diazoacetamides are the least reactive.\textsuperscript{4} \(\alpha\)-Alkyl-\(\alpha\)-diazoacetates have been less explored because they are prone to alkene formation by a 1,2-hydrogen shift. A few significant examples of intramolecular asymmetric C-H
activation by using alkyl-substituted diazoacetates are known, and the presence of the alkyl group appears to enhance the enantioselectivity.\textsuperscript{25}

Fig. 1: Diazo compounds that contain one electron-withdrawing substituent

Another type of diazo compound contains two electron-withdrawing substituents (Fig. 2).\textsuperscript{7} This includes diazoacetoacetates, diazomalonates, diazodiketones, diazoacetoacetamides, and α-methoxycarbonyl-α-diazoacetamides. Due to the added stabilization of the diazo compound towards N\textsubscript{2} loss by the presence of the second electron-withdrawing group, very active catalysts are required to decompose these diazo compounds.\textsuperscript{4} The carbene complex once formed is highly electrophilic and very capable of C-H activation. Common side reactions for this carbenoid system are carbene dimerization and hydrogen transfer to form zwitterionic intermediates. Again, intramolecular C-H insertion reactions are the most synthetically useful to date.\textsuperscript{4} Even though these diazo compounds would be expected to be less selective, there is evidence that the opposite is the case, at least in cyclopropanation reactions.\textsuperscript{1,26,27}
Fig. 2: Diazo compounds that contain two electron-withdrawing substituents

A third class of diazo compounds contains both an electron-donating and an electron-withdrawing group (Fig. 3). The donor substituent is typically a vinyl or aryl group that is capable of interacting with the carbene carbon through resonance. Very few reports on this class of diazo existed prior to 1985, and the first example of C-H activation with this class of carbenoid was reported in 1997. In the past few years, this situation has changed dramatically with the recognition that this class of diazo is capable of undergoing highly chemoselective intermolecular C-H activation. The aryl and vinyl groups also stabilize the diazo form with respect to N₂ extrusion and very active catalysts are required to effectively utilize this class of diazo compounds.

Fig. 3: Diazo compounds that contain both an electron-withdrawing and an electron-donating substituent.
Cyclopropanation Reactions Using Diazo Reagents

The great importance of the cyclopropyl moiety in chemistry and biochemistry is represented by its frequent occurrence in natural products, insecticides, modern pharmaceuticals, and critical synthetic intermediates.\(^4,9,32\) Practically, cyclopropanes can best be made from the metal-mediated cycloaddition of a carbene fragment to an olefin in the so-called olefin cyclopropanation reaction. Metal complexes which facilitate such reactions range from stoichiometric metal carbene transfer reagents\(^33\) to catalysts.\(^9,34\) Iron is rather unique among the transition metals capable of cyclopropanation, because iron complexes have been used extensively in both stoichiometric\(^33-36\) as well as catalytic\(^37-39\) reactions.

Hossain and co-workers reported the use of \([\text{CpFe(CO)}_2(\text{THF})](\text{BF}_4)\) as the catalyst in the cyclopropanation of a variety of olefins, with either ethyl diazoacetate (EDA) or phenyl diazoacetate as the carbene source, to synthesize cyclopropanes in good yields and with high cis selectivity.\(^37,40,41\) Optimal conditions for these reactions included a nitrogen atmosphere with dichloromethane as the solvent at 40 °C. In 1995, our group reported the use of several iron(II) and iron(III) porphyrins as cyclopropanation catalysts to yield mainly trans-cyclopropanes from various terminal alkenes and EDA.\(^38\) Before most of the iron(III) porphyrins could be used as efficient catalysts, reduction to iron(II) was involved, either by the use of cobaltocene\(^38\) or by heating with EDA, which can act as a mild reducing agent.\(^42\) An exception to this was chloro[meso-tetrakis(pentafluorophenyl)porphyrin]iron(III), which functioned as a catalyst at room temperature. Although iron(III) porphyrins are air-stable, the reduced iron(II) species are rapidly oxidized and need to be handled under an inert atmosphere. Iron(II)
tetramethyldibenzotetraaza[14]annulene (tmtaa) has also been used as cyclopropanation catalysts as well. This latter study also reported the ability of a Fe(saldach) complex (saldach = dianion of trans-1,2-cyclohexanediamino-N,N'-salicylidene) to catalyze the cyclopropanation of styrene, albeit with low efficiency (the combined cyclopropane and carbene dimer yields were less than 30% with EDA as the carbene source).

Iron(III) and iron(IV) corroles have also been shown to catalyze various cyclopropanation reactions. Usually cyclopropanation reactions with iron-based catalysts had to be carried out under an inert atmosphere. More recently a series of µ-oxo-bis[(salen)iron(III)] complexes were found to be active towards cyclopropanation of alkenes. The complex [Fe(3,3',5,5'-Bu4salen)]O was identified as the most efficient catalyst in the series, which successfully catalyzed the cyclopropanation not only of styrene but also of less reactive substrates such as α-methylstyrene, α-(trifluoromethyl)styrene, 1,1-diphenylethylene, methylenecyclohexane, and n-butyl vinyl ether and internal olefins such as trans- and cis-β-methylstyrene and ethylidenecyclohexane. In contrast to other known iron-based catalysts, no carbene dimers were observed in the cyclopropanation of mono- and disubstituted terminal olefins using µ-oxo-bis[(salen)iron(III)] as a catalyst. This is quite remarkable considering that the reactions were done in refluxing toluene. This suggests that the trapping of the postulated metal carbene intermediate by the styrene substrate is quite efficient. Dimerization was only observed when internal olefins were used as substrates. Interestingly, in all cases only the diethyl maleate (cis) dimer was formed. When trans- and cis-methylstyrene were used as substrates about 25% were cyclopropanated and 16%
of diethylmaleate was formed after 23 h, while in the case of ethylidenecyclohexane, 27% of cyclopropanation product and 20% of the cis dimer were obtained after 19 hours.

**N-H Insertion Reactions Using Diazo Reagents**

The catalytic insertion of diazo compounds into N-H bonds is a very powerful tool for the construction of versatile building blocks used in the synthesis of α-amino acids, peptides and β-lactam antibiotics.\(^{4,7,34,45}\) Intra- and intermolecular N–H insertion reactions have received much attention in the last few decades. Yates reported the first catalytic N-H insertion using copper bronze.\(^{46}\) Saegusa et al.\(^{47}\) and Nicoud and Kagan\(^{48}\) employed CuCN as a catalyst for the insertion of diazo compounds into N-H bonds. Later Rh\(_2\)(OAc)\(_4\) and its derivatives have emerged as powerful catalysts for the N-H insertion reaction with diazo compounds.\(^{49}\) Simonneaux and co-workers reported similar catalysis using ruthenium complexes.\(^{50}\) Recently, our group discovered that iron porphyrins such as Fe(TPP)Cl were very efficient catalysts for N-H insertions using ethylidiazooacetate as the carbene source.\(^{51}\) This work demonstrated that iron porphyrins were the most efficient catalysts for N-H insertion reactions involving EDA and a variety of amines without the need for slow addition of the diazo reagent. The most outstanding features of this one-pot process were high selectivity, very high yields in very short times and the high recyclability of the catalyst of up to 10 times with no decrease in yields.

**Intramolecular Carbenoid C-H Activation**

Intramolecular C-H activation reactions permit remote functionalization through C-C bond formation, presenting a general approach for the synthesis of a variety of
carbocyclic and heterocyclic structures in a regio- and stereocontrolled manner. The most effective catalysts for intramolecular C-H activation of diazoacetates have been Doyle's chiral rhodium carboxamidate complexes. In addition to achieving very high asymmetric induction in this system, the catalysts have considerable influence on the chemoselectivity and regioselectivity of the chemistry. For instance, Rh$_2$(OAc)$_4$ or rhodium(II) caprolactamate-catalyzed decomposition of 2-substituted ethyl diazoacetates generates products arising from intermolecular processes such as carbene dimerization and insertion into adventitious water. However, the corresponding reactions conducted with chiral Rh(II) carboxamidates favor formation of the $\gamma$-butyrolactone. All of the chiral carboxamidates studied in the reaction of diazoacetate generally displayed the same levels of chemo- and regioselectivity, showing a strong tendency for five-membered ring formation over benzylic C-H activation. The first-generation catalysts, the pyrrolidinone complex Rh$_2$(MEPY)$_4$ and the oxazolidinone complex Rh$_2$(MEOX)$_4$, gave moderate asymmetric induction (51-72% ee), whereas the second-generation imidazolidinone catalyst Rh$_2$(MPPIM)$_4$ was far superior (87-97% ee). The unrivaled success of Rh$_2$(MPPIM)$_4$ is thought to be due to the greater steric influence of the N-3-phenylpropanoyl substituent, which provides greater control over the orientation and access of the carbene intermediate than with the more open structures of Rh$_2$(MEPY)$_4$ and Rh$_2$(MEOX)$_4$. The asymmetric synthesis of $\gamma$-butyrolactones by intramolecular C-H activation has been elegantly applied to the synthesis of various lignans such as isodeoxypodophyllotoxin and enterolactone (Scheme 1). The chemistry has also been utilized in the synthesis of (S)-(+)−imperanene and (R)-(−)-baclofen.
Scheme 1: Asymmetric synthesis of various lactones by intramolecular C-H activation using dirhodium tetraacetates as catalyst.


**Intermolecular C-H Activation Reactions**

Over the past few years the intermolecular C-H activation by carbenoids has undergone explosive growth.\(^{30,31}\) For a long time the intermolecular reaction was considered to be of little synthetic utility because the process displayed very poor chemoselectivity and carbene dimerization was a major side reaction.\(^{4,9,59}\) The situation has now totally changed with the development of the phenyldiazoacetates, which are exceptional reagents for intermolecular C-H activation.\(^{30,31}\) This area of chemistry is probably the most graphic example of the significant difference in reactivity that exists between the various diazo reagents. During the very early development of catalysts for C-H insertions using diazo reagents it was found that dirhodium tetracarboxylates were far superior to the copper catalysts at inducing intermolecular C-H activation.\(^{60-64}\) The reaction, however, was not generally considered to be of much synthetic utility because the regioselectivity was poor and carbene dimerization dominated unless the diazo compound was added very slowly.\(^{4,9,59}\) An example of the regiochemical challenges associated with this chemistry is the reaction of ethyl diazoacetate with 2-methylbutane.\(^{63}\) A mixture of all four of the possible C-H activation products was formed. Even though there was a preference for insertion into the methylene C-H bond and the catalyst did influence the ratio of products, no catalyst was capable of mediating the reaction such that only a single product was formed. These seminal results demonstrated not only that metal-carbene intermediates were capable of C-H activation of alkanes but also that much more chemoselective reagents would be required for this transformation to be of practical utility.\(^{61-64}\) The present study involves the use of metalloporphyrins, mainly the
Fe(TPP)Cl as a catalyst for N-H, OH and C-H insertion reactions using various diazo compounds.

References


CHAPTER 2: IRON PORPHYRIN CATALYZED N-H INSERTION REACTIONS WITH ETHYL DIAZOOACETATE

A paper in press in *Organometallics*

Lynnette K. Baumann, Harun M. Mbuvi, Guodong Du, and L. Keith Woo*

Department of Chemistry

Iowa State University

Ames, IA 50011-3111

Abstract. A series of metalloporphyrin complexes were surveyed as catalysts for carbene insertion from ethyl diazooacetate into N-H bonds of amines. Iron(III) tetraphenylporphyrin chloride, Fe(TPP)Cl, was found to be an efficient catalyst for N-H insertion reactions with a variety of aliphatic and aromatic amines, with yields ranging from 68-97%. Primary amines were able to undergo a second insertion when another equiv of EDA was added by slow addition. N-Heterocyclic compounds were poor substrates giving low yields or no N-H insertion products. Competition reactions and linear free energy relationships provided mechanistic insights for the insertion reaction. The relative rates for N-H insertion into *para*-substituted aniline derivatives correlated with Hammett $\sigma^+$ parameters. Electron donating groups enhanced the reaction as indicated by the negative value of $\rho$ ($\rho = -0.66 \pm 0.05$, $R^2 = 0.93$). These results are consistent with a rate determining nucleophilic attack of the amine on an iron carbene complex. In addition, the decomposition of EDA catalyzed by Fe$^{II}$(TPP) or Fe$^{III}$(TPP)Cl
was examined under various amounts of added pyridine. The Fe(II) catalyst is strongly inhibited by the presence of pyridine. In contrast, catalysis by the Fe(III) porphyrin is accelerated by amines. These experiments suggested that an iron(III) porphyrin carbene complex is the active catalyst.

**Introduction**

Iron porphyrins are useful catalysts for a variety of organic reactions. These include cyclopropanation,\(^1\) epoxidation,\(^2\) and aziridination\(^3\) of olefins. Recently, iron porphyrins were shown to catalyze the olefination of aldehydes and ketones in the presence of triphenylphosphine by our group\(^4\) and others.\(^5\) This suggested to us that iron porphyrins may have the potential to mediate a variety of other processes.

Using diazo compounds as carbene sources, transition metal complexes that catalyze N-H insertion reactions include methyl trioxorhenium,\(^6\) rhodium,\(^7\) and copper\(^8\) complexes, and ruthenium porphyrins.\(^9\) Reactions that use diazoacetate reagents for insertion into N-H bonds may provide useful precursors for amino acids. In addition, intramolecular insertions resulting in N-heterocyclic compounds, such as indoles\(^10\) and imidazolones are also of great synthetic interest. We now report insertion reactions into aliphatic and aromatic N-H bonds using ethyl diazoacetate (EDA) as the carbene source and iron(III) tetraphenylporphyrin chloride, Fe(TPP)Cl,\(^11\) as the catalyst.\(^12\) Similar work appeared recently that also illustrated the utility of Fe(III/IV) corrole and Fe(III) porphyrin complexes for catalytic reactions between EDA and amines.\(^13\)
Results and Discussion

The activity of a series of metalloporphyrin complexes as catalysts for N-H insertion reactions was surveyed, using piperidine and EDA (eq 1). Among the catalysts examined, iron porphyrins proved to be the most active, giving high yields in relatively short periods of time (Table 1).

\[
\text{Fe(TPP)Cl, was found to be one of the most efficient in catalyzing the insertion of EDA into the piperidine N-H bond, resulting in a quantitative yield in under 10 minutes. The reactions were run in CH}_2\text{Cl}_2 \text{ under mild conditions at ambient temperature in a one-pot fashion, without the need for slow addition of EDA. The insertion reactions proceeded rapidly and the reaction mixtures warmed up upon addition of EDA, accompanied by observable gaseous N}_2 \text{ release. Evidence of the desired piperidine insertion product was obtained by }^1\text{H NMR spectroscopy with the appearance of a new two-proton singlet at 3.17 ppm for the N-acetate methylene hydrogens and the disappearance of the one-proton singlet at 4.72 ppm for the methine proton of EDA. No formation of diethyl fumarate or maleate was observed by GC analysis. These results illustrate that Fe(TPP)Cl is among the best porphyrin catalysts for amine N-H insertion reactions. For example, a ruthenium porphyrin catalyzed N-H insertion required longer reaction times (2-18 h) and afforded lower yields (63-81%).}^{9n}\text{ The only results comparable with Fe(TPP)Cl were obtained}
\]
with copper complexes bearing homoscorpionate (trispyrazolylborate) ligands. An osmium porphyrin complex, Os(TTP)(CO), was also able to catalyze the insertion of EDA into an N-H bond. While the reaction yield was low at ambient temperature, it afforded 90% yield of insertion product after heating at reflux for 20 minutes.

**Table 1.** Piperidine N-H insertion with EDA catalyzed by metalloporphyrins in CH$_2$Cl$_2$.  

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>time</th>
<th>% yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fe(TPP)Cl</td>
<td>&lt;5 min</td>
<td>&gt;97</td>
</tr>
<tr>
<td>2</td>
<td>Mn(TPP)Cl</td>
<td>24 h</td>
<td>nd</td>
</tr>
<tr>
<td>3</td>
<td>Zn(TPP)</td>
<td>24 h</td>
<td>nd</td>
</tr>
<tr>
<td>4</td>
<td>Co(TTP)</td>
<td>24 h</td>
<td>nd</td>
</tr>
<tr>
<td>5</td>
<td>Os(TTP)(CO)</td>
<td>28 h</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>Os(TTP)(CO)$^c$</td>
<td>20 min</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>no catalyst</td>
<td>24 h</td>
<td>nd</td>
</tr>
<tr>
<td>8</td>
<td>Fe(TMeO-PP)Cl</td>
<td>&lt;5 min</td>
<td>&gt;97</td>
</tr>
<tr>
<td>9</td>
<td>Fe(TPPF$_{20}$)Cl</td>
<td>40 min</td>
<td>&gt;97</td>
</tr>
<tr>
<td>10</td>
<td>Fe(TMP)Cl</td>
<td>1 h</td>
<td>80</td>
</tr>
<tr>
<td>11</td>
<td>Fe(Saldach)Cl</td>
<td>22 h</td>
<td>nd</td>
</tr>
</tbody>
</table>

$^a$ A molar ratio of 1:100:120 for catalyst:EDA:piperidine was used at ambient temperature. Yields were determined by GC. $^b$ nd = not detected. $^c$ Reaction with this catalyst was carried out under refluxing conditions.

A number of iron porphyrins with different steric and electronic properties were examined in catalytic N-H insertions (Table 1, entries 8-11). The varying completion times and yields indicated that the catalytic activity of these complexes depended on their steric and electronic properties. Electron-donating groups on the porphyrin periphery enhanced the activity. Fe(TMeO-PP)Cl appeared to be the best catalyst among those
investigated with the reaction reaching completion in under 5 minutes. In contrast, the
electron deficient complex, Fe(TPPF\textsubscript{20})Cl, required 40 minutes to complete the N-H
insertion into piperidine with EDA. Fe(TMP)Cl catalyzed the same reaction affording an
80% yield after 1 h, suggesting that steric hindrance also plays a role.

The subsequent studies focused on Fe(TPP)Cl because it is commercially
available and relatively inexpensive. The catalyst loadings can be lowered to 0.1 mol%,
albeit requiring longer reaction times at ambient temperature (Table 2). A variety of
amine substrates were used to study the scope of Fe(TPP)Cl as a catalyst for insertion
into N-H bonds with EDA. Originally, amines were used in slight excess to EDA based
on previous methods used to suppress maleate and fumarate formation.\textsuperscript{9a} However, 1:1
ratios of EDA:amine could be used with Fe(TPP)Cl without significant formation of side
products. N-H insertions were successfully achieved using primary and secondary alkyl
amines (eq 2) in good to high yields of 68 to 97% (Table 1, entry 1; Table 3, entries 1-4).

\[
\begin{align*}
\text{R}_1^1 \text{N-H} + \text{N}_2 \text{CHCO}_2\text{Et} & \xrightarrow{\text{Fe(TPP)Cl} \text{1 mol \%}} \text{R}_1^1 \text{N} \begin{array}{c} \text{O} \\ \text{OEt} \end{array} + \text{N}_2 \\
& \text{N}_2 \text{room temp} \\
\end{align*}
\]

Evidence of the desired insertion product with diethyl amine was observed in the \textsuperscript{1}H
NMR spectrum with the appearance of a new two-proton N-acetate methylene singlet at
3.27 ppm and the disappearance of the one-proton singlet at 4.72 ppm for the methine
proton of EDA.
Table 2. N-H insertion using EDA with various loadings of Fe(TPP)Cl in CH₂Cl₂.ᵃ

<table>
<thead>
<tr>
<th>entry</th>
<th>amine</th>
<th>% catalyst</th>
<th>time</th>
<th>% yieldᵇ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>aniline</td>
<td>1.0</td>
<td>1 min</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
<td>aniline</td>
<td>0.50</td>
<td>5 min</td>
<td>87</td>
</tr>
<tr>
<td>3</td>
<td>aniline</td>
<td>0.25</td>
<td>10 min</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>aniline</td>
<td>0.14</td>
<td>25 min</td>
<td>88</td>
</tr>
<tr>
<td>5</td>
<td>aniline</td>
<td>0.10</td>
<td>1 h</td>
<td>89</td>
</tr>
<tr>
<td>6</td>
<td>piperidine</td>
<td>1.0</td>
<td>10 min</td>
<td>&gt;95</td>
</tr>
<tr>
<td>7</td>
<td>piperidine</td>
<td>0.5</td>
<td>10 min</td>
<td>&gt;95</td>
</tr>
<tr>
<td>8</td>
<td>piperidine</td>
<td>0.1</td>
<td>5 h</td>
<td>82</td>
</tr>
</tbody>
</table>

ᵃ Amounts used were 1.0 mmol EDA and 1.2 mmol amine at ambient temperature.ᵇ Yields determined by GC.

Aryl amine substrates also gave successful insertion reactions (eq 3) with yields of 58 to 95% (Table 3, entries 8-14), comparable to reported yields for reactions catalyzed by copper, ruthenium, and rhenium complexes.⁶,⁷,⁸,⁹ The ¹H NMR spectrum of the product from EDA and aniline showed a new two-proton methylene singlet at 3.91 ppm.

\[
\text{N}₂\text{C}_\text{H}_\text{C}_\text{O}_\text{Et}^+ + \text{N}₂\text{EtCHCO}_\text{Et} \xrightarrow{\text{Fe(TPP)Cl}} \text{O}\text{CO}_\text{Et} + \text{N}₂ \ (3)
\]

Almost all of the single N-H insertion reactions reached completion in 20 minutes or less. The exception was the p-nitroaniline reaction that took 1 hour for complete consumption.
of the reagents. Also, insertion of EDA into the N-H bond of benzamide was not successful (Table 3, entry 7).

**Table 3.** Results for single EDA insertion into amines with 1 mol % Fe(TPP)Cl.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>amine</th>
<th>amine:EDA</th>
<th>time</th>
<th>% yield(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Et₂NH</td>
<td>1:1.1</td>
<td>10 min</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>t-Bu-NH₂</td>
<td>1:1</td>
<td>10 min</td>
<td>68</td>
</tr>
<tr>
<td>3</td>
<td>C₅H₁₀NH</td>
<td>1:1.2</td>
<td>10 min</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>PhCH₂NH₂</td>
<td>1:1</td>
<td>10 min</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>Ph₂NH</td>
<td>1:1.1</td>
<td>1 h, 60 °C</td>
<td>&lt;5</td>
</tr>
<tr>
<td>6</td>
<td>Tetramethylpiperidine(^c)</td>
<td>1:1.1</td>
<td>48 h</td>
<td>NR</td>
</tr>
<tr>
<td>7</td>
<td>Benzamide</td>
<td>1:1.1</td>
<td>48 h</td>
<td>NR</td>
</tr>
<tr>
<td>8</td>
<td>p-CH₃O-C₆H₄-NH₂</td>
<td>1:1.2</td>
<td>10 min</td>
<td>82</td>
</tr>
<tr>
<td>9</td>
<td>p-CH₃-C₆H₄-NH₂</td>
<td>1:1.2</td>
<td>10 min</td>
<td>95</td>
</tr>
<tr>
<td>10</td>
<td>C₆H₅-NH₂</td>
<td>1:1.2</td>
<td>10 min</td>
<td>91</td>
</tr>
<tr>
<td>11</td>
<td>p-Cl-C₆H₄-NH₂</td>
<td>1:1</td>
<td>20 min</td>
<td>58 (13)(^d)</td>
</tr>
<tr>
<td>12</td>
<td>p-Br-C₆H₄-NH₂</td>
<td>1:1.1</td>
<td>10 min</td>
<td>92</td>
</tr>
<tr>
<td>13</td>
<td>p-CN-C₆H₄-NH₂</td>
<td>1:1.2</td>
<td>20 min</td>
<td>87</td>
</tr>
<tr>
<td>14</td>
<td>p-NO₂-C₆H₄-NH₂</td>
<td>1:1.1</td>
<td>1 hr</td>
<td>91</td>
</tr>
<tr>
<td>15</td>
<td>Imidazole</td>
<td>1:1.4</td>
<td>48 h</td>
<td>51</td>
</tr>
<tr>
<td>16</td>
<td>Pyrrole</td>
<td>1:1.3</td>
<td>48 h</td>
<td>0 (37)(^e)</td>
</tr>
<tr>
<td>17</td>
<td>Indole</td>
<td>1:1.4</td>
<td>48 h</td>
<td>NR</td>
</tr>
</tbody>
</table>

\(^a\) Reactions were run with 1.0 mmol amine in 7.0 mL CH₂Cl₂ at ambient temperature. \(^b\) NMR yields using Ph₃CH as an internal standard. \(^c\) 2,2,6,6-tetramethylpiperidine. \(^d\) Yield of double insertion product in parenthesis. \(^e\) α-C-H insertion product.

Side products from dimerization of EDA, diethyl maleate and diethyl fumarate, were generally observed in only trace amounts and reactions could be run in a practical one-pot fashion. Therefore, it was not necessary to add EDA and/or amine slowly to the catalyst solution. This also indicated that Fe(TPP)Cl is not poisoned by coordination of
amine. In contrast, an amine poisoning effect was reported for a ruthenium porphyrin\textsuperscript{10a} and a rhodium catalyst.\textsuperscript{14}

Primary amines were able to undergo a double N-H insertion reaction (Table 4) with excess EDA. The double insertion product of aniline gives a four-proton NMR singlet at 4.14 ppm for the methylene hydrogens of the two N-acetate groups, exhibiting a smaller upfield shift than observed for the methylene fragment of the single insertion product. This dual reaction could be done step-wise, first forming the single insertion product then introducing a second equivalent of EDA by slow addition. Addition of two equivalents of EDA to the substrate in one aliquot, resulted mainly in the single insertion product, low yields of double insertion product, and more dimeric side products. The second insertion is a slower reaction, allowing more dimer to form in these reactions compared to the single insertion reaction. Increasing the electron-withdrawing ability of

<table>
<thead>
<tr>
<th>entry</th>
<th>amine</th>
<th>amine:EDA</th>
<th>time</th>
<th>% yield\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCH\textsubscript{2}NH\textsubscript{2}</td>
<td>1:3</td>
<td>15 min</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td>p-CH\textsubscript{3}O-C\textsubscript{6}H\textsubscript{4}-NH\textsubscript{2}</td>
<td>1:2.8</td>
<td>1 h</td>
<td>81</td>
</tr>
<tr>
<td>3</td>
<td>p-CH\textsubscript{3}-C\textsubscript{6}H\textsubscript{4}-NH\textsubscript{2}</td>
<td>1:2.4</td>
<td>1 h</td>
<td>76</td>
</tr>
<tr>
<td>4</td>
<td>C\textsubscript{6}H\textsubscript{5}-NH\textsubscript{2}</td>
<td>1:2.9</td>
<td>2 h</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td>p-Cl-C\textsubscript{6}H\textsubscript{4}-NH\textsubscript{2}</td>
<td>1:2.4</td>
<td>1.5 h</td>
<td>72 (16)\textsuperscript{c}</td>
</tr>
<tr>
<td>6</td>
<td>p-Br-C\textsubscript{6}H\textsubscript{4}-NH\textsubscript{2}</td>
<td>1:4.1</td>
<td>2 h</td>
<td>78 (14)\textsuperscript{c}</td>
</tr>
<tr>
<td>7</td>
<td>p-CN-C\textsubscript{6}H\textsubscript{4}-NH\textsubscript{2}</td>
<td>1:4</td>
<td>4 h</td>
<td>&lt; 20 (81)\textsuperscript{c}</td>
</tr>
<tr>
<td>8</td>
<td>p-NO\textsubscript{2}-C\textsubscript{6}H\textsubscript{4}-NH\textsubscript{2}</td>
<td>1:4</td>
<td>48 h</td>
<td>0 (91)\textsuperscript{c}</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reactions were run with 1.0 mmol amine in 7.0 mL CH\textsubscript{2}Cl\textsubscript{2} at ambient temperature. \textsuperscript{b} NMR yields of double insertion products using Ph\textsubscript{3}CH as an internal standard. \textsuperscript{c} Single insertion product yield listed in parentheses.
the substituents on the aniline made the second insertion more difficult and prolonged the reaction times. When aminobenzonitrile was the substrate, the double insertion product was observed in low yield as monitored by GC and GC-MS, but could not be isolated from the single insertion product. No double insertion product was formed when p-nitroaniline was the substrate (Table 4, entry 8), indicating that the strong electron-withdrawing effect of the nitro substituent was reinforced by the first N-acetate fragment.

Reactions with N-heterocyclic compounds gave significantly different results from the aniline derivatives. With imidazole as the substrate, the N-H insertion product was formed in a 51% yield (eq 4). Under the same conditions, carbene insertion from EDA occurred at the α-C-H bond of pyrrole in low yields and no reaction was observed with indole. Carbene insertion from EDA into the C-H bond of pyrrole was previously reported. Imidazole is more basic than pyrrole and indole and is a better nucleophile for attack at the carbene intermediate (vide infra).

![Reaction Scheme]

Several ortho-substituted anilines were also evaluated (Table 5). A single insertion of carbene from EDA into 2-chloroaniline gave a yield of 70% and insertion into 2-aminoacetophenone resulted in a 57% yield. Additional equivalents of EDA did not
Table 5. Single insertion of EDA into ortho-substituted anilines with 1 mol % Fe(TPP)Cl. $^a$

<table>
<thead>
<tr>
<th>entry</th>
<th>amine</th>
<th>amine:EDA</th>
<th>time</th>
<th>% yield$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>2-chloroaniline</td>
<td>1:1.2</td>
<td>10 min</td>
<td>70</td>
</tr>
<tr>
<td>1b</td>
<td>2-chloroaniline</td>
<td>1:2.5</td>
<td>48 h</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>2-aminoacetophenone</td>
<td>1:1.2</td>
<td>20 min</td>
<td>57</td>
</tr>
<tr>
<td>3</td>
<td>2,6-dimethylaniline</td>
<td>1:1.5</td>
<td>24 h</td>
<td>NR</td>
</tr>
</tbody>
</table>

$^a$ Reaction were run with 1.0 mmol amine in 7.0 mL CH$_2$Cl$_2$ at ambient temperature.

$^b$ NMR yield.

result in any double insertion product of either substrate, indicating the reaction site may be too sterically hindered after the initial insertion reaction. Single insertion into 2,6-dimethylaniline was unsuccessful, also indicating steric hindrance affects the reaction. Steric hindrance was also observed with 2,2,6,6-tetramethylpiperidine (Table 3, entry 6).

Dimethyl diazomalonate (DMM) and methyl 2-phenyldiazoacetate (MPDA, Scheme 1) were also investigated as carbene sources for insertion into aniline. Catalytic reactions with MPDA and aniline gave a 92% yield of the N-H insertion product. This reaction required refluxing in methylene chloride for 40 hours, harsher conditions compared to the ambient temperature used for insertions with EDA.

Scheme 1

![Scheme 1](image-url)
The $^1$H NMR spectrum of the product showed a new one-proton singlet at 5.09 ppm for the new malonyl methine hydrogen. Insertion reactions with DMM and aniline in refluxing benzene for 72 hours yielded only a trace of the single insertion product as detected by GC-MS analysis: 224 (M+1), 104 (base peak).

Our group previously used Fe(TPP)Cl as a pre-catalyst for the cyclopropanation of olefins using EDA as both a reductant and a carbene source. In the present study, a competition experiment between cyclopropanation of styrene and N-H insertion of aniline was conducted. Equimolar amounts of aniline, styrene and EDA were used with 1.0 mole % Fe(TPP)Cl in methylene chloride. The reaction was run at both room temperature and in refluxing methylene chloride. Under both conditions, only the N-H insertion product was observed by GC-MS and $^1$H NMR. The preference for X-H insertion over cyclopropanation has been previously reported for ruthenium catalyzed N-H and S-H insertions, a rhodium catalyzed O-H insertion, and iron porphyrin and iron corrole catalyzed N-H insertions.

**Mechanistic Considerations**

Competition reactions were undertaken to gain insight into the mechanism of the insertion reaction. *Para*-substituted anilines were paired with aniline in equimolar amounts and treated with EDA in the presence of Fe(TPP)Cl. Relative rate data are summarized in a Hammett plot (Fig. 1). A better correlation was found with $\sigma^+$ ($R^2 = 0.93$) than with $\sigma$ ($R^2 = 0.88$) or $\sigma^-$ ($R^2 = 0.70$), indicating that a partial positive charge develops in the transition state that is stabilized by resonance effects. Electron-donating groups on the aniline derivatives increased the reaction rate as indicated by a negative
value of $\rho$ ($\rho = -0.66 \pm 0.05$). This is consistent with a nucleophilic attack of the amine on the electron deficient carbon of a putative carbene intermediate as the rate determining effect.

**Figure 1.** Hammett plot from competition reactions.

Competitive N-H/N-D experiments were undertaken to measure the kinetic isotope effects on the insertion reaction. The reaction of Et$_2$NH and Et$_2$ND (88.5% D) in a 1:1 molar ratio was treated with a limiting amount of EDA with 1 mol % Fe(TPP)Cl in C$_6$D$_6$ at ambient temperature. The resulting kinetic products ratio was determined on a 700 MHz Bruker NMR spectrometer by integrating the baseline-resolved methylene proton peaks of the products, Et$_2$NCH$_2$CO$_2$Et (s) and Et$_2$NCHDCO$_2$Et (t). After correcting for the % H content in Et$_2$ND, the measured $k_{H}/k_{D}$ was 1.41 ± 0.05. A similar competition experiment with aniline and aniline-$d_7$ (98% D) produced a comparable ratio, $k_{H}/k_{D} = 1.40 \pm 0.04$. 
Initially, the catalytic cycle for N-H insertion was thought to parallel the proposed mechanism for the cyclopropanation of olefins by Fe(TPP)Cl, involving the reduction of Fe(III) to Fe(II) as shown in Scheme 2. These cyclopropanation reactions were done under an inert atmosphere to prevent oxidation of the iron(II) species. EDA is a mild reducing agent and we have proposed previously that EDA reduces Fe\textsuperscript{III} porphyrins to Fe\textsuperscript{II} porphyrins in refluxing methylene chloride.\textsuperscript{1c} After the reduction, the resulting Fe\textsuperscript{II}(TPP) is sufficiently nucleophilic to displace N\textsubscript{2} from the \(\alpha\)-carbon of EDA to produce a reactive iron(II) carbene complex. The carbene ligand is subsequently attacked by the amine and proton migration from nitrogen to carbon produces the amino acid ester. While (TPP)Fe=CHCO\textsubscript{2}Et is very reactive and has not been detected, the reaction of Fe(II)(TTP) and mesityl diazomethane or trimethylsilyl diazomethane produced carbene complexes that have been spectroscopically detected.\textsuperscript{1b,c} The osmium analogue prepared from EDA, (TTP)Os=CHCO\textsubscript{2}Et, has been isolated and fully characterized.\textsuperscript{19}

A series of experiments indicate that reduction of the Fe(III) does not appear to be necessary in the N-H insertion process with EDA. For example, the insertion reactions

\[\text{EDA} \rightarrow \text{Fe}^\text{II}(TPP) \rightarrow \text{[Reactive Carbene Complex]} \]

\[\text{[Reactive Carbene Complex]} \rightarrow \text{EDA} \rightarrow \text{[Amino Acid Ester]} \]
could be done in air with only a slight decrease in yield. In assessing a possible prereduction step at ambient temperature, the Fe(TPP)Cl-catalyzed decomposition of EDA was examined in the presence and absence of tertiary amines that could coordinate to the porphyrin complex, but not undergo N-H insertion. These reactions were followed by $^1$H NMR using CHPh$_3$ as an internal standard. GC analysis was unreliable as the temperature in the injection port was sufficient to convert EDA to butene diolates in the absence of a catalyst. When no amine was added, EDA dimerized slowly (eq 5) in 6 hours to form diethyl fumarate (DEF) and diethyl maleate (DEM).

When small amounts (1-3%) of amine were present, the reaction times were significantly reduced to 20 min (Table 6). This indicated that the amine is important to the active Fe(III) catalytic species. To probe further the nature of the catalytic species, a comparison of Fe$^{III}$(TPP)Cl and Fe$^{II}$(TPP) was undertaken for the dimerization of EDA. As shown in Table 6, Fe$^{II}$(TPP) is a more efficient catalyst (entry 6) than Fe$^{III}$(TPP)Cl (entry 1), promoting the formation of DEF and DEM in a shorter time in the absence of amine with slightly higher yields, albeit with similar product ratios. However, addition of 1% pyridine to Fe$^{III}$(TPP)Cl (py:Fe = 1:1, entry 2) substantially enhanced the catalytic rate of dimerization of EDA and improved the product yields.
Table 6. Dimerization of EDA by 1 mol% iron porphyrin complexes at 20 °C under \( \text{N}_2 \).\(^a\)

<table>
<thead>
<tr>
<th>run</th>
<th>catalyst</th>
<th>mol% amine</th>
<th>yield %(^b)</th>
<th>time to completion</th>
<th>DEM:DEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>( \text{Fe}^{\text{III}}(\text{TPP})\text{Cl} )</td>
<td>0</td>
<td>82</td>
<td>6 h</td>
<td>33:1</td>
</tr>
<tr>
<td>2</td>
<td>( \text{Fe}^{\text{III}}(\text{TPP})\text{Cl} )</td>
<td>1% pyridine</td>
<td>94</td>
<td>20 min</td>
<td>6:1</td>
</tr>
<tr>
<td>3</td>
<td>( \text{Fe}^{\text{III}}(\text{TPP})\text{Cl} )</td>
<td>2% pyridine</td>
<td>95</td>
<td>20 min</td>
<td>6:1</td>
</tr>
<tr>
<td>4</td>
<td>( \text{Fe}^{\text{III}}(\text{TPP})\text{Cl} )</td>
<td>3% pyridine</td>
<td>93</td>
<td>20 min</td>
<td>6:1</td>
</tr>
<tr>
<td>5</td>
<td>[( \text{Fe}^{\text{III}}(\text{TPP})\text{py}_2 )] BF(_4)</td>
<td>0</td>
<td>96</td>
<td>20 min</td>
<td>6:1</td>
</tr>
<tr>
<td>6</td>
<td>( \text{Fe}^{\text{II}}(\text{TPP}) )</td>
<td>0</td>
<td>94</td>
<td>50 min</td>
<td>32:1</td>
</tr>
<tr>
<td>7</td>
<td>( \text{Fe}^{\text{II}}(\text{TPP}) )</td>
<td>1% pyridine</td>
<td>56</td>
<td>16 h</td>
<td>11:1</td>
</tr>
<tr>
<td>8</td>
<td>( \text{Fe}^{\text{II}}(\text{TPP}) )</td>
<td>2% pyridine</td>
<td>&lt;2</td>
<td>16 h</td>
<td>NA</td>
</tr>
<tr>
<td>9</td>
<td>( \text{Fe}^{\text{III}}(\text{TPP})\text{Cl} )</td>
<td>1% 2,6-lutidine</td>
<td>86</td>
<td>8 h</td>
<td>31:1</td>
</tr>
<tr>
<td>10</td>
<td>( \text{Fe}^{\text{III}}(\text{TPP})\text{Cl} )</td>
<td>2% 2,6-lutidine</td>
<td>86</td>
<td>8 h</td>
<td>30:1</td>
</tr>
<tr>
<td>11</td>
<td>( \text{Fe}^{\text{III}}(\text{TPP})\text{Cl} )</td>
<td>3% 2,6-lutidine</td>
<td>88</td>
<td>8 h</td>
<td>32:1</td>
</tr>
<tr>
<td>12</td>
<td>( \text{Fe}^{\text{II}}(\text{TPP}) )</td>
<td>1% 2,6-lutidine</td>
<td>92</td>
<td>50 min</td>
<td>32:1</td>
</tr>
<tr>
<td>13</td>
<td>( \text{Fe}^{\text{II}}(\text{TPP}) )</td>
<td>2% 2,6-lutidine</td>
<td>93</td>
<td>50 min</td>
<td>36:1</td>
</tr>
</tbody>
</table>

\(^a\) Reaction were run with 0.08 mmol of EDA in 5 mL CH\(_2\)Cl\(_2\). \(^b\) NMR yields using CHPh\(_3\) as an internal standard.

In contrast, the addition of 1% pyridine to \( \text{Fe}^{\text{II}}(\text{TPP}) \) had the opposite effect (entry 7), degrading the reaction time by more than 16-fold and decreasing the yield by approximately one half. In both cases, the DEM:DEF ratio also dropped significantly with the addition of 1% pyridine. Increasing the amount of pyridine above 1% in the Fe(III) system did not produce any further changes (entries 3-4). Moreover, the previously characterized Fe(III) bispyridine complex, [\( \text{Fe}(\text{TPP})\text{py}_2 \)] BF\(_4\),\(^{20}\) catalyzed the decomposition of EDA (entry 5) in a manner similar to the \( \text{Fe}^{\text{III}}(\text{TPP})\text{Cl}-\text{pyridine} \) system. However, addition of 2% pyridine to \( \text{Fe}^{\text{II}}(\text{TPP}) \) (py:Fe = 2:1, entry 8) drastically inhibited the dimerization of EDA. These results indicate that if Fe(III) is reduced to Fe(II), the
presence of pyridine would strongly inhibit its catalytic behavior. Thus, it is highly likely that prereduction of Fe(III) is not necessary for catalytic carbene insertion from EDA into N-H bonds of amines.

Additional support for ligand binding effects on the catalytic dimerization of EDA by Fe\textsuperscript{III}(TPP)Cl was illustrated with 2,6-lutidine (Table 6, entries 9-11). Since 2,6-lutidine is sterically hindered and a poor ligand for metalloporphyrins,\textsuperscript{21} no enhancement was expected as was observed when pyridine was added to a catalytic Fe\textsuperscript{III}(TPP)Cl system. Indeed, the rate of EDA dimerization by Fe\textsuperscript{III}(TPP)Cl with 1-3 eq. of 2,6-lutidine was qualitatively the same as that by Fe\textsuperscript{III}(TPP)Cl alone. In complementary experiments, addition of 1-2 eq. of 2,6-lutidine to Fe\textsuperscript{II}(TPP) also had no effect on the catalytic dimerization of EDA. Thus, the rate acceleration of EDA dimerization on addition of pyridine must involve binding of the amine to the metal center of Fe\textsuperscript{III}(TPP)Cl.

The proposed mechanism for N-H insertion into aniline is shown in Scheme 3. In the presence of unhindered bases, Fe(TPP)Cl typically forms bis-amine complexes, [(TPP)FeL\textsubscript{2}]\textsuperscript{+}.\textsuperscript{22} Dissociation of a ligand produces a five-coordinate mono-amine species that has sufficient electron density and an open coordination site at the metal center so that a six-coordinate Fe(III) porphyrin carbene complex can be produced readily. Formation of the carbene complex is extremely rapid as evident by the notable evolution of gas on addition of EDA to the reaction flask. In the absence of amine, formation of a carbene complex directly from Fe(TPP)Cl is unfavorable. The carbene carbon then undergoes nucleophilic attack by an additional amine to form the insertion product. The amine nitrogen is more nucleophilic than EDA and single N-H insertion occurs faster than dimerization. Moreover, the qualitative variation of rates as a function of the amine
indicated that the rate-determining step is the addition of amine to the carbene carbon. In addition, the hydrogen transfer step exhibits N-H/N-D isotope effects, $k_H/k_D = 1.41 \pm 0.05$ (diethyl amine) and $1.40 \pm 0.04$ (aniline).

**Scheme 3**

The N-glycine ester formed from the first insertion is less nucleophilic than the original amine, resulting in a slower second N-H insertion step. Since the second insertion process is less competitive with carbene dimerization, step-wise addition of EDA is necessary to optimize the formation of the double insertion product. Although it is possible that the N-H insertion reactions catalyzed by the related Fe(III) corrole complexes$^{13}$ may involve a similar mechanism, it is unclear what pathway the corresponding Fe(IV) corrole compounds employ. Although no induction period was reported for the Fe(IV) case, a possibility involves reduction of the iron center from IV to III.
Conclusion

Catalytic carbene insertion from EDA into N-H bonds mediated by Fe(TPP)Cl is a very efficient process. Fe(TPP)Cl appears to be among the best catalysts for insertion of EDA into amine N-H bonds and insertion reactions could also be performed at ambient temperatures and atmospheric conditions in relatively short reaction times. Aliphatic and aromatic amines were both shown to be good substrates giving high yields (>85%). Single and double insertion products were successfully obtained when primary amines were used as the substrate. Unlike other reported N-H insertion catalysts, the insertion reaction was faster than EDA dimerization and slow addition of EDA is not necessary with Fe(TPP)Cl. Mechanistic studies and comparisons with FeII(TPP) suggest that an Fe(III) form of the porphyrin complex is the active catalyst. Moreover, FeIII(TPP)Cl has the advantages of not being poisoned by the amine, producing little of the dimerization side products from EDA, is commercially available, and relatively inexpensive.

Experimental Procedures

General methods. EDA, solvents and amines were used as received, except as noted. Fe(TPP)Cl, Mn(TPP)Cl, Fe(TMeO-PP)Cl, and Fe(TPFPP)Cl were all used as received. Os(TTP)(CO)23 Fe(saldach)Cl24 and Zn(TPP)25 were prepared according to literature procedures. Co(TTP) was prepared using a modified literature procedure.26 DMM27 and MPDA28 were synthesized following literature procedures. Aniline was distilled from CaH2 under reduced pressure. Diethyl amine was distilled from KOH pellets. The reaction progress and competition reactions were monitored by gas chromatography on a HP5890 Series II Plus gas chromatograph using a HP-5 cross-
linked 5% PH ME silicone column, 30 m × 0.32 mm × 0.25 µm film thickness. 

$^1$H and $^{13}$C spectra were obtained in CDCl$_3$ on a Varian VXR-300 spectrometer. MS analysis was done on a Finnigan Magnum GC-MS. Elemental analyses for new compounds were performed on a Perkin-Elmer Model 2400 Series II CHN/S elemental analyzer. Fe(TMP)Cl was prepared according to a literature procedure$^{29}$ then reduced with Zn/Hg in toluene. 

$[^{13}]$Fe(TPP)py$_2$BF$_4$ was synthesized as reported previously.$^{20}$

**General procedure for single insertion reactions (Method A).** In a typical experiment, an amine (0.250–1.0 mmol) was dissolved in 5 mL methylene chloride in a 25 mL round bottom flask. Fe(TPP)Cl (0.0025–0.010 mmol, 1 mol%) was added and nitrogen was bubbled through the solution for 20 minutes. Ethyl diazoacetate (EDA) (1.20 equiv., 0.275–1.20 mmol) in 2 mL CH$_2$Cl$_2$ was added in one aliquot and the reaction mixture was stirred 10 minutes. Almost immediate release of N$_2$ was evident in most reactions. Upon completion of the reaction as indicated by GC analysis, the solvent was removed in vacuo and the reaction yield was determined by $^1$H NMR with triphenylmethane as an internal standard. Products were purified by column chromatography on silica gel (2.5 cm × 11 cm) and eluted with hexane:ethyl acetate (10:1) unless specified otherwise.

**General procedure for double insertion reactions (Method B).** The single insertion product was formed using the reaction conditions described above. An additional 1.20 equiv. EDA in 2 mL CH$_2$Cl$_2$ was added by syringe over one minute and the reaction was stirred for an additional hour and monitored by GC. Upon completion of the reaction, the solvent was removed in vacuo and the reaction mixture was analyzed by $^1$H NMR with triphenylmethane as an internal standard. Products were purified by
column chromatography (2.5 cm × 11 cm) on silica gel and eluted with hexane:ethyl acetate (10:1) unless specified otherwise.

**General procedure for competition reactions.** Equimolar quantities (0.300 mmol) of aniline and an aniline derivative and Fe(TPP)Cl (0.0030 mmol) in 4 mL methylene chloride were stirred under nitrogen. EDA (0.300 mmol) in 2 mL methylene chloride was added by syringe in one aliquot. After five minutes, a sample was removed and the ratio of product yields was determined by gas chromatography using dodecane as an internal standard.

**Synthesis of Et₂NCH₂CO₂CH₂CH₃.** Method A was followed using diethylamine (43.7 mg, 0.597 mmol), EDA (83.5 mg, 0.732 mmol), Fe(TPP)Cl (4.2 mg, 0.0060 mmol). A yellow oil was isolated (74.0 mg). ¹H-NMR δ ppm: 1.02 (t, 6H, NCH₂CH₃), 1.27 (t, 3H, OCH₂CH₃), 2.61 (q, 4H, CH₂CH₃), 3.27 (s, 2H, NCH₂CO), 4.14 (q, 2H, OCH₂CH₃). ¹³C-NMR δ ppm: 12.4 (NCH₂CH₃), 14.5 (OCH₂CH₃), 48.0 (NCH₂CH₃), 54.5 (NCH₂CO), 60.6 (OCH₂CH₃), 171.8 (CO). MS: 160 (M+1). Anal. Calcd.: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.26; H, 10.83; N, 8.42.

**Synthesis of t-BuNH(CH₂CO₂CH₂CH₃).** A yellow oil (87.9 mg) was obtained using method A with t-butylamine (75.8 mg, 1.04 mmol), EDA (126.6 mg, 1.11 mmol), Fe(TPP)Cl (7.4 mg, 0.011 mmol). ¹H-NMR δ ppm: 1.11 (s, 9H, CCH₃), 1.28 (t, 3H, OCH₂CH₃), 1.7 (broad, NH), 3.40 (s, 2H, NCH₂CO), 4.19 (q, 2H, OCH₂CH₃). ¹³C-NMR δ ppm: 14.3 (CCH₃), 28.9, 45.0, 50.3, 60.9, 173.1 (CO). MS: 160 (M+1). Spectral results match reported values.⁶

**Synthesis of C₅H₁₀NCH₂CO₂CH₂CH₃.** A yellow oil (83.0 mg) was obtained using method A with piperidine (48.7 mg, 0.572 mmol), EDA (78.3 mg, 0.687 mmol),
Fe(TPP)Cl (3.5 mg, 0.0050 mmol). $^1$H-NMR δ ppm: 1.27 (t, 3H, OCH$_2$CH$_3$), 1.43 (m, 2H, C$_5$H$_{10}$), 1.62 (m, 4H, C$_5$H$_{10}$), 2.50 (m, 4H, C$_5$H$_{10}$), 3.17 (s, 2H, NCH$_2$CO), 4.18 (q, 2H, OCH$_2$CH$_3$). $^{13}$C-NMR δ ppm: 14.3, 23.9, 25.8, 54.4, 60.4, 60.5, 170.7. MS: 172 (M+1), 98 (base peak). Spectral results match reported values.  

**Synthesis of PhCH$_2$NH(CH$_2$CO$_2$CH$_2$CH$_3$).** A yellow oil (164.2 mg) was obtained using method A with benzyl amine (124.8 mg, 1.16 mmol), EDA (148.0 mg, 1.30 mmol), Fe(TPP)Cl (7.5 mg, 0.011 mmol). $^1$H-NMR δ ppm: 1.27 (t, 3H, OCH$_2$CH$_3$), 1.85 (s, 1H, NH), 3.41 (s, 2H, NC$_2$H$_4$CO), 3.81 (s, 2H, PhC$_6$H$_5$N), 4.19 (q, 2H, OCH$_2$CH$_3$), 7.27 to 7.34 (m, 5H, C$_6$H$_5$). $^{13}$C-NMR δ ppm: 14.5, 50.3, 53.5, 60.9, 127.4, 128.5, 128.7, 139.7, 172.6. MS: 194 (M+1), 91 (base peak). Spectral results match reported values.

**Synthesis of PhCH$_2$N(CH$_2$CO$_2$CH$_2$CH$_3$)$_2$.** Procedure B was followed using an overall amine:EDA ratio of 1:3 and total reaction time of 15 minutes: benzylamine (60.9 mg, 0.568 mmol), EDA (218.4 mg, 1.92 mmol), Fe(TPP)Cl (3.8 mg, 0.0054 mmol). A yellow-green oil was obtained (153.5 mg). $^1$H-NMR δ ppm: 1.29 (t, 6H, OCH$_2$CH$_3$), 3.59 (s, 4H, NCH$_2$CO), 3.96 (s, 2H, PhCH$_2$N), 4.20 (q, 4H, OCH$_2$CH$_3$), 7.21 to 7.37 (m, 5H, C$_6$H$_5$). $^{13}$C-NMR δ ppm: 14.2, 54.2, 57.8, 60.4, 127.3, 128.3, 129.0, 138.1, 171.1. MS: 280 (M+1), 206 (base peak). Spectral results match that of the commercially available compound from Aldrich.

**Synthesis of p-CH$_3$O-C$_6$H$_4$-NH(CH$_2$CO$_2$CH$_2$CH$_3$).** Anisidine (123.3 mg, 1.001 mmol) was treated with EDA (128.7 mg, 1.128 mmol) and Fe(TPP)Cl (6.5 mg, 0.0092 mmol) using method A. A white solid (125.0 mg) was isolated. $^1$H-NMR δ ppm: 1.29 (t, 3H, OCH$_2$CH$_3$), 3.74 (s, 3H, CH$_3$O), 3.86 (s, 2H, NCH$_2$CO), 4.23 (q, 2H, OCH$_2$CH$_3$), 6.59 (d, 2H, C$_6$H$_4$), 6.79 (d, 2H, C$_6$H$_4$), NH not observed. $^{13}$C-NMR δ ppm: 14.2, 46.8,

**Synthesis of p-CH₃O-C₆H₄-N(CH₂CO₂CH₂CH₃)₂.** A yellow-orange oil (245.7 mg) was obtained using method B: p-anisidine (126.7 mg, 1.029 mmol), EDA (235.7 mg, 2.854 mmol), Fe(TPP)Cl (7.5 mg, 0.011 mmol). ¹H-NMR δ ppm: 1.26 (t, 6H, OCH₂CH₃), 3.73 (s, 3H, OCH₃), 4.10 (s, 4H, NCH₂CO), 4.20 (q, 4H, OCH₂CH₃), 6.61 (m, 2H, C₆H₄), 6.80 (m, 2H, C₆H₄). ¹³C-NMR δ ppm: 14.2, 54.0, 55.6, 60.9, 114.4, 114.7, 142.3, 152.6, 171.1. MS: 295 (M). Anal. Calcd.: C, 61.00; H, 7.17; N, 4.74. Found: C, 60.32; H, 7.70; N, 5.27.

**Synthesis of p-CH₃-C₆H₄-NH(CH₂CO₂CH₂CH₃).** A white solid (86.8 mg) was obtained using method A; toluidine (53.5 mg, 0.499 mmol), EDA (65.6 mg, 0.575 mmol), Fe(TPP)Cl (3.7 mg, 0.0053 mmol). ¹H-NMR δ ppm: 1.29 (t, 3H, OCH₃), 2.24 (s, 3H, CH₃C₆H₄), 3.88 (s, 2H, NCH₂CO), 4.24 (q, 2H, OCH₂CH₃), 6.53 (m, 2H, C₆H₄), 7.00 (d, 2H, C₆H₄), NH not observed. ¹³C-NMR δ ppm: 14.2, 20.4, 46.2, 61.2, 113.1, 127.4, 129.8, 144.8, 171.3. MS: 193 (M+1). Spectral results match reported values.⁶

**Synthesis of p-CH₃-C₆H₄-N(CH₂CO₂CH₂CH₃)₂.** A yellow oil (405.3 mg) was isolated using method B; toluidine (206.7 mg, 1.929 mmol), EDA (500.1 mg, 4.383 mmol), Fe(TPP)Cl (12.8 mg, 0.0182 mmol). ¹H-NMR δ ppm: 1.30 (t, 6H, OCH₂CH₃), 2.27 (s, 3H, CH₃C₆H₃), 4.15 (s, 4H, NCH₂CH₃), 4.24 (q, 4H, OCH₂CH₃), 6.59 (d, 2H, C₆H₄), 7.07 (d, 2H, C₆H₄). ¹³C-NMR δ ppm: 14.2, 54.0, 55.6, 60.9, 114.4, 114.7, 142.3, 152.6, 171.1. MS: 279 (M), 206 (base peak). Anal. Calcd.: C, 64.49; H, 7.58; N, 5.02. Found: C, 63.93; H, 7.70; N, 5.41.
**Synthesis of C₆H₅-NH(CH₂CO₂CH₂CH₃).** A yellow oil (115.0 mg) was obtained using method A: aniline (68.7 mg, 0.738 mmol), EDA (99.7 mg, 0.874 mmol), Fe(TPP)Cl (4.0 mg, 0.0057 mmol). ¹H-NMR δ ppm: 1.30 (t, 3H), 3.91 (s, 2H), 4.25 (q, 2H), 6.65 (d, 2H), 6.77 (t, 1H), 7.21 (t, 2H), NH not observed. ¹³C-NMR δ ppm: 14.1, 45.8, 61.2, 112.9, 118.1, 129.2, 146.9, 171.0. MS: 180 (M+1, base peak). Spectral results match reported values.⁶

**Synthesis of C₆H₅-N(CH₂CO₂CH₂CH₃)₂.** A yellow oil (106.4 mg) was isolated using method B with an overall amine: EDA ratio of 1:2.9 and a reaction time of 2 hours after the second addition of EDA: aniline (47.1 mg, 0.506 mmol), EDA (169.5 mg, 1.485 mmol), Fe(TPP)Cl (3.5 mg, 0.0050 mmol). ¹H-NMR δ ppm: 1.28 (t, 6H, OCH₂CH₃), 4.14 (s, 4H, NC₃H₂CO), 4.22 (q, 4H, OCH₂CH₃), 6.60-6.65 (m, 2H, C₆H₅), 6.75-6.80 (m, 1H, C₆H₅), 7.19-7.25 (m, 2H, C₆H₅). ¹³C-NMR δ ppm: 14.0, 53.3, 60.9, 112.3, 118.0, 129.1, 147.7, 170.7. MS: 265 (M). Anal. Calcd.: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.17; H, 7.68; N, 5.57.

**Synthesis of p-Cl-C₆H₄-N(CH₂CO₂CH₂CH₃).** A pale yellow solid (42.4 mg) was isolated using method A: p-chloroaniline (63.3 mg, 0.496 mmol), EDA (57.3 mg, 0.502 mmol), Fe(TPP)Cl (3.7 mg, 0.0053 mmol). ¹H-NMR δ ppm: 1.30 (t, 3H, OCH₂CH₃), 3.88 (s, 2H, NCH₂CO), 4.25 (q, 2H, OCH₂CH₃), 6.52-6.56 (m, 2H, C₆H₄), 7.12-7.16 (m, 2H, C₆H₄), NH not observed. ¹³C-NMR δ ppm: 14.2, 45.9, 61.5, 114.1, 122.9, 129.1, 145.5, 170.8. MS: 213 (M), 140 (base peak). Spectral results match reported values.⁶

**Synthesis of p-Cl-C₆H₄-N(CH₂CO₂CH₂CH₃)₂.** A yellow oil (91.8 mg) was isolated using method B: p-chloroaniline (64.4 mg, 0.505 mmol), EDA (140.0 mg, 1.227
mmol), Fe(TPP)Cl (3.5 mg, 0.0050 mmol). $^1$H-NMR δ ppm: 1.28 (t, 6H, OCH$_2$CH$_3$), 4.10 (s, 4H, NCH$_2$CO), 4.21 (q, 4H, OCH$_2$CH$_3$), 6.54 (d, 2H, C$_6$H$_4$), 7.16 (d, 2H, C$_6$H$_4$).

$^{13}$C-NMR δ ppm: 14.4, 53.8, 61.4, 114.0, 123.4, 129.3, 146.8, 170.7. MS: 299(M), 154 (base peak). Anal. Calcd.: C, 56.09; H, 6.05; N, 4.67. Found: C, 55.69; H, 6.49; N, 4.92.

**Synthesis of p-Br-C$_6$H$_4$-NH(CH$_2$CO$_2$CH$_2$CH$_3$).** A pale yellow solid (183.6 mg) was obtained using method A: p-bromoaniline (153.9 mg, 0.8947 mmol), EDA (108.1 mg, 0.9473 mmol), Fe(TPP)Cl (6.5 mg, 0.0092 mmol). $^1$H-NMR δ ppm: 1.30 (t, 3H, OCH$_2$C), 3.86 (s, 2H, NC$_2$HCO), 4.25 (q, 2H, OC$_2$H$_2$CH$_3$), 6.49 (d, 2H, C$_6$H$_4$), 7.27 (d, 2H, C$_6$H$_4$), NH not observed. $^{13}$C-NMR δ ppm: 14.2, 45.7, 61.5, 109.9, 114.5, 132.0, 146.0, 170.6. MS: 258 (M+1). Anal. Calcd.: C, 46.53; H, 4.69; N, 5.43. Found: C, 46.65; H, 4.79; N, 5.57.

**Synthesis of p-Br-C$_6$H$_4$-N(CH$_2$CO$_2$CH$_2$CH$_3$)$_2$.** A yellow oil (208.8 mg) was isolated using method B with an overall amine:EDA ratio of 1:4.1 and a reaction time of 24 hours after the second addition of EDA; p-bromoaniline (143.3 mg, 0.8330 mmol), EDA (389.3 mg, 3.412 mmol), Fe(TPP)Cl (5.4 mg, 0.0077 mmol). $^1$H-NMR δ ppm: 1.27 (t, 6H, OCH$_2$CH$_3$), 4.09 (s, 4H, NCH$_2$CO), 4.21 (q, 4H, OCH$_2$CH$_3$), 6.49 (d, 2H, C$_6$H$_4$), 7.29 (d, 2H, C$_6$H$_4$). $^{13}$C-NMR δ ppm: 14.2, 53.6, 61.2, 110.4, 114.2, 131.9, 146.9, 170.5. MS: 343 (M-1), 59 (base peak). Anal. Calcd.: C, 48.85; H, 5.27; N, 4.07. Found: C, 48.38; H, 5.84; N, 3.90.

**Synthesis of p-CN-C$_6$H$_4$-NH(CH$_2$CO$_2$CH$_2$CH$_3$).** A pale yellow solid (166.2 mg) was obtained using method A and a reaction time of 20 minutes with p-cyanoaniline (110.5 mg, 0.9353 mmol), EDA (123.4 mg, 1.081 mmol), Fe(TPP)Cl (7.0 mg, 0.0099 mmol). The chromatography eluent was hexane:ethyl acetate 5:1. $^1$H-NMR δ ppm: 1.29
(t, 3H, OCH₃CH₂), 3.90 (s, 2H, NCH₂CO), 4.25 (q, 2H, OCH₂CH₃), 6.55 (d, 2H, C₆H₄), 7.42 (d, 2H, C₆H₄), NH not observed. ¹³C-NMR δ ppm: 14.1, 44.7, 61.7, 99.6, 112.4, 120.1, 133.6, 150.0, 169.9. MS: 204(M), 131 (base peak). Anal. Calcd.: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.64; H, 6.12; N, 13.89.

Synthesis of p-CN-C₆H₄-N(CH₂CO₂CH₂CH₃)₂. Procedure B was followed using an overall amine:EDA ratio of 1:4 and a reaction time of 4 hours after the second addition of EDA. This reaction had a low double insertion yield (<20%) and the desired product could not be isolated from the single insertion product. MS: 290 (M⁺), 217 (base peak).

Synthesis of p-NO₂-C₆H₄-NH(CH₂CO₂CH₂CH₃). A yellow solid (200.6 mg) was obtained using method A, requiring 18 hours p-nitroaniline (141.0 mg, 1.02 mmol), EDA (128 mg, 1.12 mmol), Fe(TPP)Cl (7.2 mg, 0.010 mmol). The chromatography eluent was hexane:ethyl acetate 5:1. ¹H-NMR δ ppm: 1.33 (t, 3H, OCH₂CH₃), 3.98 (s, 2H, NCH₂CO), 4.29 (q, 2H, OCH₂CH₃), 6.56 (d, 2H, C₆H₄), 8.12 (d, 2H, C₆H₄), NH not observed. ¹³C-NMR δ ppm: 14.4, 45.1, 62.2, 111.7, 126.6, 139.1, 152.1, 169.9. MS: 224 (M), 151 (base peak). Anal. Calcd.: C, 53.56; H, 5.39; N, 12.50. Found: C, 53.20; H, 5.58; N, 12.35.

Insertion into Imidazole. A yellow oil (157.4 mg) was obtained using method A with the reaction being complete in 48 hours: imidazole (135.4 mg, 1.989 mmol), EDA (321.7 mg, 2.819 mmol), Fe(TPP)Cl (13.3 mg, 0.019 mmol). The chromatography eluent was ethyl acetate: methanol 10:1. ¹H-NMR δ ppm: 1.26 (t, 3H, OCH₂CH₃), 4.21 (q, 2H, OCH₂CH₃), 4.66 (s, 2H, NCH₂CO) 6.93 (s, 1H, C=CH), 7.06 (s, 1H, C=CH) 7.47 (s, 1H, NCH₃). ¹³C-NMR δ ppm: 14.3, 48.3, 62.3, 120.2, 129.9, 138.1, 167.6. MS: 154 (M), 81.

**Insertion of MPDA into aniline.** A yellow-white solid (69.6 mg, 92% yield) was prepared using method A except the reaction solution was refluxed: aniline (29.2mg, 0.314 mmol), MPDA (63.9 mg, 0.363mmol) with the reaction being complete in 40 hours. The chromatography eluent was hexane: ethyl acetate 10:1.  

$^1$H-NMR δ ppm: 3.74 (s, 3H, CH$_3$), 4.97 (s, 1H, NH), 5.09 (s, 1H, NCHCO), 6.57 (d, 2H, C$_6$H$_5$), 6.71 (t,1H, C$_6$H$_5$), 7.13 (t,2H, C$_6$H$_5$), 7.35 (m, 3H, C$_6$H$_5$), 7.51 (dd, 2H, C$_6$H$_5$).  

$^{13}$C-NMR δ ppm: 52.8, 60.7, 113.4, 118.1, 127.2, 128.3, 128.8, 129.2, 137.6, 145.9, 172.3.  

MS: 242(M+1), 121 (base peak).

**General procedure for dimerization of EDA using Fe(TPP)Cl.** In a typical experiment, Fe(TPP)Cl (1.1 mg, 0.0015 mmol) was dissolved in 2 mL of deuterated methylene chloride and the mixture stirred under nitrogen. From a pyridine- or a 2,6-lutidine-stock solution (0.018 mmol/mL of CD$_2$Cl$_2$), an appropriate volume was added to the Fe(TPP)Cl mixture to produce the required catalyst:amine ratio. EDA (18 mg, 0.15 mmol) in 1 mL of deuterated methylene chloride was added by syringe in one aliquot. The progress of the reactions was monitored by $^1$H NMR spectroscopy. Triphenylmethane (24 mg, 0.1 mmol) was used as an internal standard to determine the yields.

**General procedure for dimerization of EDA using Fe(II)(TPP).** In a typical experiment, Fe(TPP)Cl (2.1 mg, 0.0030 mmol) was dissolved in 2 mL of THF and excess Zn/Hg amalgam (6-8 mg) added in a glove box. This mixture was stirred overnight (about 16 hours). The resulting solution was then filtered through a fine frit to remove
the Zn/Hg amalgam. The solvent was removed under reduced pressure. The resulting Fe(TPP) was then redissolved in 2 mL of deuterated methylene chloride. From this solution, an appropriate volume of FeTPP (0.0008 mmol) was measured and placed in a 5 mL round bottom flask. From a pyridine- or a 2,6-lutidine-stock solution (0.018 mmol/mL of CD$_2$Cl$_2$), an appropriate volume was added to the Fe(TPP) mixture to produce the required catalyst:amine ratio. EDA (9.0 mg, 0.08 mmol) in 1 mL of deuterated methylene chloride was added by syringe in one aliquot. The progress of the reactions was monitored by $^1$H NMR spectroscopy. Triphenylmethane (12 mg, 0.05 mmol) was used as an internal standard to determine the yields.

**Et$_2$N-D.** $N$-deuterated diethylamine was prepared by three fractional distillations of a mixture of the amine and a tenfold molar excess of D$_2$O using a 20-cm Vigreux column.$^{30}$ The product was dried and distilled from calcium hydride. The percent deuteration was determined by reaction with excess EDA to form monodeuterated Et$_2$NCHDCO$_2$Et catalyzed by Fe(TPP)Cl in CD$_2$Cl$_2$. Residual H-N protons resulted in the production of Et$_2$NCH$_2$CO$_2$Et and amounts of the $d_0/d_1$ products could be quantitatively measured by $^1$H NMR at 700 MHz by integration of the baseline separated N-methylene signals. A $d_1/d_0$ product ratio of 7.72:1 was obtained (88.5 atom % $d$). Aniline-$d_7$ was obtained from Aldrich and used as received.

**Kinetic isotope effect.** C$_6$D$_6$ was dried by stirring with phosphorus pentoxide for 18 h in a sealed Schlenk tube under reduced pressure. Using vacuum line techniques, ca. 0.6 mL of dry, C$_6$D$_6$ was added by trap-to-trap distillation to a dry 20 mL round bottom flask containing Fe(TPP)Cl, (0.5 mg, 0.07 µmoles) and a magnetic bar. The flask was warmed to ambient temperature, backfilled with dry nitrogen, and immediately capped
using a rubber septum under a positive flow of N₂. Diethylamine (10.0 µL, 7.07 mg, 96.7 µmoles) and diethylamine-N-d₁ (10.0 µL, 7.07 mg, 96.6 µmoles, 88.5 atom % D) were added to the stirred solution using a gas tight syringe. To initiate the reaction, a limiting amount of ethyldiazoacetate (10.0 µL, 8.50 mg, 74.6 µmoles) was added by syringe. The resulting contents were transferred to an NMR tube and the kinetic ratio of products was determined on a 700 MHz Bruker NMR spectrometer by integrating the baseline-resolved methylene proton peaks of the products, Et₂NCH₂CO₂Et (s) and Et₂NCHDCO₂Et (t). A similar procedure was used for deuterated aniline. The kinetic isotope effect was determined from averaging the results of three separate reactions.

Acknowledgement. We gratefully acknowledge funding from the Petroleum Research Fund and the National Science Foundation.

References


(11) Abbreviations: TPP – *meso*-tetraphenylporphyrin, TMeO-PP – *meso*-tetra(*p*-methoxyphenyl)porphyrin, TPFPP – *meso*-tetakis(pentafluorophenyl)porphyrin, TMP – *meso*-tetramesitylporphyrin, Saldach – N,N′-bis(salicylidene)-1,2-cyclohexyldiamine.


(13) Aviv, I.; Gross, Z.; *Synlett*, 2006, 951.


CHAPTER 3: CATALYTIC C-H INSERTIONS USING SILVER(II), COPPER(II) AND IRON(III) Porphyrin Complexes

Harun M. Mbuvi, L. Keith Woo

To be submitted to Organometalics

Abstract. Fe(III), Cu(II) and Ag(II) porphyrin complexes are active catalysts for benzylic and ring C-H insertions by carbene transferred from methyl diazomalonate, 2. Temperatures above 100 °C are required and yields greater than 70% have been achieved. C-H insertions with cyclohexane and tetrahydrofuran are catalyzed at a lower temperature of 60 °C with 60% yields when using para-substituted methyl 2-phenyldiazoacetates, 15a-d, as carbene sources. The rate for Fe(TPP)Cl-catalyzed insertion into the C-H bond of cyclohexane was found to be first order in methyl 2-(p-chlorophenyl)diazoacetates, [p-Cl-MPDA], indicating that formation of a carbene complex is the rate-determining step. Competition reactions for cyclohexane insertion with para-substituted methyl 2-phenyldiazoacetates correlated linearly with $\sigma^+$ Hammett parameters with a $\rho$ value of $-1.11 \pm 0.05$ when Fe(TPP)Cl was used as catalyst, implying that electron-donating para-substituents on the phenyl group of the methyl 2-aryldiazoacetates enhanced reactivity. These data support the involvement of an electrophilic iron-carbene complex in the catalytic cycle. A mechanistic model for the iron-mediated C-H insertion reactions is proposed.
Introduction

Transition metal catalyzed decomposition of diazo compounds and subsequent transformations constitute a variety of useful synthetic reactions. For example, cyclopropanation of olefins with diazo compounds has been extensively studied. Iron(II) porphyrins and dirhodiumtetracarboxylate complexes are among the most efficient catalysts reported for this reaction. High yields of cyclopropanation products have been achieved with styrene using iron(II) porphyrins complexes. Currently, dirhodiumtetracarboxylate complexes are also among the best catalysts for C-H insertion reactions using diazo reagents. Although both iron(II) porphyrin and dirhodium complexes complexes are also efficient and selective catalysts for other reactions such as the epoxidation of olefins, iron porphyrins have not been studied as catalysts for C-H insertion using diazo compounds.

The development of practical methods for catalytic C-H activation has been a long-term goal of the organometallic chemical community. One method for C-H activation involves the use of metal carbene complexes. Impressive advances have been made in asymmetric intramolecular C-H insertions involving diazo compounds. In contrast to numerous studies on intramolecular C-H insertions; the intermolecular analogue has not enjoyed widespread application. Indeed until very recently, the intermolecular C-H insertion was not considered to be of great synthetic utility. A major difficulty with intermolecular reactions is that the most widely studied alkyl diazoacetates are very prone to carbene dimerization. Furthermore, this carbene source exhibits poor chemoselectivity in intermolecular C-H insertions. Consequently, in order for
intermolecular C-H insertion to become a convenient method, it is necessary to develop systems with improved chemoselectivity.

In this paper, we report the application of iron(III) porphyrin complexes in catalytic intermolecular C-H insertion using different classes of diazo compounds. The ability of silver(I) scorpionate complexes (Tp\textsuperscript{Br3}Ag\textsubscript{2}·CH\textsubscript{3}COCH\textsubscript{3} and Tp\textsuperscript{Br3}Ag(THF) to catalyze the insertion of the carbene fragment from ethyl diazoacetate (EDA) into the saturated C-H bonds of several C\textsubscript{5}, C\textsubscript{6}, and C\textsubscript{8} linear and branched alkanes, including secondary and tertiary sites\textsuperscript{10} led us to also examine Ag and Cu porphyrins.

**Results and Discussion**

**Diazomalonate Reactions.** Dimethyl diazomalonate, 2, undergoes benzylic C-H insertion with toluene to give dimethyl 2-benzylmalonate (3a, eq 1) as the major product when Ag(TPP), Cu(TPP) and Fe(TPP)Cl (TPP = 5,10,15,20-tetraphenylporphyrinato) are used as catalysts. No products were formed when Mn(TPP)Cl, Co(TPP) and Zn(TPP) were tried as catalysts. This reaction was found to require temperatures above 100 °C and

\[
\text{2} + 2\text{N}_2 + \text{Catalyst} \xrightarrow{110^\circ C} \text{3a}
\]

\[\text{1} \quad \text{2} \quad \text{3a}
\]

\[
\text{a. } X = H
g. \quad \text{b. } X = \text{Cl}
d. \quad \text{c. } X = \text{CH}_3
\]
32 to 54 h when 2 mol% catalyst was used. Furthermore, anaerobic conditions were necessary to avoid side reactions that produced uncharacterized products. The insertion products were identified by $^1$H NMR spectroscopy and mass spectrometry. For example, formation of dimethyl 2-benzylmalonate, 3a, was established by $^1$H NMR with the appearance of a diagnostic 2-proton resonance for the benzylic hydrogens at 3.23 (d) ppm. The composition of the product was also verified by its mass of 222 m/z. The $^1$H and $^{13}$C NMR data for 3a were found to match literature values.\textsuperscript{11} Minor species with masses identical to 3a were observed by GC/MS. These products were identified by $^1$H NMR as ring C-H insertion products. Partial separation of the product mixture was achieved by silica gel chromatography using hexane/ethyl acetate (20:1) as the eluent. Compound 3a could be isolated cleanly but the toluene ring C-H insertion products o-, p-4a were not separable from each other. The $^1$H NMR spectrum of the o,p-mixture gave a broad singlet at 2.35 revealing aromatic CH$_3$ groups. Furthermore, the $^1$H NMR signals at 4.63 and 4.92 ppm, in an integrated ratio of 1:1, agree with the methine protons of dimethyl p-tolylmalonate\textsuperscript{12} and dimethyl o-tolylmalonate,\textsuperscript{13} respectively, that would result from ring C-H insertions. Reactions with p-chlorotoluene, 1b, were found to result in lower yields and a higher ratio of benzylic C-H insertion, 3b, to ring C-H insertion products (10:1) as indicated in Table 1. In this case, the ring C-H insertion products o-, p-4b were minor and detectable by GC, but could not be isolated. GC yields of the products varied slightly as a function of the catalyst as shown in Table 1. When p-xylene was used as the substrate, a benzylic C-H insertion product, dimethyl (p-methylbenzyl)malonate, 3c, was obtained along with a ring C-H insertion product, dimethyl 2,5-xylylmalonate, 4c, in ratio of about 5:1, respectively. Benzylic product 3c could be obtained in relatively
Table 1. Summary of catalytic reactions with dimethyl diazomalonate\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>catalyst</th>
<th>products</th>
<th>Time (hrs)</th>
<th>Yields(^b)</th>
<th>ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>toluene</td>
<td>Fe(TPP)Cl</td>
<td>3a:4a</td>
<td>54</td>
<td>68</td>
<td>2:1</td>
</tr>
<tr>
<td>2</td>
<td>toluene</td>
<td>Ag(TPP)</td>
<td>3a:4a</td>
<td>54</td>
<td>74</td>
<td>2:1</td>
</tr>
<tr>
<td>3</td>
<td>toluene</td>
<td>Cu(TPP)</td>
<td>3a:4a</td>
<td>54</td>
<td>72</td>
<td>2:1</td>
</tr>
<tr>
<td>4</td>
<td>toluene</td>
<td>Fe(TPPF(_{20}))Cl(^c)</td>
<td>3a:4a</td>
<td>72</td>
<td>51</td>
<td>2:1</td>
</tr>
<tr>
<td>5</td>
<td>toluene</td>
<td>ZnTPP</td>
<td>NR(^d)</td>
<td>72</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>6</td>
<td>toluene</td>
<td>CoTPP</td>
<td>NR</td>
<td>72</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>7</td>
<td>toluene</td>
<td>MnTPPCl</td>
<td>Mixture(^e)</td>
<td>72</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>8</td>
<td>(p)-Cl-toluene</td>
<td>Ag(TPP)</td>
<td>3b:4b</td>
<td>54</td>
<td>52</td>
<td>10:1</td>
</tr>
<tr>
<td>9</td>
<td>(p)-xylene</td>
<td>Fe(TPP)Cl</td>
<td>3c:4c</td>
<td>24</td>
<td>76</td>
<td>5:1</td>
</tr>
<tr>
<td>10</td>
<td>mesitylene</td>
<td>Fe(TPP)Cl</td>
<td>6:7</td>
<td>24</td>
<td>78</td>
<td>9:1</td>
</tr>
<tr>
<td>11</td>
<td>mesitylene</td>
<td>Ag(TPP)</td>
<td>6:7</td>
<td>24</td>
<td>79</td>
<td>9:1</td>
</tr>
<tr>
<td>12</td>
<td>mesitylene</td>
<td>Cu(TPP)</td>
<td>6:7</td>
<td>24</td>
<td>78</td>
<td>9:1</td>
</tr>
<tr>
<td>13</td>
<td>mesitylene</td>
<td>Fe(TPPF(_{20}))Cl(^c)</td>
<td>6:7</td>
<td>48</td>
<td>56</td>
<td>9:1</td>
</tr>
<tr>
<td>14</td>
<td>(C_6H_5Cl)</td>
<td>Fe(TPP)Cl</td>
<td>9:10</td>
<td>54</td>
<td>56</td>
<td>2:1</td>
</tr>
<tr>
<td>15</td>
<td>(C_6H_5Cl)</td>
<td>Ag(TPP)</td>
<td>9:10</td>
<td>54</td>
<td>62</td>
<td>2:1</td>
</tr>
<tr>
<td>16</td>
<td>(C_6H_5Cl)</td>
<td>Cu(TPP)</td>
<td>9:10</td>
<td>54</td>
<td>58</td>
<td>2:1</td>
</tr>
<tr>
<td>17</td>
<td>anisole</td>
<td>Fe(TPP)Cl</td>
<td>12a:13a</td>
<td>16</td>
<td>74</td>
<td>5:1</td>
</tr>
<tr>
<td>18</td>
<td>anisole</td>
<td>Ag(TPP)</td>
<td>12a:13a</td>
<td>16</td>
<td>78</td>
<td>5:1</td>
</tr>
<tr>
<td>19</td>
<td>anisole</td>
<td>Cu(TPP)</td>
<td>12a:13a</td>
<td>16</td>
<td>75</td>
<td>5:1</td>
</tr>
<tr>
<td>20</td>
<td>(p)-Me-anisole(^f)</td>
<td>Fe(TPP)Cl</td>
<td>12b:13b</td>
<td>16</td>
<td>76</td>
<td>8:1</td>
</tr>
</tbody>
</table>

\(^a\)Substrate used as solvent (5 mL), dimethyl diazomalonate (30.0 mg, 0.19 mmol), (TPP)FeCl (2.7 mg, 2 mol%), the mixture thoroughly purged with dry nitrogen, heated at 110 °C with continuous stirring. \(^b\)Combined yields of all products determined by GC. \(^c\)TPPF\(_{20}\) = tetrakis(pentafluorophenyl)-porphyrinato. \(^d\)No reaction. \(^e\)Several unidentified minor products. \(^f\)\(p\)-Me-anisole = \(p\)-methylanisole.
pure form and its $^1$H NMR spectrum showed signals that matched with literature values.\textsuperscript{14} A small amount of dimethyl 2-(2,5-xylyl)malonate, 4c, was produced but could not be isolated in pure form.

When mesitylene was heated to 110 °C in the presence of 2 mol\% catalyst and dimethyl diazomalonate, dimethyl 2-(3,5-dimethylbenzyl)malonate (6, eq 2) could be isolated pure in 74\% yield. A minor ring C-H insertion product, 2-(mesityl)malonate, 7, was detected by GC, but could not be isolated in pure form. The 9:1 ratio of 6 to 7 suggested that the ring C-H insertion products could be minimized by steric factors. Reactions run in the absence of catalysts did not yield products 6 or 7 but other minor, unidentified compounds were detected by GC.

\begin{center}
\includegraphics[width=0.6\textwidth]{reaction_diagram.png}
\end{center}

To explore further ring C-H insertions, other aromatic substrates were examined. Benzene did not undergo reaction, presumably due to its low boiling point. However, chlorobenzene was found to give the ortho- 9 and para-products 10 resulting from ring C-H insertions as shown in (eq 3). With all catalysts in Table 1, the ortho/para product ratios were approximately 2. Trace amounts of the meta product were detected but not isolable. Surprisingly, when anisole was treated under identical conditions dimethyl phenoxyxomalonate, 12a, was isolated as the major product in a yield of 60\% (eq 4). This product had a mass of 224 m/z and exhibited a new $^1$H resonance at 5.25 (s) ppm due to
the new methine proton. The new carbon α to the oxygen of 12a produced a 13C NMR signal at 82.29 ppm. A mixture of two minor ring C-H insertion isomers was also obtained from the anisole reaction and constituted a combined yield of about 10%. These two compounds had molecular ion masses of 238 m/z. The proton NMR spectrum of the minor isomer mixture gave resonances at 4.6 (s) and 5.1 (s) ppm that corresponded to the methine hydrogen of dimethyl p-methoxyphenylmalonate15 and dimethyl o-methoxyphenylmalonate,16 with an integrated ratio of 1:1. p-Methylanisole was found to give similar reaction results as anisole (eq 4) in addition to 4% benzylic C-H insertion. Attempts to use meta directing substituents with substrates such as benzonitrile and nitrobenzene resulted in no reactions after 3 days at 110 °C. Nonetheless, given the general success with Fe(TPP)Cl in catalysis, iron porphyrins were utilized in the remainder of this study.
**Substituted methyl 2-phenyldiazoacetates.** Catalytic C-H activation using Fe(TPP)Cl was extended to the chemistry of another class of diazo compounds, substituted methyl 2-phenyldiazoacetates. These diazo reagents contain an electron-withdrawing ester and an electron-donating aryl group on the incipient carbene carbon. The substituents on these compounds result in higher chemoselectivity and lower tendency towards carbene dimerization compared to alkyl diazoacetates.\(^{17}\) These properties should lead to more proficient intermolecular C-H insertion. The feasibility of the intermolecular C-H insertion reaction was demonstrated by treatment of a series of \(p\)-substituted methyl 2-phenyldiazoacetates in neat cyclohexane with catalytic amounts of iron porphyrins (eq 5). Yields of the C-H insertion products were found to be about 20% higher and fewer unidentified side products were detected when the reactions were conducted under anaerobic conditions at 60 °C as compared to reactions run under air. C-H insertion products were obtained in yields ranging from 66 to 74%. These yields are comparable to those obtained when dirhodium tetracarboxylate catalysts were used and \(^1\)H NMR data for the products matched literature values.\(^{18}\) The efficiency of the \(p\)-substituted methyl 2-phenyldiazoacetates for C-H insertion is in sharp contrast to the
results that were obtained when alkyl diazoacetates and dimethyl diazomalonate were used as the carbene sources. The reactions with ethyl diazoacetate or dimethyl diazomalonate did not generate any C-H insertion products with cyclohexane but a significant amount of butenedioate product is formed in the case of ethyl diazoacetate. Only trace amounts of dimeric carbene products were detected in the reactions with p-substituted methyl 2-phenyldiazoacetates.

Extension of the reaction to tetrahydrofuran using Fe(TPP)Cl as a catalyst (eq 6) illustrated that the C-H insertion of p-substituted methyl 2-phenyldiazoacetates was highly regioselective (Table 2). No insertion into the β-position of THF was observed. The catalyzed decomposition of p-substituted methyl 2-phenyldiazoacetates in the presence of tetrahydrofuran, heated under reflux, resulted in the formation of products 18a-d in yields ranging from 58-63%. These products are formed by C-H insertion into the methylene group adjacent to the oxygen. A minor ring-opened product 19a-d (~20% yield) was also isolated in pure form. These products were identified by 1H and 13C NMR spectroscopy. For example, in 19c, the 3-butenyl fragment exhibited proton signals at 5.84 (m, 1H, vinyl CH), 5.09 (dm, 1H, vinyl CH2) 5.04 (dm, 1H, vinyl CH2) 3.57 (m, 1H, methylene CH2) 3.48 (m, 1H, methylene CH2), 2.45 (m, 2H, methylene CH2). Formation of these ring-opened products likely arises from nucleophilic attack by the THF oxygen on an electron deficient carbene ligand (vide infra) followed by C-O bond cleavage and hydrogen transfer.
Mesitylene was found to undergo reaction at both benzylic C-H and ring C-H positions (eq 7) and the two products were not separable from each other except in the reaction with p-MeO-MPDA, 15d. \(^1\)H NMR data from the isolated methoxy substituted compounds 21d and 22d aided in the proton peak assignments for the inseparable mixtures. The electronic nature of the *para*-substituent in the substituted methyl 2-phenyl diazoacetates slightly influenced the product ratio. The less electron-donating Cl in methyl 2-(*p*-chlorophenyl)diazoacetate resulted in a ring C-H insertion as the major product, 22. As the electron donor ability of the aryl substituent was increased this product decreased. The methoxy substituent produced benzylic C-H insertion as the major product (Table 2, entries 9-12). This suggests that a more electrophilic carbene complex favors ring C-H insertion over benzylic C-H insertion. However, a fluorinated porphyrin iron(III) complex that would result in a more electrophilic carbene intermediate produced anomalous results. Surprisingly, in all the cases the ratio of the ring C-H insertion product was significantly lowered as indicated in Table 2, entries 13-16.
Table 2. Summary of catalytic reactions of substituted methyl 2-phenyldiazoacetate compounds.

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>catalyst</th>
<th>diazo products</th>
<th>Time (h)</th>
<th>% yields&lt;sup&gt;b&lt;/sup&gt;</th>
<th>ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cyclohexane</td>
<td>Fe(TPP)Cl</td>
<td>15a 16a</td>
<td>24</td>
<td>66</td>
<td>n/a</td>
</tr>
<tr>
<td>2</td>
<td>Cyclohexane</td>
<td>Fe(TPP)Cl</td>
<td>15b 16b</td>
<td>24</td>
<td>58</td>
<td>n/a</td>
</tr>
<tr>
<td>3</td>
<td>Cyclohexane</td>
<td>Fe(TPP)Cl</td>
<td>15c 16c</td>
<td>24</td>
<td>72</td>
<td>n/a</td>
</tr>
<tr>
<td>4</td>
<td>Cyclohexane</td>
<td>Fe(TPP)Cl</td>
<td>15d 16d</td>
<td>24</td>
<td>78</td>
<td>n/a</td>
</tr>
<tr>
<td>5</td>
<td>THF</td>
<td>Fe(TPP)Cl</td>
<td>15a 18a:19a</td>
<td>32</td>
<td>62</td>
<td>3.4:1</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>Fe(TPP)Cl</td>
<td>15b 18b:19b</td>
<td>32</td>
<td>67</td>
<td>3.5:1</td>
</tr>
<tr>
<td>7</td>
<td>THF</td>
<td>Fe(TPP)Cl</td>
<td>15c 18c:19c</td>
<td>32</td>
<td>75</td>
<td>3.7:1</td>
</tr>
<tr>
<td>8</td>
<td>THF</td>
<td>Fe(TPP)Cl</td>
<td>15d 18d:19d</td>
<td>32</td>
<td>82</td>
<td>3.6:1</td>
</tr>
<tr>
<td>9</td>
<td>Mesitylene</td>
<td>Fe(TPP)Cl</td>
<td>15a 21a:22a</td>
<td>12</td>
<td>82&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1:1.5</td>
</tr>
<tr>
<td>10</td>
<td>Mesitylene</td>
<td>Fe(TPP)Cl</td>
<td>15b 21b:22b</td>
<td>12</td>
<td>78&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1:2.3</td>
</tr>
<tr>
<td>11</td>
<td>Mesitylene</td>
<td>Fe(TPP)Cl</td>
<td>15c 21c:22c</td>
<td>12</td>
<td>84&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1:0.9</td>
</tr>
<tr>
<td>12</td>
<td>Mesitylene</td>
<td>Fe(TPP)Cl</td>
<td>15d 21d:22d</td>
<td>12</td>
<td>86&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1:0.7</td>
</tr>
<tr>
<td>13</td>
<td>Mesitylene</td>
<td>Fe(TPPF&lt;sub&gt;20&lt;/sub&gt;)Cl&lt;sup&gt;d&lt;/sup&gt;</td>
<td>15a 21a:22a</td>
<td>16</td>
<td>79&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1:0.7</td>
</tr>
<tr>
<td>14</td>
<td>Mesitylene</td>
<td>Fe(TPPF&lt;sub&gt;20&lt;/sub&gt;)Cl&lt;sup&gt;d&lt;/sup&gt;</td>
<td>15b 21b:22b</td>
<td>16</td>
<td>72&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1:1.3</td>
</tr>
<tr>
<td>15</td>
<td>Mesitylene</td>
<td>Fe(TPPF&lt;sub&gt;20&lt;/sub&gt;)Cl&lt;sup&gt;d&lt;/sup&gt;</td>
<td>15c 21c:22c</td>
<td>16</td>
<td>79&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1:0.4</td>
</tr>
<tr>
<td>16</td>
<td>Mesitylene</td>
<td>Fe(TPPF&lt;sub&gt;20&lt;/sub&gt;)Cl&lt;sup&gt;d&lt;/sup&gt;</td>
<td>15d 21d:22d</td>
<td>16</td>
<td>72&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1:0.3</td>
</tr>
<tr>
<td>17</td>
<td>2,2,4-TMP&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Fe(TPP)Cl</td>
<td>15b 24b:others</td>
<td>54</td>
<td>36&lt;sup&gt;e&lt;/sup&gt;</td>
<td>2:1&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>18</td>
<td>2,2,4-TMP&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Fe(TPP)Cl</td>
<td>15c 24c:others</td>
<td>54</td>
<td>41&lt;sup&gt;e&lt;/sup&gt;</td>
<td>3:1&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>19</td>
<td>2,2,4-TMP&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Fe(TPP)Cl</td>
<td>15d 24d:others</td>
<td>54</td>
<td>46&lt;sup&gt;e&lt;/sup&gt;</td>
<td>4:1&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Substrate used as solvent (5 mL), substituted methyl phenyldiazoacetates (0.19 mmol), (TPP)FeCl (2.5 mg, 2 mol%), mixture thoroughly flashed with dry nitrogen, heated at 110 °C with continuous stirring. <sup>b</sup>Isolated yields. <sup>c</sup>Combined isolated yields of all products. <sup>d</sup>TPPF<sub>20</sub> = tetrakis(pentafluorophenyl)-porphyrinato. <sup>e</sup>2,2,4-TMP = 2,2,4-trimethylpentane. <sup>f</sup>Ratio of major product to all other isomers combined.
Competition experiments with \( p\text{-MeO-MPDA, } 15\text{d} \), using cyclohexane and THF in equimolar amounts and 1 mol\% \( \text{Fe(TPP)Cl} \) catalyst loading resulted in the formation of products 16d (cyclohexane C-H insertion), 18d (THF C-H insertion), and 19d (THF ring-opening) in a ratio of 11:4:1, respectively. A similar competition experiment with cyclohexane and mesitylene gave products 16d (cyclohexane C-H insertion), 21d (benzylic C-H insertion), and 22d (aromatic C-H insertion) in a ratio of 2.7:1.2:1, respectively. This indicates that the substrate reactivity using methyl 2-\((p\text{-methoxyphenyl})\text{diazoacetate follows the trend cyclohexane} > \text{mesitylene} > \text{THF. This is in contrast to the dirhodium tetraacetate catalyst which catalyzes the insertion of carbenes from MPDAs, 15a-d, 1700 times faster with THF than for cyclohexane.}^\text{18} \) However, the study also found that similar to our observations, secondary C-H insertion was more favored than benzylic C-H insertion.

To explore the reactivity profile between primary, secondary and tertiary sites, the reaction of substituted methyl 2-phenyldiazoacetates with 2,2,4-trimethylpentane was examined. In these reactions a mixture of isomeric C-H insertion products was obtained as determined by GC-MS. In each reaction, three GC-MS peaks were observed with the same molecular masses. In all cases these three isomeric products were not cleanly
separable. However, a major isomer was produced and identified in the reaction mixture by $^1$H NMR spectroscopy. For example, treatment of $p$-Me-MPDA with 2,2,4-trimethylpentane at 60 °C in the presence of 2 mol% Fe(TPP)Cl resulted in formation of methine C-H insertion species 24d as the major product (Scheme 1). The newly formed methine proton of the major isomer appeared as a singlet at 3.45 ppm. The lack of coupling of this methine hydrogen to other protons indicated that insertion for the major product occurred at the tertiary site of the substrate. Isomers formed by insertion at primary and secondary sites result in splitting of the new methine resonance due to 3-bond proton-proton coupling. It was not possible to clearly identify the minor isomers by either GC or NMR methods. The ratio of tertiary C-H insertion to all other insertion products combined was 4:1. The selectivity for tertiary insertion decreased as the electron withdrawing nature at the para position of the diazo reagent increased (Table 2). These trends are consistent with C-H insertions occurring via an electrophilic transition state.

Scheme 1

An attempt to effect an intramolecular benzylic C-H insertion with 2-phenylethyl diazoacetate, 25, resulted in formation of a carbene dimer product 26 (eq 8) at both ambient temperature and 40 °C. The reaction progress was monitored by $^1$H NMR spectroscopy. Loss of the singlet at 3.96 ppm for the proton attached to the diazo carbon was accompanied by the appearance of a new vinyl proton NMR signal at 6.23 ppm. This
dimer formed even when a very dilute solution of substrate was used and in all cases only one geometric isomer was observed. The vinyl signal at 6.23 ppm identifies the product as the Z-isomer, in agreement with the olefin signal of diethyl maleate at 6.2 ppm. In comparison, the diethyl fumarate (E-isomer) vinyl signal is observed at 6.8 ppm. The absence of cyclized product is in contrast to use of Rh(II) acetates as catalysts where a similar substrate resulted in intramolecular C-H insertion at the benzylic carbon to give a substituted lactone.\textsuperscript{19}

\begin{center}
\includegraphics[width=\textwidth]{reaction_diagram.png}
\end{center}

In another effort towards catalyzing an intramolecular reaction, 1-(2-methylphenyl)-2-diazo-1,3-butanedione, 27, was examined and found to be unreactive at ambient temperature in the presence of Fe(TPP)Cl. However, refluxing conditions in toluene produced 46\% of 2-methylbenzaldehyde, 28, along with other unidentified products (Scheme 2). The presence of a signal of a \textsuperscript{1}H NMR signal at 10.27 ppm from a sample of the reaction mixture indicated the presence of the aldehyde. Co-injection of reaction mixture with authentic aldehyde 28 confirmed the results. The NMR spectrum of product was also found to be identical with that of the authentic aldehyde.
Mechanistic Studies. Initial rates for C-H insertion with cyclohexane catalyzed by Fe(TPP)Cl were determined under pseudo-first order conditions at 70 °C with different concentrations of p-Cl-MPDA. The rates were found to be first order with respect to the concentration of the diazo compound (0.095 mM, 3.70 ± 0.4 µM/h; 0.19 mM, 7.2 ± 0.4 µM/h; 0.29 mM, 10.3 ± 0.6 µM/h). This confirmed that the formation of a metal carbene complex is the rate-determining step. This concurs well with homogeneous metal catalyzed C-H activation via diazocarbonyl reagents which are generally assumed to involve an intermediate metal carbene complex, produced by metal-mediated extrusion of nitrogen from the diazo compound, followed by concerted C-H activation and C-C bond formation.\(^\text{18}\) DFT and saturation kinetics studies using dirhodium tetracarboxylate catalysts suggested that the rate-determining step is either nitrogen extrusion when highly reactive substrates are involved or insertion into the C-H bond when less reactive substrates are used.\(^\text{20,21}\)

Competition experiments with substituted methyl 2-phenylidiaoacetates were used to investigate the electronic effects on cyclohexane C-H activation using Fe(TPP)Cl and its fluorinated analog, Fe(TPPF\(_{20}\))Cl, as catalysts (Table 3). Methyl 2-phenylidiaoacetates with electron-donating p-substituents were more effective reagents for C-H insertion with either of the catalysts. A Hammett analysis showed a stronger
correlation to $\sigma^+$ ($R = 0.99$) than to $\sigma$ ($R = 0.59$) for Fe(TPP)Cl. Similar correlations were obtained for Fe(TPPF$_{20}$)Cl ($\sigma^+$, $R = 0.98$; $\sigma$, $R = 0.59$). The $\rho$ value of $-1.11 \pm 0.05$ for Fe(TPP)Cl and $-0.82$ for Fe(TPPF$_{20}$)Cl suggests that the C-H insertion involves a positive charge buildup in the transition state. In both complexes, this charge build up is

Table 3. Competition reactions of cyclohexane with $p$-substituted methyl 2-phenyl diazoacetates using Fe(TPP)Cl and Fe(TPPF$_{20}$)Cl as a catalysts.$^a$

<table>
<thead>
<tr>
<th>$p$-substituent</th>
<th>$\sigma^+$</th>
<th>$\sigma^+$</th>
<th>$\sigma^+$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\text{Fe(TPP)Cl}$</td>
<td>$\text{Fe(TPPF}_{20}\text{Cl}$</td>
<td></td>
</tr>
<tr>
<td>OMe</td>
<td>$-0.78$</td>
<td>$8.7$</td>
<td>$5.53$</td>
</tr>
<tr>
<td>Me</td>
<td>$-0.31$</td>
<td>$2.2$</td>
<td>$1.89$</td>
</tr>
<tr>
<td>Cl</td>
<td>$0.11$</td>
<td>$0.9$</td>
<td>$1.03$</td>
</tr>
</tbody>
</table>

$^a$Substrate used as solvent (10 mL), methyl 2-phenyl diazoacetate (30.6 mg, 0.17 mmol), equivalent amount of substituted methyl 2-phenyl diazoacetate, $p$-X-MPDA (0.17 mmol), (TPP)FeCl (2.40 mg, 2.0 mol%) or (TPPF$_{20}$)FeCl (3.60 mg, 2.0 mol%), reaction stirred at 70 °C for 8h.

stabilized by resonance with the para-substituents. The electrophilic nature of the carbene intermediate is also supported by its selectivity towards tertiary C-H groups and the 2-position of tetrahydrofuran. These sites are best suited to stabilizing a positive charge buildup. Additional support for the intermediate electrophilic carbene complex is provided by the formation of minor ring-opened products in the Fe(TPP)Cl-catalyzed reaction of THF with $p$-substituted methyl 2-phenyl diazoacetates (eq 6). It is likely that these side reactions occur by nucleophilic attack of the THF oxygen on an electron deficient carbene ligand coordinated to Fe(TPP). Subsequent C-O bond cleavage and hydrogen transfer produces the butenyl fragment (Scheme 2). Moreover, the intermediate
electrophilic carbene complex is unreactive towards aryl substrates with electron withdrawing groups such as benzonitrile and nitrobenzene.

**Scheme 2**

The C-H insertion process was found to exhibit a kinetic isotope effect (KIE) of 1.97 ± 0.03 when a 1:1 mixture of cyclohexane and d$_{12}$-cyclohexane was heated at 70 °C with methyl 2-(p-methoxyphenyl)diazoacetate and catalytic amounts of Fe(TPP)Cl. The KIEs were also measured for methyl 2-(p-tolyl)diazoacetate (1.96 ± 0.03) and methyl 2-(p-methoxyphenyl)diazoacetate (1.97 ± 0.03). This indicates that after the rate-determining N$_2$ extrusion step to form a carbene complex, a subsequent C-H activation state occurs in which the C-H bond is partially broken (Fig 1).

Several theories exist for the reaction mechanism of transition metal catalyzed carbene insertion, including Taber's four-centered hypothesis, Doyle's three-centered concerted bond formation process, Davies's concerted yet nonsynchronous process and Pirrung's stepwise pathway. The generally accepted mechanism for intermolecular C-H insertions involves a direct three-centered interaction between the carbene complex
and the C-H bond.\textsuperscript{18,27,28} The kinetic isotope effect of $1.97 \pm 0.03$ that was observed for the Fe(TPP)Cl-catalyzed process, is most consistent with a C-H insertion that occurs in a concerted but nonsynchronous manner with build up of positive charge at the reacting carbon of the substrate (Scheme 3).\textsuperscript{18,29} The overall mechanism involves metalloporphyrin mediated extrusion of N$_2$ in the slow step to form a metal carbene complex followed by insertion of the carbene fragment between a C-H bond in a concerted step to regenerate the active catalyst (Scheme 4).

**Fig. 1.** Energy profile of the Fe(TPP)Cl-catalyzed reaction of methyl ($p$-chlorophenyl)diazoacetate with cyclohexane

**Scheme 3**
Conclusion

Ag(II), Cu(II) and Fe(III) porphyrins serve as effective catalysts for C-H activation and provide a general method for insertion of carbene fragments from diazo reagents into aromatic and aliphatic C-H bonds with high yields. Reactions can be run conveniently in one-pot without the need for slow addition of the diazo compound and with a low catalyst loading of 1-2%. The Fe(TPP)Cl complex, easily prepared and also commercially available, can be used to achieve this useful and simple catalytic process.

Initial rates for reactions with cyclohexane catalyzed by Fe(TPP)Cl were found to be first order with respect to p-Cl-MPDA. This indicates that the slow step is formation of a reactive carbene intermediate coordinated to the iron porphyrin. The reaction of MPDAs with cyclohexane-$d_0/d_{12}$ was found to exhibit a kinetic isotope effect of $1.97 \pm 0.03$. This indicates that after the rate-determining step, a product-forming step subsequently occurs in which the substrate C-H bond is partially broken. Hammett studies on the reaction of $para$-substituted-MPDAs with cyclohexane support the involvement of an electrophilic carbene complex. On the basis of these mechanistic
studies and reactivity trends, the C-H activation step in these Fe(TPP)Cl-catalyzed insertion reactions appear to involve a concerted, nonsynchronous process.\textsuperscript{30}

**Experimental Section**

Fe(TPP)Cl was obtained from Aldrich. Ag(TPP) and Cu(TPP) were synthesized using literature methods.\textsuperscript{31} Toluene was deoxygenated and dried by passage through columns of reduced copper and alumina as described by Grubb’s et al.\textsuperscript{32} Dimethyl diazomalonate was prepared by transferring a diazo group from tosylazide to dimethylmalonate under basic conditions.\textsuperscript{33} Substituted methyl 2-phenyldiazoacetates were prepared as outlined in the literature.\textsuperscript{34} Synthesis of 2-phenyleth-1-yl diazoacetate (25) was done using a literature method.\textsuperscript{35} Proton NMR and $^{13}$C NMR spectra were run in CDCl$_3$ and recorded on a Varian VXR 300 or a Bruker DRX400 spectrometer. $^1$H NMR peak positions were referenced against residual proton resonances of CDCl$_3$ ($\delta$, 7.27). Gas chromatographic analysis was performed on a HP 5890 series II or a Finnigan GC-MS instrument. Dodecane was used as an internal standard. All reactions were performed under an atmosphere of nitrogen.

**General Procedure for C-H Insertion Reactions.** About 30.0 mg of the diazo reagent were accurately weighed and placed in a 50-mL round bottom flask containing a stir bar. A condenser, fitted with a rubber septum, was then attached to the round bottom flask and the contents thoroughly flushed with nitrogen. A catalyst (1-2 mol %) was placed in a separate flask, dissolved in 5 mL of substrate, and the contents were bubbled with dry nitrogen for 15 min. This solution was transferred to the diazo reagent by a cannula. The mixture was then heated to an appropriate temperature while stirring until
the diazo reagent was consumed. The products were separated or purified by eluting on a silica gel column (4 cm diameter, 30 cm, hexane/ethyl acetate; 20:1).

**Dimethyl Diazomalonate Insertion with Toluene.** The general procedure was used with dimethyl diazomalonate (30.5 mg, 0.193 mmol), (TPP)FeCl (2.70 mg, 1.99 mol%) and 5.0 mL of toluene. The mixture was stirred at 100 °C for 48 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. Pure benzylic C-H insertion product dimethyl-2-benzylmalonate, 3a, (23.0 mg, 0.104 mmol, 53.7% yield based on dimethyl diazomalonate) was obtained as a yellow oil. The proton NMR and $^{13}$C NMR spectra matched literature values.$^{11}$ A mixture of dimethyl $p$-tolylmalonate$^{12}$ and dimethyl $o$-tolylmalonate$^{13}$ (6.10 mg, 0.0275 mmol, 14.2% yield based on dimethyl diazomalonate) was obtained but not separable. $^{1}$H NMR of 3a (400 MHz) δ: 7.32-7.26 (m, 2H, aryl-H), 7.25-7.18 (m, 3H, aryl-H), 3.71 (s, 6H, OCH$_3$), 3.69 (t, 1H, J$_{HH}$ = 7.8, methine C-H), 3.23 (d, 2H, J$_{HH}$ = 7.8, Ar-CH$_2$). $^{13}$C NMR (100.5 MHz) δ: 169.5, 138.0, 128.9, 128.7, 127.0, 53.8, 52.8, 35.0. MS {EI}: 223 [M+1]$^+$, 161 [M - 2(OMe)], 131 [M - C$_6$H$_5$CH$_2$]. Ring insertion products **$o$.p$^-$$4$**: $^{1}$H NMR (400 MHz) δ: 7.15-7.33 (m, 8H, $o$.p$^-$$4$-aryl-H), 4.92 (s, 1H, o-4a-methine C-H), 4.63 (s, 1H, p-4a-methine C-H), 3.77 (s, 6H, $o$.4a-OCH$_3$), 3.76 (s, 6H, $p$.4a-OCH$_3$), 2.35 (b, 6H, $o$.p$^-$$4$-CH$_3$).

**Dimethyl Diazomalonate Insertion with $p$-Chlorotoluene.** The general procedure was used with dimethyl diazomalonate (30.2 mg, 0.191 mmol), (TPP)FeCl (2.60 mg, 1.93 mol%) and 5.0 mL of $p$-chlorotoluene. The mixture was stirred at 100 °C for 48 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. Pure benzylic C-H insertion product dimethyl ($p$-
chlorobenzyl)malonate, 3b, (24.8 mg, 0.0969 mmol, 50.7% yield based on dimethyl diazomalonate) was obtained as a yellow oil. The proton NMR and $^{13}$C NMR spectra matched literature values. Small amounts of ring C-H insertion products were detected on GC but not isolatable. Benzylic insertion product 3b: $^1$H NMR (400 MHz) δ: 7.26 (dd, 2H, J_H = 8.4, aryl-H), 7.14 (dd, 2H J_H = 8.4, aryl-H), 3.71 (s, 6H, OCH$_3$), 3.65 (t, 1H, J_H = 7.8 methine C-H), 3.19 (d, 2H, J_H = 7.8, aryl-CH$_2$). $^{13}$C NMR (100.5 MHz) δ: 169.2, 136.4, 130.4, 130.3, 129.0, 53.6, 52.9, 34.3, MS{EI}: 256 [M]$^+$, 191 [M - (OMe) - Cl], 177 [M - CO$_2$Me].

**Dimethyl diazomalonate Insertion with p-Xylene.** The general procedure was used with dimethyl diazomalonate (30.5 mg, 0.193 mmol), (TPP)FeCl (2.70 mg, 1.99 mol%) and 5.0 mL of p-xylene. The mixture was stirred at 100 °C for 32 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. A mixture of the benzylic C-H insertion product dimethyl (p-methylbenzyl)malonate, 3c, and ring C-H insertion product dimethyl 2,5-xylylmalonate, 4c, (34.4 mg, 0.146 mmol, 75.5% yield based on dimethyl diazomalonate) was obtained as a yellow oil. Although it was possible to get a pure portion of the major product dimethyl (p-methylbenzyl)malonate, 3c, the minor ring C-H product 4c was not obtained in pure form. The proton NMR and $^{13}$C NMR spectra of the benzylic C-H product matched literature values. Benzylic insertion product 3c: $^1$H NMR (400 MHz) δ: 7.09 (b, 4H, aryl-H), 3.71 (s, 6H, OCH$_3$), 3.66 (t, 1H, J_H = 8.0, methine C-H), 3.19 (d, 2H, J_H = 8.0, aryl-CH$_2$), 2.32 (s, 3H, aryl-CH$_3$). $^{13}$C NMR (100.5 MHz) δ: 169.3, 136.4, 134.7, 129.3, 128.7, 53.8, 52.6, 34.4, 21.1. MS {EI}: 237 [M+1]$^+$, 204 [M - (HO-Me)], 177 [M - CO$_2$Me]. Ring insertion product 4c: $^1$H NMR (400 MHz) δ: 7.19 (b, 1H, aryl-H), 7.10-
69

7.04 (m, 2H, aryl-H), 4.89 (s, 1H, methine C-H), 3.77 (s, 3H, OCH3), 2.33 (s, 3H, Ar-CH3), 2.30 (s, 3H, Ar-CH3). MS{EI}: 236 [M]+, 205 [M - (OMe)], 175 [M - HCO2Me].

Dimethyl Diazomalonate Insertion with Mesitylene. The general procedure was used with dimethyl diazomalonate (30.4 mg, 0.192 mmol), (TPP)FeCl (2.70 mg, 2.00 mol%) and 5.0 mL of mesitylene. The mixture was stirred at 100 °C for 32 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. Pure benzyl C-H insertion product 3,5-dimethyl 2-(3,5-dimethylbenzyl)malonate, 6, was obtained as a yellow oil (35.4 mg, 0.142 mmol, 73.8% yield based on dimethyl diazomalonate). The proton NMR and 13C NMR spectra matched literature values.37 Small amounts of ring C-H insertion products were detected by GC but were not isolated. 1H NMR of 6 (400 MHz) δ: 6.86 (b, 1H, p-H), 6.81 (b, 2H, o-H), 3.71 (s, 6H, OCH3), 3.66 (t, 1H, JH = 8.0, methine C-H), 3.15 (d, 2H, JH = 8.0, aryl-CH2), 2.28 (s, 6H, m-CH3). 13C NMR (100.5 MHz) δ: 169.6, 138.2, 137.9, 128.8, 126.7, 53.9, 52.8, 34.8, 21.5. MS{EI}: 250 [M]+, 190 [M - (HCOOMe)], 159 [M - C6H5CH2].

Dimethyl Diazomalonate Insertion with Chlorobenzene. The general procedure was used with dimethyl diazomalonate (30.6 mg, 0.194 mmol), (TPP)FeCl (2.70 mg, 1.98 mol%) and 5.0 mL of chlorobenzene. The mixture was stirred at 100 °C for 32 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. Pure dimethyl-o-chlorophenylmalonate, 9, (18.2 mg, 0.0752 mmol, 38.8% yield based on dimethyl diazomalonate) and dimethyl-p-chlorophenylmalonate, 10, (10.2 mg, 0.0421 mmol, 21.7% yield based on dimethyl diazomalonate) were obtained. The 1H NMR and 13C NMR spectra matched literature values.15,16 Para product 10 1H NMR (300 MHz) δ: 7.35 (br, 4H, aryl-H), 4.63 (s, 1H,
methine-CH), 3.78 (s, 6H, OCH₃). ¹³C NMR (75.4 MHz) δ: 168.4, 134.6, 131.1, 129.8, 127.4, 54.3, 53.3. Product 9 ¹H NMR (300 MHz) δ: 7.46 (m, 1H, aryl-H), 7.40 (m, 1H, aryl-H), 7.30 (m, 2H, aryl-H), 5.27 (s, 1H, methine-CH), 3.79 (s, 6H, OCH₃). ¹³C NMR (75.4 MHz) δ: 168.4, 134.7, 131.2, 130.9, 129.1, 127.4, 54.3, 53.3. MS{EI}: 242 [M]⁺, 201[M - HOMe], 183 [M - COOMe].

**Dimethyl Diazomalonate Insertion with Anisole.** The general procedure was used with dimethyl diazomalonate (30.7 mg, 0.194 mmol), (TPP)FeCl (2.70 mg, 1.98 mol%) and 5.0 mL of anisole. The mixture was stirred at 100 °C for 16 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The major product dimethyl phenoxyxmalonate, 12a, (27.7 mg, 0.124 mmol, 63.7% yield based on dimethyl diazomalonate) was obtained in pure form as a white solid. Small amounts of ring C-H insertion products were detected on GC but not isolatable. ¹H NMR (400 MHz) δ: 7.30 (m, 2H, aryl-H), 7.03 (m, 1H, aryl-H), 6.95 (m, 2H, aryl-H), 5.25 (s, 1H methine-CH), 3.84 (s, 6H, OCH₃). ¹³C NMR (100.5 MHz) δ: 166.2, 157.0, 130.0, 123.0, 115.6, 82.3, 53.5. MS{EI}: 224 [M]⁺. Elemental analysis: Found (calcd.) %C: 58.62 (58.93), %H: 4.92 (5.39).

**Dimethyl Diazomalonate Insertion with p-Methylanisole.** The general procedure was used with dimethyl diazomalonate (30.5 mg, 0.193 mmol), (TPP)FeCl (2.60 mg, 1.91 mol%) and 5.0 mL of p-methylanisole. The mixture was stirred at 100 °C for 32 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The major product dimethyl p-methylphenoxymalonate, 12b, (31.2 mg, 0.131 mmol, 67.9% yield based on dimethyl diazomalonate) was obtained along with 4% benzylic C-H insertion product. Small
amounts of ring C-H insertion products were also detected on GC but not isolatable.\textsuperscript{1}H NMR (400 MHz) δ: 7.10 (m, 2H, aryl-H), 6.84 (m, 2H, aryl-H), 5.21 (s, 1H methine-\textit{H}), 3.84 (s, 6H, OCH\textsubscript{3}), 2.28 (s, 3H, aryl-CH\textsubscript{3}). \textsuperscript{13}C NMR (100.5 MHz) δ: 166.3, 155.0, 132.4, 130.4, 115.6, 76.8, 53.5, 20.7. MS\{EI\}: 238 [M]+. HRMS: 242.2249, Calcd. 242.2256.

**Methyl 2-Phenyldiazoacetate Insertion with Cyclohexane.** The general procedure was used with methyl 2-phenyldiazoacetate (30.1 mg, 0.171 mmol), (TPP)FeCl\textsubscript{2} (2.50 mg, 2.08 mol%) and 5.0 mL of cyclohexane. The mixture was stirred at 80 °C for 32 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl-cyclohexylphenylacetate, 16a, (26.2 mg, 0.113 mmol, 66.0% yield based on methyl 2-phenyldiazoacetate) was obtained. The proton NMR and \textsuperscript{13}C NMR spectra matched literature values.\textsuperscript{18} \textsuperscript{1}H NMR (400 MHz) δ: 7.24-7.34 (m, 5H, aryl-H), 3.65 (s, 3H OCH\textsubscript{3}), 3.23 (d, 1H, \textit{J}_H = 14.0, benzylic C-H), 1.95-2.10 (m, 1H, methine C-H), 1.69-1.86 (m, 2H, CH\textsubscript{2}), 1.55-1.70 (m, 2H, CH\textsubscript{2}), 1.23-1.40 (m, 2H, CH\textsubscript{2}), 0.99-1.20 (m, 3H, CH\textsubscript{2}), 0.67-0.82 (m, 1H, CH\textsubscript{2}). \textsuperscript{13}C NMR (100.5 MHz) δ: 174.6, 138.1, 128.8, 128.6, 127.4, 58.3, 52.3, 41.4, 32.1, 30.6, 26.4, 26.2, 26.2. MS\{EI\}: 238 [M]+.

**Methyl 2-(p-chlorophenyl)diazoacetate Insertion with Cyclohexane.** The general procedure was used with methyl 2-(p-chlorophenyl)diazoacetate (30.6 mg, 0.145 mmol), (TPP)FeCl\textsubscript{2} (2.20 mg, 2.16 mol%) and 5.0 mL of cyclohexane. The mixture was stirred at 80 °C for 48 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl-cyclohexyl-4-chloro-phenylacetate, 16b, (26.2 mg, 0.0985 mmol, 67.9% yield based on Methyl 2-(p-}
chlorophenyl)diazoacetate) was obtained. (80% purity) The proton NMR and $^{13}$C NMR matched literature values. $^{18}$ $^1$H NMR (400 MHz) δ: 7.40-7.44 (m, 2H, aryl-H), 7.32-7.37 (m, 2H, aryl-H), 3.65 (s, 3H, OCH$_3$), 3.20 (d, 1H, $J_{HH}$ = 10.4, benzylic C-H), 1.90-2.04 (m, 1H, methine C-H), 1.70-1.83 (m, 2H, CH$_2$), 1.56-1.70 (m, 2H, CH$_2$), 1.26-1.41 (m, 2H, CH$_2$), 1.12-1.23 (m, 2H, CH$_2$), 0.98-1.12 (m, 1H, CH$_2$), 0.67-0.81 (m, 1H, CH$_2$).

**Methyl 2-($p$-tolyl)diazoacetate Insertion with Cyclohexane.** The general procedure was used with methyl 2-($p$-tolyl)diazoacetate (30.3 mg, 0.159 mmol), (TPP)FeCl$_2$ (2.20 mg, 1.97 mol%) and 5.0 mL of cyclohexane. The mixture was stirred at 80 °C for 48 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl-cyclohexyl-4-methyl-phenylacetate, 16c, (28.2 mg, 0.114 mmol, 71.5% yield based on methyl 2-($p$-tolyl)diazoacetate) was obtained. The proton NMR and $^{13}$C NMR spectra matched literature values. $^{18}$ $^1$H NMR (300 MHz) δ: 7.22 (d, 2H, $J_{HH}$ = 8.1, aryl-H), 7.12 (d, 2H, $J_{HH}$ = 8.1, aryl-H), 3.64 (s, 3H, OCH$_3$), 3.20 (d, 1H, $J_{HH}$ = 10.8, benzylic C-H), 2.33 (s, 3H, Ar-CH$_3$), 1.93-2.08 (m, 1H, methine C-H), 1.68-1.84 (m, 2H, CH$_2$), 1.56-1.68 (m, 2H, CH$_2$), 1.20-1.42 (m, 2H, CH$_2$), 0.98-1.20 (m, 3H, CH$_2$), 0.66-0.82 (m, 1H, CH$_2$). $^{13}$C NMR (75.4 MHz) δ: 174.8, 137.0, 135.1, 129.4, 128.7, 58.6, 51.9, 41.2, 32.2, 30.7, 26.5, 26.2, 21.3.

**Methyl 2-($p$-methoxyphenyl)diazoacetate Insertion with Cyclohexane.** The general procedure was used with methyl 2-($p$-methoxyphenyl)diazoacetate (30.4 mg, 0.148 mmol), (TPP)FeCl$_2$ (2.20 mg, 2.11 mol%) and 5.0 mL of cyclohexane. The mixture
was stirred at 80 °C for 48 h. The products were isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl-cyclohexyl-4-methoxy-phenylacetate, **16d**, (30.2 mg, 0.115 mmol, 77.9% yield based on Methyl 2-(p-methoxyphenyl)diazoacetate) was obtained. The proton NMR and $^{13}$C NMR spectra matched literature values.$^{18}$ $^1$H NMR (400 MHz) δ: 7.25 (d, 2H, $J_{HH} = 8.4$, aryl-H), 6.85 (d, 2H, $J_{HH} = 8.4$, aryl-H), 3.79 (s, 3H, ArOCH$_3$), 3.64 (s, 3H, OCH$_3$), 3.18 (d, 1H, $J_{HH} = 10.8$, benzylic C-H), 1.91-2.04 (m, 1H, methine C-H), 1.70-1.83 (m, 2H, CH$_2$), 1.55-1.70 (m, 2H, CH$_2$), 1.24-1.40 (m, 2H, CH$_2$), 0.98-1.12 (m, 1H, CH$_2$), 0.66-0.81 (m, 1H, CH$_2$). $^{13}$C NMR (100.5 MHz) δ: 174.9, 158.9, 130.1, 129.7, 114.0, 58.1, 55.4, 51.9, 41.3, 32.2, 30.6, 26.5, 26.2, 26.2. MS{EI}: 262 [M]$^+$.

**Methyl 2-phenyldiazoacetate Insertion with THF.** The general procedure was used with methyl 2-(phenyl)diazoacetate (30.2 mg, 0.172 mmol), (TPP)FeCl (2.20 mg, 1.82 mol%) and 10.0 mL of tetrahydrofuran. The mixture was stirred at 80 °C for 48 h. The products were separated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl 2-phenyl-2-(tetrahydrofuran-2-yl)acetate, **18a**, (21.9 mg, 0.100 mmol, 58.4% yield based on methyl 2-phenyldiazoacetate) and **19a**, (6.40 mg, 0.0293 mmol, 17.1% yield based on methyl 2-phenyldiazoacetate) were obtained. The proton NMR and $^{13}$C NMR spectra for **18a** matched literature values.$^{18}$ $^1$H NMR (400 MHz) δ: 7.53 (m, 2H, aryl-H) 7.28-7.39 (m, 3H, aryl-H), 3.97 (m, 1H, benzyl C-H), 3.78 (m, 1H, methine C-H), 3.72 (s, 3H, OCH$_3$), 2.56 (m, 1H, CH$_2$), 1.83-1.95 (m, 1H, CH$_2$), 1.72-1.82 (m, 1H, CH$_2$), 1.53-1.70 (m, 3H, CH$_2$). $^{13}$C NMR (100.5 MHz) δ: 173.4, 141.1, 128.6, 127.9, 125.4, 81.0, 65.3, 52.7, 33.9, 30.6, 25.3, 20.9. Minor product **19a**: $^1$H NMR (400 MHz) δ: 7.46 (m, 2H, aryl-H), 7.27-
7.37 (m, 3H, aryl-H), 5.83 (m, 1H, vinyl-CH), 5.10 (m, 1H, geminal-CH₂), 5.04 (m, 1H, geminal-CH₂), 4.90 (s, 1H, benzylic C-H), 3.72 (s, 3H, OCH₃), 3.60 (m, 1H, CH₂), 3.49 (m, 1H, CH₂), 2.43 (m, 2H, CH₂). HRMS: 218.13071, Calcd. 218.13068.

Methyl 2-(p-chlorophenyl)diazoacetate Insertion with THF. The general procedure was used with methyl 2-(p-chlorophenyl)diazoacetate (30.4 mg, 0.144 mmol), (TPP)FeCl (2.20 mg, 2.17 mol%) and 10.0 mL of tetrahydrofuran. The mixture was stirred at 80 °C for 48 h. The products were separated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl 4-chlorophenyl(tetrahydrofuran-2-yl)acetate, 18b, (19.1 mg, 0.0752 mmol, 52.2% yield based on methyl 2-(p-chloro)diazoacetate) and 19b, (5.50 mg, 0.0216 mmol, 15.0% yield based on methyl 2-phenyldiazoacetate) were obtained. The proton NMR and ¹³C NMR spectra of 18b matched literature values.¹⁸ ¹H NMR (400 MHz) δ: 7.47 (d, 2H, J_H = 11.6, aryl-H), 7.32 (d, 2H, J_H = 11.6, aryl-H), 3.96 (m, 1H, methine C-H), 3.76 (m, 1H, benzyl C-H), 3.72 (s, 3H, OCH₃), 2.48-2.57 (m, 1H, CH₂), 1.74-1.87 (m, 2H, CH₂), 1.54-1.65 (m, 3H, CH₂). ¹³C NMR (100.5 MHz) δ: 173.1, 139.9, 133.9, 128.8, 126.9, 80.6, 65.4, 52.9, 33.9, 25.2, 20.9. MS{EI} : 255 [M+1]⁺. Minor product 19b: ¹H NMR (400 MHz) 7.40 (d, 2H, J_H = 8.8), 7.34 (d, 2H, J_H = 8.8), 5.82 (m, 1H, vinyl-CH), 5.15 (m, 1H, geminal-CH₂), 5.05 (m, 1H, geminal-CH₂), 4.87 (s, 1H, benzyl C-H), 3.72 (s, 3H, OCH₃), 3.60 (m, 1H, CH₂), 3.48 (m, 1H, CH₂), 2.42 (dd, 2H, J_H = 6.8, CH₂). ¹³C NMR (100.5 MHz) δ: 171.0, 135.0, 134.6, 131.6, 128.9, 128.5, 116.8, 80.4, 69.4, 52.4, 34.0. HRMS: 252.09187; Calcd. 252.09171.

Methyl 2-(p-tolyl)diazoacetate Insertion with THF. The general procedure was used with methyl 2-(p-tolyl)diazoacetate (30.3 mg, 0.159 mmol), (TPP)FeCl (2.20 mg,
1.97 mol%) and 10.0 mL of tetrahydrofuran. The mixture was stirred at 80 °C for 48 h. The product was isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl-4-methylphenyl(tetrahydrofuran-2-yl)acetate, 18c, (22.2 mg, 0.949 mmol, 59.7% yield based on methyl 2-(p-tolyl)diazoacetate) and 19c, (6.00 mg, 0.0256 mmol, 16.1% yield based on methyl 2-(p-tolyl)diazoacetate) were obtained. The proton NMR and 13C NMR for spectra 18c matched literature values.18 1H NMR (400 MHz) δ: 7.40 (dd, 2H, J_H = 8.0, aryl-H), 7.17 (dd, 2H, J_H = 8.0, aryl-H), 3.92-3.99 (m, 1H, methine C-H), 3.72 (s, 3H, OCH3), 3.72-3.79 (m, 1H, benzyl C-H), 2.48-2.52 (m, 1H, CH2), 2.35 (s, 3H, Ar-CH3), 1.80-1.93 (m, 1H, CH2), 1.74-1.77 (m, 1H, CH2), 1.50-1.60 (m, 3H, CH2). 13C NMR (100.5 MHz) δ: 173.5, 137.7, 129.3, 128.1, 125.4, 80.8, 65.2, 52.7, 33.8, 25.3, 21.3, 20.9. Minor product 19c: 1H NMR (400 MHz) δ: 7.35 (d, 2H, J_H = 8.0, aryl-H), 7.18 (d, 2H, J_H = 8.0, aryl-H), 5.83 (m, 1H, vinyl-CH), 5.09 (m, 1H, geminal-CH2), 5.04 (m, 1H, geminal-CH2), 4.87 (s, 1H, benzylic-CH), 3.72 (s, 3H, OCH3), 3.58 (m, 1H, CH2), 3.48 (m, 1H, CH2), 2.42 (m, 2H, CH2), 2.36 (s, 3H, Ar-CH3). 13C NMR (100.5 MHz) δ: 171.7, 138.8, 134.9, 133.7, 129.5, 127.4, 116.9, 81.1, 69.3, 52.5, 34.3, 21.5. Elemental analysis: Found (calcd.) %C: 71.44 (71.77), %H: 7.46 (7.74).

**Methyl 2-(p-methoxyphenyl)diazoacetate Insertion with THF.** The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (30.4 mg, 0.148 mmol), (TPP)FeCl (2.20 mg, 2.11 mol%) and 10.0 mL of tetrahydrofuran. The mixture was stirred at 80 °C for 48 h. The products were separated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The products methyl-4-methoxyphenyl(tetrahydrofuran-2-yl)acetate, 18d, (23.6 mg, 0.0944 mmol, 63.8% yield
based on methyl 2-(p- methoxyphenyl)diazoacetate) and 19d, (6.60 mg, 0.0264 mmol, 17.8% yield based on methyl 2-(p-methoxyphenyl)diazoacetate) were obtained. The proton NMR and $^{13}$C NMR spectra for 18d matched literature values.$^{18}$ $^1$H NMR (300 MHz) $\delta$: 7.45 (d, 2H, $J_H = 8.7$, aryl-H), 6.88 (d, 2H, $J_H = 8.7$, aryl-H), 3.94 (m, 1H, methine C-H), 3.80 (s, 3H, ArOCH$_3$), 3.75 (m, 1H, benzylic C-H), 3.71 (s, 3H, OCH$_3$), 2.51 (m, 1H, CH$_2$), 1.90 (m, 1H, CH$_2$), 1.77 (m, 1H, CH$_2$), 1.61 (m, 3H, CH$_2$). $^{13}$C NMR (75.4 MHz) $\delta$: 173.6, 159.3, 126.8, 113.9, 80.6, 65.1, 55.5, 52.6, 33.6, 25.3, 20.9. Minor product 19d: $^1$H NMR (400 MHz) 7.37 (d, 2H, $J_H = 8.7$, aryl-H), 6.90 (dd, 2H, $J_H = 8.7$, aryl-H), 5.82 (m, 1H, vinyl-CH), 5.08 (m, 1H, geminal-CH$_2$), 5.03 (m, 1H, geminal-CH$_2$), 4.85 (s, 1H, benzylic C-H), 3.80 (s, 3H, ArOCH$_3$), 3.72 (s, 3H, OCH$_3$), 3.52 (m, 2H, CH$_2$), 2.41 (m, 2H, CH$_2$). $^{13}$C NMR (100.5 MHz) $\delta$: 171.8, 160.1, 134.9, 128.9, 128.8, 116.8, 114.2, 80.8, 69.2, 55.5, 52.4, 34.2. HRMS: 250.12087; Calcd. 250.12051.

**Methyl 2-phenyldiazoacetate Insertion with mesitylene.** The general procedure was used with methyl 2-phenyldiazoacetate (30.6 mg, 0.174 mmol), (TPP)FeCl$_2$ (2.40 mg, 1.96 mol%) and 5.0 mL of mesitylene. The mixture was stirred at 80 °C for 16 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. A mixture of the benzylic C-H insertion product, 21a, and the ring C-H insertion product, 22a, (38.2 mg, 0.143 mmol, 81.9% yield based on methyl methyl 2-phenyldiazoacetate) were obtained. Benzylic C-H insertion product 21a: $^1$H NMR (400 MHz) $\delta$: 7.24-7.38 (m, 5H, aryl-H), 6.83 (s, 1H, aryl-H), 6.75 (s, 2H, aryl-H), 3.85 (dd, 1H, $J_H = 9.2$, $J_H = 6.0$, methine C-H), 3.61 (s, 3H, O-CH$_3$), 3.45 (dd, 1H, $J_H = 13.6$, $J_H = 9.2$, Ar-CH$_2$), 2.95 (dd, 1H, $J_H = 13.6$, $J_H = 6.0$, Ar-CH$_2$), 2.26 (s, 6H, Ar-CH$_3$). Ring C-H insertion product 22a: $^1$H NMR (400 MHz) $\delta$: 7.22-7.32 (m, 3H, aryl-H), 7.11
(m, 2H, aryl-H), 6.93 (s, 2H, aryl-H), 5.39 (s, 1H, methine C-H), 3.74 (s, 3H, OCH₃), 2.32 (s, 3H, Ar-CH₃), 2.26 (s, 6H, Ar-CH₃).

**Methyl 2-(p-chlorophenyl)diazoacetate Insertion with mesitylene.** The general procedure was used with methyl 2-(p-chlorophenyl)diazoacetate (30.3 mg, 0.144 mmol), (TPP)FeCl (2.10 mg, 2.07 mol%) and 5.0 mL of mesitylene. The mixture was stirred at 80 °C for 16 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. A mixture of the benzylic C-H insertion product, 21b, and the ring C-H insertion product, 22b, (33.9 mg, 0.112 mmol, 78.0% yield based on methyl 2-(p-chlorophenyl)diazoacetate) were obtained. Benzylic C-H insertion product 21b: ¹H NMR (300 MHz) δ: 7.44 (d, 2H, J_H = 8.7 aryl-H), 7.37 (d, 2H, J_H = 8.7 aryl-H), 6.83 (s, 1H, aryl-H), 6.72 (s, 2H, aryl-H), 3.82 (dd, 1H, J_H = 8.8, J_H = 5.6, methine C-H), 3.62 (s, 3H, O-CH₃), 3.33 (dd, 1H, J_H = 13.5, J_H = 8.7, Ar-CH₂), 2.91 (dd, 1H, J_H = 13.5, J_H = 6.6, Ar-CH₂), 2.26 (s, 6H, Ar-CH₃). Ring C-H insertion product 22b: ¹H NMR (300 MHz) δ: 7.25 (d, 2H, J_H = 8.7, aryl-H), 7.06 (d, 2H, J_H = 8.7, aryl-H), 6.92 (s, 2H, aryl-H), 5.32 (s, 1H, methine C-H), 3.74 (s, 3H, OCH₃), 2.31 (s, 3H, Ar-CH₃), 2.16 (s, 6H, Ar-CH₃).

**Methyl 2-(p-tolyl)diazoacetate Insertion with mesitylene.** The general procedure was used with methyl 2-(p-tolyl)diazoacetate (30.7 mg, 0.162 mmol), (TPP)FeCl (2.30 mg, 2.02 mol%) and 5.0 mL of mesitylene. The mixture was stirred at 80 °C for 16 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. A mixture of the benzylic C-H insertion product, 21c, and the ring C-H insertion product, 22c, (38.9 mg, 0.138 mmol, 85.1% yield based on methyl methyl 2-(p-tolyl)diazoacetate) were obtained. Benzylic C-
H insertion product 21c: $^1$H NMR (400 MHz) δ: 7.24 (d, 2H, $J_H = 8.4$, aryl-H), 7.15 (d, 2H, $J_H = 8.4$, aryl-H), 6.84 (s, 1H, aryl-H), 6.78 (s, 2H, aryl-H), 3.84 (dd, 1H, $J_H = 9.2$, $J_H = 6.0$, methine C-H), 3.61 (s, 3H, OCH$_3$), 3.36 (dd, 1H, $J_H = 13.6$, $J_H = 9.1$, Ar-CH$_2$), 2.93 (dd, 1H, $J_H = 13.6$, $J_H = 6.3$, Ar-CH$_2$), 2.35 (s, 3H, Ar-CH$_3$), 2.28 (s, 6H, Ar-CH$_3$). Ring C-H insertion product 22c: $^1$H NMR (CDCl$_3$) δ: 7.11 (d, 2H, $J_H = 8.4$, aryl-H), 7.01 (d, 2H, $J_H = 8.4$, aryl-H), 6.93 (s, 2H, aryl-H), 5.35 (s, 1H, methine C-H), 3.74 (s, 3H, O-CH$_3$), 2.34 (s, 3H, Ar-CH$_3$), 2.32 (s, 3H, Ar-CH$_3$), 2.19 (s, 6H, Ar-CH$_3$).

Methyl 2-($p$-methoxyphenyl)diazoacetate Insertion with mesitylene. The general procedure was used with methyl 2-($p$-methoxyphenyl)diazoacetate (30.5 mg, 0.148 mmol), (TPP)FeCl$_3$ (2.30 mg, 2.21 mol%) and 5.0 mL of mesitylene. The mixture was stirred at 80 °C for 16 h. The products were partially isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. A mixture of the benzylic C-H insertion product, 21d, and the ring C-H insertion product, 22d, (37.9 mg, 0.127 mmol, 85.9% yield based on methyl 2-($p$-methoxyphenyl)diazoacetate) were obtained. Benzylic C-H insertion product 21d: $^1$H NMR (400 MHz) δ: 7.25 (d, 2H, $J_H = 8.8$, aryl-H), 6.86 (d, 2H, $J_H = 8.8$, aryl-H), 6.82 (b, 1H, aryl-H), 6.75 (b, 2H, aryl-H), 3.81 (dd, 1H, $J_H = 9.1$, $J_H = 6.3$, methine C-H), 3.80 (s, 3H, ArOCH$_3$), 3.61 (s, 3H, CO$_2$CH$_3$), 3.33 (dd, 1H, $J_H = 13.8$, $J_H = 9.1$, Ar-CH$_2$), 2.92 (dd, 1H, $J_H = 13.8$, $J_H = 6.3$, Ar-CH$_2$), 2.26 (s, 6H, Ar-CH$_3$). $^{13}$C NMR (100.5 MHz) δ: 174.3, 158.9, 139.1, 137.8, 131.1, 129.0, 128.0, 126.8, 55.3, 52.8, 51.9, 39.8, 30.6, 21.3. Elemental analysis: Found (calcd.) %C: 76.20 (76.48), %H: 7.41 (7.43). Ring C-H insertion product 22d: $^1$H NMR (400 MHz) δ: 7.05 (d, 2H, $J_H = 8.8$, aryl-H), 6.93 (b, 2H, aryl-H), 6.84 (d, 2H, $J_H = 8.8$ aryl-H), 5.32 (s, 1H, methine C-H), 3.80 (s, 3H, ArOCH$_3$), 3.74 (s, 3H, CO$_2$CH$_3$), 2.32 (s, 3H, Ar-CH$_3$), 2.19 (s, 6H, Ar-
CH₃). ¹³C NMR (100.5 MHz) δ: 174.2, 158.4, 137.3, 136.8, 132.6, 129.9, 129.8, 128.6, 113.6, 55.3, 52.3, 50.0, 21.0, 20.8. Elemental analysis: Found (calcd.) %C: 76.56 (76.48), %H: 7.36 (7.43).

Methyl 2-(p-methoxyphenyl)diazoacetate Insertion with 2,2,4-Trimethylpentane. The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (30.4 mg, 0.148 mmol), (TPP)FeCl (2.20 mg, 2.11 mol%) and 10.0 mL of 2,2,4-trimethylpentane. The mixture was stirred at 80 °C for 54 h. The major product, methine C-H insertion, 24d, with 20% of the other C-H insertion products was obtained by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture (20.5 mg, 0.0702 mmol 47.4% yield based on methyl 2-(p-methoxyphenyl)diazoacetate). ¹H NMR (400 MHz) δ: 7.31 (d, 2H, J_H = 8.8, aryl-H), 6.84 (d, 2H, J_H = 8.8, aryl-H), 3.80 (s, 3H, ArOCH₃), 3.63 (s, 3H, CO₂CH₃), 3.45 (s, 1H, methine C-H), 1.53 (d, 1H, J_H = 14.4, -CH₂-), 1.29 (d, 2H, J_H = 14.4, -CH₂-), 1.12 (s, 3H, CH₃), 1.03 (s, 3H, CH₃), 0.98 (s, 9H, CH₃). ¹³C NMR (100.5 MHz) δ: 174.0, 158.7, 131.4, 129.0, 113.1, 62.3, 55.2, 51.9, 51.3, 38.8, 32.2, 26.0. MS{EI}: 292 [M]+, 233 [M-OCOMe], 180 [M-C(CH₃)₂CH₂C(CH₃)₂]. HRMS: 292.20347; Calcd. 292.20304.

Methyl 2-(p-chloro)diazoacetate Insertion with 2,2,4-Trimethylpentane. The general procedure was used with methyl 2-(p-chlorophenyl)diazoacetate (30.6 mg, 0.145 mmol), (TPP)FeCl (2.10 mg, 2.06 mol%) and 10.0 mL of 2,2,4-trimethylpentane. The mixture was stirred at 80 °C for 54 h. The major product, methine C-H insertion, 24b, with 30% of the other C-H insertion products were obtained by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture (16.5 mg, 0.0557 mmol 38.4% yield based on methyl methyl 2-(p-chlorophenyl)diazoacetate). ¹H NMR (300 MHz) δ:
7.27-7.39 (m, 4H, aryl-H), 3.76 (s, 1H, methine C-H), 3.65 (s, 3H, OCH₃), 1.51 (d, 1H, J₇ = 14.6, -CH₂-), 1.27 (d, 2H, J₇ = 14.6, -CH₂-), 1.12 (s, 3H, CH₃), 1.03 (s, 3H, CH₃), 0.99 (s, 9H, CH₃). MS{EI}: 297 [M]⁺, 239 [M - OCOMe], 184 [M - C₈H₁₇]. HRMS: 296.15371; Calcd. 296.15431.

**Methyl 2-(p-tolyl)diazoacetate Insertion with 2,2,4-Trimethylpentane.** The general procedure was used with methyl 2-(p-tolyl)diazoacetate (30.7 mg, 0.162 mmol), (TPP)FeCl₂ (2.10 mg, 1.84 mol%) and 10.0 mL of 2,2,4-trimethylpentane. The mixture was stirred at 80 °C for 54 h. The major product, methine C-H insertion, 24c, with 25% of the other C-H insertion products was obtained by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture (18.7 mg, 0.0678 mmol, 41.8% yield based on methyl methyl 2-(p-tolyl)diazoacetate). \(^1\)H NMR (300 MHz) δ: 7.27 (d, 2H, J₇ = 8.1, aryl-H), 7.11 (d, 2H, J₇ = 8.1 aryl-H), 3.63 (s, 3H, OCH₃), 3.48 (s, 1H, methine C-H), 2.34 (s, 3H, ArCH₃), 1.55 (d, 1H, J₇ = 14.3, -CH₂-), 1.30 (d, 2H, J₇ = 14.3, -CH₂-), 1.13 (s, 3H, CH₃), 1.04 (s, 3H, CH₃), 1.00 (s, 9H, CH₃), MS{EI}: 276 [M]⁺, 217 [M - OCOMe]. HRMS: 276.20804; Calcd. 276.20893.

**Dimerization of 2-Phenyleth-1-yl Diazoacetate, 25.** In an oven-dried 25 mL round bottom flask, 2-phenyleth-1-yl diazoacetate, 25, (32.0 mg, 0.168 mmol) was dissolved in 10 mL of dry dichloromethane. The solution was flushed with nitrogen before Fe(TPP)Cl₂ (2.40 mg, 2.02 mol%) was added and the reaction was monitored by GC or TLC. The reaction reached completion in 12 h after which the solvent was removed under reduced pressure. A quantitative (27.2 mg, 0.0840 mmol, 100%) amount of dimer was obtained. \(^1\)H NMR (400 MHz) δ: 7.31 (m, 2H aryl-H), 7.24 (m, 3H aryl-H), 6.24 (s, 1H, vinyl-H), 4.38 (t, J = 7.2 Hz, 2H, CH₂) 2.98 (t, J = 7.2 Hz, 2H, CH₂). \(^13\)C
NMR (100.5 MHz) δ: 165.1, 137.5, 129.9, 128.9, 128.6, 126.7, 65.7, 34.9. Elemental analysis: Found (calcd.) %C: 74.21 (74.06), %H: 6.21 (6.28).

**Synthesis of 1-(2-Methylphenyl)-2-diazo-1,3-butanedione, 27.** The diketone, 1-(2-methylphenyl)-1,3-butanedione was prepared using literature methods. A stirred slurry of 5.99 g (0.137 mol) of NaH (55% dispersion in mineral oil) in 100 mL of anhydrous ether was cooled in an icebath. To this mixture under N₂ atmosphere was added a solution of 3.62 g (0.0271 mol) of o-methylacetophenone, 16.1 g of (0.183 mol) of ethyl acetate, and 0.4 mL of anhydrous ethanol. The solution was stirred at ambient temperature for 46 h. To the reaction mixture was added 10 mL of water. The solution was extracted with three 100-mL portions of 10% aqueous NaOH solution. The combined ether solutions were washed twice with water and dried over anhydrous MgSO₄. Distillation gave 3.42 g (72.3%) of 1-(2-methylphenyl)-1,3-butanedione. ¹H NMR (400 MHz) δ: 7.5-6.9 (m, 4H, aryl CH), 5.7 (s, 2H, CH₂), 2.4 (s, 3H, CH₃) 2.04 (s, 3H CH₃). In addition, small signals at 3.87 and 2.12 due to CH₂ and CH₃ of keto tautomer).

To a continuously stirred solution of 1-(2-methylphenyl)-1,3-butanedione (3.42 g, 19.4 mmol) mesyl azide, (3.34 g, 28.2 mmol) in 50 mL of dried CH₃CN, triethylamine, (5.11 g, 50.0 mmol) was added dropwise and the mixture stirred overnight. The mixture was diluted with NaOH and extracted with ethyl acetate and dried under reduced pressure. The crude product purified on a silica gel column to afford 2.60 g of 1-(2-Methylphenyl)-2-diazo-1,3-butanedione, 27, (67.4%). ¹H NMR (CDCl₃, 400 MHz) δ: 7.5-7.2 (m, 4H, aryl-H), 2.53 (s, 3H,CH₃) 2.41 (s, 3H CH₃).
In an oven-dried 25-mL round bottom flask 1-(2-methylphenyl)-2-diazo-1,3-butanedione, 27, (60.0 mg, 0.297 mmol) was dissolved in 10 mL of dry toluene. The solution was flushed with nitrogen before Fe(TPP)Cl (2.10 mg, 0.994 mol%) was added and the reaction was monitored by GC or TLC. The reaction was done in 8 h after which all the solvent was removed under reduced pressure. The contents were then separated on a silica gel column using a 30:1 hexane/ethyl acetate mixture. The portion that contained o-tolualdehyde was concentrated and solvent removed under reduced pressure. o-Tolualdehyde (16.4 mg, 0.137 mmol, 46.1%) was recovered. $^1$H NMR (CDCl$_3$) $\delta$: 10.3 (s, 1H, aldehyde-H), 7.82-7.26 (m, aromatic) 2.69 (s, 3H, CH$_3$).

**Determination of $k_H/k_D$ for Cyclohexane C-H Insertion.** Determination of the kinetic isotope effect for C-H insertion in cyclohexane was done following a literature procedure.$^{18}$ Equimolar amounts of cyclohexane (3.00 mL, 2.32 g, 27.6 mmol) and cyclohexane-$d_{12}$ (99.6 atom % D, 2.97 mL, 2.65 g, 27.6 mmol) were placed in a 25 mL round bottom flask. Methyl 2-(p-methoxyphenyl)diazoacetate (30.4 mg, 0.147 mmol) and (TPP)FeCl (2.20 mg, 2.12 mol%) were added and the contents flushed with nitrogen for about 5 minutes. The mixture was then refluxed for 8 hours after which the mixture was analyzed by GC-MS (Finnigan 4500 ITD) (detecting masses 262 and 274). Baseline-resolved GC peak areas for the $d_{12}$ and $d_0$ products were integrated and corrected for the $k_H/k_D$ of ionization. The observed kinetic isotope effect was 1.97 ± 0.03 and represents an average of three runs each of two reactions. Similar procedures used for the determination of the K.I.E for methyl 2-(p-tolyldiazoacetate and methyl 2-(p-methoxyphenyl)diazoacetate.
**Kinetic experiments for cyclohexane insertion with p-Cl-MPDA.** Three 10-mL two-necked round-bottom flasks were charged with the same amounts of Fe(TPP)Cl (2.50 mg, 3.55 µmol) and dodecane (14.4 mg, 0.09 mmol) dissolved in 2.00 mL of cyclohexane. To each flask, a different amount of p-Cl-MPDA was added [flask 1: (40.0 mg, 0.190 mmol), flask 2: (81.0 mg, 0.385 mmol), flask 3: (121.0 mg, 0.575 mmol)]. A condenser was inserted in one neck, all openings sealed with septa, the assembly was purged with nitrogen and then stirred under nitrogen at 70 °C. The formation of product was monitored hourly with GC by extracting samples via syringe through the septum. The amount of product was determined using dodecane as an internal standard. The initial rate was found to be first order with respect to the diazo reagent (40.0 mg, 3.7 ± 0.4 µM/h; 81.0 mg, 7.2 ± 0.4 µM/h; 121.0 mg, 10.3 ± 0.6 µM/h).

**Competition experiments with para-substituted MPDAs and cyclohexane.** In a round-bottom flask, methyl 2-phenyl diazoacetate (30.6 mg, 0.174 mmol), an equiv amount of a para-substituted methyl 2-phenyl diazoacetate, p-X-MPDA (0.174 mmol), (TPP)FeCl (2.40 mg, 1.96 mol%) were dissolved in 10.0 mL of cyclohexane. The mixture was purged with nitrogen, and heated and 70 °C for 8 hours while stirring. The contents were then cooled to room temperature and volatiles were removed under reduced pressure. The ratio of the products was determined using $^1$H NMR by integrating the signal of the benzylic methine protons which appear at doublets at 3.23 ppm for the unsubstituted product, methyl-cyclohexyl phenylacetate, 16a, and at slightly higher field for the substituted products.
Acknowledgement. The authors are grateful for funding provided by the Petroleum Research Fund administered by the American Chemical Society and the National Science Foundation.

References


(28) Davies, H. M. L.; *Journal of Molecular Catalysis A*, 2002, 189, 125


CHAPTER 4: ADDITION OF CARBENES DERIVED FROM 2-ARYLDIAZOACETATES TO ARENES USING CHLORO(TETRAPHENYLPORPHYRINATO)IRON AS CATALYST

Harun M. Mbuvi, L. Keith Woo

To be submitted to Organometallics

Abstract. Chloro(tetraphenylporphyrinato)iron, Fe(TPP)Cl, is an active catalyst for the Büchner addition of para-substituted methyl 2-phenyldiazoacetates, 1a-d, to substituted benzenes. Temperatures from 60-100 °C are required and yields greater than 70% have been achieved. Reactions of substituted methyl 2-phenyldiazoacetates with benzene gave rapidly equilibrating mixtures of norcaradiene-cycloheptatriene valence isomers 2a-d/2’a-d in yields over 70%. Chlorobenzene gave a regioisomeric mixture of 7-carbomethoxy-2-chloro-7-phenylnorcaradiene/7-carbomethoxy-2-chloro-7-phenylcycloheptatriene, 3a/3’a and 7-carbomethoxy-3-chloro-7-phenylnorcaradiene/7-carbomethoxy-3-chloro-7-phenylcycloheptatriene, 4a/4’a, when treated with methyl 2-phenyldiazoacetate. When p-methylanisole was treated with methyl 2-phenylacetate at 80 °C, a product that largely favored a fused cyclopropane structure, 7-carbomethoxy-2-methoxy-5-methyl-7-phenylnorcaradiene, 12a, was obtained along with the benzylic C-H insertion product methyl 3-(p-methoxyphenyl)-2-phenylpropionoate, 13a. Heating the norcaradiene product 12a at 110 °C yielded the ring-opened diarylacate, 14a. The dienes of the fluxional norcaradiene-cycloheptatriene systems were trapped with benzyne...
to give one stereoisomer of 3,3-disubstituted benzhomobarralenes, 18a-d. The cycloheptatriene-norcaradiene valence isomers quantitatively converted to ring-opened diaryl acetate products upon acidification in acetonitrile. Rates for the addition of methyl (p-chlorophenyl)diazoacetate to benzene were first order with respect to the diazo reagent. A concerted mechanism is proposed for these iron porphyrin-catalyzed Büchner reactions.

**Introduction**

The thermal or photochemical reaction of ethyl diazoacetate with arenes to give a mixture of isomeric cycloheptatrienes is a prototypical example of the Büchner reaction, a process that has been known for over 100 years.\(^1\) The daunting complexity of the product mixtures was reduced or eliminated with the advent of copper-based Büchner catalysts. In the early 1980’s Rh\(_2\)(OAc)\(_4\) and its analogues became the catalyst of choice for this reaction.\(^2\) Subsequently, Rh\(_2\)(OAc)\(_4\)-catalyzed cyclopropanations of arenes, especially intramolecular versions, have enjoyed popularity due to the high regio- and stereoselectivity, which can be achieved.\(^3\) The related sequential cyclopropanation-Cope rearrangement method that has been applied fruitfully to a variety of synthetic challenges and includes examples of Büchner-type cyclopropanations of benzenes, pyrroles, and furans.\(^4\)

Bicyclo[4.1.0]hepta-2,4-diene (norcaradiene, NCD) and the unusually rich chemistry of rearrangements involved with it have been extensively studied for half a century. In 1957, Woods\(^5\) observed the thermal valence isomerization of
bicyclo[2.2.1]heptadiene (norbornadiene, NBD) to 1,3,5-cycloheptatriene (CHT). Considerable mechanistic and synthetic interests continue to evolve with these processes.

While investigating the scope of metal-mediated diazo chemistry, we examined the Fe(TPP)Cl-catalyzed reaction of methyl 2-phenyldiazoacetate (MPDA) with benzene. This reaction was expected to lead to a ring C-H insertion based on our previous work. Instead, the reaction afforded a mixture whose NMR spectra indicated that it consisted of rapidly interconverting norcaradiene-cycloheptatriene valence isomers. Furthermore, upon acidification in acetonitrile these fluxional NCD/CHT products quantitatively converted to ring-opened diaryl acetate products, structural motifs that are present in a number of important pharmaceuticals such as tolterodine, CDP-840, and nomifensine. The details of Fe(TPP)Cl-catalyzed reactions with a variety of arenes and p-substituted MPDAs are reported herein.

**Results and discussion**

The iron(III) tetraphenylporphyrinato complex Fe(TPP)Cl catalyzes the decomposition of para-substituted methyl 2-phenyldiazoacetates, 1a-d, in benzene to produce rapidly equilibrating mixtures of substituted norcaradiene-cycloheptatriene adducts, 2a-d and 2'a-d (eq 1). This reaction required temperatures of 80 °C for 12 to 16 h when 2 mol% catalyst was used. No carbene dimerization to form butenedioates was observed. The rapidly equilibrating valence isomers were characterized by ¹H NMR, ¹³C NMR, mass spectrometry and elemental analysis. For example, the formation of 7-carbomethoxy-7-phenylnorcaradiene, 2a, and its ring expansion valence isomer 7-carbomethoxy-7-phenylcycloheptatriene, 2'a, was established by ¹H NMR spectroscopy.
at 20 °C with the appearance of diagnostic resonances for the olefinic hydrogens at 6.28 (m, 2H) and 6.03 (m, 2H) ppm. The rapid equilibration of the two species was indicated by the appearance of the 1,6-proton resonance at 4.31 ppm, a position intermediate between those expected for the cyclopropyl hydrogens of static 7-methoxycarbonyl-7-phenyldibenzonorcaradiene (~3.67 ppm)\(^\text{11}\) and the 1,6-hydrogens of the static 7-carbomethoxycycloheptatriene (~5.43 ppm)\(^\text{12}\). Furthermore, the \(^{13}\)C NMR spectrum exhibited a broad signal at 72.3 for the 1,6-carbons. This also represented a time-averaged value due to the exchanging vinyl and cyclopropyl carbon atoms at the 1,6-positions. Equilibration of the valence isomers remained rapid even at -60 °C. The composition of the product was verified further by its molecular mass of 226 \(m/z\). In addition, the \(^1\)H NMR data for 2a/2’a was found to match literature values.\(^\text{13}\)

\[
\begin{align*}
\text{Fe(TPP)Cl} + \text{N}_2 + \text{Cl} - \text{H} = 1a \\
\text{Me} = 1b \\
\text{OMe} = 1c \\
\end{align*}
\]

\[
\begin{align*}
2a-d \quad \text{Yields > 70%} \\
2'a-d \\
\end{align*}
\]

When chlorobenzene was treated with methyl 2-phenyldiazoacetate, 1a, and heated at 80 °C with 2 mol% Fe(TPP)Cl for 16 h, two regioisomers of the fluxional NCD-CHT products were produced (eq 2). In all cases, positions 1 and 6 of the valence isomers always maintained a C-H group. Thus, the Büchner addition did not involve the
chlorinated double bond of the substrate. The ratio of the 2-chloro-products, 3a/3'a, to the 3-chloro-isomers, 4a/4'a, was 1:1. Separation of the product mixture by silica gel chromatography using hexane/ethyl acetate (30:1) as the eluent produced a pure sample of the 2-chloro isomers, 3a/3'a. The 3-chloro fraction, 4a/4'a, contained some residual 2-chloro products and could not be obtained cleanly. The 1H NMR spectrum of 3a/3'a exhibited signals for the 1,6-protons at 3.30 (dd) and 3.36 (d) ppm respectively. Furthermore, the 13C NMR signal of C7 appeared at 26.2 ppm while C1 and C6 appeared at 43.0 and 44.6 ppm respectively. In contrast, the 1H NMR signals for H1 and H6 of 4a/4'a appeared together at 4.38 (m) ppm while 13C NMR signals for C7 appears at 38.7 and those of C1 and C6 appeared as broad peaks at 74.7 and 73.5, respectively. These NMR data suggested that the equilibrating valence isomers of 3a/3'a favor the norcaradiene form more than is the case with 4a/4'a. Similar cycloheptatriene-norcaradiene adducts 3b/3'b and 4b/4'b were obtained when chlorobenzene was treated under the same conditions with p-Cl-MPDA, 1b. The reaction mixture was separated on a silica gel column to give a pure sample of the 2-chloro isomers, 3b/3'b. The 3-chloro isomers 4b/4'b contained traces of 3b/3'b and could not be purified further. Proton NMR signals for H1 and H6 appear at 3.32 (d) and 3.25 (dd) ppm respectively for the 2-chloro isomer, 3b/3'b while the related protons appear together at 4.25 (m) ppm for the 3-chloro isomer, 4b/4'b. Although the C1 and C6 13C NMR signals for the 2-chloro isomer, 3b/3'b, were detected as broad peaks at 43.7 and 42.0, the same carbons were not detectable for the 3-chloro isomer case owing to the rapid equilibration of the cycloheptatriene-norcaradiene adduct 4b/4'b, presumably resulting in coalescence of the signals into the baseline. The reaction of chlorobenzene with p-MeO-MPDA, 1d, was
found to produce low yields of both regioisomers 3d/3'd and 4d/4'd. Refluxing for three days using 2\% catalyst resulted in less than 50\% conversion and about 32\% combined yield of the CHT-NCD isomers 3d/3'd and 4d/4'd.

Toluene underwent concomittant C-H activation and Büchner addition reactions with substituted methyl 2-phenyldiazoacetates to give benzylic insertion products, 5a-d, and the two regioisomers of the fluxional NCD-CHT systems 6a-d/6'a-d and 7a-d/7'a-d (eq 3). Although it was not possible to obtain all of the products in high purity, some were separated cleanly. This provided sufficient samples to allow assignment of all the proton NMR signals for this family of products. MPDA, 1a, reacted with toluene to give the benzylic insertion product methyl 2,3-diphenylpropionate, 5a, and the fluxional NCD-CHT products 7-carbomethoxy-2-methyl-7-phenynorcaradiene/7-carbomethoxy-2-methyl-7-phenylcycloheptatriene, 6a/6'a, and 7-carbomethoxy-3-methyl-7-phenynorcaradiene/7-carbomethoxy-3-methyl-7-phenylcycloheptatriene 7a/7'a. It was not possible to cleanly isolate methyl 2,3-diphenylpropionate, 5a. The benzyl product contained ~20\% of 7a/7'a after eluting the reaction mixture through a silica gel column with a hexane/ethyl acetate (30:1) solvent mixture. Nonetheless, the proton NMR
resonances of 5a were found to match literature values. The 2-methyl isomers 6a/6'a were obtained in pure form while the 3-methyl fraction 7a/7'a could not be fully separated from 6a/6'a. As in the case of the chlorobenzene products, the 1,6 protons of 6a/6'a appeared separately at 3.05 ppm and 3.20 ppm respectively while those of 7a/7'a appear together as multiplets at 3.88 ppm. These signals are all upfield relative to those in the chloro analogues 4a/4'a. The electronic nature of the para-substituent of the substituted methyl 2-phenyldiazoacetates influenced the benzyl/Büchner product ratios slightly. The less electron-donating chloride in methyl 2-(p-chlorophenyl)diazoacetate, 1b, resulted in Büchner addition as the major products, 5b:6b/6'b:7b/7'b = 1:2:2. As the electron donor ability of the aryl substituent on the diazo reagent increased, the ratio of the Büchner product decreased. For example, the p-methoxy substituted MPDA, 1d, produced more benzylic C-H insertion (5d:6d/6'd:7d/7'd = 2:1:1, Table 1, entries 9-12).

Contrary to expectations, the more electron rich anisole substrate (eq 4) was found to give low yields of the Büchner-type products that decomposed to unknown compounds on standing. In this reaction, GC analysis showed that most of the diazo reagent was not consumed after 12 hours under refluxing conditions. Column chromatography did not result in clean separation of the product mixture. Unlike the chlorobenzene and toluene cases, products with methoxy substitution at position 2 gave 1,6-proton NMR signals at
lower field as compared to those with substitution at position 3. For example, the 1,6-protons of 7-carbomethoxy-2-methoxy-7-phenylnorcaradiene/7-carbomethoxy-2-methoxy-7-phenylcycloheptatriene, 8a/8'a, gave NMR signals at 4.25 and 4.09 ppm whereas 1,6-hydrogens of the 3-methoxy isomers 9a/9'a appear at 3.10 ppm.

Substituted methyl 2-phenyldiazoacetates reacted with \( p \)-xylene to give both cyclopropanation and benzylic C-H insertion products (eq 5). The equivalence of the vinyl methyl groups of the norcaradiene products indicated that these compounds retained mirror symmetry and that the cyclopropanation occurred only at the 2,3-xylyl double bond. The 1,6-protons of 7-carbomethoxy-2,5-dimethyl-7-phenylnorcaradiene, 10a, gave \(^1\)H NMR signals at 2.94 ppm while \(^{13}\)C NMR signals for the 1,6-carbons appear at 41.4 ppm. These data suggest that 10a favors the norcaradiene form. Electron withdrawing groups on the aryl of the diazo reagents favored cyclopropanation over benzylic insertion with the chloro substituent giving a 10/11 product ratio of 3:1. As the
electron donating nature of the diazo substituent is increased this ratio decreased (Table 1
entries 17-20). Thus, the \( p \)-methoxy substituted MPDA produced a 1:1 product ratio.

Table 1. Summary of catalytic reactions of substituted methyl 2-phenyldiazoacetate compounds.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>catalyst</th>
<th>diazo</th>
<th>products</th>
<th>yields</th>
<th>ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>benzene</td>
<td>Fe(TPP)Cl</td>
<td>1a</td>
<td>2a</td>
<td>76(^b)</td>
<td>n/a</td>
</tr>
<tr>
<td>2</td>
<td>benzene</td>
<td>Fe(TPP)Cl</td>
<td>1b</td>
<td>2b</td>
<td>78(^b)</td>
<td>n/a</td>
</tr>
<tr>
<td>3</td>
<td>benzene</td>
<td>Fe(TPP)Cl</td>
<td>1c</td>
<td>2c</td>
<td>79(^b)</td>
<td>n/a</td>
</tr>
<tr>
<td>4</td>
<td>benzene</td>
<td>Fe(TPP)Cl</td>
<td>1d</td>
<td>2d</td>
<td>82(^b)</td>
<td>n/a</td>
</tr>
<tr>
<td>5</td>
<td>( C_6H_5Cl )</td>
<td>Fe(TPP)Cl</td>
<td>1a</td>
<td>3a:4a</td>
<td>78(^c)</td>
<td>1:1</td>
</tr>
<tr>
<td>6</td>
<td>( C_6H_5Cl )</td>
<td>Fe(TPP)Cl</td>
<td>1b</td>
<td>3b:4b</td>
<td>72(^c)</td>
<td>1:1</td>
</tr>
<tr>
<td>7</td>
<td>( C_6H_5Cl )</td>
<td>Fe(TPP)Cl</td>
<td>1c</td>
<td>3c:4c</td>
<td>&lt;10(^d)</td>
<td>1:1</td>
</tr>
<tr>
<td>8</td>
<td>( C_6H_5Cl )</td>
<td>Fe(TPP)Cl</td>
<td>1d</td>
<td>3d:4d</td>
<td>32(^c)</td>
<td>1:1</td>
</tr>
<tr>
<td>9</td>
<td>toluene</td>
<td>Fe(TPP)Cl</td>
<td>1a</td>
<td>5a:6a:7a</td>
<td>77(^c)</td>
<td>1:1.5:1.5</td>
</tr>
<tr>
<td>10</td>
<td>toluene</td>
<td>Fe(TPP)Cl</td>
<td>1b</td>
<td>5b:6b:7b</td>
<td>68(^c)</td>
<td>1:2:2</td>
</tr>
<tr>
<td>11</td>
<td>toluene</td>
<td>Fe(TPP)Cl</td>
<td>1c</td>
<td>5c:6c:7c</td>
<td>74(^c)</td>
<td>1:1:1</td>
</tr>
<tr>
<td>12</td>
<td>toluene</td>
<td>Fe(TPP)Cl</td>
<td>1d</td>
<td>5d:6d:7d</td>
<td>79(^c)</td>
<td>2:1:1</td>
</tr>
<tr>
<td>13</td>
<td>anisole</td>
<td>Fe(TPP)Cl</td>
<td>1a</td>
<td>8a:9a</td>
<td>38(^c)</td>
<td>1:0.7</td>
</tr>
<tr>
<td>14</td>
<td>anisole</td>
<td>Fe(TPP)Cl</td>
<td>1b</td>
<td>8b:9b</td>
<td>&lt;10(^d)</td>
<td>1:1.3</td>
</tr>
<tr>
<td>15</td>
<td>anisole</td>
<td>Fe(TPP)Cl</td>
<td>1c</td>
<td>8c:9c</td>
<td>&lt;10(^d)</td>
<td>1:1</td>
</tr>
<tr>
<td>16</td>
<td>anisole</td>
<td>Fe(TPP)Cl</td>
<td>1d</td>
<td>8d:9d</td>
<td>42(^c)</td>
<td>1:1</td>
</tr>
<tr>
<td>17</td>
<td>( p )-xylene</td>
<td>Fe(TPP)Cl</td>
<td>1a</td>
<td>10a:11a</td>
<td>83(^c)</td>
<td>2:1</td>
</tr>
<tr>
<td>18</td>
<td>( p )-xylene</td>
<td>Fe(TPP)Cl</td>
<td>1b</td>
<td>10b:11b</td>
<td>84(^c)</td>
<td>3:1</td>
</tr>
<tr>
<td>19</td>
<td>( p )-xylene</td>
<td>Fe(TPP)Cl</td>
<td>1c</td>
<td>10c:11c</td>
<td>86(^c)</td>
<td>1:1:1</td>
</tr>
<tr>
<td>20</td>
<td>( p )-xylene</td>
<td>Fe(TPP)Cl</td>
<td>1d</td>
<td>10d:11d</td>
<td>88(^c)</td>
<td>1:1</td>
</tr>
<tr>
<td>21</td>
<td>( p )-Me-anisole</td>
<td>Fe(TPP)Cl</td>
<td>1a</td>
<td>12a:13a</td>
<td>74(^c)</td>
<td>1.5:1</td>
</tr>
<tr>
<td>22</td>
<td>( p )-Me-anisole</td>
<td>Fe(TPP)Cl</td>
<td>1b</td>
<td>13b:14b</td>
<td>75(^c)</td>
<td>2:1</td>
</tr>
<tr>
<td>23</td>
<td>( p )-Me-anisole</td>
<td>Fe(TPP)Cl</td>
<td>1c</td>
<td>12c:13c</td>
<td>78(^c)</td>
<td>1.2:1</td>
</tr>
<tr>
<td>24</td>
<td>( p )-Me-anisole</td>
<td>Fe(TPP)Cl</td>
<td>1d</td>
<td>12d:13d</td>
<td>77(^c)</td>
<td>1:3</td>
</tr>
<tr>
<td>25</td>
<td>( p )-Cl-toluene</td>
<td>Fe(TPP)Cl</td>
<td>1a</td>
<td>15a:16a</td>
<td>62(^c)</td>
<td>1:3</td>
</tr>
<tr>
<td>26</td>
<td>( p )-Cl-toluene</td>
<td>Fe(TPP)Cl</td>
<td>1b</td>
<td>15b:16b</td>
<td>68(^c)</td>
<td>1:4</td>
</tr>
<tr>
<td>27</td>
<td>( p )-Cl-toluene</td>
<td>Fe(TPP)Cl</td>
<td>1c</td>
<td>15c:16c</td>
<td>73(^c)</td>
<td>1:2</td>
</tr>
<tr>
<td>28</td>
<td>( p )-Cl-toluene</td>
<td>Fe(TPP)Cl</td>
<td>1d</td>
<td>16d:17d</td>
<td>85(^c)</td>
<td>1:1</td>
</tr>
</tbody>
</table>

\(^a\)Substrates used as solvent (5 mL), substituted methyl phenyldiazoacetates (0.19 mmol),
(TPP)FeCl (2.5 mg, 2.0 mol%), mixture thoroughly purged with dry nitrogen, heated at
100 °C for 12-16 h with stirring. \(^b\) Isolated yields. \(^c\) Combined isolated yields of all
products. \(^d\) Detected but not isolated.

When \( p \)-methylanisole was treated with methyl 2-phenyldiazoacetate at 80 °C for
16 h in the presence of 2 mol% Fe(TPP)Cl, both the cyclopropanation product, 7-
carbomethoxy-2-methoxy-5-methyl-7-phenynorcaradiene, 12a, and the benzylic C-H insertion product, methyl 3-(p-methoxyphenyl)-2-phenylpropionoate, 13a, were obtained (eq 6). However, when the reaction was done at 110 °C, a ring C-H insertion product, methyl 2-(2-methoxy-5-methylphenyl)-2-phenylacetate, 14a, was produced instead of the cyclopropanation product (eq 7). Similarly, p-Cl-MPDA, 1b, was found to afford the cyclopropanation product only when the reactions was done at 60 °C, otherwise a ring C-H insertion product, 14b, formed at higher temperature. To probe this behavior further, pure 7-carbomethoxy-2-methoxy-5-methyl-7-phenynorcaradiene, 12a, was dissolved in p-methylanisole and the mixture heated at 110 °C for 6 h. Quantitative conversion to the diarylacate, 14a, (eq 8) was observed. Similarly, heating 7-carbomethoxy-7-(p-chlorophenyl)-2-methoxy-5-methylnorcaradiene, 12b, at 110 °C resulted in rearrangement to product 14b.

Although the cyclopropane moiety in product 12a can theoretically rearrange to two ring-opened products, 14a and 15a, only one isomer was observed by ^1H NMR
spectroscopy based on the appearance of a single methine signal at 5.27 ppm. The product stereochemistry was confirmed by a 2D noesy NMR experiment. The aryl proton H₃ (6.86 ppm, see eq. 8 for proton numbering), assigned definitively by its appearance as a unique singlet at 6.86 ppm, interacted through space with the aryl methyl group (C-4) at 2.25 ppm. This NOE result is only possible in product 14a. In isomer 15a the aryl proton H₂ would also appear as a singlet, but is too far to exhibit a NOE interaction with the aryl methyl group at C-4.

When p-chlorotoluene was stirred with methyl 2-phenyldiazoacetate, 1a, at 80 °C for 16 h in the presence of 2 mol% catalyst, both the cyclopropanation product, 7-carbomethoxy-2-chloro-5-methyl-7-phenylnorcaradiene, 16a, and the benzylic C-H insertion product, 17a, were obtained (eq 9). Chloro and methyl substituted methyl 2-phenyldiazoacetates gave similar products but the proportion of the cyclopropanation product was found to be higher for the chloro substituent (Table 1 entries 25-26).
However, methyl 2-\((p\text{-methoxyphenyl})\)diazoacetate was found to give the cyclopropanation product, \(16d\), and benzylic insertion product, \(17d\), in almost equal amounts.

\[ \begin{align*}
\text{Cl} & \quad \overset{2 \text{ (1a-c)}}{\xrightarrow{2 \text{ mol\% Fe(TPP)Cl}}} \\
\text{Cl} & \quad 80 \, ^\circ\text{C} \\
12-16 \, \text{h} & \quad -2 \, \text{N}_2 \\
\text{Cl} & \quad 16a-d + 17a-d
\end{align*} \]

**Trapping Fluxional Dienes.** To explore further these fluxional NCD-CHT systems, trapping experiments with benzyne were undertaken. Benzyne was generated in situ using 2-(trimethylsilyl)phenyltriflate and CsF dissolved in acetonitrile\(^\text{15}\) in the presence of the NCD-CHT systems. In each case, a single isomer was produced in yields greater than 94\%. \(^1\)H NMR spectroscopy allowed unambiguous characterization and identification of the products as 3-carbomethoxy-3-aryl-8,9-benzhomobarralenes, \(18a-d\), resulting from \([2+4]\) cycloaddition reactions (eq 10-13). For example, after reaction of benzyne with the 7-carbomethoxy-7-\((p\text{-methylphenyl})\)-norcaradiene/cycloheptatriene valence isomers, \(2c/2'c\), the 1,6-hydrogen signals moved upfield from 4.32 ppm to 2.33 (m, 2H) ppm. The retention of chemical equivalence of these protons and their peak position indicated that the new product retained mirror symmetry and contained a cyclopropyl fragment. Furthermore, a new chemical shift at 4.24 (m, 2H) ppm is consistent with bridgehead protons as reported previously for benzhomobarrelene compounds.\(^\text{16}\) The existence of a mirror plane in the product ruled out \([2+4]\) addition of
benzyne to the cycloheptatriene form of the valence isomers. Moreover, all [2+2] adducts can be ruled out by the presence of bridgehead protons in the product. This was somewhat unexpected since treatment of cycloheptatriene with benzyne produced a [2+2] product along with 7-phenylcycloheptatriene as a minor product.\textsuperscript{17} However, in the cases reported here, it is apparent that benzyne reacts preferentially with the norcaradiene form of the valence isomers. Precedence for the [2+4] products is provided by the work of Abbasoglu \textit{et al.}\textsuperscript{18} in which the reaction of 7-carbomethoxycycloheptatriene with benzyne resulted in the formation of only one benzhomobarrelene isomer. To our knowledge, benzhomobarralenes, 18a-d, are the first examples with disubstitution at the 3-position.
Two norcaradiene stereoisomers (I and III, Scheme 1) can interconvert with each other through the cycloheptatriene structure (II). Since these cycloheptatriene-norcaradiene system are dynamic and the proton NMR signals of the products produce a simple time averaged spectrum, it is not possible to determine a priori which norcaradiene isomer reacts with benzyne. An endo attack by benzyne on either norcaradiene is likely to be disfavored due to steric reasons. The most likely benzomobarrelene products are isomers IV and V (Scheme 1). A noesy NMR experiment performed on benzomobarrelene 18c revealed that the cyclopropyl hydrogens at 2.33 ppm interact through space with the methyl hydrogens of the ester group. In addition, a through-space interaction between the hydrogens of the $p$-tolyl
group (6.99 ppm) with the vinyl protons (5.51 ppm) was observed. These NOE relationships indicate that the benzhomobarrelenes adopt structure V.

Scheme 1

Acidification of Fluxional Dienes. Acid treatment of the NCD-CHT valence isomers resulted in ring opening of the cyclopropane and formation of diaryl acetates. For example, 7-carbomethoxy-7-(p-tolyl)-norcaradiene/7-carbomethoxy-7-(p-tolyl)cycloheptatriene, 2c/2’c, quantitatively converted to methyl 2-phenyl-2-p-tolylacetate, 22c, upon acidification with sulfuric acid and warming to 60 °C in acetonitrile solution (eq 14). Similarly, 2,5-dimethyl-7-(p-chlorophenyl)-7-carbomethoxy norcaradiene/2,5-dimethyl-7-(p-chlorophenyl)-7-carbomethoxycycloheptatriene, 10b/10’b, readily converted to methyl 2-(2,5-dimethylphenyl)-2-p-chlorophenylacetate, 23b, upon acidification (eq 15).
Mechanistic Considerations. The present work has shown that MPDAs substituted with electron withdrawing groups such as Cl tended to favor Büchner addition to arenes whereas the electron rich methoxy substituted MPDA preferred benzylic insertion products. This suggests that an increase in electrophilicity of intermediate carbene favors the cyclopropanation of arenes. This concurs well with earlier research done by Anciaux et al.\textsuperscript{19} which found that use of tetrakis(carboxylato)dirhodium(II) complexes with carboxylate ligands of very strong organic acids such as trifluoroacetic and perfluorobenzoic acids led to cyclopropanation of benzene and toluene with EDA in quantitative yields while the parent acetate complex gave yields of less than 30%. Whether the addition of the carbenoid to the aromatic molecule is concerted or takes place via a stepwise ionic mechanism remains to be answered. However, if the addition was a stepwise ionic mechanism, one would expect some 1,2-hydrogen shift byproduct that would produce ring C-H insertion products (Scheme 2).\textsuperscript{20} Lack of these hydrogen transfer products suggests a concerted mechanism.
Initial rates of catalysis with \(p\)-Cl-MPDA and benzene were determined under pseudo-first order condition at different diazo reagent concentrations. These rates were found to be first order with respect to the concentration of the diazo compound (0.095 mM, 2.40 \(\mu\)M/h; 0.19 mM, 4.75 \(\mu\)M/h; 0.29 mM, 7.0 \(\mu\)M/h). This indicates that formation of a metal carbene complex is the rate-determining step. This concurs well with metal-complexes catalyzed cyclopropanation via diazocarbonyl reagents which are generally assumed to involve an intermediate metal carbene complex, proceeding through metal-mediated extrusion of nitrogen from the diazo compound, followed by a concerted cyclopropanation process.\(^{21,22}\) The NCD-CHT valence isomers convert to diarylacettes when acidified. Scheme 3 outlines how this 1,2 hydrogen transfer ring opening mechanism can be facilitated by presence of acid.

**Scheme 2**
Scheme 3

Conclusion

Fe(TPP)Cl is an effective catalyst for the cyclopropanation of arenes using \(p\)-substituted methyl phenyldiazoacetates as carbene sources. This reaction produced valence isomeric norcaradiene-cycloheptatriene products. The compounds obtained from insertion of carbenes derived from MPDAs gave \(^1\)H NMR diagnostic resonances for olefinic hydrogens at approximately 6.3 ppm (m, 2H) and 6.0 (m, 2H) ppm and rapidly equilibrating 1,6-proton resonance at 4.3 ppm when spectra are run at 20 °C. When the same NMR sample is run at -60 °C, the olefinic protons broaden, but remain at similar chemical shifts of 6.2 (b, 2H) and 6.0 (b, 2H) ppm. The 1,6-protons also broaden and move to slightly higher field, resonating at around 4.1 ppm. This indicates that even at -60 °C these isomers are in rapid equilibration on the NMR time scale, thus giving a time-averaged signal due to the exchanging vinyl and cyclopropyl carbon atoms at the 1,6-positions. Insertion of MPDA into chlorobenzene produces 2-chloro 3a/3'a and 3-chloro 4a/4'a isomers. These regioisomers are easily distinguished by their \(^1\)H NMR signals
with 1,6-protons that are surprisingly very different. The 1,6-proton signals of the 2-chloro 3a/3’a product appear at 3.30 (dd) and 3.36 (d) ppm, respectively, while those of 4a/4’a appear together at 4.38 (m) ppm.

The fluxional nature the NCD-CHT system was confirmed further by trapping with benzyne to give one isomer of substituted benzhomobarralenes resulting from [2+4] cycloaddition reactions. Trapping 2-chloro 3b/3’b and 3-chloro 4b/4’b with benzyne helped confirm the configuration of two regioisomers. The benzhomobarralene product derived from the 2-chloro 3b/3’b isomer exhibited a bridgehead signal at 4.23 ppm (m) that integrates to one proton and a vinyl signal at 5.57 that integrates to two protons. However, trapping the 3-chloro 4b/4’b isomer produced 20b which has two different bridgehead signals at 4.15 ppm (m) and 4.30 ppm (m) intergrating to one proton each and a vinyl signal at 5.42 ppm that intergrates as one proton. These fluxional systems have also be aromatized by acidification to afford biaryl products which are same as one would expect from an aromatic C-H insertion process.

Initial rate of reactions studies for p-Cl MPDA addition to benzene indicate that formation of an iron carbene complex is the rate-limiting step. Absence of a 1,2-hydrogen shift byproduct suggested that a concerted mechanism is involved.

**Experimental Section**

Fe(TPP)Cl was obtained from Aldrich. Toluene was dried by passage through a column of catalytic copper and alumina as described by Grubbs et al. Substituted methyl phenyldiazoacetates were prepared as outlined in the literature. Proton NMR and 13C NMR spectra were recorded on a Varian VXR 300 or a Bruker DRX400
spectrometer. $^1$H NMR peak positions were referenced against residual proton resonances of deuterated CDCl$_3$ (δ, 7.27 ppm). Gas chromatography analysis was performed on a HP 5890 series II or a Finnigan GC-MS. Dodecane was used as an internal standard. All reactions were performed under an atmosphere of nitrogen.

**General Procedure for Büchner and C-H Insertion Reactions.** About 30.0 mg of the diazo reagent were accurately weighed and placed in a 50-mL round bottom flask containing a stir bar. A condenser fitted with a rubber septum was then attached to the round bottom flask and the contents thoroughly flushed with nitrogen. Fe(TPP)Cl (2 mol %) was placed in a separate flask, dissolved in 5 mL of substrate, and the contents were bubbled with dry nitrogen for 15 minutes. This solution was transferred to the diazo reagent by a cannula. The mixture was then heated to an appropriate temperature while continuously stirring until the diazo reagent was consumed. The products were separated or purified by eluting on a silica gel column (4 cm diameter x 30 cm, hexane/ethyl acetate; 30:1).

**General Procedure for Trapping Fluxional Norcaradiene-Cycloheptatriene Systems.** About 10.0 mg of the norcaradiene-cycloheptatriene product was dissolved in 10.0 mL of acetonitrile and placed in a 4-dram vial that contained a stir bar. To this solution, 1.2 equiv of 2-(trimethylsilyl)phenyl triflate were added and the mixture was stirred briefly before adding 2 equivalent of cesium fluoride. The vial was then sealed and the mixture stirred for 8 h. The product was purified by silica gel chromatography (4 cm diameter x 30 cm long, hexane/ethyl acetate; 20:1).

**Reaction of Methyl 2-phenyldiazoacetate with Benzene.** The general procedure was used with methyl 2-phenyldiazoacetate (30.1 mg, 0.171 mmol),
Fe(TPP)Cl (2.40 mg, 1.99 mol%) and 10.0 mL of benzene. The mixture was stirred at 80 °C for 32 h. The product was isolated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The products, 7-carbomethoxy-7-phenylnorcaradiene/7-carbomethoxy-7-phenyl-cycloheptatriene, 2a/2'a, (29.3 mg, 0.130 mmol, 76% yield based on methyl 2-phenyldiazoacetate) were obtained as a white solid. The proton NMR and $^{13}$C NMR matched literature values.\(^5\) $^1$H NMR (300 MHz): 7.19 (m, 5H, aryl C-H), 6.28 (m, 2H, vinyl C-H), 6.03 (m, 2H, vinyl C-H), 4.31 (m, 2H, cyclopropyl-H), 3.65 (s, 3H, OCH\(_3\)). $^{13}$C NMR (75.4 MHz): 176.0, 135.6, 131.3, 127.4, 127.1, 126.9, 125.1, 72.3, 53.0. MS\{EI\}: 226 [M]\(^+\). Elemental analysis: Found (calcd.): %C: 79.85 (79.62), %H: 6.26 (6.24).

**Reaction of Methyl 2-(p-chlorophenyl)diazoacetate with Benzene.** The general procedure was used with methyl 2-(p-chlorophenyl)diazoacetate (30.7 mg, 0.146 mmol), Fe(TPP)Cl (2.10 mg, 2.04 mol%) and 10.0 mL of benzene. The mixture was stirred at 80 °C for 32 h. The product was isolated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The products 7-carbomethoxy-7-(p-chlorophenyl)norcaradiene/7-carbomethoxy-7-(p-chlorophenyl)cycloheptatriene, 2b/2'b, (29.6 mg, 0.114 mmol, 78% yield based on methyl 2-(p-chlorophenyl)diazoacetate) were obtained as a white solid. $^1$H NMR (300 MHz): 7.14 (d, 2H, J\(_H\) = 10.7, aryl C-H), 7.09 (d, 2H, J\(_H\) = 10.7 aryl C-H), 6.24 (m, 2H, vinyl C-H), 5.98 (m, 2H, vinyl C-H), 4.32 (d, 2H, cyclopropyl-H), 3.66 (s, 3H, OCH\(_3\)). $^{13}$C NMR (75.4 MHz): 175.9, 133.7, 133.2, 132.8, 129.3, 127.6, 127.5, 125.2, 67.6, 53.2. MS\{EI\}: 260 [M]\(^+\). Elemental analysis: Found (calcd.) %C: 69.32 (69.10), %H: 5.21 (5.03).
**Reaction of Methyl 2-(p-tolyl)diazoacetate with Benzene.** The general procedure was used with methyl 2-(p-tolyl)diazoacetate (30.4 mg, 0.160 mmol), Fe(TPP)Cl (2.30 mg, 2.04 mol%) and 10.0 mL of benzene. The mixture was stirred at 80 °C for 32 h. The product was isolated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The products 7-carbomethoxy-7-(p-tolyl)norcaradiene/7-carbomethoxy-7-(p-tolyl)cycloheptatriene, 2c/2'c, (30.3 mg, 0.126 mmol, 79% yield based on methyl 2-(p-tolyl)diazoacetate) were obtained as a white solid. $^1$H NMR (400 MHz): 7.08 (d, 2H, J_H = 8.0, aryl C-H), 7.00 (d, 2H, J_H = 8.0, aryl C-H), 6.28 (m, 2H, vinyl C-H), 6.04 (m, 2H, vinyl C-H), 4.31 (m, 2H, cyclopropyl-H), 3.64 (s, 3H, OCH$_3$), 2.29 (s, 3H, ArCH$_3$). $^{13}$C NMR (100.5 MHz): 176.4, 136.6, 132.7, 131.2, 128.2, 127.6, 125.3, 73.1, 53.2, 41.0, 21.5. MS{EI}: 241 [M+1]$^+$. Elemental analysis: Found (calcd.) %C: 79.52 (79.97), %H: 6.83 (6.71).

**Reaction of Methyl 2-(p-methoxyphenyl)diazoacetate with Benzene.** The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (30.5 mg, 0.148 mmol), Fe(TPP)Cl (2.10 mg, 2.02 mol%) and 10.0 mL of benzene. The mixture was stirred at 80 °C for 32 h. The products were isolated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The products, 7-carbomethoxy-7-(p-methoxyphenyl)norcaradiene/7-carbomethoxy-7-(p-methoxyphenyl)cycloheptatriene, 2d/2'd, (31.1 mg, 0.121 mmol, 82% yield based on methyl 2-(p-methoxyphenyl)diazoacetate) were obtained as a white solid. $^1$H NMR (400 MHz, CDCl$_3$): 7.09 (d, 2H, J_H = 9.0, aryl C-H), 6.72 (d, 2H, J_H = 9.0 aryl C-H), 6.25 (m, 2H, vinyl C-H), 6.02 (m, 2H, vinyl C-H), 4.21 (m, 2H, cyclopropyl-H), 3.76 (s, 3H, ArOCH$_3$), 3.65 (s, 3H, OCH$_3$). $^{13}$C NMR (100.5 MHz): 176.4, 158.2, 132.4, 127.3, 125.0,
Reaction of Methyl 2-phenyldiazoacetate with Chlorobenzene. The general procedure was used with methyl 2-phenyldiazoacetate (30.1 mg, 0.171 mmol), Fe(TPP)Cl (2.40 mg, 1.99 mol%) and 5.0 mL of chlorobenzene. The mixture was stirred at 80 °C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. It was not possible to fully separate the two products. A combined yield of 34.6 mg, 0.133 mmol, of both products, 3a/3'a and 4a/4'a, 78% yield based on methyl 2-phenyldiazoacetate were obtained. However, 8.20 mg (18% yield) of pure 7-carbomethoxy-3-chloro-7-phenylnorcaradiene/7-carbomethoxy-3-chloro-7-phenylcycloheptatriene, 3a/3'a, was obtained from a center-cut of a band. 3a/3'a: \( ^1 \text{H NMR (400 MHz)}: 7.20-7.25 (m, 3H, aryl C-H), 7.11-7.15 (m, 2H, aryl C-H), 6.13 (dd, 1H, J_H = 9.2, J_H = 5.6 vinyl C-H), 5.84 (d, J_H = 6.8, 1H vinyl C-H), 5.71(dd, J_H = 9.2, J_H = 6.8, 1H, vinyl C-H), 3.67 (s, 3H, OCH\_3), 3.36 (d, J_H = 8.8, 1H, cyclopropyl-H), 3.30 (dd, J_H = 8.8, J_H = 5.6, 1H, cyclopropyl-H). \(^{13}\text{C NMR (100.5 MHz): 176.1, 132.3, 132.0, 131.4, 127.5, 127.4, 125.6, 123.1, 123.0, 53.3, 44.6, 43.0, 26.2. MS{EI}: 260 [M]^+} \). Elemental analysis: Found (calcd.) %C: 68.97 (69.10), %H: 5.11 (5.03). 7-Carbomethoxy-3-chloro-7-phenylnorcaradiene/7-carbomethoxy-3-chloro-7-phenylcycloheptatriene 4a/4'a (11.4 mg, 25%) containing ~10% of 3a/3'a were obtained. 4a/4'a: \( ^1 \text{H NMR (400 MHz)}: 7.19-7.24 (m, 3H, aryl C-H), 7.12-7.18 (m, 2H, aryl C-H), 6.28 (m, 2H, vinyl C-H), 6.02 (d, J_H =8.8, 1H, vinyl C-H), 4.38 (m, 2H, cyclopropyl-H), 3.66 (s, 3H, OCH\_3). \(^{13}\text{C NMR (100.5 MHz): 175.2, 134.9, 132.2, 130.9, 128.3, 127.4, 127.3, 126.3, 123.5, 74.7, 73.5, 53.2, 38.7. MS{EI}: 260 [M]^+} \).
Reaction of Methyl 2-(p-chlorophenyl)diazoacetate with Chlorobenzene. The general procedure was used with methyl 2-(chlorophenyl)diazoacetate (30.6 mg, 0.145 mmol), Fe(TPP)Cl (2.20 mg, 2.16 mol%) and 5.0 mL of chlorobenzene. The mixture was stirred at 80 °C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. It was not possible to fully separate the two products. A combined yield of 30.9 mg, 0.105 mmol, 72% yield based on methyl 2-(chlorophenyl)diazoacetate) was obtained. However, collecting a center fraction of the 7-carbomethoxy-2-chloro-7-(p-chlorophenyl)norcaradiene/7-carbomethoxy-2-chloro-7-(p-chlorophenyl)cycloheptatriene, 3b/3'b, band produced a pure sample (10.4 mg, 24% yield). 3b/3'b: 1H NMR (400 MHz): 7.20 (d, 2H, J_H = 8.6, aryl C-H), 7.06 (d, 2H, J_H = 8.6, aryl C-H), 6.11 (dd, 1H, J_H = 9.2, J_H = 5.6, vinyl C-H), 5.84 (d, 1H, J_H = 6.8, vinyl C-H), 5.73 (dd, 1H, J_H = 9.2, J_H = 6.8, vinyl C-H), 3.67 (s, 3H, OCH_3), 3.32 (d, 1H, J_H = 9.0, cyclopropyl-H), 3.25 (dd, 1H, J_H = 9.0, J_H = 5.6, cyclopropyl-H). ^13C NMR (100.5 MHz): 175.6, 133.7, 133.3, 131.3, 130.4, 127.9, 125.8, 123.1, 122.8, 53.3, 43.7, 42.0, 25.2. MS{EI}: 295 [M+1]^+. Elemental analysis: Found (calcd.) %C: 59.96 (61.04), %H: 4.21 (4.10). 7-Carbomethoxy-3-chloro-7-(p-chlorophenyl)norcaradiene/7-carbomethoxy-3-chloro-7-(p-chlorophenyl)cycloheptatriene, 4b/4'b, (9.40 mg, 22% yield) containing ~ 2% of 3b/3'b was obtained. 4b/4'b: 1H NMR (300 MHz): 7.18 (d, 2H, J_H = 8.7, aryl C-H), 7.08 (d, 2H, J_H = 8.7, aryl C-H), 6.27 (m, 2H, vinyl C-H), 6.02 (dd, 1H, J_H = 8.7, J_H = 1.5, vinyl C-H), 4.25 (m, 2H, cyclopropyl-H), 3.68 (s, 3H, OCH_3). ^13C NMR (75.4 MHz): 175.0, 133.8, 132.7, 132.4, 131.7, 128.7, 127.9, 126.6, 123.4, 53.4. MS{EI}: 295 [M]^+. 
Reaction of Methyl 2-(p-methoxyphenyl)diazoacetate with Chlorobenzene.

The general procedure was used with methyl 2-(methoxyphenyl)diazoacetate (30.3 mg, 0.147 mmol), Fe(TPP)Cl (2.20 mg, 2.13 mol%) and 5.0 mL of chlorobenzene. The mixture was stirred at 80°C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The products 7-carbomethoxy-2-chloro-7-(p-methoxyphenyl)norcaradiene/7-carbomethoxy-2-chloro-7-(p-methoxyphenyl)cycloheptatriene, 3d/3’d, and 7-carbomethoxy-3-chloro-7-(p-methoxyphenyl)norcaradiene/7-carbomethoxy-3-chloro-7-(p-methoxyphenyl)cycloheptatriene, 4d/4’d, and unreacted p-MeO-MPDA could not be fully separated from each other. The proton NMR of the product was assigned by comparison with the spectra of 3b/3’b and 4b/4’b. An NMR yield of 16% of 3b/3’b and 17% of 4b/4’b were obtained. 3d/3’d: 1H NMR (400 MHz): 7.05 (d, 2H, J_H = 8.8, aryl C-H), 6.75 (d, 2H, J_H = 8.8, aryl C-H), 6.12 (dd, 1H, J_H = 9.0, J_H = 5.6, vinyl C-H), 5.84 (d, 1H, J_H = 6.8, vinyl C-H), 5.72 (dd, 1H, J_H = 9.0, J_H = 6.8, vinyl C-H), 3.77 (s, 3H, ArOCH3), 3.67 (b, 3H, OCH3), 3.31 (d, 1H, J_H = 9.0, cyclopropyl-H), 3.25 (dd, 1H, J_H = 9.0, J_H = 5.6, cyclopropyl-H). MS{EI}: 290 [M]^+.

4d/4’d: 1H NMR (300 MHz): 7.07 (d, 2H, J_H = 8.3, aryl C-H), 6.74 (d, 2H, J_H = 8.3, aryl C-H), 6.25 (m, 2H, vinyl C-H), 6.03 (m, 1H, vinyl C-H), 4.30 (m, 2H, cyclopropyl-H), 3.77 (s, 3H, ArOCH3), 3.67 (b, 3H, OCH3). MS{EI}: 290 [M]^+.

Reaction of Methyl 2-phenyldiazoacetate with Toluene. The general procedure was used with methyl 2-phenyldiazoacetate (30.1 mg, 0.171 mmol), Fe(TPP)Cl (2.40 mg, 1.99 mol%) and 5.0 mL of toluene. The mixture was stirred at 80 °C for 32 h. The benzylic C-H insertion product methyl 2,3-diphenylpropionate (5a) and two Büchner
products  7-carbomethoxy-2-methyl-7-phenynorcaradiene/7-carbomethoxy-2-methyl-7-phenylcycloheptatriene, 6a/6’a, and 7-carbomethoxy-3-methyl-7-phenynorcaradiene/7-carbomethoxy-3-methyl-7-phenylcycloheptatriene, 7a/7’a, were partially separated using silica gel chromatography and hexane/ethyl acetate 30:1 as eluent. It was not possible to fully separate the three products. A combined yield of 31.6 mg, 0.132 mmol 77% yield was obtained. A mixture (6.40 mg) of 5a containing ~ 30% of 7a/7’a was used for spectroscopic analysis. The proton NMR data for the benzylic C-H product, methyl 2,3-diphenylpropionate, was found to match literature values.\textsuperscript{14} 5a: \textsuperscript{1}H NMR (400 MHz): 7.22-7.34 (m, 5H, aryl C-H), 7.09-7.22 (m, 5H, aryl C-H), 3.86 (dd, 1H, J\textsubscript{H} = 8.8, J\textsubscript{H} = 6.8, methine C-H), 3.62 (s, 3H, OCH\textsubscript{3}), 3.43 (dd, 1H, J\textsubscript{H} = 13.6, J\textsubscript{H} = 8.8, ArCH\textsubscript{2}R), 3.04 (dd, 1H, J\textsubscript{H} = 13.6, J\textsubscript{H} = 6.8, ArCH\textsubscript{2}R). MS\{EI\}: 240 [M]\textsuperscript{+}. Pure 6a/6’a (8.60 mg, 21% yield) was obtained from a center-cut of a band. \textsuperscript{1}H NMR (400 MHz): 7.17-7.22 (m, 3H, aryl C-H), 7.01-7.07 (m, 2H, aryl C-H), 6.04 (dd, 1H, J\textsubscript{H} = 8.4, J\textsubscript{H} = 5.6, vinyl C-H), 5.73 (dd, 1H, J\textsubscript{H} = 8.4, J\textsubscript{H} = 6.4 vinyl C-H), 5.56 (d, 1H, J\textsubscript{H} = 6.4, vinyl C-H), 3.65 (s, 3H, OCH\textsubscript{3}), 3.24 (dd, 1H, J\textsubscript{H} = 8.6, J\textsubscript{H} = 5.6, cyclopropyl-H), 3.10 (d, 1H, J\textsubscript{H} = 8.6, cyclopropyl-H), 2.10 (s, 3H, vinyl-CH\textsubscript{3}). \textsuperscript{13}C NMR (100.5 MHz): 177.3, 133.7, 133.1, 132.5, 127.2, 127.0, 126.1, 122.1, 121.8, 53.0, 44.6, 42.1, 26.7, 24.1. MS\{EI\}: 240 [M]\textsuperscript{+}. Pure 7a/7’a (2.60 mg, 6% yield) was obtained from a center-cut of a band. \textsuperscript{1}H NMR (400 MHz): 7.11-7.22 (m, 5H, aryl C-H), 6.16 (m, 1H, vinyl C-H), 5.96 (m, 1H, vinyl C-H), 5.74 (d, 1H, J\textsubscript{H} = 9.2, vinyl C-H), 3.88 (m, 2H, cyclopropyl-H), 3.65 (s, 3H, OCH\textsubscript{3}), 1.61 (s, 3H, vinyl-CH\textsubscript{3}). \textsuperscript{13}C NMR (100.5 MHz): 176.4, 135.3, 135.1, 132.0, 129.0, 128.7, 128.6, 125.1, 122.3, 52.8, 21.9.
Reaction of Methyl 2-(p-chlorophenyl)diazoacetate with Toluene. The general procedure was used with methyl 2-(p-chlorophenyl)diazoacetate (30.4 mg, 0.144 mmol), Fe(TPP)Cl (2.00 mg, 1.97 mol%) and 5.0 mL of toluene. The mixture was stirred at 80 °C for 32 h. The benzylic C-H insertion product, 5b, and two Büchner products 7-carbomethoxy-2-methyl-7-(p-chlorophenyl)norcaradiene/7-carbomethoxy-2-methyl-7-(p-chlorophenyl)cycloheptatriene, 6b/6'b, and 7-carbomethoxy-3-methyl-7-(p-chlorophenyl)norcaradiene/7-carbomethoxy-3-methyl-7-(p-chlorophenyl)cycloheptatriene, 7b/7'b, were partially separated using silica gel chromatography and hexane/ethyl acetate 30:1 as eluent. It was not possible to fully separate the three products. A combined yield of 27.2 mg, 0.0993 mmol 69% yield was obtained. It was impossible to separate 5b from 7b/7'b and about 15.2 mg, 38% yield, containing a 1:1 ratio of these products were obtained. The \(^1\)H NMR of the benzylic C-H product, 5b, was found to match literature values.\(^{14}\) 5b: \(^1\)H NMR (300 MHz): 7.16-7.27 (m, 5H, aryl C-H), 7.07-7.16 (m, 4H, aryl C-H), 3.82 (m, 1H, methine C-H), 3.65 (s, 3H, OCH\(_3\)), 3.39 (dd, 1H, \(J_H = 13.5, J_H = 8.3,\) ArCH\(_2\)R), 3.00 (dd, 1H, \(J_H = 13.5, J_H = 7.2,\) ArCH\(_2\)R). A mixture (9.20 mg, 23% yield) of 6b/6'b containing ~15% of 7b/7'b was used for spectroscopic analysis. 6b/6'b: \(^1\)H NMR (300 MHz): 7.15 (d, 2H, \(J_H = 8.6,\) aryl C-H), 6.95 (d, 2H, \(J_H = 8.6,\) aryl C-H), 6.02 (dd, 1H, \(J_H = 9.3, J_H = 5.6,\) vinyl C-H), 5.74 (dd, 1H, \(J_H = 9.3, J_H = 6.3,\) vinyl C-H), 5.58 (d, 1H, \(J_H = 5.6,\) vinyl C-H), 3.65 (s, 3H, OCH\(_3\)), 3.20 (dd, 1H, \(J_H = 8.6, J_H = 6.3,\) cyclopropyl-H), 3.06 (d, 1H, \(J_H = 8.6,\) cyclopropyl-H), 2.08 (s, 3H, vinyl-CH\(_3\)). 7b/7'b: \(^1\)H NMR (400 MHz): 7.05 (m, 2H, aryl C-H), 6.95 (d, 2H, aryl C-H), 6.14 (m, 1H, vinyl C-H), 5.93 (m, 1H, vinyl C-H), 5.73 (d,
1H, J_H = 9.2, vinyl C-H), 3.73 (m, 2H, cyclopropyl-H), 3.64 (s, 3H, OCH_3), 1.61 (s, 3H, vinyl-CH_3). MS{EI}: 275 [M+1]^+.

**Reaction of Methyl 2-(p-tolyl)diazoacetate with Toluene.** The general procedure was used with methyl 2-(p-chlorophenyl)diazoacetate (30.3 mg, 0.159 mmol), Fe(TPP)Cl (2.20 mg, 1.97 mol%) and 5.0 mL of toluene. The mixture was stirred at 80 °C for 32 h. The benzylic C-H insertion product, 5c, and two Büchner products 7-carbomethoxy-2-methyl-7-(p-tolyl)norcaradiene/7-carbomethoxy-2-methyl-7-(p-tolyl)cycloheptatriene, 6c/6'e, and 7-carbomethoxy-3-methyl-7-(p-tolyl)norcaradiene/7-carbomethoxy-3-methyl-7-(p-tolyl)cycloheptatriene, 7c/7'e, were partially separated using silica gel chromatography and hexane/ethyl acetate 30:1 as eluent. It was not possible to separate the three products. A combined yield of 30.1 mg, 0.119 mmol, 75% yield was obtained. A mixture (7.20 mg, 18%) of benzylic C-H product 5c containing 20% 7c/7'c was obtained. The ^1H NMR of 5c was found to match literature values.^14 5c:

^1H NMR (300 MHz): 7.18-7.25 (m, 5H, aryl C-H), 7.11-7.19 (m, 4H, aryl C-H), 3.84 (dd, 1H, J_H = 9.0, J_H = 6.6, methine C-H), 3.61 (s, 3H, OCH_3), 3.42 (dd, 1H, J_H = 13.6, J_H = 9.0, ArCH_2R), 3.02 (dd, 1H, J_H = 13.6, J_H = 6.6, ArCH_2R), 2.34 (s, 3H, ArCH_3). MS{EI}: 254 [M]^+. Pure 6c/6'e (7.40 mg, 18% yield) was obtained from a center-cut of a band. ^1H NMR (300 MHz): 7.00 (d, 2H, J_H = 8.1, aryl C-H), 6.91 (d, 2H, J_H = 8.1, aryl C-H), 6.03 (dd, 1H, J_H = 9.3, J_H = 5.6, vinyl C-H), 5.74 (dd, 1H, J_H = 9.3, J_H = 6.5, vinyl C-H), 5.57 (d, 1H, J_H = 5.6, vinyl C-H), 3.65 (s, 3H, OCH_3), 3.23 (dd, 1H, J_H = 8.4, J_H = 6.5, cyclopropyl-H), 3.08 (d, 1H, J_H = 8.4, cyclopropyl-H), 2.29 (s, 3H, ArCH_3), 2.09 (s, 3H, vinyl-CH_3). ^13C NMR (75.4 MHz): 177.7, 136.6, 133.8, 132.4, 130.2, 129.3, 128.2, 126.3, 122.3, 122.0, 53.2, 24.2, 21.5. MS{EI}: 254 [M]^+. Elemental analysis: Found
(calcd.) %C: 80.02 (80.28), %H: 6.97 (7.13). A mixture (2.20 mg, 5% yield) of 7c/7′c containing ~15% 5c was used for spectroscopic analysis. 7c/7′c: 1H NMR (300 MHz): 7.04 (d, 2H, J_H = 8.1, aryl C-H), 6.99 (d, 2H, J_H = 8.1, aryl C-H), 6.15 (m, 1H, vinyl C-H), 5.96 (m, 1H, vinyl C-H), 5.77 (d, 1H, J_H = 8.4, vinyl C-H), 3.93 (m, 2H, cyclopropyl-H), 3.63 (s, 3H, OCH_3), 2.28 (s, 3H, ArCH_3), 1.64 (s, 3H, R vinyl-CH_3). MS{EI}: 275 [M]+.

**Reaction of Methyl 2-(p-methoxyphenyl)diazoacetate with Toluene.** The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (30.5 mg, 0.148 mmol), Fe(TPP)Cl (2.10 mg, 2.02 mol%) and 5.0 mL of toluene. The mixture was stirred at 80 °C for 32 h. Pure benzylic C-H insertion product 5d (11.6 mg, 29% yield), pure Büchner product 7-carbomethoxy-2-methyl-7-(p-methoxyphenyl)norcaradiene/7-carbomethoxy-2-methyl-7-(p-methoxyphenyl)cycloheptatriene, 6d/6′d (6.50 mg, 16% yield), and partially pure 7-carbomethoxy-3-methyl-7-(p-methoxyphenyl)norcaradiene/7-carbomethoxy-3-methyl-7-(p-methoxyphenyl)cycloheptatriene, 7d/7′d (13.5 mg, 34%) were obtained from silica gel chromatography with hexane/ethyl acetate 30:1 as eluent. The 1H NMR spectrum of 5d was found to match literature data: 14 1H NMR (300 MHz): 7.17-7.27 (m, 5H, aryl C-H), 7.12 (d, 2H, J_H = 8.7, aryl C-H), 6.86 (d, 2H, J_H = 8.4, aryl C-H), 3.81 (m, 1H, methine C-H), 3.80 (s, 3H, ArOCH_3), 3.61 (s, 3H, ROCH_3), 3.39 (dd, 1H, J_H = 13.7, J_H = 8.7, ArCH_2R), 3.01 (dd, 1H, J_H = 13.7, J_H = 6.9, ArCH_2R). 13C NMR (95.4 MHz): 174.4, 159.1, 139.3, 130.9, 129.3, 128.5, 126.6, 114.2, 55.5, 52.9, 52.2, 40.1. MS{EI}: 270 [M]+. 6d/6′d: 1H NMR (400 MHz): 6.94 (d, 2H, J_H = 8.8, aryl C-H), 6.72 (d, 2H, J_H = 8.8, aryl C-H), 6.01 (dd, 1H, J_H = 9.2, J_H = 5.6, vinyl C-H), 5.74 (dd, 1H, J_H = 9.2, J_H = 6.5, vinyl C-H), 5.57 (d, 1H, J_H = 6.5, vinyl C-H), 3.76 (s, 3H, ArOCH_3), 3.65 (s, 3H, OCH_3), 3.20 (dd, 1H, J_H = 8.4, J_H = 5.6, cyclopropyl-H), 3.05 (d, 1H, J_H = 8.4,
cyclopropyl-H), 2.08 (s, 3H, R vinyl-CH₃). ¹³C NMR (100.5 MHz): 177.6, 158.2, 133.6, 133.4, 126.2, 125.0, 122.1, 121.7, 112.7, 55.0, 53.0, 44.3, 41.8, 25.8, 24.1. MS{EI}: 270 [M⁺]. A mixture (4.20 mg, 9%) of 7d/7'd containing ~ 25% of 5d was used for spectroscopic analysis. ¹H NMR (300 MHz): 7.04 (d, 2H, J_H = 8.7, aryl C-H), 6.72 (d, 2H, J_H = 8.7, aryl C-H), 6.14 (m, 1H, vinyl C-H), 5.94 (m, 1H, vinyl C-H), 5.75 (d, 1H, J_H = 9.0, vinyl C-H), 3.81 (m, 2H, cyclopropyl-H), 3.77 (s, 3H, ArOCH₃), 3.64 (s, 3H, OCH₃), 1.63 (s, 3H, R vinyl-CH₃). MS{EI}: 270 [M⁺].

**Reaction of Methyl 2-phenyldiazoacetate with Anisole.** The general procedure was used with methyl 2-phenyldiazoacetate (30.1 mg, 0.171 mmol) Fe(TPP)Cl (2.40 mg, 1.99 mol%) and 5.0 mL of anisole. The mixture was stirred at 80 °C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. Two Büchner products 7-carbomethoxy-2-methoxy-7-phenylnorcaradiene/7-carbomethoxy-2-methoxy-7-phenylecycloheptatriene, 8a/8'a, and 7-carbomethoxy-3-methoxy-7-phenylnorcaradiene/7-carbomethoxy-3-methoxy-7-phenylecycloheptatriene, 9a/9'a, were partially separated using silica gel chromatography and hexane/ethyl acetate 30:1 as eluent. It was not possible to fully separate the two products. A combined yield of 16.6 mg, 0.0648 mmol, 38% yield based on methyl 2-phenyldiazoacetate was obtained. A sample of 8a/8'a containing ~ 5% of 9a/9'a was used for spectroscopic analysis. ¹H NMR (400 MHz): 7.19 (b, 5H, aryl C-H), 6.24 (m, vinyl C-H), 5.58 (m, vinyl C-H), 5.51 (m, vinyl C-H), 4.25 (m, 1H, cyclopropyl-H), 4.09 (m, 1H, cyclopropyl-H), 3.64 (s, 3H, ArOCH₃), 3.43 (s, 3H, ROCH₃). MS{EI}: 256 [M⁺]. 9a/9'a: ¹H NMR (400 MHz): 7.18 (m, 3H, aryl C-H), 7.09 (m, 2H, aryl C-H), 5.72 (m, 2H, vinyl
C-H), 4.79 (d, 1H, J_H = 8.0, vinyl C-H), 3.62 (s, 3H, ROCH_3), 3.61 (s, 3H, ROCH_3), 3.10 (m, 2H, cyclopropyl-H). MS{EI}: 256 [M]^+.

**Reaction of Methyl 2-(p-methoxyphenyl)diazoacetate with Anisole.** The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (30.4 mg, 0.148 mmol), Fe(PP)Cl (2.10 mg, 2.02 mol%) and 5.0 mL of anisole. The mixture was stirred at 80 °C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. Two Büchner products 7-carbomethoxy-2-methoxy-7-(p-methoxyphenyl)norcaradiene/7-carbomethoxy-2-methoxy-7-(p-methoxyphenyl)cycloheptatriene, 8d/8'd, and 7-carbomethoxy-3-methoxy-7-(p-methoxyphenyl)norcaradiene/7-carbomethoxy-3-methoxy-7-(p-methoxyphenyl)cycloheptatriene, 9d/9'd, were partially separated using silica gel column and hexane/ethyl acetate 30:1 as eluent. It was not possible to fully separate the two products. A combined yield of 17.8 mg, 0.0622 mmol, 42% yield based on methyl 2-(p-methoxyphenyl)diazoacetate was obtained. A sample of 8d/8'd containing some minor impurities was used for spectroscopic analysis. ^1H NMR (400 MHz): 7.09 (d, 2H, J_H = 8.8, aryl C-H), 6.72 (d, 2H, J_H = 8.8, aryl C-H), 6.22 (m, vinyl C-H), 5.59 (m, J_H = 2.6, vinyl C-H), 5.48 (m, vinyl C-H), 4.13 (m, 1H, cyclopropyl-H), 3.99 (m, 1H, vinyl C-H), 3.77 (s, 3H, ArOCH_3), 3.64 (s, 3H, ROCH_3), 3.45 (s, 3H, ROCH_3), MS{EI}: 286 [M]^+. A sample of 9d/9'd containing minor impurities was used for spectroscopic analysis. ^1H NMR (400 MHz): 7.01 (d, 2H, J_H = 8.4, aryl C-H), 6.72 (d, 2H, J_H = 8.4, aryl C-H), 5.73 (m, 2H, vinyl C-H), 4.82 (m, 1H, vinyl C-H), 3.77 (s, 3H, ArOCH_3), 3.63 (s, 3H, ROCH_3), 3.62 (s, 3H, ROCH_3), 3.08 (m, 2H, cyclopropyl-H). MS{EI}: 286 [M]^+. 
**Reaction of Methyl 2-phenyldiazoacetate with p-Xylene.** The general procedure was used with methyl 2-phenyldiazoacetate (30.3 mg, 0.172 mmol), Fe(TPP)Cl (2.40 mg, 1.98 mol%) and 5.0 mL of p-xylene. The mixture was stirred at 80 °C for 8 hours. The cyclopropanation product 7-carbomethoxy-2,5-dimethyl-7-phenylnorcaradiene, 10a, and the benzylic C-H insertion product, 11a, were partially separated using silica gel column and hexane/ethyl acetate 30:1 as eluent. A combined yield of 35.9 mg, 0.141 mmol, 82% yield based on methyl 2-phenyldiazoacetate was obtained. However, 12.6 mg, 29% yield of pure 10a were obtained: $^1$H NMR (300 MHz): 7.19 (m, 3H, aryl C-H), 6.97 (m, 2H, aryl C-H), 5.47 (s, 2H, vinyl C-H), 3.65 (s, 3H, ROCH$_3$), 2.94 (s, 2H, cyclopropyl-H), 2.09 (s, 6H, RCH$_3$). $^{13}$C NMR (75.4 MHz): 177.8, 133.1, 132.0, 130.7, 127.5, 127.2, 122.2, 53.1, 41.4, 23.9. MS{EI}: 254 [M]$^+$.

Elemental analysis: Found (Calcd.) %C: 80.28 (80.06) %H: 7.28 (7.13). Pure 11a (8.60 mg, 20% yield) was obtained from a center-cut of a band. $^1$H NMR and $^{13}$C NMR data for 11a were found to much literature values.$^{14}$

$^1$H NMR (300 MHz): 7.28 (m, 5H, aryl C-H) 7.03 (m, 4H, aryl C-H) 3.84 (dd, 1H, J$_H$ = 9.0, J$_H$ = 6.6, methine C-H), 3.61(s, 3H, OCH$_3$) 3.39 (dd, 1H, J$_H$ = 13.8, J$_H$ = 9.0, ArCH$_2$R) 3.00 (dd, 1H, J$_H$ = 13.8, J$_H$ = 6.6, ArCH$_2$R) 2.30 (s, 3H, ArCH$_3$) $^{13}$C NMR (75.4) 174.1, 139.8, 136.2, 136.1, 129.3, 129.0, 128.9, 128.2, 127.6, 53.9, 52.2, 39.6, 21.3 MS{EI}: 254 [M]$^+$. 

**Reaction of Methyl 2-(p-chlorophenyl)diazoacetate with p-Xylene.** Methyl 2-(p-chlorophenyl)diazoacetate (30.2 mg, 0.143 mmol) was placed in a round bottom flask. In a different round bottom flask, the catalyst Fe(TPP)Cl (2.00 mg, 1.99 mol%) was dissolved in 5.0 mL of p-xylene under an atmosphere of dry nitrogen. Both flasks were thoroughly flushed with nitrogen before the dissolved catalyst was transferred to the flask.
containing the diazo by a cannula. The mixture was stirred at 80 °C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The cyclopropanation product 7-carbomethoxy-2,5-dimethyl-7-(p-chlorophenyl)norcaradiene, 10b, and the benzylic C-H insertion product, 11b, were partially separated using silica gel column and hexane/ethyl acetate 30:1 as eluent: A combined yield of 34.4 mg, 0.119 mmol, 83% yield based on methyl 2-(p-chlorophenyl)diazoacetate) were obtained. Pure 10b (16.8 mg, 41% yield) was obtained from a center-cut of a band. 1H NMR (400 MHz): 7.15 (d, 2H, J_H = 8.4, aryl C-H), 6.88 (d, 2H, J_H = 8.4, aryl C-H), 5.49 (s, 2H, vinyl C-H), 3.66 (s, 3H, ROCH3), 2.94 (s, 2H, cyclopropyl-H), 2.07 (s, 6H, RCH3). 13C NMR (100.5 MHz): 177.1, 133.2, 132.8, 131.4, 130.3, 127.7, 122.3, 53.0, 41.2, 23.7. MS{EI}: 289 [M+1]. Elemental analysis: Found (Calcd.) %C: 70.46 (70.71) %H: 5.71 (5.93). Pure 11b (5.40 mg, 13% yield) was obtained from a center-cut of a band. 1H NMR (400 MHz): 7.20 (m, 4H, aryl C-H), 7.14 (d, 2H, J_H = 8.0, aryl C-H), 7.06 (d, 2H, J_H = 8.0, aryl C-H), 3.80 (t, 1H, J_H = 8.8, J_H = 6.8, methine C-H), 3.62 (s, 3H, ROCH3), 3.37 (dd, 1H, J_H = 14.0, J_H = 8.8, ArCH2R), 2.98 (dd, 1H, J_H = 14.0, J_H = 6.8, ArCH2R), 2.30 (s, 3H, RCH3). 13C NMR (100.5 MHz): 173.8, 137.7, 137.3, 135.3, 132.2, 130.4, 129.5, 128.5, 127.8, 53.1, 52.1, 39.1, 21.1. MS{EI}: 289 [M+1].

**Reaction of Methyl 2-(p-tolyl)diazoacetate with p-Xylene.** The general procedure was used with methyl 2-(p-tolyl)diazoacetate (30.6 mg, 0.161 mmol), Fe(TPP)Cl (2.20 mg, 1.94 mol%) and 5.0 mL of p-xylene. The mixture was stirred at 80 °C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The cyclopropanation product 7-
carbomethoxy-2,5-dimethyl-7-(p-tolyl)norcaradiene, 10c, and the benzylic C-H insertion product, 11c, were partially separated using silica gel column and hexane/ethyl acetate 30:1 as eluent: A combined yield of 37.1 mg, 0.138 mmol, 86% yield based on methyl 2-(p-tolyl)diazoacetate were obtained. A pure sample of 10c (12.6 mg, 29% yield) was obtained from a center-cut of a band. \(^1\)H NMR (300 MHz): 7.01 (d, 2H, J\(_H\) = 8.1, aryl C-H), 6.86 (d, 2H, J\(_H\) = 8.1, aryl C-H), 5.49 (s, 2H, vinyl C-H), 3.66 (s, 3H, ROCH\(_3\)), 2.93 (s, 2H, cyclopropyl-H), 2.23 (s, 3H, ArCH\(_3\)), 2.08 (s, 6H, RCH\(_3\)). \(^1\)C NMR (75.4 MHz): 178.0, 136.7, 131.8, 130.7, 130.0, 128.4, 122.2, 53.1, 41.5, 25.8, 23.9, 21.5. MS\{EI\}: 268 [M]+. Elemental analysis: Found (Calcd.) %C: 79.86 (80.56), %H: 7.32 (7.51). 

Pure benzylic C-H product, 11c, (10.6 mg, 25% yield) was obtained from a center-cut of a band. \(^1\)H NMR (400 MHz): 7.23 (d, 2H, J\(_H\) = 8.0, aryl C-H), 7.14 (d, 2H, J\(_H\) = 8.0, aryl C-H), 7.07 (d, 2H, J\(_H\) = 8.0, aryl C-H), 7.03 (d, 2H, J\(_H\) = 8.0, aryl C-H), 3.83 (dd, 1H, J\(_H\) = 9.0, J\(_H\) = 6.8, methine C-H), 3.61 (s, 3H, ROCH\(_3\)), 3.39 (dd, 1H, J\(_H\) = 13.4, J\(_H\) = 9.0, ArCH\(_2\)R), 2.99 (dd, 1H, J\(_H\) = 13.4, J\(_H\) = 6.8, ArCH\(_2\)R), 2.35 (s, 3H, ArCH\(_3\)), 2.31 (s, 3H, RCH\(_3\)). \(^1\)C NMR (100.5 MHz): 174.3, 137.2, 136.3, 136.0, 129.6, 129.3, 129.0, 128.0, 53.5, 52.2, 39.6, 21.3, 21.2. MS\{EI\}: 268 [M]+. Elemental analysis: Found (Calcd.) %C: 80.32 (80.56), %H: 7.21 (7.51).

**Reaction of Methyl 2-(p-methoxyphenyl)diazoacetate with p-Xylene.** The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (30.4 mg, 0.148 mmol), Fe(TPP)Cl (2.30 mg, 2.21 mol%) and 5.0 mL of p-xylene. The mixture was stirred at 80 °C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The cyclopropanation product 7-carbomethoxy-2,5-dimethyl-7-(p-methoxyphenyl)norcaradiene, 10d, and the benzylic C-
H insertion product, 11d, were partially separated using silica gel column and hexane/ethyl acetate 30:1 as eluent: A combined yield of 39.9 mg, 0.140 mmol, 88% yield based on methyl 2-(p-methoxyphenyl)diazoacetate was obtained. Pure 10d (9.70 mg, 21% yield) was obtained from a center-cut of a band. 1H NMR (400 MHz): 6.88 (d, 2H, JH = 9.6, aryl C-H), 6.73 (d, 2H, JH = 9.6, aryl C-H), 5.49 (s, 2H, vinyl C-H), 3.80 (s, 3H, ArOCH3), 3.66 (s, 3H, ROCH3), 3.01 (s, 2H, cyclopropyl-H), 2.07 (s, 6H, RCH3). 13C NMR (100.5 MHz): 178.3, 158.3, 138.6, 132.8, 130.5 122.1, 112.8, 55.0, 53.0, 41.3, 23.7. MS{EI} : 284 [M]+. Pure benzylic C-H product, 11d (12.3 mg, 27%) was obtained from a center-cut of a band and used for spectroscopic analysis. 1H NMR (400 MHz): 7.25 (d, 2H, JH = 8.0, aryl C-H), 7.05 (d, 2H, JH = 8.0, aryl C-H), 7.01 (d, 2H, JH = 8.0, aryl C-H), 6.73 (d, 2H, JH = 8.0, aryl C-H), 3.81 (s, 3H, ArOCH3), 3.79 (m, 1H, methine C-H, overlaps with ArOCH3), 3.61 (s, 3H, ROCH3), 3.32 (dd, 1H, JH = 13.8, JH = 8.6, ArCH2R), 2.94 (dd, 1H, JH = 13.8, JH = 6.8, ArCH2R), 2.27 (s, 3H, ArCH3). 13C NMR (100.5 MHz): 174.4, 159.0, 136.3, 136.0, 133.0, 131.1, 129.2, 129.0, 114.2, 55.5, 53.0, 52.2, 39.7, 21.3. MS{EI}: 284 [M]+. Found (Calcd.) %C: 75.58 (76.03), %H: 6.97 (7.03).

**Reaction of Methyl 2-phenyldiazoacetate with p-Methylanisole.** The general procedure was used with methyl 2-phenyldiazoacetate (30.3 mg, 0.172 mmol), Fe(TPP)Cl (2.40 mg, 1.98 mol%) and 5.0 mL of p-methylanisole. The mixture was stirred at 80 °C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The cyclopropanation product 7-carbomethoxy-2-methoxy-5-methyl-7-phenylnorcaradiene, 12a, and the benzylic C-H insertion product, 13a, were partially separated using silica gel column and hexane/ethyl acetate 30:1 as eluent: A combined yield of 34.4 mg, 0.127 mmol, 74% yield based on
methyl 2-phenyl diazoacetate were obtained. Pure 12a (11.3 mg, 24% yield) was obtained from a center-cut of a band. $^1$H NMR (400 MHz): 7.20 (m, 3H, aryl C-H), 7.06 (m, 2H, aryl C-H), 5.45 (d, 1H, $J_H = 6.8$, vinyl C-H), 4.74 (d, 1H, $J_H = 6.8$, vinyl C-H), 3.64 (s, 3H, ArOCH$_3$), 3.60 (s, 3H, ROCH$_3$), 3.05 (d, 1H, $J_H = 9.6$, cyclopropyl-H), 2.96 (d, 2H, $J_H = 9.6$, cyclopropyl-H), 2.05 (s, 3H, RCH$_3$). $^{13}$C NMR (100.5 MHz): 177.1, 154.5, 133.0, 131.9, 127.6, 127.3, 124.6, 121.6, 95.9, 55.5, 53.1, 46.8, 36.8, 25.1, 23.3. MS{EI}: 270 [M]$^+$. Found (Calcd.) %C: 75.32 (75.53), %H: 6.53 (6.71).

Pure 13a (7.70 mg, 17% yield) was obtained from a center-cut of a band. The $^1$H and $^{13}$C NMR data of 13a was found to match literature values. $^{25}$ $^1$H NMR (400 MHz) 7.21-7.31 (m, 5H, aryl C-H), 7.04 (d, 2H, $J_H = 8.4$, aryl C-H) 6.78 (d, 2H, $J_H = 8.4$, aryl C-H) 3.81 (dd, 1H, $J_H = 8.8$, methine C-H) 3.78 (s, 3H, ArOCH$_3$), 3.61 (s, 3H, ROCH$_3$), 3.36 (dd, 1H, $J_H = 13.8$, $J_H = 8.8$, ArCH$_3$R), 2.98 (dd, 1H, $J_H = 13.8$, $J_H = 6.8$, ArCH$_3$R). $^{13}$C NMR (100.5 MHz): 174.0, 158.1, 138.7, 131.1, 130.0, 128.7, 128.0, 127.4, 113.8, 55.2, 53.9, 52.0, 39.0. MS{EI}: 270 [M]$^+$. Found (Calcd.) %C: 75.32 (75.53), %H: 6.53 (6.71).

Thermal rearrangement of 12a: Compound 12a (10.2 mg, 0.0378 mmol) was dissolved in 5 mL of $p$-methylanisole and the solution stirred at 110 °C for 3 h. All solvent was removed under reduced pressure and the ring-opened product, 14a, was purified using silica gel chromatography and hexane/ethyl acetate 30:1 to afford 9.90 mg (97% yield). $^1$H NMR (400 MHz): 7.28-7.38 (m, 5H, aryl C-H), 7.05 (d, 1H, $J_H = 8.4$, aryl C-H), 6.86 (s, 1H, aryl C-H), 6.78 (d, 1H, $J_H = 8.4$, ring C-H), 5.31 (s, 1H, methine C-H), 3.83 (s, 3H, ArOCH$_3$), 3.74 (s, 3H, ROCH$_3$), 2.23 (s, 3H, ArCH$_3$). $^{13}$C NMR (100.5 MHz): 173.6, 154.8, 137.9, 129.8, 129.1, 128.8, 128.6, 127.4, 127.2, 110.5, 55.7, 52.3, 50.8, 20.7. MS{EI}: 270 [M]$^+$. Found (Calcd.) %C: 75.41 (75.53), %H: 6.64 (6.71).
Reaction of Methyl 2-\((p\text{-chlorophenyl})\)diazoacetate with \(p\)-Methylanisole.

The general procedure was used with methyl 2-\((p\text{-chlorophenyl})\)diazoacetate (30.3 mg, 0.144 mmol), Fe(TPP)Cl (2.00 mg, 1.97 mol%) and 5.0 mL of \(p\)-methylanisole. The mixture was stirred at 60 °C for 32 h. The benzylic C-H insertion product, 13b, and 7-carbomethoxy-2-methoxy-5-methyl-7-(\(p\)-chlorophenyl)norcaradiene, 12b, were partially separated using silica gel chromatography and hexane/ethyl acetate 30:1 as eluent. A combined yield of 32.8 mg, 0.107 mmol, 74% yield based on methyl 2-\((p\text{-chlorophenyl})\)diazoacetate was obtained. Pure 13b (8.30 mg, 19% yield) was obtained from a center-cut of a band and used for spectroscopic analysis. \(^1\text{H}\) NMR (400 MHz): 7.28 (d, 2H, \(J_H = 8.4\), aryl C-H), 7.23 (d, 2H, \(J_H = 8.4\), aryl C-H), 7.01 (d, 2H, \(J_H = 8.6\), aryl C-H), 6.78 (d, 2H, \(J_H = 8.6\), aryl C-H), 3.78 (dd, 1H, \(J_H = 8.6\), \(J_H = 7.2\), methine C-H), 3.78 (s, 3H, ArOCH₃), 3.62 (s, 3H, ROCH₃), 3.33 (dd, 1H, \(J_H = 13.6\), \(J_H = 8.4\), ArCH₂R), 2.94 (dd, 1H, \(J_H = 13.6\), \(J_H = 7.2\), ArCH₂R). \(^{13}\text{C}\) NMR (100.5 MHz): 173.6, 158.2, 137.1, 133.3, 130.6, 130.0, 129.4, 128.8, 113.8, 55.2, 53.3, 52.2, 39.0. MS\{EI\}: 305 [M+1]⁺.

Pure 12b (13.4 mg, 31% yield) was obtained from a center-cut of a band. \(^1\text{H}\) NMR (400 MHz): 7.17 (d, 2H, \(J_H = 7.8\), aryl C-H), 6.96 (m, 2H, \(J_H = 7.8\), aryl C-H), 5.46 (d, 1H, \(J_H = 6.6\), vinyl C-H), 4.75 (d, 1H, \(J_H = 6.6\), vinyl C-H), 3.64 (s, 3H, ArOCH₃), 3.59 (s, 3H, ROCH₃), 3.04 (d, 1H, \(J_H = 9.2\), cyclopropyl-H), 2.95 (d, 2H, \(J_H = 9.2\), cyclopropyl-H), 2.03 (s, 3H, RCH₃). \(^{13}\text{C}\) NMR (100.5 MHz): 176.4, 154.1, 133.1, 133.0, 131.3, 127.8, 124.2, 121.7, 95.9, 55.3, 53.0, 46.8, 36.6, 24.2, 23.1. Found (Calcd.) %C: 66.46 (67.00), %H: 5.53 (5.62).

**Thermal rearrangement of 12b.** Compound 12b (11.2 mg, 0.0368 mmol) was dissolved in 5 mL of \(p\)-methylanisole and the solution stirred at 100 °C for 3 h. All
solvent was removed under reduced pressure and the ring-opened product, 14b, was purified using silica gel chromatography and hexane/ethyl acetate 30:1 as eluent to afford 10.8 mg (96% yield). $^1$H NMR (400 MHz): 7.31 (d, 2H, $J_H = 8.8$, aryl C-H), 7.26 (d, 2H, $J_H = 8.8$, aryl C-H), 7.07 (d, 1H, $J_H = 8.2$, aryl C-H), 6.87 (s, 1H, aryl C-H), 6.79 (d, 1H, $J_H = 8.2$, aryl C-H), 5.27 (s, 1H, methine C-H), 3.80 (s, 3H, ArOCH$_3$), 3.74 (s, 3H, ROCH$_3$), 2.25 (s, 3H, ArCH$_3$). $^{13}$C NMR (100.5 MHz): 173.3, 154.7, 136.6, 133.1, 130.5, 130.0, 130.6, 129.6, 129.0, 128.7, 127.0, 55.7, 52.4, 50.2, 20.7. MS{EI}: 305 [M]+. Found (Calcd.) %C: 66.53 (67.00), %H: 5.56 (5.62).

**Reaction of Methyl 2-(p-tolyl)diazoacetate with p-Methylanisole.** The general procedure was used with methyl 2-(p-tolyl)diazoacetate (30.6 mg, 0.161 mmol), Fe(TPP)Cl (2.30 mg, 2.03 mol%) and 5.0 mL of p-methylanisole. The mixture was stirred at 80 °C for 32 h. The cyclopropanation product 7-carbomethoxy-2-methoxy-5-methyl-7-(p-tolyl)norcaradiene, 12c, and the benzylic C-H insertion product, 13c, were partially separated using silica gel chromatography and hexane/ethyl acetate 30:1 as eluent. A combined yield of 35.2 mg, 0.124 mmol, 77% yield based on methyl 2-(p-tolyl)diazoacetate were obtained. Pure 12c (12.4 mg, 27% yield) was obtained from a center-cut of a band. $^1$H NMR (400 MHz): 7.01 (d, 2H, $J_H = 7.6$, aryl C-H), 6.93 (d, 2H, $J_H = 7.6$, aryl C-H), 5.46 (d, 1H, $J_H = 7.0$, vinyl C-H), 4.76 (d, 1H, $J_H = 7.0$, vinyl C-H), 3.64 (s, 3H, ROCH$_3$), 3.60 (s, 3H, ROCH$_3$), 3.03 (d, 1H, $J_H = 9.4$, cyclopropyl-H), 2.94 (d, 2H, $J_H = 9.4$, cyclopropyl-H), 2.30 (s, 3H, ArCH$_3$), 2.04 (b, 3H, RCH$_3$). $^{13}$C NMR (100.5 MHz): 177.1, 154.3, 136.6, 131.5, 129.7, 128.3, 124.5, 121.4, 95.7, 55.3, 52.9, 40.3, 36.6, 24.5, 23.1, 21.4. MS{EI}: 284 [M]+. Pure benzylic C-H product, 13c (8.90 mg, 19% yield) was obtained from a center-cut of a band. $^1$H NMR (400 MHz): 7.22 (d,
2H, J_H = 8.0, aryl C-H), 7.13 (d, 2H, J_H = 8.0, aryl C-H), 7.05 (d, 2H, J_H = 8.0, aryl C-H), 6.79 (d, 2H, J_H = 8.0, aryl C-H), 3.79 (dd, 1H, J_H = 8.8, J_H = 6.6, methine C-H), 3.78 (s, 3H, ArOCH_3), 3.60 (s, 3H, ROCH_3), 3.35 (dd, 1H, J_H = 13.8, J_H = 8.8, ArCH_2R), 2.96 (dd, 1H, J_H = 13.8, J_H = 6.6, ArCH_2R), 2.33 (s, 3H, ArCH_3).

\[ ^{13} \text{C NMR (100.5 MHz):} \]

174.1, 158.1, 137.0, 131.3, 129.9, 129.4, 127.8, 113.7, 55.2, 53.5, 52.0, 39.0, 21.1.

MS{EI}: 284 [M]^+.

**Reaction of Methyl 2-(p-methoxyphenyl)diazoacetate with p-Methylanisole.**

The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (30.5 mg, 0.148 mmol), Fe(TPP)Cl (2.10 mg, 2.02 mol%) and 5.0 mL of p-methylanisole. The mixture was stirred at 80 °C for 32 h. The cyclopropanation product 7-carbomethoxy-2-methoxy-5-methyl-7-(p-methoxyphenyl)norcaradiene, \textbf{12d}, and the benzylic C-H insertion product, \textbf{13d}, were partially separated using silica gel chromatography and hexane/ethyl acetate 30:1 as eluent. A combined yield of 34.6 mg, 0.115 mmol, 78% yield based on methyl 2-(p-tolyl)diazoacetate were obtained. A sample of \textbf{12d} containing about 10% of \textbf{13d} was used for spectroscopic analysis. \(^1\text{H NMR (400 MHz):} \) 6.95 (d, 2H, J_H = 8.2, aryl C-H), 6.73 (d, 2H, J_H = 8.2, aryl C-H), 5.47 (d, 1H, J_H = 6.8, vinyl C-H), 4.76 (d, 1H, J_H = 6.8, vinyl C-H), 3.77 (s, 3H, ArOCH_3), 3.64 (s, 3H, ROCH_3), 3.59 (s, 3H, ROCH_3), 3.03 (d, 1H, J_H = 9.6, cyclopropyl-H), 2.93 (d, 1H, J_H = 9.6, cyclopropyl-H), 2.03 (b, 3H, R-CH_3). MS{EI}: 300 [M]^+. Pure \textbf{13d} (15.6 mg, 35%) was obtained from a center-cut of a band. The \(^1\text{H and} \(^{13} \text{C NMR data of} \textbf{13d} \) was found to match literature values. \(^{25} \text{H NMR (400 MHz):} \) 7.23 (d, 2H, J_H = 8.4, aryl C-H), 7.03 (d, 2H, J_H = 8.4, aryl C-H), 6.85 (d, 2H, J_H = 8.4, aryl C-H), 6.78 (d, 2H, J_H = 8.4, aryl C-H), 3.80 (s, 3H, ArOCH_3), 3.77 (s, 3H, ArOCH_3), 3.76 (dd, 1H, J_H = 8.8, J_H = 6.8, methine C-H), 3.60
(s, 3H, ROCH₃), 3.33 (dd, 1H, Jₗ = 14.0, Jᵢ = 8.8, ArCH₂R), 2.94 (dd, 1H, Jₗ = 14.0, Jᵢ = 6.8, ArCH₂R). ¹³C NMR (100.5 MHz): 174.3, 158.9, 158.1, 131.2, 130.8, 130.2, 130.0, 129.0, 114.0, 113.7, 55.3, 55.2, 53.0, 39.1. MS{EI}: 300 [M⁺].

**Reaction of Methyl 2-phenylidazoaacetate with p-Chlorotoluene.** The general procedure was used with methyl 2-phenylidazoaacetate (30.3 mg, 0.172 mmol), Fe(TPP)Cl (2.40 mg, 1.98 mol%) was dissolved in 5.0 mL of p-chlorotoluene. The mixture was stirred at 80 °C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The cyclopropanation product cyclopropanation product 7-carbomethoxy-2-chloro-5-methyl-7-phenylnorcaradiene 16a and the benzylic C-H insertion product 17a were partially separated using silica gel column and hexane/ethyl acetate 30:1 as eluent: A combined yield of 29.3 mg, 0.107 mmol, 62% yield based on methyl 2-phenylidazoaacetate were obtained. Pure 16a (4.20 mg, 9% yield) was obtained from a center-cut of a band. ¹H NMR (400 MHz): 7.23 (b, 3H, aryl C-H), 7.09 (b, 2H, aryl C-H), 5.74 (d, 1H, Jₗ = 6.6, vinyl C-H), 5.46 (d, 1H, Jₗ = 6.6, vinyl C-H), 3.67 (s, 3H, ROCH₃), 3.20 (d, 1H, Jₗ = 9.2, cyclopropyl-H), 3.00 (s, 1H, Jₗ = 9.2, cyclopropyl-H), 2.09 (b, 3H, R-CH₃). ¹³C NMR (100.5 MHz): 176.4, 132.4, 132.0, 131.7, 128.2, 127.7, 127.5, 123.1, 121.4, 53.2, 42.1, 41.2, 25.6, 23.6. MS{EI}: 275 [M⁺]. Benzylic C-H product 17a (15.7 mg, 33% yield) of containing trace impurities was obtained from a center-cut of a band. ¹H NMR (400 MHz): 7.21-7.35 (m, 5H, aryl C-H), 7.21 (d, 2H, Jₗ = 7.8, aryl C-H), 7.04 (d, 2H, Jₗ = 7.8, aryl C-H), 3.81 (dd, 1H, Jₗ = 8.6, Jᵢ = 6.6, methine C-H), 3.62 (s, 3H, ArOCH₃), 3.38 (dd, 1H, Jₗ = 13.6, Jᵢ = 8.6, ArCH₂R), 3.00 (dd, 1H, Jₗ = 13.6, Jᵢ = 6.6, ArCH₂R). ¹³C
NMR (100.5 MHz): 173.7, 138.3, 137.5, 132.2, 130.4, 128.8, 128.5, 128.0, 127.6, 53.5, 52.1, 39.1. MS{EI}: 275 [M+1].

**Reaction of Methyl 2-(p-chlorophenyl)diazoacetate with p-Chlorotoluene.**

The general procedure was used with methyl 2-(p-chlorophenyl)diazoacetate (30.4 mg, 0.144 mmol), Fe(TPP)Cl (2.00 mg, 1.97 mol%) and 5.0 mL of p-chlorotoluene. The mixture was stirred at 80 °C for 32 h. The products were partially separated by eluting through a silica gel column using a 30:1 hexane/ethyl acetate mixture. The 7-carbomethoxy-2-chloro-5-methyl-7-(p-chlorophenyl)norcaradiene, 16b, and the benzylic C-H insertion product, 17b, were partially separated using silica gel column and hexane/ethyl acetate 30:1 as eluent. A combined yield of 25.9 mg, 0.0841 mmol, 58% yield based on methyl 2-(p-chlorophenyl)diazoacetate was obtained. Pure 16b (3.20 mg, 7% yield) was obtained from a center-cut of a band. $^1$H NMR (400 MHz): 7.21 (d, 2H, $J_H = 8.6$, aryl C-H), 7.01 (d, 2H, $J_H = 8.6$, aryl C-H), 5.76 (d, 1H, $J_H = 6.8$, vinyl C-H), 5.48 (d, 1H, $J_H = 6.8$, vinyl C-H), 3.68 (s, 3H, ROCH$_3$), 3.18 (d, 1H, $J_H = 9.2$, cyclopropyl-H), 2.99 (d, 2H, $J_H = 9.2$, cyclopropyl-H), 2.08 (b, 3H, RCH$_3$). $^{13}$C NMR (100.5 MHz): 175.9, 133.3, 133.0, 132.2, 130.4, 128.1, 128.0, 123.3, 121.7, 53.3, 42.1, 41.1, 24.8, 23.6. MS{EI}: 309 [M+1]. A mixture 17b (14.2 mg, 32%) containing trace impurities was obtained. $^1$H NMR (300 MHz): 7.30 (d, 2H, $J_H = 8.4$, aryl C-H), 7.21 (d, 4H, $J_H = 8.4$, aryl C-H), 7.02 (d, 2H, $J_H = 8.4$, aryl C-H), 3.78 (dd, 1H, $J_H = 8.1$, $J_H = 7.2$, methine C-H), 3.62 (s, 3H, ROCH$_3$), 3.35 (dd, 1H, $J_H = 13.8$, $J_H = 8.1$, ArCH$_2$R), 2.97 (dd, 1H, $J_H = 13.8$, $J_H = 7.2$, ArCH$_2$R). $^{13}$C NMR (75.4 MHz): 173.5, 137.2, 133.7, 131.1, 130.5, 129.7, 129.5, 129.1, 128.8, 53.0, 52.4, 39.2. MS{EI}: 309 [M+1].
Reaction of Methyl 2-(p-tolyl)diazoacetate with p-Chlorotoluene. The general procedure was used with methyl 2-(p-tolyl)diazoacetate (30.6 mg, 0.161 mmol), Fe(TPP)Cl (2.30 mg, 2.03 mol%) and 5.0 mL of p-chlorotoluene. The mixture was stirred at 80 °C for 32 h. The cyclopropanation product 7-carbomethoxy-2-chloro-5-methyl-7-(p-methylphenyl)norcaradiene, 16c, and the benzylic C-H insertion product, 17c, were partially separated using silica gel chromatography and hexane/ethyl acetate 30:1 as eluent. A combined yield of 29.3 mg, 0.103 mmol, 64% yield based on methyl 2-(p-tolyl)diazoacetate) was obtained. It was impossible to get pure 16c, (1H and 13C NMR data were assigned by subtracting the spectrum of pure 17c from that of the mixture). 1H NMR (300 MHz) 7.13 (d, 2H, J_H = 8.1, aryl C-H), 6.95 (d, 2H, J_H = 8.1, aryl C-H), 5.75 (d, 1H, J_H = 6.6, vinyl C-H), 5.47 (d, 1H, J_H = 6.6, vinyl C-H), 3.60 (s, 3H, ROCH3), 3.18 (d, 1H, J_H = 9.0, cyclopropyl-H), 3.00 (d, 2H, J_H = 9.0, cyclopropyl-H), 2.31 (s, 3H, ArCH3), 2.09 (b, 3H, RCH3). 13C NMR (75.4 MHz): 176.8, 137.3, 132.6, 131.6, 129.0, 128.4, 123.3, 121.6, 53.4, 42.4, 41.5, 25.4, 23.7, 21.5. MS{EI}: 289 [M+1]+. Pure benzylic C-H product 17c (5.90 mg, 13%) was obtained from a center-cut of a band. 1H NMR (400 MHz): 7.22 (d, 2H, J_H = 8.4, aryl C-H), 7.19 (d, 2H, J_H = 8.4, aryl C-H), 7.13 (d, 2H, J_H = 8.0, aryl C-H), 7.06 (d, 2H, J_H = 8.0, aryl C-H), 3.78 (dd, 1H, J_H = 8.8, J_H = 6.8, methine C-H), 3.76 (s, 3H, ROCH3), 3.36 (dd, 1H, J_H = 14.0, J_H = 8.8, ArCH2R), 3.00 (dd, 1H, J_H = 14.0, J_H = 6.8, ArCH2R), 2.34 (s, 3H, ArCH3). 13C NMR (100.5 MHz): 173.8, 137.6, 137.3, 132.2, 130.4, 129.5, 128.5, 127.8, 53.1, 52.1, 39.1, 21.1. MS{EI}: 289 [M+1]+.

Reaction of Methyl 2-(p-methoxyphenyl)diazoacetate with p-Chlorotoluene. The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (30.4 mg,
0.148 mmol), Fe(TPP)Cl (2.10 mg, 2.02 mol%) and 5.0 mL of \textit{p}-chlorotoluene. The mixture was stirred at 80 °C for 32 h. A cyclopropanation product 7-carbomethoxy-2-chloro-5-methyl-7-(\textit{p}-methoxyphenyl)norcaradiene, 16\textit{d}, and a benzylic C-H insertion product, 17\textit{d}, were partially separated using silica gel chromatography and hexane/ethyl acetate 30:1 as eluent. A combined yield of 24.7 mg, 0.0813 mmol, 55% yield based on methyl 2-(\textit{p}-methoxyphenyl) diazoacetate was obtained. It was not possible to isolate pure 16\textit{d}, (\textit{H} and \textit{C} NMR data were assigned by subtracting the spectrum of pure 17\textit{d} from that of the mixture). \textit{H} NMR (400 MHz): 7.00 (d, 2H, \textit{J}\textsubscript{H} = 8.4, aryl C-H), 6.78 (d, 2H, \textit{J}\textsubscript{H} = 8.4, aryl C-H), 5.76 (d, 1H, \textit{J}\textsubscript{H} = 6.8, vinyl-H), 5.47 (d, 1H, \textit{J}\textsubscript{H} = 6.8, vinyl-H), 3.77 (s, 3H, ArOCH\textsubscript{3}), 3.68 (s, 3H, ROCH\textsubscript{3}), 3.17 (d, 1H, \textit{J}\textsubscript{H} = 9.6, cyclopropyl-H), 2.97 (d, 1H, \textit{J}\textsubscript{H} = 9.6, cyclopropyl-H), 2.08 (s, 3H, RCH\textsubscript{3}). \textit{C} NMR (100.5 MHz): 176.7, 158.7, 132.7, 128.2, 123.9, 123.2, 121.5, 113.2, 55.1, 53.2, 42.2, 41.3, 24.8, 23.6. Pure benzylic C-H product 17\textit{d} (6.30 mg, 14%) was obtained from a center-cut of a band. \textit{H} NMR (300 MHz): 7.20 (m, 4H, aryl C-H), 7.03 (d, 2H, \textit{J}\textsubscript{H} = 8.7, aryl C-H), 6.85 (d, 2H, \textit{J}\textsubscript{H} = 8.7, aryl C-H), 3.80 (s, 3H, ArOCH\textsubscript{3}), 3.73 (dd, 1H, \textit{J}\textsubscript{H} = 8.6, \textit{J}\textsubscript{H} = 6.9, methine C-H), 3.61 (s, 3H, ROCH\textsubscript{3}), 3.35 (dd, 1H, \textit{J}\textsubscript{H} = 13.6, \textit{J}\textsubscript{H} = 8.6, ArCH\textsubscript{2}R), 2.97 (dd, 1H, \textit{J}\textsubscript{H} = 13.6, \textit{J}\textsubscript{H} = 6.9, ArCH\textsubscript{2}R). \textit{C} NMR (75.4 MHz) 173.9, 159.0, 137.6, 132.2, 130.4, 130.3, 129.0, 128.5, 114.1, 55.3, 52.6, 52.1, 39.2. MS\{EI\}: 305 [M+1]\. Elemental analysis: Found (calcd.) %C: 66.56 (67.00), %H: 5.83 (5.62).

**Reaction of 7-Carbomethoxy-7-(\textit{p}-chlorophenyl)norcaradiene/7-Carbomethoxy-7-(\textit{p}-chlorophenyl)cycloheptatriene, 2b/2'\textit{b}, with benzyne.** Valence isomers 2\textit{b}/2'\textit{b} (20.6 mg, 0.0792 mmol) were placed in a 4 dram vial that was equipped with a stir bar and dissolved in 10.0 mL of acetonitrile. After adding 2-
(trimethylsilyl)phenyl triflate (28.1 mg, 0.0951 mmol, 1.2 equiv), the mixture stirred for 5 min. CsF (24.1 mg, 0.158 mmol, 2 equiv) was added, the vial sealed and the mixture was stirred for 8 h. The product was isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. Pure benzhomobarrelene, 18b, (25.8 mg, 0.0768 mmol, 97% yield) was obtained as a white solid. $^1$H NMR (400 MHz): 7.26 (m, 4H, aryl C-H), 7.05 (m, 4H, aryl C-H), 5.54 (m, 2H, vinyl C-H), 4.24 (m, 2H, methine-H), 3.53 (s, 3H, ROCH$_3$), 2.33 (t, 2H, J$_H$ = 2.0, cyclopropyl-H). $^{13}$C NMR (100.5 MHz): 173.0, 147.2, 136.5, 134.6, 132.3, 128.4 125.0, 123.4, 57.0, 52.9, 47.4, 41.5, 36.1. MS{EI}: 336 [M]$^+$. Elemental analysis: Found (calcd.) %C: 83.36 (83.51), %H: 6.39 (6.37).

**Reaction of 7-Carbomethoxy7-(p-tolyl)norcaradiene/7-Carbomethoxy7-(p-tolyl)cycloheptatriene, 2c/2'c, with Benzyne.** Valence isomers 2c/2'c (10.3 mg, 0.0429 mmol) were placed in a 4 dram vial that was equipped with a stir bar and dissolved in 10 mL of acetonitrile. After adding 2-(trimethylsilyl)phenyl triflate (15.2 mg, 0.0515 mmol, 1.2 equiv), the mixture stirred for 5 minutes. CsF (13.1 mg, 0.0862 mmol, 2 equiv) was added, the vial sealed and the mixture was stirred for 8 hours. The product was isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture to produce pure benzhomobarrelene, 18c, (12.7 mg, 0.0402 mmol, 94% yield) as a white solid. $^1$H NMR (400 MHz): 7.22 (dd, 2H, J$_H$ = 5.2, J$_H$ = 3.2, aryl C-H), 7.09 (d, 2H, J$_H$ = 7.8, aryl C-H), 7.02 (dd, 2H, J$_H$ = 5.2, J$_H$ = 3.2, aryl C-H), 6.99 (d, 2H, J$_H$ = 7.8, aryl C-H), 5.51 (dd, 2H, J$_H$ = 4.4, J$_H$ = 3.6, vinyl C-H), 4.24 (m, 2H, methine-H), 3.52 (s, 3H, ROCH$_3$), 2.39 (s, 3H, ArCH$_3$), 2.33 (t, 2H, J$_H$ = 2.2, cyclopropyl-H). $^{13}$C NMR (100.5 MHz): 173.5, 147.4, 136.0, 133.9, 130.7, 128.8 124.6, 123.1, 52.6, 41.3, 35.7, 21.3.
MS\{EI\}: 316 [M]⁺. Elemental analysis: Found (calcd.) %C: 74.62 (74.89), %H: 5.15 (5.09).

**Reaction of 7-Carbomethoxy-2-chloro-7-(p-chlorophenyl)norcaradiene/7-Carbomethoxy-2-chloro-7-(p-chlorophenyl)cycloheptatriene, 3b/3'b, with Benzyne.**

Valence isomers 3b/3'b (15.4 mg, 0.0524 mmol) was placed in a 4 dram vial that was equipped with a stir bar and dissolved in 10 mL of acetonitrile. After adding 2-(trimethylsilyl)phenyl triflate (18.6 mg, 0.0629 mmol, 1.2 equiv), the mixture stirred for 5 minutes. CsF (15.9 mg, 0.105 mmol, 2 equiv) was added, the vial sealed, and the mixture was stirred for 8 hours. The product was isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. Pure product, 19b, (18.6 mg, 0.0503 mmol, 96% yield) was obtained as a colorless oil. ¹H NMR (300 MHz): 7.22-7.38 (m, 4H, aryl C-H), 7.00-7.21 (m, 4H, aryl C-H), 5.57 (m, 2H, vinyl C-H), 4.23 (m, 1H, methine-H), 3.56 (s, 3H, ROCH₃), 2.67 (dd, 1H, J_H = 7.2, J_H = 0.6, cyclopropyl-H), 2.52 (dd, 2H, J_H = 7.2, J_H = 2.7, cyclopropyl-H). ¹³C NMR (75.4 MHz): 172.0, 146.1, 145.1, 138.7, 135.1, 132.7, 131.8, 128.7, 128.5, 125.7, 122.8, 121.1, 69.6, 52.9, 47.8, 42.8, 40.6, 37.4. MS\{EI\}: 371 [M+1]⁺. Elemental analysis: Found (calcd.) %C: 67.66 (67.94), %H: 4.56 (4.34).

**Reaction of 7-Carbomethoxy-3-chloro-7-(p-chlorophenyl)norcaradiene/7-Carbomethoxy-3-chloro-7-(p-chlorophenyl)cycloheptatriene, 4b/4'b, with Benzyne.**

Valence isomers 4b/4'b (17.9 mg, 0.0609 mmol) were placed in a 4 dram vial that was equipped with a stir bar and dissolved in 10 mL of acetonitrile. After adding 2-(trimethylsilyl)phenyl triflate (21.6 mg, 0.0731 mmol, 1.2 equiv), the mixture stirred for 5 minutes. CsF (18.4 mg, 0.121 mmol, 2 equiv) was added, the vial sealed, and the
mixture was stirred for 8 hours. The product was isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. Pure product, 20b, (21.8 mg, 0.0589 mmol, 97% yield) was obtained as a colorless oil. $^1$H NMR (400 MHz): 7.20-7.34 (m, 4H, aryl C-H), 7.02-7.11 (m, 4H, aryl C-H), 5.42 (dd, 1H, J_H = 7.2, J_H = 2.6, vinyl C-H), 4.30 (dt, 1H, J_H = 6.8, J_H = 2.0, methine-H), 4.15 (q, 1H, J_H = 1.6, methine-H), 3.53 (s, 3H, ROCH$_3$), 2.38 (t, 2H, J_H = 2.4, cyclopropyl-H). $^{13}$C NMR (100.5 MHz): 172.5, 145.4, 135.9, 134.3, 132.3, 132.1, 131.6, 131.3 128.7, 127.9, 125.1, 123.5, 123.2, 52.8, 49.2 47.6, 42.1, 35.7, 35.1. MS{EI}: 370 [M$^+$].

**Reaction of 7-Carboxymethoxy-2-methyl-7-phenynorcaradiene/7-Carboxymethoxy-2-methyl-7-phenylcycloheptatriene, 6a/6'a, with Benzyne.** Valence isomers 6a/6'a (7.40 mg, 0.0308 mmol) were placed in a 4 dram vial that was equipped with a stir bar and dissolved in 10 mL of acetonitrile. After adding 2-(trimethylsilyl)phenyl triflate (11.0 mg, 0.0370 mmol, 1.2 equiv), the mixture was stirred for 5 minutes. CsF (9.40 mg, 0.0618 mmol, 2 equiv) was added, the vial was sealed, and the reaction stirred for 8 h. The product was isolated by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. Pure product, 21a, (9.30 mg, 0.0294 mmol, 96% yield based on diene) was obtained as a colorless oil. $^1$H NMR (400 MHz): 7.22-7.34 (m, 5H, aryl C-H), 7.00-7.19 (m, 4H, aryl C-H), 5.51 (t, 1H, J_H = 6.8, vinyl C-H), 5.26 (d, 1H, J_H = 7.2, vinyl C-H), 4.22 (m, 1H, methine-H), 3.53 (s, 3H, ROCH$_3$), 2.43 (dd, 1H, J_H = 9.2, J_H = 4.4, cyclopropyl-H), 2.11 (d, 2H, J_H = 9.2, cyclopropyl-H), 1.92 (s, 3H, ROCH$_3$). $^{13}$C NMR (100.5 MHz): 173.4, 138.5, 137.7, 134.0, 131.1, 130.9, 128.1, 128.0, 126.3, 124.3, 122.9, 120.1, 52.6, 48.1, 44.1, 41.5, 37.5, 33.9, 20.0. MS{EI}: 316 [M$^+$].
Acidification of 7-Carbomethoxy-7-(p-tolyl)norcaradiene/7-Carbomethoxy-7-(p-tolyl)cycloheptatriene, 2c/2\textsuperscript{c}. Valence isomers 2c/2\textsuperscript{c} (14.2 mg, 0.0592 mmol) were dissolved in 3 mL of acetonitrile. Three drops of conc. sulfuric acid were to the solution and the mixture was warmed to 60 °C while stirring. After allowing the mixture to cool, 5 mL of water were added and the product was extracted with methylene chloride (3 x 5 mL). Removal of CH\textsubscript{2}Cl\textsubscript{2} under reduced pressure afforded methyl 2-phenyl-2-(p-tolyl)benzeneacetate, 22c. The \textsuperscript{1}H and \textsuperscript{13}C NMR data was found to match literature values.\textsuperscript{26} (13.6 mg, 0.0567 mmol, 96 % yield). \textsuperscript{1}H NMR (400 MHz): 7.25-7.35 (m, 5H, aryl C-H), 7.21 (d, 2H, J\textsubscript{H} = 8.0, aryl C-H), 7.14 (d, 2H, J\textsubscript{H} = 8.0, aryl C-H), 5.01 (s, 1H, methine C-H), 3.75 (s, 3H, ROCH\textsubscript{3}), 2.33 (s, 3H, Ar-CH\textsubscript{3}). \textsuperscript{13}C NMR (100.5 MHz): 173.2, 138.9, 137.0, 135.7, 129.4, 128.63, 128.57, 128.5, 127.3, 56.7, 52.4, 21.1. MS{EI}: 241 [M+1]\textsuperscript{+}.

Acidification of 7-Carbomethoxy-2,5-dimethyl-7-(p-chlorophenyl)norcaradiene, 10b. 7-Carbomethoxy-2,5-dimethyl-7-(p-chlorophenyl)norcaradiene 10b (15.8 mg, 0.0590 mmol) was dissolved in 3 mL of acetonitrile. Three drops of conc. sulfuric acid were to the solution and the mixture warmed to 60 °C while stirring. After cooling to ambient temperature, 5 mL of water were added and the product was extracted with methylene chloride (3 x 5 mL). Removal of CH\textsubscript{2}Cl\textsubscript{2} under reduced pressure afforded methyl 2-(2,5-dimethylphenyl)-2-(p-chlorophenyl)benzeneacetate, 23b, (15.2 mg, 0.0567 mmol, 96% yield). \textsuperscript{1}H NMR (400 MHz): 7.29 (d, 2H, J\textsubscript{H} = 8.8, aryl C-H), 7.17 (d, 2H, J\textsubscript{H} = 8.4, aryl C-H), 7.08 (d, 1H, J\textsubscript{H} = 8.4, aryl C-H), 7.02 (d, 2H, J\textsubscript{H} = 8.8, aryl C-H), 5.16 (s, 1H, methine C-H), 3.76 (s, 3H, ROCH\textsubscript{3}), 2.31 (s, 3H, Ar-CH\textsubscript{3}), 2.22 (s, 3H, Ar-CH\textsubscript{3}). \textsuperscript{13}C NMR (100.5 MHz): 173.1,
136.5, 136.2, 136.0, 133.2, 133.1, 130.8, 129.4, 128.7, 128.5, 128.4, 126.2, 53.0, 52.5, 21.2, 19.3. MS{EI}: 269 [M+1]. Elemental analysis: Found (calcd.) %C: 70.34 (70.71), %H: 5.76 (5.93).

Acknowledgement. The authors are grateful for funding provided by the Petroleum Research Fund administered by the American Chemical Society and the National Science Foundation.

References


(6) Mbuvi, H. M.; Woo, L. K., manuscript in preparation for Organometallics.


CHAPTER 5: O-H INSERTION AND TANDEM N-H INSERTION/CYCLIZATION REACTIONS USING AN IRON PORPHYRIN AS CATALYST WITH DIAZOO COMPOUNDS AS CARBENE SOURCES.

Abstract. Iron(III) tetraphenylporphyrin chloride, Fe(TPP)Cl, is an efficient catalyst for O-H insertion reactions with both aliphatic and aromatic alcohols giving yields above 80% when methyl 2-phenyldiazoacetates were used as carbene sources. Unlike analogous N-H insertion reactions, which are very fast at room temperatures, O-H insertions required refluxing in methylene chloride for about 8 h using 1% catalyst. Fe(TPP)Cl was also found to be very effective for tandem N-H insertion/cyclization reactions when EDA is treated with ethylenediamine and ethanolamine to give 2-piperazinone and 2-morpholinone, respectively. This reaction provides a new simple route for synthesizing these classes of heterocyclic products.

Introduction

The synthesis of α-hydroxy and α-alkoxy carboxylic acid derivatives is of considerable importance since these compounds are useful synthetic intermediates for the construction of natural products and other biologically active molecules. The ready availability, relative kinetic stability, and facile decomposition (under thermal, photochemical, and transition-metal-catalyzed conditions) of diazocarbonyl compounds make them useful intermediates for the synthesis of these types of derivatives. Transition-metal-catalyzed procedures are often the method of choice, taking place under relatively mild conditions. The original catalysts were based on copper metal or simple copper(II) salts. Rhodium(II) carboxylates were introduced later by Teyssie and co-workers in the
early 1970’s. In recent years, new transition-metal catalysts have been developed that are now widely used since they mediate a broad range of carbenoid transformations such as cyclopropanation, C-H insertion, addition to aromatic rings, and ylide formation. Consequently, synthetic uses of diazocarbonyl compounds have increased dramatically.

Our own interest in iron porphyrin reactivity centers on O-H and N-H insertions, which despite their potential in synthesis, have not been widely studied. Earlier work done by our group established that iron tetraphenylporphyrin chloride, Fe(TPP)Cl, is one the most effective catalysts for insertion of carbenes from diazo esters into N-H bonds. The present study attempted to establish if the effectiveness of iron porphyrins could be extended to O-H insertion reactions and also determine if the highly efficient N-H insertion process could extended with subsequent cyclization reactions to give products that contain piperizanone or morpholinone moeties. Piperazinone polypeptides are useful as analgesics and psychotherapeutic agents. Novel syntheses (Scheme 1) could lead to important 2-piperazinone intermediates, which may facilitate the production and use of peptide nucleic acids (PNAs). This has the potential for rapid identification of PNA oligomers for use in therapeutics, diagnostics and/or gene characterization tools. Derivatives of 2-piperazinones are known to have therapeutic properties and have been patented. These generally act by controlling or inhibiting cell-adhesion.

Scheme 1
Results and Discussion.

When ethyldiazoacetate (EDA) was used as a carbene source for O-H insertion reactions using Fe(TPP)Cl catalyst, only maleates and fumarates were formed. This is in contrast to analogous N-H insertions reactions where EDA was shown to be an excellent carbene source. However, substituted methyl 2-phenyl diazoacetates (MPDAs) were found to be efficient carbene sources for O-H insertion reactions with alcohols when Fe(TPP)Cl was used as a catalyst (eq. 1). Treating an alcohol with one equiv of substituted methyl 2-phenyl diazoacetate in refluxing methylene chloride using 1% catalyst efficiently produced O-H insertion products. Yields as high as 88% were obtained (Table 1). No aromatic C-H insertion products were detected by GC when phenol was used as substrate. These products were characterized by mass spectrometry

\[ \begin{align*}
\text{R-OH} + \overset{\text{1% Fe(TPP)Cl}}{\overset{\text{CH}_2\text{Cl}_2, \text{reflux}}{\overset{\text{R-}}{\text{Me-X-CO}_2\text{Me}}}} \\
\text{X} = \begin{array}{l}
\text{H} = a \\
\text{Cl} = b \\
\text{Me} = c \\
\text{OMe} = d \\
\end{array} \\
\text{Phenyl} = 1 \\
\text{cyclohexyl} = 2 \\
\text{ethyl} = 3 \\
\text{propyl} = 4
\end{align*} \]

and \(^1\)H and \(^{13}\)C NMR spectroscopy. For example, methyl 2-phenoxy-4-methyl-phenylacetate, \(1c\), produced from phenol and methyl 2-(p-tolyl)diazoacetate, gave a characteristic methine singlet \(^1\)H NMR signal at 5.63 ppm while the methine carbon exhibited a \(^{13}\)C NMR signal at 78.5 ppm. Both the \(^1\)H and \(^{13}\)C NMR spectra were found to match literature values. This reaction was extended to aliphatic alcohols. Treatment of
ethanol with \( p \)-MeO-MPDA in refluxing methylene chloride and 1% Fe(TPP)Cl produced methyl 2-ethoxy-4-tolylacetate, 3c. This product was purified by elution through a silica gel column using 20:1 hexanes/ethyl acetate as the eluent and yields above 80% were obtained. The product exhibits a \(^1\)H NMR signal for the methine proton at 4.84 ppm while the two \( \alpha \)-methylene hydrogens give diastereotopic multiplets at 3.53 ppm. No C-H insertion products were detected in this reaction.

**Table 1:** Summary of catalytic reactions of \( para \)-substituted methyl 2-phenyldiazoacetate compounds with various alcohols.\(^a\)

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>MPDA ( p-X )</th>
<th>% Yield(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>phenol</td>
<td>CH(_3)-</td>
<td>81</td>
</tr>
<tr>
<td>phenol</td>
<td>CH(_3)O-</td>
<td>83</td>
</tr>
<tr>
<td>cyclohexanol</td>
<td>CH(_3)-</td>
<td>86</td>
</tr>
<tr>
<td>cyclohexanol</td>
<td>CH(_3)O-</td>
<td>88</td>
</tr>
<tr>
<td>ethanol</td>
<td>CH(_3)O-</td>
<td>84</td>
</tr>
<tr>
<td>( n )-propanol</td>
<td>CH(_3)-</td>
<td>81</td>
</tr>
<tr>
<td>2-propanol</td>
<td>CH(_3)O-</td>
<td>56(^c)</td>
</tr>
</tbody>
</table>

\(^a\)Conditions: CH\(_2\)Cl\(_2\) used as solvent, 40 °C for 8 hours, alcohol:diazo reagent ratio of 2:1, 1% Fe(TPP)Cl catalyst. \(^b\) Isolated yield. \(^c\) Methine C-H insertion product detected by NMR.

Isopropanol was found to react with p-MeO-MPDA to give a mixture of O-H product 5d and C-H insertion product 6d in a ratio of 6:1 respectively (eq 2). The O-H insertion product 5d exhibited characteristic NMR signals for the two types of methine
protons. The isopropyl methine hydrogen appeared at 3.67 (1H, m) and a singlet at 4.95 ppm was assigned to the methine hydrogen alpha to the ester group. The diastereotopic nature of the isopropyl methyl groups is manifested by distinct doublets at 1.24 and 1.19 ppm, each integrating as three protons. Although it was not possible to isolate a pure sample of the C-H insertion product, the presence of doublets for the terminal CH₃ proton signal at 0.96 ppm (3H) and multiplets at 3.65 (2H) and 4.03 ppm (1H) for the methylene and methine protons, respectively, suggested that an insertion into the terminal C-H group occurred to give 6d. These results illustrate that Fe(TPP)Cl is an effective catalyst for O-H insertion reactions. This catalyst is better than more expensive rhodium catalysts which typically require similar conditions to effect O-H insertions, but at lower yields.⁹

Ethylenediamine reacted rapidly with ethyl diazoacetate in the presence of 1% catalyst at ambient temperature to give 2-piperazinone in yields above 80% (eq 3). This was confirmed by the absence of the ¹H NMR methine signal for EDA that appears at 4.72 ppm. The absence of ¹H NMR signals at 4.23 (q) and 1.25 (t) indicated that the ethyl group of the ester had been lost. The highly polar 2-piperazinone was found to be soluble in water and insoluble in organic solvents and could not therefore be purified by silica gel chromatography. However, it was extracted from methylene chloride with a 1:1 mixture
of methanol and water to give a 90% pure product. This product exhibits a proton NMR singlet at 3.50 ppm for the two hydrogens at C3, a multiplet at 3.33 ppm for two protons at C6 and a triplet at 3.01 for the two protons at C5. The amide N-H proton was detected as a broad peak at 6.76 ppm while the amine proton was not detected. These NMR data compare well with spectra of other 2-piperazinone nucleoside analogs substituted at the amine nitrogen.\(^{10}\)

When 2 equiv of EDA were added dropwise to ethylenediamine and 1 mol% Fe(TPP)Cl in CH\(_2\)Cl\(_2\), about 40% of a new product was observed that had a molecular ion peak at 186 \(m/z\) along with formation of about 60% yield of maleates and fumarates. The product mass and NMR data are consistent with a subsequent carbene insertion with 2-piperazinone to form product 7 (eq 4). Although this product could not be isolated cleanly for full characterization, its formation is consistent with our earlier study that clearly demonstrated that insertion at the secondary amine nitrogen is strongly favored over insertion at the amide nitrogen.\(^{4}\)

Ethanolamine reacted analogously with one equiv of EDA to give a single product with a mass of 101 \(m/z\) as detected by GC/MS. This product also results from an N-H insertion followed by a cyclization process to give 2-morpholinone and ethanol (eq 5).
The product was extracted from methylene chloride using a 1:1 methanol/water mixture. Characteristic of these heterocycles is the singlet NMR signal for the methylene protons at C3. In 2-morpholinone, this signal appears at 3.14 ppm. No product derived from O-H insertion was observed. This is consistent with our earlier observations that have clearly shown that iron porphyrins are very efficient catalysts for N-H insertion reaction but less competent for O-H insertions. Slow addition of 2 equiv of EDA to ethanolamine yielded about 30% of a new product with a mass of 187 m/z suggesting that an analogous product similar to 7 was formed arising from carbene insertion into the N-H bond of 2-morpholinone.
The reaction of 2-aminophenol with one equiv of EDA afforded a mixture of products. The major species was a N-H insertion product 8 (eq 6) which exhibited a characteristic glycyl methylene proton singlet at 3.91 ppm.\(^4\) GC-MS analysis revealed the formation of about 10% of another minor product. Although this product could not be isolated, its molecular ion peak of 150 m/z suggested it to be cyclization product 9 (eq. 6). When a second equivalent of EDA was added slowly, three different products were detected by GC-MS along with maleates and fumarates. However, when the contents were placed on a column for separation only one product, 10 was obtained in 42% yield. The morpholinone fragment of 10 gave a characteristic methylene singlet at 4.0 ppm for the two protons at C3. In addition, the ethyl protons of the ester group appeared at 4.23 (q, 2H) and 1.29 (t, 3H) ppm.

Treatment of 1,2-phenylenediamine with EDA in methylene chloride and 1% catalyst afforded one major product in 74% yield as detected by GC-MS. Purification by silica gel chromatography using an ethyl acetate/hexanes (10:1) eluent yielded product 11 (eq 7). The \(^1H\) NMR spectrum of the product showed a new singlet at 3.91 ppm for the N-acetate methylene hydrogens. No cyclization product was detected. However,
acidification of the solution of 11 in THF with HCl yielded about 30% of a product that had a molecular ion peak at m/z of 148. This suggested formation of cyclized product by loss of ethanol from product 11. Treatment of 1,2-phenylenediamine with 2 equiv of EDA yielded product 12 in which both the amine groups had undergone an N-H insertion. This double insertion product gives a four-proton NMR singlet at 5.00 ppm for the new methylene hydrogens of the two N-acetate groups.

In an attempt to synthesize substituted piperazinones, ethylenediamine was treated with methyl 2-(p-methoxyphenyl)acetate in refluxing THF in the presence of 1% Fe(TPP)Cl. A GC-MS analysis detected two products at m/z values of 206 and 204 in a ratio of 3:1. This suggested that the N-H insertion/cyclization product 13 and its dehydrogenated form 14 were formed (eq 8). However, eluting of the mixture through a alumina column enabled the isolation of only 5,6-dihydro-3-phenyl pyrazinone (14) in a yield of 54%. This suggested that further dehydrogenation occurred on the column. Treatment of ethylenediamine with p-Cl-MPDA in refluxing THF yielded products with masses of 208 and 211 m/z in a ratio of 1:10 respectively. A similar reaction of methyl 2-(p-methoxyphenyl)acetate with ethanoamine yielded a products with masses of 207 and 210 m/z as detected by a GC-MS spectrometry. Although these products were not
isolated, their masses suggested that they were substituted morpholinones and dehydromorpholinones similar to 13 and 14.

$$\text{H}_2\text{N}$$ $$\text{NH}_2^+$$ $$\text{X}$$ $$\text{N}$$ $$\text{O}$$ $$\text{Me}$$ $1\%$ $\text{Fe(TPP)Cl}_\text{CH}_2\text{Cl}_2, \text{reflux}$ $\text{NH}_2$ $\text{O}$ $\text{X}$

(8)

a, $X=\text{OMe}$  
b, $X=\text{Cl}$  
(m/e) 206  
(m/e) 208  
(m/e) 204  
(m/e) 211

**Conclusion**

Fe(TPP)Cl is an effective catalyst for O-H insertion reactions with alcohols when substituted MPDAs are used as carbene sources. Aromatic and normal aliphatic alcohols give O-H insertion as the only product. Treatment of isopropanol with $\rho$-Cl-MPDA and Fe(TPP)Cl yielded O-H insertion as the major product and a minor C-H insertion at the terminal position. This catalyst was also found to be very efficient in the syntheses of 2-piperazinone and 2-morpholinone through a tandem N-H insertion/cyclization process when EDA is the carbene source. Substituted MPDAs can be used to synthesize substituted piperazinones and morpholinones. The tandem N-H insertion/cyclization process provides an easy one-pot procedure for the syntheses of novel piperazinones, morpholinones and their substituted analogues.
Experimental Section

Fe(TPP)Cl was obtained from Aldrich and used without further purification. Substituted methyl 2-phenyldiazoacetates were prepared as outlined in the literature. Proton NMR and $^{13}$C NMR spectra were run in CDCl$_3$ and recorded on a Varian VXR 300 or a Bruker DRX400 spectrometer. $^1$H NMR peak positions were referenced against residual proton resonances of CDCl$_3$ ($\delta$, 7.27). Gas chromatographic analyses were performed on a HP 5890 series II or a Finnigan GC-MS instrument. All reactions were performed under an atmosphere of nitrogen.

**General Procedure for O-H Insertion Reactions.** About 30.0 mg of the alcohol were accurately weighed and placed in a 50-mL round bottom flask containing a stir bar and dissolved in 5 mL of methylene chloride. A condenser, fitted with a rubber septum, was then attached to the round bottom flask and the contents thoroughly flushed with nitrogen. The catalyst (1 mol%) and one equiv diazo reagent were then added and the contents bubbled with dry nitrogen for 5 min. The mixture was then heated at reflux while stirring until the diazo reagent was consumed. The products were separated or purified by eluting on a silica gel column (4 cm diameter, 30 cm height, hexane/ethyl acetate; 20:1).

**Methyl 2-(p-tolyl)diazoacetate Insertion with Phenol.** The general procedure was used with methyl 2-(p-tolyl)diazoacetate (60.8 mg, 0.320 mmol), (TPP)FeCl (2.20 mg, 1.0 mol%), phenol (30.0 mg, 0.320 mmol) and 5.0 mL of methylene chloride. The mixture was refluxed at 40 °C for 8 h. The products were purified by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl 2-phenoxy-(4-methylphenyl)acetate, 1c, (66.2 mg, 0.262 mmol, 81% yield) was obtained.
The proton NMR and $^{13}$C NMR spectra matched literature values.\textsuperscript{7} $^1$H NMR (400 MHz) δ: 7.47 (d, 2H, $J_\text{H} = 7.9$, aryl-H), 7.29 (d, 2H, $J_\text{H} = 7.9$, aryl-H), 7.22 (d, 2H, $J_\text{H} = 7.9$, aryl-H), 6.97 (m, 3H, aryl-H), 5.63 (s, 1H, methine C-H), 3.75 (s, 3H, OCH$_3$), 2.37 (s, 3H, Ar-CH$_3$). $^{13}$C NMR (100.5 MHz) δ: 170.6, 157.4, 139.0, 132.5, 129.6, 129.5, 127.1, 121.8, 115.5, 78.5, 52.6, 21.3. MS{EI}: 258 [M$^+$.  

**Methyl 2-(p-methoxyphenyl)diazoacetate Insertion with Phenol.** The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (65.9 mg, 0.320 mmol), (TPP)FeCl (2.20 mg, 1 mol%), phenol (30.0 mg, 0.320 mmol) and 5.0 mL of methylene chloride. The mixture was refluxed for 8 h. The products were purified by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl 2-phenoxy-(4-methoxyphenyl)acetate, \textbf{1d}, (72.2 mg, 0.270 mmol, 83% yield) was obtained. The proton NMR and $^{13}$C NMR spectra matched literature values.\textsuperscript{5} $^1$H NMR (400 MHz) δ: 7.50 (d, 2H, $J_\text{H} = 8.4$, aryl-H), 7.36 (d, 2H, $J_\text{H} = 8.4$, aryl-H), 6.95 (m, 5H, aryl-H), 5.61 (s, 1H, methine C-H), 3.82 (s, 3H, ArOCH$_3$), 3.75 (s, 3H, OCH$_3$). $^{13}$C NMR (100.5 MHz) δ: 170.7, 160.2, 157.3, 129.6, 128.6, 127.5, 121.8, 115.5, 114.3, 78.2, 55.4, 52.6. MS{EI}: 272 [M$^+$.  

**Methyl 2-(p-tolyl)diazoacetate Insertion with Cyclohexanol.** The general procedure was used with methyl 2-(p-tolyl)diazoacetate (60.8 mg, 0.320 mmol), (TPP)FeCl (2.20 mg, 1 mol%), cyclohexanol (48.0 mg, 0.480 mmol) and 5.0 mL of methylene chloride. The mixture was refluxed at 40 °C for 8 h. The products were purified by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl 2-cyclohexanoxy-(4-methylphenyl)acetate, \textbf{2c}, (72.2 mg, 0.273 mmol, 86% yield) was obtained. $^1$H NMR (400 MHz) δ: 7.36 (d, 2H, $J_\text{H} = 8.0$, aryl-H),
7.17 (d, 2H, $J_H = 8.0$, aryl-H), 5.03 (s, 1H, methine C-H), 3.71 (s, 3H, OCH$_3$), 3.34 (m, 1H, cyclo-methine C-H), 2.35 (s, 3H, ArCH$_3$), 1.99 (m, 1H), 1.88 (m, 1H), 1.74 (m, 2H), 1.53 (m, 1H) 1.41 (m, 2H), 1.23 (m, 3H). $^{13}$C NMR (100.5 MHz) $\delta$: 172.3, 138.3, 134.4, 129.3, 127.1, 78.0, 52.2, 32.3, 32.2, 25.7, 24.2, 21.2. MS (EI): 262 [M$^+$].

**Methyl 2-(p-methoxyphenyl)diazoacetate Insertion with Cyclohexanol.** The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (65.9 mg, 0.320 mmol), (TPP)FeCl$_2$ (2.20 mg, 1 mol%), cyclohexanol (48.0 mg, 0.480 mmol) and 5.0 mL of methylene chloride. The mixture was refluxed at 40 °C for 8 h. The products were purified by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl 2-cyclohexanoxy-(4-methoxyphenyl)acetate, 2d, (78.3 mg, 0.280 mmol, 88% yield) was obtained. $^1$H NMR (400 MHz) $\delta$: 7.38 (d, 2H, $J_H = 8.4$, aryl-H), 6.89 (d, 2H, $J_H = 8.4$, aryl-H), 5.00 (s, 1H, methine C-H), 3.81 (s, 3H, ArOCH$_3$), 3.71 (s, 3H, OCH$_3$), 3.32 (m, 1H, cyclo-methine C-H), 1.99 (m, 1H), 1.87 (m, 1H), 1.73 (m, 2H), 1.53 (m, 1H) 1.39 (m, 2H), 1.22 (m, 3H). $^{13}$C NMR (100.5 MHz) $\delta$: 172.3, 159.7, 129.5, 128.5, 114.0, 77.6, 55.3, 52.2, 32.3, 32.2, 25.7, 24.2. MS (EI): 278 [M$^+$].

**Methyl 2-(p-methoxyphenyl)diazoacetate Insertion with Ethanol.** The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (65.9 mg, 0.320 mmol), (TPP)FeCl$_2$ (2.20 mg, 1 mol%), ethanol (29.4 mg, 0.640 mmol) and 5.0 mL of methylene chloride. The mixture was refluxed at 40 °C for 8 h. The products were purified by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl 2-ethoxy-(4-methoxyphenyl)acetate, 3d, (53.0 mg, 0.240 mmol, 74% yield) was obtained. $^1$H NMR (400 MHz) $\delta$: 7.38 (d, 2H, $J_H = 8.8$, aryl-H), 6.90 (d, 2H, $J_H = 8.8$, aryl-H), 4.84 (s, 1H, methine C-H), 3.81 (s, 3H, ArOCH$_3$), 3.72 (s, 3H, OCH$_3$),
3.53 (m, 2H, OCH2), 1.27 (t, 3H, JH = 8.8, RCH3). 13C NMR (100.5 MHz) δ: 170.3, 159.2, 128.8, 128.6, 114.1, 80.5, 65.1, 55.3, 52.3, 15.2. MS{EI}: 224 [M]+.

**Methyl 2-(p-tolyl)diazoacetate Insertion with n-Propanol.** The general procedure was used with methyl 2-(p-tolyl)diazoacetate (60.8 mg, 0.320 mmol), (TPP)FeCl (2.20 mg, 1 mol%), n-propanol (39.7 mg, 0.640 mmol) and 5.0 mL of methylene chloride. The mixture was refluxed at 40 °C for 8 h. The products were purified by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl 2-propanoxy-(4-methoxyphenyl)acetate, 4c, (50.4 mg, 0.230 mmol, 71% yield) was obtained. 1H NMR (400 MHz) δ: 7.35 (d, 2H, JH = 8.0, aryl-H), 7.18 (d, 2H, JH = 8.0, aryl-H), 4.85 (s, 1H, methine C-H), 3.71 (s, 3H, OCH3), 3.48 (m, 1H, OCH2), 3.40 (m, 1H, OCH2), 2.35 (s, 3H, ArCH3), 1.67 (m, 2H, CH2), 0.94 (t, 3H, JH = 7.6, CH3). 13C NMR (100.5 MHz) δ: 171.7, 138.5, 133.8, 129.3, 127.2, 80.9, 71.5, 52.2, 22.8, 21.2, 10.5. MS{EI}: 222 [M]+.

**Methyl 2-(p-methoxyphenyl)diazoacetate Insertion with isopropanol.** The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (65.9 mg, 0.320 mmol), (TPP)FeCl (2.2 mg, 1 mol%), ethanol (39.4 mg, 0.640 mmol) and 5.0 mL of methylene chloride. The mixture was refluxed at 40 °C for 8 h. The products were purified by eluting through a silica gel column using a 20:1 hexane/ethyl acetate mixture. The product methyl 2-isopropanoxy-(4-methoxyphenyl)acetate, 5d, (42.6 mg, 0.180 mmol, 56% yield) was obtained. 1H NMR (400 MHz) δ: 7.39 (d, 2H, JH = 8.6, aryl-H), 6.89 (d, 2H, JH = 8.6, aryl-H), 4.95 (s, 1H, methine C-H), 3.81 (s, 3H, ArOCH3), 3.71 (s, 3H, OCH3), 3.65 (m, 1H, OCH), 1.24 (d, 3H, JH = 6.2, RCH3), 1.19 (d, 3H, JH = 6.2,
EDA Insertion with Ethylenediamine. Ethylenediamine (30.0 mg, 0.500 mmol) and (TPP)FeCl (3.50 mg, 1 mol%) were placed in a 50-mL round bottom flask and dissolved in 5.0 mL of methylene chloride. The mixture was flushed with nitrogen after which ethyldiazoacetate (57.0 mg, 0.500 mmol) dissolved in 3 mL of methylene chloride was added dropwise using a dropping funnel while continuously stirring the flask contents. The product was extracted using distilled water and dried under reduced pressure to obtain 2-piperazinone (43.1 mg, 0.431 mmol, 86% yield). $^1$H NMR (400 MHz) δ: 6.76 (b, 1H, N-H), 3.50 (s, 2H, CH$_2$), 3.33 (m, 2H, CH$_2$), 3.01 (t, 2H, J$_H$ = 5.2, CH$_2$). $^{13}$C NMR (100.5 MHz) δ: 170.1, 49.9, 43.0, 42.3.

EDA Insertion with Ethanolamine. Ethanoamine (30.0 mg, 0.500 mmol) and (TPP)FeCl (3.50 mg, 1 mol%) were placed in a 50-mL round bottom flask and dissolved in 5.0 mL of methylene chloride. The mixture was flushed with nitrogen after which ethyldiazoacetate (57.0 mg, 0.500 mmol) dissolved in 3 mL of methylene chloride was added dropwise using a dropping funnel while continuously stirring the flask contents. The product was extracted using distilled water and placed under reduced pressure overnight to obtain 2-morpholinone (44.2 mg, 0.442 mmol, 88% yield). $^1$H NMR (400 MHz) δ: 3.43 (t, 2H, J$_H$ = 5.2, CH$_2$), 3.14 (s, 2H, CH$_2$), 2.63 (t, 2H, J$_H$ = 5.2, CH$_2$). $^{13}$C NMR (100.5 MHz) δ: 172.7, 63.2, 52.2, 43.8.

EDA Reaction with 2-Aminophenol (1:1). 2-Aminophenol (54.2 mg, 0.500 mmol) and (TPP)FeCl (3.5 mg, 1 mol%) were placed in a 50-mL round bottom flask and dissolved in 5.0 mL of methylene chloride. The mixture was flushed with nitrogen after
which ethyldiazoacetate (57.0 mg, 0.500 mmol) dissolved in 3 mL of methylene chloride was added dropwise using a dropping funnel while continuously stirring the flask contents. The product was extracted using distilled water and dried under reduced pressure to obtain N-(2-hydroxyphenyl)glycine ethyl ester, 8, (69.3 mg, 0.360 mmol, 71% yield). $^1$H NMR (400 MHz) δ: 6.6-7.1 (m, 4H, aryl-H) 4.23 (m, 2H, CH$_2$), 3.91 (s, 2H, CH$_2$), 1.29 (m, 3H, CH$_3$). $^{13}$C NMR (100.5 MHz) δ: 172.4, 153.6, 127.9, 126.4, 120.4, 116.0, 61.7, 56.4, 14.5. MS{EI}: 195 [M]$.  

**EDA Reaction with 2-Aminophenol (2:1).** 2-Aminophenol (54.2 mg, 0.500 mmol) and (TPP)FeCl (3.50 mg, 1 mol%) were placed in a 50-mL round bottom flask and dissolved in 5.0 mL of methylene chloride. The mixture was flushed with nitrogen after which ethyldiazoacetate (114 mg, 1.00 mmol) dissolved in 3 mL of methylene chloride was added dropwise using a dropping funnel while continuously stirring the flask contents. The product 10 was extracted using distilled water and dried under reduced pressure to obtain (49.4 mg, 0.210 mmol, 42% yield). $^1$H NMR (400 MHz) δ: 7.07 (m, 2H, aryl-H), 6.89 (t, 1H, J$_H$ = 8.0, aryl-H), 6.62 (d, 1H, J$_H$ = 8.0, aryl-H), 4.23 (q, 2H, J$_H$ = 7.0, CH$_2$), 4.13 (s, 2H, CH$_2$), 4.00 (s, 2H, CH$_2$), 1.29 (t, 2H, J$_H$ = 7.0, CH$_3$)). $^{13}$C NMR (100.5 MHz) δ: 169.5, 164.6, 141.9, 133.6, 125.5, 120.7, 117.4, 112.7, 61.7, 51.3, 51.0, 14.2. MS{EI}: 236 [M+1]$^+$.  

**EDA Insertion on 1,2 phenylenediamine (1:1).** 1,2-Phenylenediamine (54.3 mg, 0.500 mmol) and (TPP)FeCl (3.50 mg, 1 mol%) were placed in a 50-mL round bottom flask and dissolved in 5.0 mL of methylene chloride. The mixture was flushed with nitrogen after which ethyldiazoacetate (57.0 mg, 0.500 mmol) dissolved in 3 mL of methylene chloride was added dropwise using a dropping funnel while continuously
stirring the flask contents. The product was extracted using distilled water and dried under reduced pressure to obtain N-(2-aminophenyl)glycine ethyl ester, 11, (78.4 mg, 0.400 mmol, 81% yield). $^1$H NMR (400 MHz) δ: 6.50-6.85 (m, 4H, aryl-H) 4.25 (m, 2H, CH$_2$), 3.91 (s, 2H, CH$_2$), 1.29 (m, 3H, CH$_3$). $^{13}$C NMR (100.5 MHz) δ: 171.5, 136.6, 136.5, 120.6, 120.1, 119.7, 112.6, 61.3, 46.5, 14.3.

EDA Insertion on 1,2 phenylenediamine 2:1. 1,2-Phenylenediamine (54.3 mg, 0.500 mmol) and (TPP)FeCl (3.50 mg, 1 mol%) were placed in a 50-mL round bottom flask and dissolved in 5.0 mL of methylene chloride. The mixture was flushed with nitrogen after which ethylidiazoacetate (114 mg, 1.00 mmol) dissolved in 3 mL of methylene chloride was added dropwise using a dropping funnel while continuously stirring the flask contents. The product was extracted using distilled water and dried under reduced pressure to obtain N,N- bis(2-aminophenyl)glycine ethyl ester, 12, (95.2 mg, 0.34 mmol, 58% yield). $^1$H NMR (400 MHz) δ: 7.26 (m, 2H, aryl-H), 7.03 (m, 2H, aryl-H) 5.00 (s, 4H, CH$_2$), 4.26 (q, 4H, CH$_2$), 1.29 (t, 6H, CH$_3$). $^{13}$C NMR (100.5 MHz) δ: 167.0, 126.8, 125.0, 115.0, 62.5, 44.8, 14.4.

Methyl 2-(p-methoxyphenyl)diazoacetate Insertion on Ethylenediamine. The general procedure was used with methyl 2-(p-methoxyphenyl)diazoacetate (65.9 mg, 0.32 mmol), (TPP)FeCl (2.20 mg, 1 mol%), ethylenediamine (60.4 mg, 1.00 mmol) and 5.0 mL of THF. The mixture was refluxed at 80 °C for 8 h. The products were purified by eluting through a alumina column using a 20:1:1 hexane/ethyl acetate/methanol mixture. The product 5,6-dihydro-3-(p-methoxyphenyl) pyrazinone, 14, (35.4 mg, 0.11 mmol, 54% yield) was obtained. $^1$H NMR (400 MHz) δ: 7.93 (d, 2H, $J_H = 8.8$, aryl-H), 7.39 (b, 1H, N-H) 6.93 (d, 2H, $J_H = 8.8$, aryl-H), 3.91 (t, 2H, $J_H = 6.2$, CH$_2$), 3.84 (s, 3H,
ArOCH$_3$), 3.48 (m, 2H, CH$_2$). $^{13}$C NMR (100.5 MHz) $\delta$: 161.5, 161.3, 158.1, 130.5, 127.9, 113.5, 55.4, 48.1, 39.1. MS{EI}: 205 [M+1].

References


(7) Mbuvi, H. M.; Woo, L. K., manuscript in preparation for *Organometallics*. 


GENERAL CONCLUSIONS

This dissertation focuses on the use of metalloporphyrins, mainly iron(III), Fe(TPP)Cl, as catalysts for N-H, C-H and O-H insertion reactions and cyclopropanation of arenes using various diazo reagents as sources of carbenes. A tandem N-H insertion/cyclization reaction using ethylenediamine and ethanolamine to give 2-piperazinone and 2-morpholinone, respectively, was also developed.

Fe(TPP)Cl is one of the most efficient catalysts for insertion of the carbene derived from EDA into amine N-H bonds. This insertion reaction can be performed at room temperature and atmospheric conditions in relatively short reaction times. The vast majority of systems capable of mediating this reaction also readily convert ethyl diazoacetate into diethyl fumarate and maleate. Unlike these others catalytic systems, N-H insertions catalyzed by Fe(TPP)Cl are faster than EDA dimerization and therefore no side products are formed. Mechanistic studies and comparisons with Fe^{II}(TPP) suggest that an Fe(III) form of the porphyrin complex is the active catalyst.

Fe(III), Cu(II) and Ag(II) porphyrin complexes are also active catalysts for benzylic and ring C-H insertions by carbene fragments transferred from methyl diazomalonate and \textit{para}-substituted methyl 2-phenyldiazoacetates. However, this insertion requires temperatures above 100 °C for methyl diazomalonate and lower temperatures of 60 °C for \textit{para}-substituted methyl 2-phenyldiazoacetates. Initial rates for Fe(TPP)Cl-catalyzed insertion into the C-H bond of cyclohexane are first order with respect to [\textit{p}-Cl-MPDA], implying that formation of a carbene complex is the rate-determining step. This result and a kinetic isotope effect of 1.97 ± 0.03 that was observed for cyclohexane suggests an overall two-step mechanism. Metalloporphyrin mediated
extrusion of N\(_2\) in the slow step to form a metal carbene complex is followed by insertion of the carbene fragment between a C-H bond in a concerted step to regenerate the active catalyst.

Reactions of substituted methyl 2-phenyldiazoacetates with arenes yield rapidly equilibrating mixtures of norcaradiene-cycloheptatriene valence isomers in yields over 70%. Evidence of the dynamic nature of these products was provided by variable temperature NMR spectroscopy. These dynamic valence isomers can be trapped with benzyne to yield one isomer of benzohomobarrelene. The exact structure of these isomers has been assigned using NOE experiments. These fluxional systems have also been aromatized by acidification to produce biaryl products.

Fe(TPP)Cl is also an effective catalyst for O-H insertion reactions with alcohols when substituted MPDAs are used as carbene sources. Aromatic and normal aliphatic alcohols give O-H insertion as the only product. Furthermore, this catalyst is very efficient in the synthesis of 2-piperazinone and 2-morpholinone through a tandem N-H/cyclization process when EDA is the carbene source. Substituted MPDAs can be used to synthesize substituted piperazinones and morpholinones.

The present work has shown that iron porphyrin, Fe(TPP)Cl, performs better than the widely used rhodium acetate complexes in catalyzing N-H insertions reactions when diazo compounds are used as carbene sources. Moreover, its performance is comparable with the rhodium acetate catalysts in catalyzing O-H insertion reactions. The ability of iron porphyrin to catalyze C-H insertion reactions using various diazo compounds is of great interest because even though rhodium acetate is still the catalyst of choice for C-H insertion reactions, iron porphyrins are relatively inexpensive and more environmentally...
friendly as compared to the rhodium catalyst. More studies geared towards making iron porphyrins or similar iron complexes better catalysts for asymmetric C-H activations are therefore desirable as this could lead to cheaper and safer catalysts.
ACKNOWLEDGEMENTS

I would like to sincerely thank professor Keith Woo for his guidance, support and patience during the course of this study. His advice that luck came to the very hard working came in handy during this study. His insight and vast knowledge aided immensely in interpreting our data and determining the next steps to take to tie up loose ends.

I also express my gratitude to my POS committee members Robert Angelici, John Verkade, William Jenks and Aaron Sadow for always being available. Additional thanks go to Steve Veysey, Dave Scott and Shu Xu for help in NMR and GC-MS experiments. I also extend my gratitude to present and former members of the Woo crew.

I would also like to thank the Petroleum Research Fund and National Science Foundation for funding the project.

Finally, I would like to sincerely give lots of gratitude to my wife Christine for the moral support she accorded me and the sacrifice of taking care of our daughter Joy singlehandedly during my study abroad and to my daughter Joy for giving me inspiration and purpose.