

CHAPTER 1

CATALYTIC, ASYMMETRIC, INTRAMOLECULAR CARBON–HYDROGEN INSERTION

MICHAEL P. DOYLE, YU LIU, AND MAXIM RATNIKOV

*Department of Chemistry and Biochemistry, University of Maryland,
College Park, Maryland 20742*

CONTENTS

	PAGE
ACKNOWLEDGMENTS	2
INTRODUCTION	2
MECHANISM AND STEREOCHEMISTRY	5
SCOPE AND LIMITATIONS	12
Preparation and Stability of Metal Carbene Precursors	12
Survey of Catalysts	16
Synthesis of Lactones by C–H Insertion	20
Monocyclic γ -Butyrolactones	20
Bicyclic γ -Butyrolactones	22
Steroidal Lactones	25
Silylated γ -Butyrolactones	26
β -Lactones	27
Synthesis of Lactams by C–H Insertion	28
γ -Lactams and β -Lactams	29
Synthesis of Cycloalkane Derivatives by C–H Insertion	35
Cyclopentanones	35
Cyclopentanes	37
Side Reactions	38
APPLICATIONS TO SYNTHESIS	39
COMPARISON WITH OTHER METHODS	41
EXPERIMENTAL CONDITIONS	42
EXPERIMENTAL PROCEDURES	44
Preparation of Diazo Compounds	44
1-Diazo-4-phenylbutan-2-one [Arndt–Eistert Reaction]	44
Methyl 2-(2-(Benzyloxy)phenyl)-2-diazoacetate [Diazo Transfer Reaction]	45
3-(3-Methoxyphenyl)propyl 2-Diazoacetate [Acyl Cleavage Reaction]	45
(<i>R</i>)-Cyclohex-2-en-1-yl 2-Diazoacetate [Direct Diazoacetylation]	46
D-(+)-Menthyl Diazoacetate [DCC Coupling Reaction]	47

Methyl 2-Diazo-3-oxo-4-(3-oxocyclohexyl)butanoate [Mukaiyama–Michael Reaction]	47
Catalytic, Asymmetric, Intramolecular C–H Insertions	48
(<i>R</i>)-4-(4-Chlorophenyl)dihydrofuran-2(3 <i>H</i>)-one [Synthesis of a β -Substituted γ -Butyrolactone from an Acyclic Diazoacetate]	48
(4 <i>S</i> ,5 <i>S</i>)-5-Ethyl-4-methyldihydrofuran-2(3 <i>H</i>)-one [Desymmetrization of a Secondary Alkyl Diazoacetate]	48
(3 <i>aS</i> ,7 <i>aS</i>)-Hexahydrobenzofuran-2(3 <i>H</i>)-one [Formation of a Bicyclic γ -Lactone from a Cyclic Diazoacetate]	49
(2 <i>S</i>) and (2 <i>R</i>)-3-(3 β -Hydroxy-5-cholesten-3 α -yl)phenylacetic Acid Lactones [β -Lactone Formation from a Phenyl diazoacetate]	49
(<i>R</i>)-1-Azabicyclo[5.2.0]nonan-9-one [β -Lactam Formation from a Diazoacetamide]	51
(2 <i>S</i> ,4 <i>aS</i> ,7 <i>aS</i>)-5-(bis(Trimethylsilyl)methyl)-2-phenyltetrahydro-[1,3]dioxino[5,4- <i>b</i>]pyrrol-6(4 <i>H</i>)-one [γ -Lactam Formation from a Diazoacetamide]	51
(<i>S</i>)-3-(2-(Benzyloxy)ethyl)-2-(3-methoxy-5-methylphenyl)-3-methylcyclopentanone [Synthesis of a Cyclopentanone from a Diazoketone]	52
(1 <i>S</i> ,2 <i>R</i>)-cis-2-phenylcyclopentane-1-carboxylate [Synthesis of a Cyclopentane from a Methyl Diazoester]	52
TABULAR SURVEY	53
Chart 1. Chiral Dirhodium Carboxamidate Catalysts	55
Chart 2. Chiral Dirhodium Carboxylate Catalysts	58
Chart 3. Chiral Arylphosphate Dirhodium Catalysts	61
Chart 4. Chiral <i>cis</i> -Orthometalated Arylphosphine Dirhodium Catalysts	62
Chart 5. Chiral Copper Catalysts	63
Table 1. Monocyclic γ -Lactones from Diazoacetates	64
Table 2. Silylative Transformations of Prochiral Cyclic Ketones	73
Table 3. β -Lactones from Diazoacetates	87
Table 4. γ -Lactams from Diazoacetamides	95
Table 5. β -Lactams from Diazoacetamides	106
Table 6. Synthesis of Cycloalkane Derivatives	113
REFERENCES	124

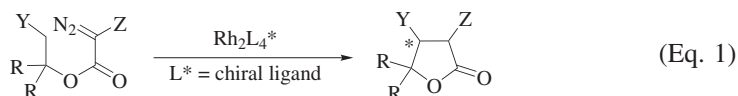
ACKNOWLEDGMENTS

We gratefully acknowledge research support from the National Science Foundation and the NIGMS of the National Institute of Health. We also thank Darren Bykowski for providing the preliminary compilations of information for this review.

INTRODUCTION

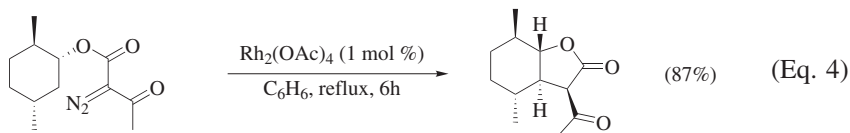
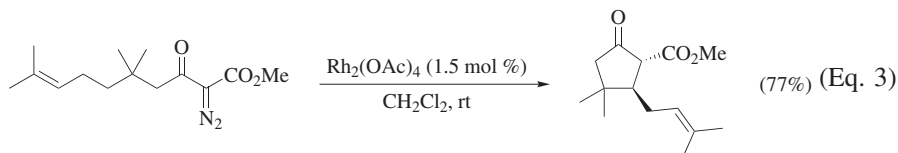
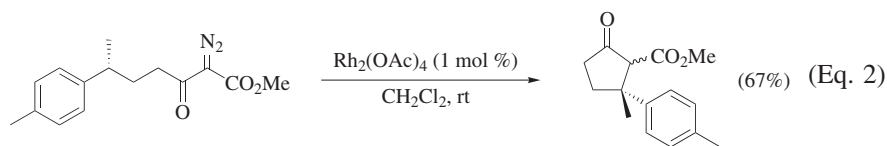
Among the most synthetically attractive methods for replacement of hydrogen on carbon are those that form new C–C bonds and, among these methods, controlled insertion of a metallo-carbene into a C–H bond has broad applications. This strategy has become popular, in large part, due to advances in

our understanding of metallo-carbene chemistry and the evolution of its catalytic applications^{1–21} over the past sixty years from an impractical curiosity to a useful strategy in synthetic organic chemistry.^{7,12–14,18,19,22–32} Intramolecular reactions of metallo-carbenes with remote C–H bonds were the first to be investigated as synthetic strategies; they provide access to more complex materials by selective functionalization at a normally unreactive C–H site (e.g. Eq. 1).^{2–7,12–19,31} Site- and stereoselective discrimination among the C–H bonds found in complex molecules is critical to the ultimate success of these strategies. Advances in the development and applications of catalyst systems that selectively insert a carbene into a specific C–H bond have been the subject of intensive investigations,^{6,7,13,18,19,24,25,31,32} and the intramolecular applications of this method are the subject of this chapter.



Although C–H insertion reactions of free carbenes have been known for several decades, it has only been through the application of metallo-carbenes that highly selective, high-yielding C–H insertions could be realized.^{33–38} Copper catalysts were employed prior to the initial reports of insertion reactions with dirhodium(II) carboxylate catalysts, but they showed limited success except with highly constrained systems.³⁹ These insertion reactions were carried out with α -diazocarbonyl compounds; the latter are ideally suited in view of their ready availability and their ability to undergo diazo decomposition to metallo-carbenes in reactions with selected transition-metal complexes.^{32,40,41} Unlike their aliphatic diazoalkane counterparts, α -diazocarbonyl compounds are conveniently prepared and relatively stable to thermal and acid-promoted decomposition. The intermediate metallo-carbenes generated from diazocarbonyl compounds by reactions with transition-metal complexes are able to react in a selective fashion with C–H bonds.^{26,42,43}

Although considerable attention has been devoted to reactions of α -diazocarbonyl compounds with transition-metal catalysts, including those of copper, silver, and gold,^{14,18,44,45} ruthenium,^{46–48} and even iron,^{49–51} only dirhodium(II) catalysts have provided a consistent, dependable, and reproducible foundation for C–H insertion chemistry. Beginning in the 1990's with the development of dirhodium(II) catalysts having chiral carboxylate^{52–54} and carboxamidate ligands,^{32,55} stereocontrol has been a primary focus of this research. Chiral catalysts are capable of providing high levels of enantioselectivity, as well as diastereo- and site-selectivity, and they are the focus of this chapter. Although C–H insertion reactions using achiral catalysts are common in organic synthesis (Eq. 2–4) and exhibit high site- and diastereoselectivity,^{32,56} this review will be devoted to C–H insertion reactions that utilize chiral catalysts to exert stereocontrol over the insertion process.



The first reports of asymmetric C–H insertion reactions focused on intramolecular processes.^{32,40,42,56} Intermolecular C–H insertion reactions were subsequently found to be controllable and synthetically useful,^{57,58} and a recent related chapter⁵⁹ provides a comprehensive overview of enantioselective intermolecular C–H insertion reactions.

In contrast to cyclopropanation reactions, for which a variety of transition-metal complexes are effective catalysts,^{32,42,60–62} dirhodium(II) compounds have emerged as the dominant catalyst class for C–H insertion reactions. The dirhodium(II) catalysts are paddlewheel-shaped dimetallic complexes in which four bidentate ligands bridge two rhodium atoms connected by a rhodium–rhodium bond and completed by two axial ligands (Fig. 1). The bridging ligands are most commonly carboxylates or carboxamides, although asymmetric catalysts based on phosphonate^{63,64} and arylphosphine^{65–68} ligands have also been reported. With identical substitution on each rhodium atom, the two axial faces of the paddlewheel-shaped complex of the dirhodium(II) catalysts are homotopic, provided the complex has D_2 symmetry. A large number of enantiomerically enriched dirhodium complexes have been reported, but only a few have found widespread application for asymmetric C–H insertion.^{25,53,69,70} Due to their stability to ambient air and moisture, these complexes are convenient to store and use.

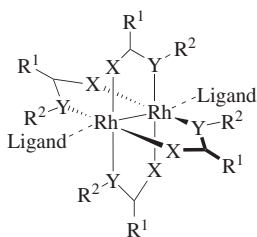


Figure 1. Dirhodium (II) paddlewheel complexes.

Because α -diazocarbonyl compounds are the most common precursors to metal carbene intermediates in catalytic reactions, numerous methods for their preparation have been reported and reviewed.^{32,40,71–82} Although caution should be exercised in the preparation and use of any diazo compound, α -diazocarbonyl compounds exhibit much greater thermal stability than the more reactive diazoalkanes.^{32,71} Ethyl diazoacetate, for example, is stable for long periods at temperatures at or below 120° and does not undergo loss of dinitrogen in glacial acetic acid. Methyl phenyldiazoacetate is even more stable.³² As evidenced by the extensive applications of α -diazocarbonyl compounds in synthesis,^{32,40} simple precautions such as the use of well ventilated fume hoods and avoidance of high temperatures are sufficient to ensure the safe handling and use of α -diazocarbonyl compounds. Other compounds (e.g., iodonium ylides) have been explored for use as carbene precursors, in conjunction with transition-metal catalysts, in intramolecular C–H insertion reactions.^{45,83–86}

Throughout this chapter we refer to the metal-catalyst-generated carbene species as a “metallo-carbene” rather than a “carbenoid”. These intermediates have been observed, and they have been directly implicated in catalytic reactions.^{87,88} Indeed, similarities exist between metal carbenes generated in copper and dirhodium(II) catalytic reactions and structurally well defined metallo-carbenes such as pentacarbonyltungstenphenyl carbene.^{89,90} The term “carbenoid” was originally coined for α -haloalkyllithium compounds.⁹¹ Although commonly used in reports of transition-metal-catalyzed reactions of diazo compounds, “carbenoid” implies more uncertainty in the structures of reaction intermediates than are revealed in mechanistic interpretations. The term “carbenoid” is used in this chapter only to infer uncertainty when appropriate to the discussion.

The “apparent C–H insertion” of metallo-carbenes into aryl C–H bonds is well known, but these reactions are unlikely to proceed through direct insertion into the aryl C–H bond.^{32,92–94} Instead, the reaction is likely to be initiated by an electrophilic addition of the metal carbene onto the aromatic ring. Because these reactions are not the result of direct insertion into a C–H bond, they are not covered in this review.

Several reviews have focused on C–H insertion reactions of metal carbenes.^{18,22,23,32,40,42,43,95,96} This review of catalytic, asymmetric, intramolecular C–H insertions, which covers the literature up to and including 2009, is organized according to the products obtained from the insertion reaction, focusing on functional groups.

MECHANISM AND STEREOCHEMISTRY

The catalytic cycle for conversion of a diazocarbonyl compound to a dirhodium-stabilized carbene, and subsequent transfer of the carbene, is believed to be applicable not only to dirhodium-stabilized carbene C–H insertion but to most, if not all, reactions of diazocarbonyl compounds using transition-metal catalysts.^{32,41,56} Dirhodium(II) compounds are 18-electron rhodium complexes only when a ligand occupies the axial coordination site; axial ligands are Lewis

bases—commonly acetonitrile—that are ordinarily loosely held by dirhodium in solution [e.g., bis(acetonitrile)dirhodium(II) tetraacetate in Fig. 2].^{97–104}

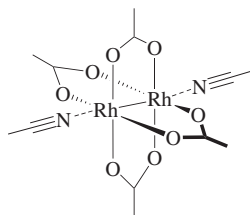
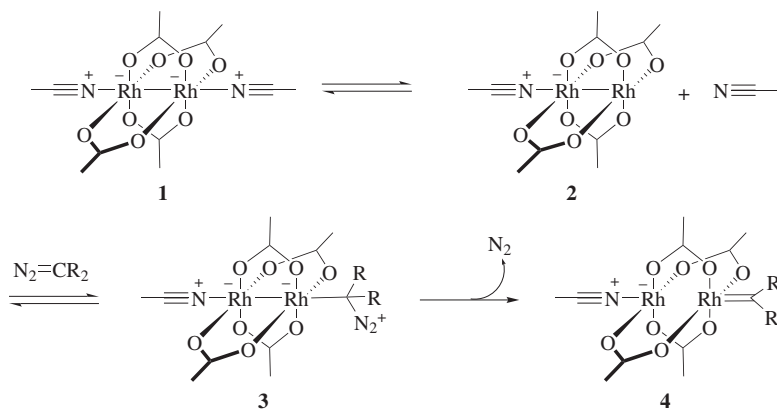


Figure 2. Dirhodium tetraacetate (bis)acetonitrile complex.

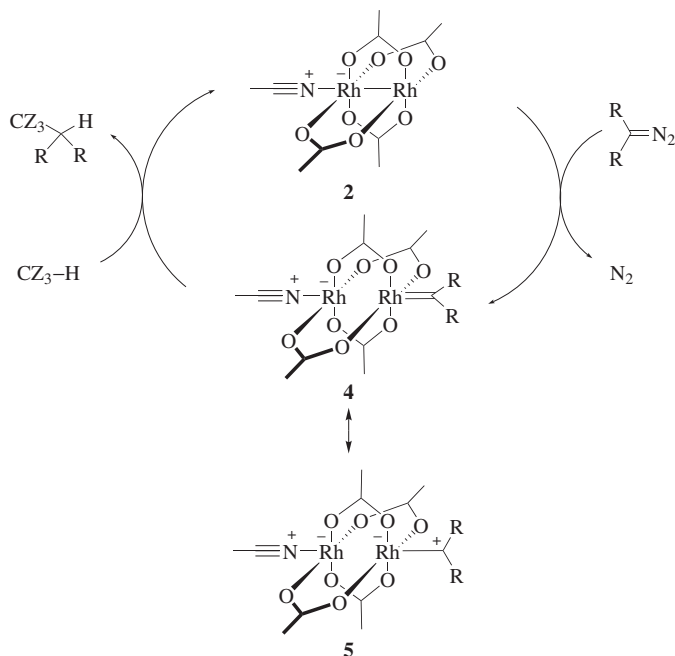
The metallo-carbene is produced by a sequence of steps beginning with ligand dissociation from dirhodium complex **1** and attack of the nucleophilic diazo carbon on the electron-deficient dirhodium(II) complex **2** (Scheme 1).^{105–108}



Scheme 1

Back-bonding from rhodium to carbon aids the extrusion of dinitrogen from intermediate **3** and the formation of the dirhodium-stabilized carbene (**4**). Experimental and computational studies have identified the extrusion of dinitrogen as the rate-limiting step within the catalytic cycle.^{106–109} Dinitrogen extrusion is first order in the dirhodium catalyst.^{105,108} A large ¹⁵N kinetic isotope effect for dinitrogen formation supports the mechanism outlined in Scheme 1.¹¹⁰ The rhodium-stabilized carbene may be depicted by two resonance structures: one that describes a rhodium–carbon double bond (**4**, Scheme 2), not unlike that used to depict stable metal carbene complexes,^{111–116} and another having a charge-separated structure (**5**) that places a formal positive charge on carbon and a formal negative charge on the metal.^{32,117} The depiction of the carbene as a charge-separated species (metal-stabilized carbocation), while deemphasizing

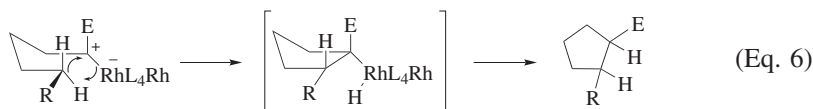
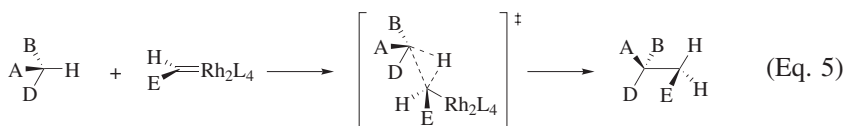
back-bonding from rhodium into the carbene, provides a simple tool with which to explain its electrophilic reactivity. Upon reaction of the metallo-carbene with a C–H bond, product formation occurs, and the catalyst is released back into the catalytic cycle. Kinetic isotope effects for C–H/C–D insertion are consistent with an increase in positive charge at the carbon of the C–H bond in the transition state,^{58,118} and calculations have reproduced the experimental data.¹⁰⁷



Scheme 2

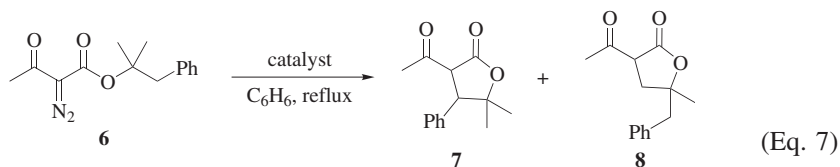
The mechanism for insertion of a metal carbene into a C–H bond has generated considerable debate. Early studies provided evidence that insertion occurs with retention of configuration at carbon.^{119,120} A primary point of contention had been whether insertion of the carbene into a C–H bond occurs through a three-centered transition state structure (concerted or stepwise)^{58,107,121} or a four-centered transition state structure.^{117,120,122–124} In the three-centered transition state structure (Eq. 5), the ligands at Rh do not dissociate, and the rhodium atom has no direct interactions with the C–H bond. The four-centered transition state (Eq. 6) implies a dissociation of a ligand from one rhodium site of the dirhodium intermediate; the reaction involves the addition of a C–H bond across the Rh–C bond to generate a metal-hydride species that undergoes reductive elimination.^{117,120,124,125} Experimental^{105,106,108} and computational^{107,126} studies have evaluated these mechanistic proposals. No convincing evidence has been provided for a four-centered transition state, and kinetic data discount dissociation of a dirhodium ligand during the insertion process.¹⁰⁶ Recent computational

studies support these data and indicate that C–H insertion proceeds through a concerted, asynchronous, three-centered transition-state structure.¹⁰⁷ Accordingly, formation of the C–H bond occurs early in the transition state with subsequent C–C bond formation and release of the catalyst occurring concomitantly. The reaction is stereospecific at the C–H bond so that insertion occurs with retention of configuration.^{32,107} Theoretical studies indicate that the second rhodium atom plays a critical role in the process, alternately accepting and donating electron density to the first rhodium atom during dinitrogen extrusion and C–C bond forming processes.¹⁰⁷ This bimetallic cooperativity is regarded as crucial to the success of C–H insertion and may explain the special role of dirhodium catalysts in carbene C–H insertion reactions.

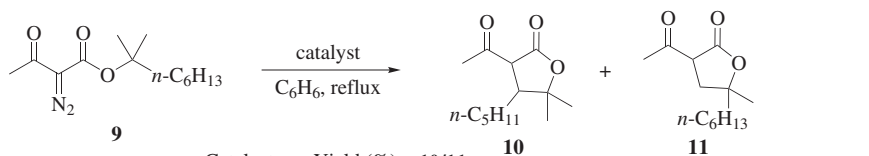


A buildup of positive charge occurs at the carbon from which hydrogen is transferred during insertion of the carbene into a C–H bond.¹⁰⁷ Consequently, substitution at the reacting C–H bond that stabilizes the developing positive charge lowers the activation energy, and promotes the insertion process.^{105,120,121} This stabilization can lead to exceptional site selectivity for intramolecular C–H insertion. Early studies into the site selectivity of C–H insertion note a general trend of reactivity toward carbene insertion to be methine > methylene >> methyl C–H bonds.^{120,121} Oxygen or nitrogen atoms also activate adjacent C–H bonds toward insertion.^{127,128} Inverse selectivity from electron-withdrawing substituents has also been reported, with esters inhibiting insertion at C–H bonds that are α , and even β ,¹²⁹ to the carbonyl carbon, although the latter has been disputed.¹³⁰ Surprisingly, an early competition study indicates that insertion into allylic and benzylic C–H bonds is disfavored,¹²⁰ however, more recent studies show that allylic and benzylic sites are preferentially reactive toward C–H insertion compared to their corresponding aliphatic counterparts.^{58,131–133} Although the electronic effects of substituents are a powerful factor in determining the site selectivity of C–H insertion, steric and conformational effects also have substantial influence, especially when chiral dirhodium catalysts are employed.^{121,134–136} An early example with 1,1-dimethyl-2-phenylethyl diazoacetoacetate (**6**) (Eq. 7) shows that insertion into the C–H bond of a methyl group (product **8**) occurs in preference to insertion into a benzylic C–H group (product **7**), independent of catalyst or temperature, whereas with 2-methyl-2-octyl diazoacetoacetate **9** (Eq. 8), site selectivity depends on the ligand (pfb = perfluorobutyrate; cap = caprolactamate) as indicated by the ratios of products **10** and **11**.¹²¹ As is readily

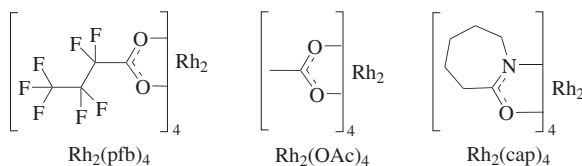
apparent from subsequent examples that will be discussed, the choice of ligand can have an impact on site selectivity as well as stereoselectivity, and, not infrequently, chemoselectivity for C–H insertion vs. competing carbene-related processes.^{121,137–142}



Catalyst	Yield (%)	7/8
Rh ₂ (pfb) ₄	31	26:74
Rh ₂ (OAc) ₄	84	29:71
Rh ₂ (cap) ₄	71	30:70

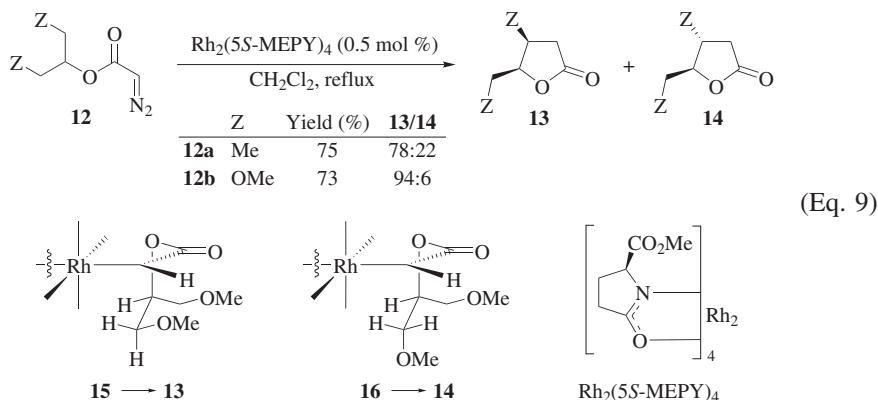


Catalyst	Yield (%)	10/11
Rh ₂ (pfb) ₄	75	34:66
Rh ₂ (OAc) ₄	84	75:25
Rh ₂ (cap) ₄	80	92:8

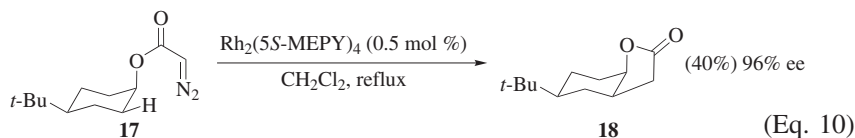


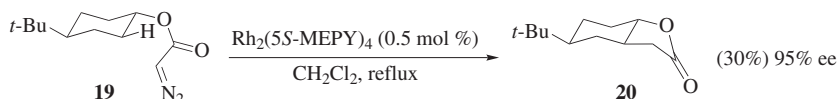
Intramolecular C–H insertion generally provides five-membered ring products; however, exceptions do exist. Conformational and electronic effects, coupled with catalyst selection, result in the predominant formation of four-membered rings in a number of instances,^{95,134,135,143,144} and insertion to form a three-membered ring has been observed in one case.¹⁴⁵ The formation of six-membered rings is comparatively rare, although several examples exist in which six-membered rings are the exclusive C–H insertion products.^{134,146–148} Other ring sizes have also been observed as C–H insertion products, however rarely, and stereocontrol is negligible.^{40,145,149–151} Conformational preferences can lead to interesting selectivities; an example is a comparison of results from catalytic asymmetric C–H insertion reactions with 3-pentyl diazoacetate (**12a**)¹⁵² and those with 1,3-dimethoxy-2-propyl diazoacetate (**12b**) (Eq. 9).^{153,154} Diastereoselectivity is significantly higher in the latter reaction than in the former. This increase in diastereoselectivity has been proposed to arise from conformational preferences due to steric and/or dipolar interactions between the polar face of the catalyst and an alkoxy group of the intermediate rhodium-bound carbene.¹⁵³ According to this

model, conformer **15** minimizes repulsive dipolar interactions between the alkoxy group and the heteroatoms of the catalyst face, providing the major diastereomer **13**. Conformer **16**, in which the polar catalyst face and an alkoxy group are proximal, generates the minor diastereomer **14**. This electronic control of conformational preferences in the transition states of **15** vs. **16** obviates the need for further catalyst ligand control that is required by 3-pentyl diazoacetate to obtain high diastereoselectivity. The electronic influence of dirhodium ligands on stereoselectivity follows the expected pattern, that is, the less electron-withdrawing the ligands, the higher the stereoselectivity.^{56,105}



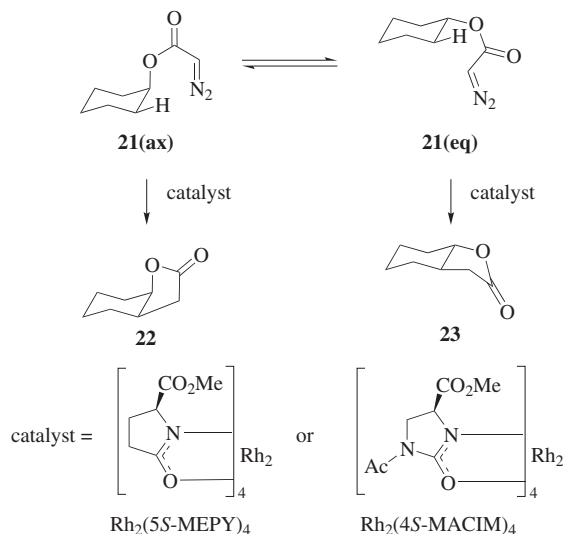
Reactions of conformationally biased 4-*tert*-butylcyclohexyl diazoacetates provide an understanding of conformational influences on C–H insertion transition state geometries.¹⁵⁵ In *cis*-4-*tert*-butylcyclohexyl diazoacetate the diazoacetate unit (and resulting metal carbene) prefers an axial position, and the neighboring equatorial C–H bonds are more available for insertion. As expected, the *cis* isomer **17** gives exclusive formation of the *cis*-bicyclic lactone isomer **18** (Eq. 10). In contrast, with *trans*-4-*tert*-butylcyclohexyl diazoacetate (**19**) the intermediate metal carbene is restricted to an equatorial position from which both neighboring axial and equatorial C–H bonds are available for insertion, potentially leading to either or both *cis*- or *trans*-bicyclic lactones. In this case only the *trans*-bicyclic lactone isomer **20** is observed (Eq. 11).¹⁵⁵ Because the *trans*-bicyclic lactone is only the minor product in the C–H insertion reaction of unsubstituted cyclohexyl diazoacetate, the implication is that C–H insertion occurs preferentially into the equatorial C–H bond from an axial carbene-bearing substituent in conformationally mobile cyclohexyl diazoacetates. Similar results are reported for the 4-methylcyclohexyl diazoacetates.¹⁵⁵





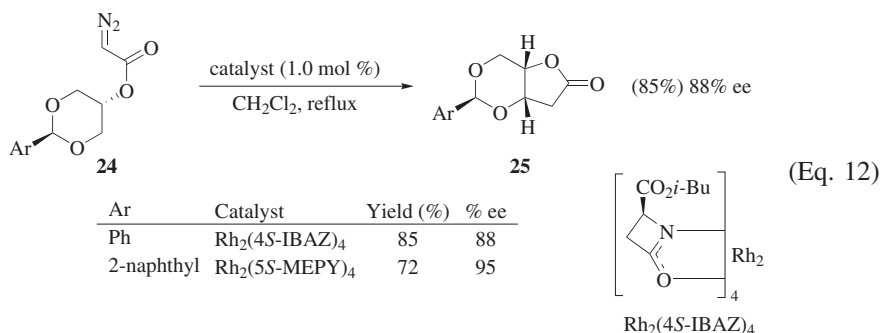
(Eq. 11)

Support for the hypothesis that insertion of the carbene in cyclohexyl systems occurs preferentially from the substituent occupying the axial position is provided by a theoretical study of diastereoselective C–H insertion reactions.¹²⁶ Using density functional theory (DFT) calculations, transition-state structures of axial or equatorial C–H insertion processes from the reaction of cyclohexyl diazoacetate **21** with $\text{Rh}_2(5S\text{-MEPY})_4$ or $\text{Rh}_2(4S\text{-MACIM})_4$ have been evaluated (Scheme 3). The lowest-energy transition structure found for this reaction stems from the carbene-bearing substituent occupying an axial position (**21ax**), allowing insertion only into the equatorial C–H bond to generate **22**. The second-lowest energy transition structure is predicted to stem from insertion of an equatorial carbene-bearing substituent (**21eq**) into the neighboring equatorial C–H bond, giving rise to **23**. This analysis is consistent with the outcome of the catalytic reaction of 4-substituted cyclohexyl diazoacetates; when the carbene-bearing substituent is forced to occupy the equatorial position, insertion also occurs into the neighboring equatorial C–H bond, yielding the *trans* isomer. Calculations of the relative transition-state energies confirm that the energy difference between the transition states leading to **22** vs. **23** is substantially greater with the catalyst $\text{Rh}_2(4S\text{-MACIM})_4$ than with $\text{Rh}_2(5S\text{-MEPY})_4$ (Scheme 3), and this is in line with observed selectivities.⁴²



Scheme 3

A departure from the conformational model used with cyclohexyl diazoacetates is observed with 2-aryl-1,3-dioxan-5-yl diazoacetates **24** (Eq. 12).¹⁵⁴ Intramolecular cyclization provides the *cis* isomer **25** exclusively, as opposed to the expected *trans* isomer. In the previously discussed six-membered ring system, the six-membered ring is assumed to adopt the chair conformation. Anomeric effects of the two oxygen atoms on the α -hydrogen atoms undergoing the insertion are likely responsible for the observed selectivity. Use of the 2-naphthyl derivative provides convenient access to the 2-naphthyl-substituted 2-deoxyribo-1,4-lactone in good yield and excellent diastereo- and enantioselectivity.

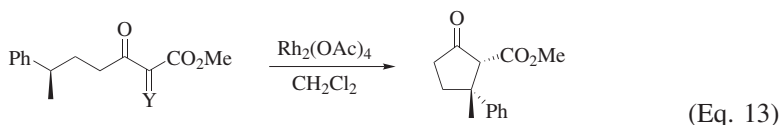


SCOPE AND LIMITATIONS

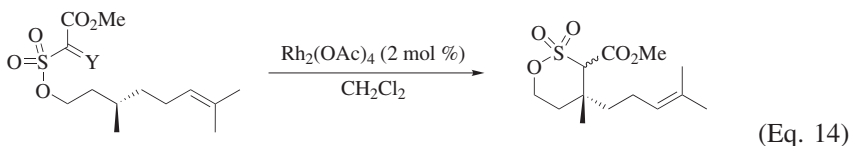
Preparation and Stability of Metal Carbene Precursors

The synthetic utility of diazocarbonyl compounds has prompted the development of several practical means of introducing the diazo functionality into substrates. Described in this section are some of the more commonly used protocols for the preparation of α -diazocarbonyl compounds; previous reviews should be consulted for a more comprehensive description of this chemistry.^{32,40,71–73,156–158} In situ methods¹⁵⁹ are also available, but they are subject to the limitations of the method that is employed.^{81,156,160} *N*-Sulfonyl-1,2,3-triazoles are promising alternatives to diazocarbonyl compounds for metal carbene reactions,^{161,162} but applications in C–H insertion reactions have not yet been reported.

A comparison of the reactivity of carbenes generated from iodonium ylides with that of the corresponding diazocarbonyl compounds shows no apparent advantage in the use of iodonium ylides other than the avoidance of the potentially explosive diazo compounds; results from both carbene precursors typically parallel each other.^{45,83–86,163–168} Because no advantage accrues from the use of iodonium ylides in the few examples reported (e.g., Eq. 13–14),^{86,169} and because the reactivity of iodonium ylides has been reviewed,⁴⁵ this chapter does not discuss these metal-carbene precursors further.

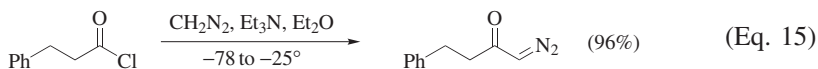


Y	Yield (%)	Temp	Time
N ₂	59	rt	30 min
IPh	57	0°	3 h



Y	Yield (%)	Conditions
N ₂	84	40°
H ₂	52	PhI=O, Cs ₂ CO ₃ , 3 Å MS

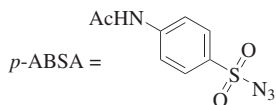
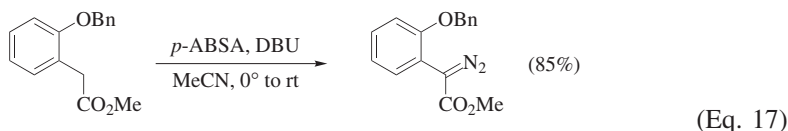
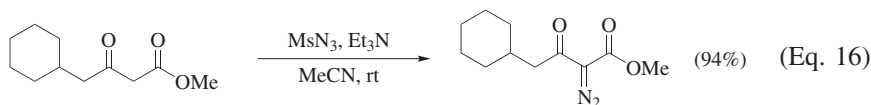
Diazo ketones having the general structure RCOCHN_2 are synthesized by addition of an acyl chloride or mixed carbonic anhydride to an ethereal solution of diazomethane.¹⁷⁰ The hydrochloric acid evolved in the course of this reaction is scavenged by an excess of diazomethane or by triethylamine (Eq. 15).¹⁷⁰ Methods for the generation of diazomethane have been described in considerable detail;^{171–173} the most commonly used reagent is the commercially available Diazald (*N*-methyl-*N*-nitroso-*p*-toluenesulfonamide).¹⁷³ Commercially available trimethylsilyldiazomethane may be used as a safer substitute for diazomethane.^{174–176} Homologs of diazomethane can also be acylated to form $\text{RCOC}(\text{N}_2)\text{R}'$, although the reaction of higher diazoalkanes is often inefficient.^{177–198}



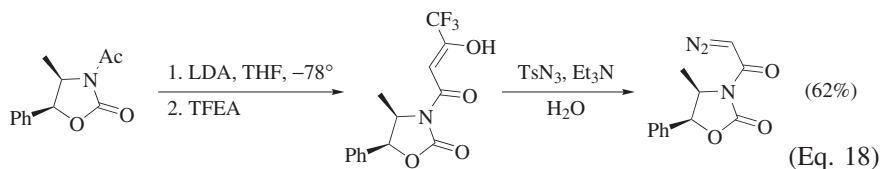
Diazo transfer between an enolate and a sulfonyl azide is used to access a wide range of α -diazocarbonyl compounds.^{32,40,71} The scope and limitations of this reaction have been described in several reviews^{32,40,71} and will be only briefly mentioned here. The thermal stability of sulfonyl azides, a large number of which have been evaluated for their synthetic utility and safety characteristics,^{32,199–202} can be a significant limitation of this method in large-scale preparations. Several of these azides have been designed to optimize diazo transfer, to reduce the explosion hazard, or to ease the separation of the product sulfonamide from the diazocarbonyl compound,^{199,203–217} and a few of them are commercially available.

Diazo transfer to the α -position of a carbonyl group requires formation of an enolate anion; if the reacting methylene group is activated by only one carbonyl group, a strong base is required. However, if the use of strong bases such as

lithium diisopropylamide (LDA) results in the formation of side products, indirect methods can be employed. When the α -position of a carbonyl group is sufficiently acidic to allow deprotonation by an organic amine, direct diazo-transfer conditions are used. Moderately basic amines such as triethylamine or DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) are typically employed. 1,3-Dicarbonyl compounds such as β -diketones, β -keto esters, and malonic esters are suitable for direct diazo transfer (Eq. 16);¹⁹⁹ an aryl or vinyl group also has an activating effect for diazo transfer (Eq. 17).²¹⁸

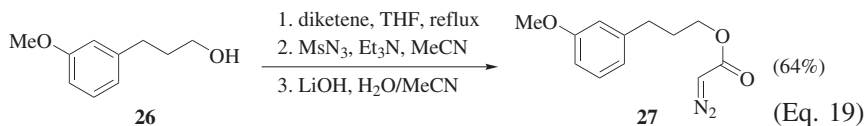


The Regitz deformylating diazo transfer protocol and its variants have found widespread application for diazo transfer to a methylene or methyl group that is not sufficiently acidic to be deprotonated by mild bases.^{32,40,71} This process begins with a Claisen condensation of the carbonyl compound with ethyl formate.^{72,73} The resulting 1,3-dicarbonyl compound is activated for diazo transfer, which occurs with subsequent deformylation (or deacylation). The formyl group is released as a sulfonamide (RSO_2NHCHO), which is usually easily separated from the diazocarbonyl product during workup due to its acidity. Variants of the Regitz conditions in which ethyl formate is replaced by TFEA (2,2,2-trifluoroethyl trifluoroacetate)^{219–221} (Eq. 18) or benzoyl chloride²²² have also been developed, and in many cases provide yields that are markedly superior to those obtained via the original protocol.

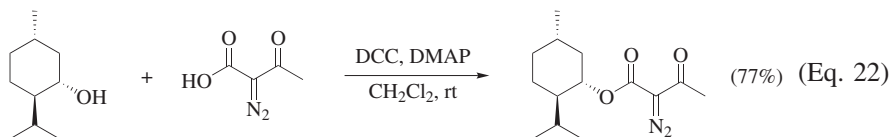
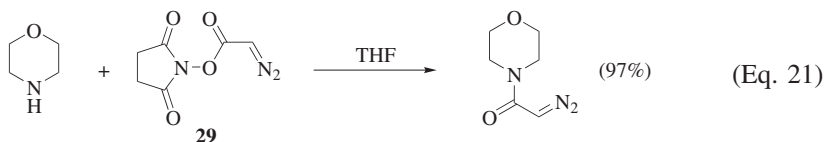
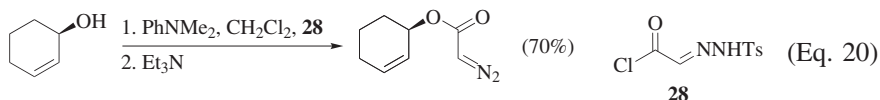


α -Diazo- β -keto esters or amides can be subjected to base-promoted acyl cleavage to generate α -diazoacetates or α -diazoacetamides. Deacylation using an alkali metal hydroxide is frequently employed for the synthesis of diazoacetates such as **27** (Eq. 19).²²³ In the complete process, alcohol **26** is treated with diketene

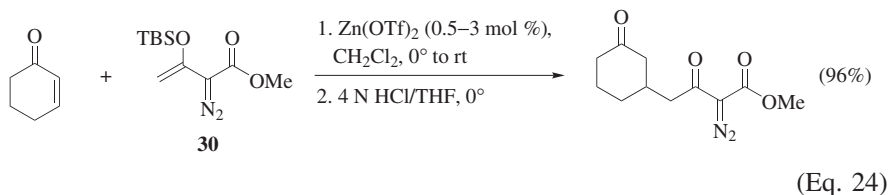
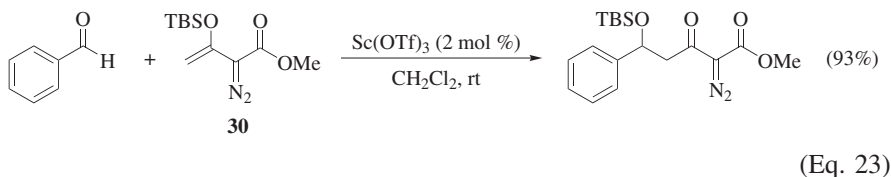
to form a β -keto ester. Reaction with mesyl azide and triethylamine generates the α -diazo- β -keto ester. Strong aqueous base cleaves the acyl group providing diazoacetate **27**.



Direct diazoacetylation of alcohols and amines provides a convenient means of accessing α -diazoacetates (Eq. 20)²²⁴ and α -diazoacetamides (Eq. 21).²²⁵ 2-(2-Tosylhydrazono)acetyl chloride (**28**)^{226,227} is an effective reagent for the synthesis of α -diazoacetates (Eq. 20). Succinimidyl diazoacetate **29** selectively transfers the acyldiazo moiety to amines and phenols (but not alcohols) under mild conditions (Eq. 21); two preparations of **29** have been reported,^{225,228} but only the latter²²⁸ has been found to be routinely reproducible in good yield. A method of preparing α -diazoacetoacetates by the direct coupling of 2-diazoacetoacetic acid and an alcohol using DCC and a catalytic amount of DMAP has recently been reported (Eq. 22).⁷⁷ Diazoacetoacetic acid is synthesized by hydrogenolysis of benzyl diazoacetoacetate catalyzed by Pd/C.⁷⁷ The main advantage of this method is that base-sensitive substrates are tolerated, thus enabling the production of diazo compounds that are difficult to make by common methods.



Silyl enol ether **30** undergoes both Mukaiyama aldol (Eq. 23)⁷⁹ and Mukaiyama–Michael (Eq. 24)⁷⁵ addition reactions with aldehydes and ketones catalyzed by a variety of Lewis acids, the most general and economical being zinc(II) triflate.^{75,229} In turn, **30** is prepared from methyl α -diazoacetoacetate.^{230,231} The products of these reactions are functionalized β -keto- α -diazoacetate esters. Ag(I)-BINAP catalysts have been used to produce enantio-enriched β -keto- α -diazoacetate esters via the Mukaiyama aldol reaction.²³² Other methods involving acid- or base-promoted reactions have also been reported.^{78,80,233–241}



Survey of Catalysts

(Note: The definitions of the abbreviations and acronyms used in the names of dirhodium catalysts are included in a list preceding the “Tabular Survey”. There are also five Charts preceding the tables that depict all the catalysts used therein. Note, however, that the bold numbers assigned to these structures and used in the tables differ from those assigned and used in the text.)

The selection of structures shown in Figs. 3–6 is intended to be representative of those that are described in this text. For a complete listing of catalysts, consult Charts 1–5.)

Chiral dirhodium(II) carboxamidate catalysts have emerged as excellent catalysts in intramolecular C–H insertion used for the synthesis of lactones and lactams.^{43,69,70} The chiral dirhodium carboxamidate catalysts (e.g., **31**–**38**, Fig. 3) that are the most widely applicable in C–H insertion reactions are prepared from rhodium acetate and enantiomerically pure amino-acid-derived lactams, carbamates, or imides with a pendant ester that serves as the stereodirecting moiety.⁶⁹ Both amino acid enantiomers are available, although the natural (*S*)-enantiomer is accessible at lower cost. The Rh₂(MEPY)₄ catalysts (**31a** and **32a**)⁵⁵ were the first effective chiral dirhodium(II) carboxamidate catalysts to be prepared, and they have enjoyed widespread application in asymmetric C–H insertion reactions. However, the use of *N*-acylimidazolidinone (**35a–d** and **36a–d**)^{223,242–244} as the chiral carboxamidate ligands gives significantly enhanced selectivities. The azetidinone-ligated catalysts **37a–d** and **38a–d**, whose OCN bite angles lengthen the rhodium–rhodium bonds, are more active than are dirhodium carboxamidate catalysts formed from five-membered ring lactams.^{245,246} The pendant CO₂R group of these catalysts is necessary for high enantiocontrol. With increased steric congestion (for example, in 1- and 2-adamantyl diazoacetates) the Rh₂(MEOX)₄ catalysts (**33a** and **34a**) can provide higher levels of enantiocontrol than the Rh₂(MEPY)₄ catalysts (**31a** and **32a**).²⁴⁷ This result is due in part to the more open nature of the catalyst face in oxazolidinate **33**, compared to pyrrolidinate (**31**)- or imidazolidinate (**35**)-ligated catalysts.

Chiral dirhodium(II) carboxylates (e.g., **39**–**48**, Fig. 4), of which the proline-based catalysts **39**^{25,54,146,248} are the most effective in intermolecular reactions that

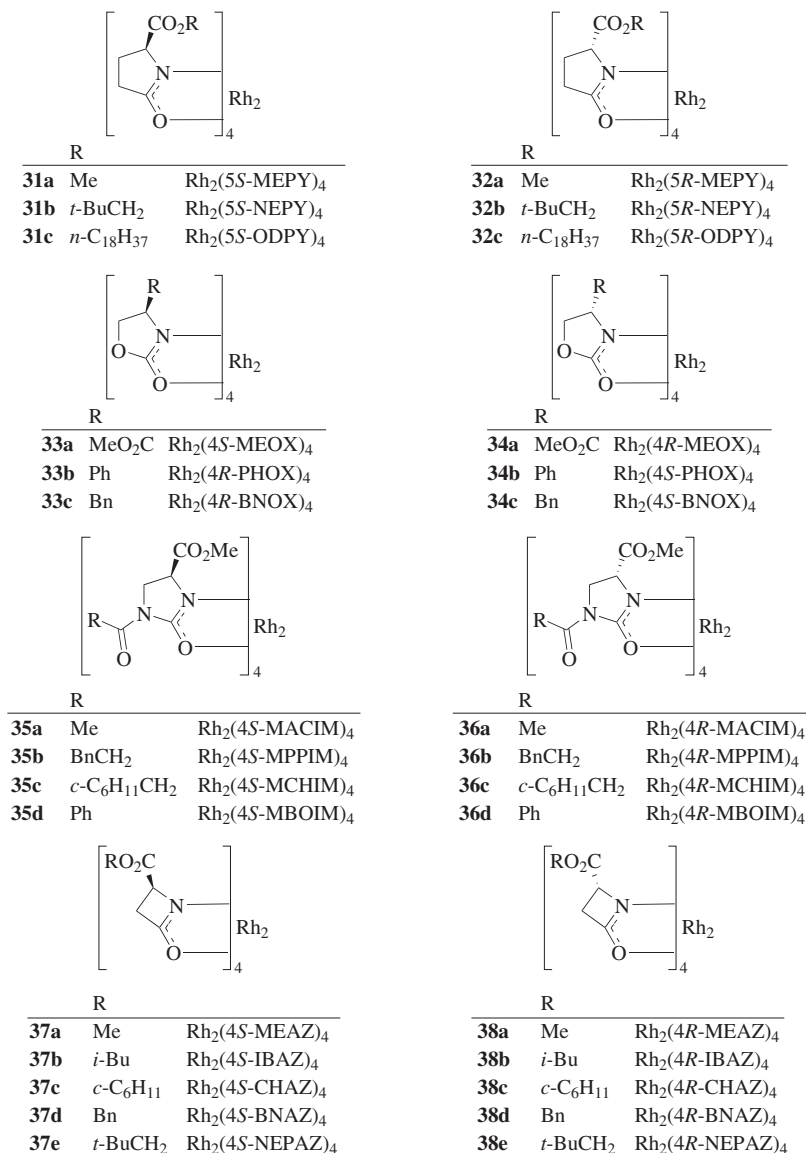


Figure 3. Chiral dirhodium(II) carboxamidate catalysts.

occur with vinyl- and aryldiazoacetates, have only rarely approached the selectivities obtained with chiral dirhodium(II) carboxamidate catalysts in the formation of lactones from diazoacetates.¹⁴³ However, chiral phthalimide-substituted amino acid ligands for dirhodium(II) (e.g., **40a–e**) are now recognized as effective alternatives to chiral carboxamidate ligands for highly enantioselective C–H insertion reactions in selected cases.^{249,250}

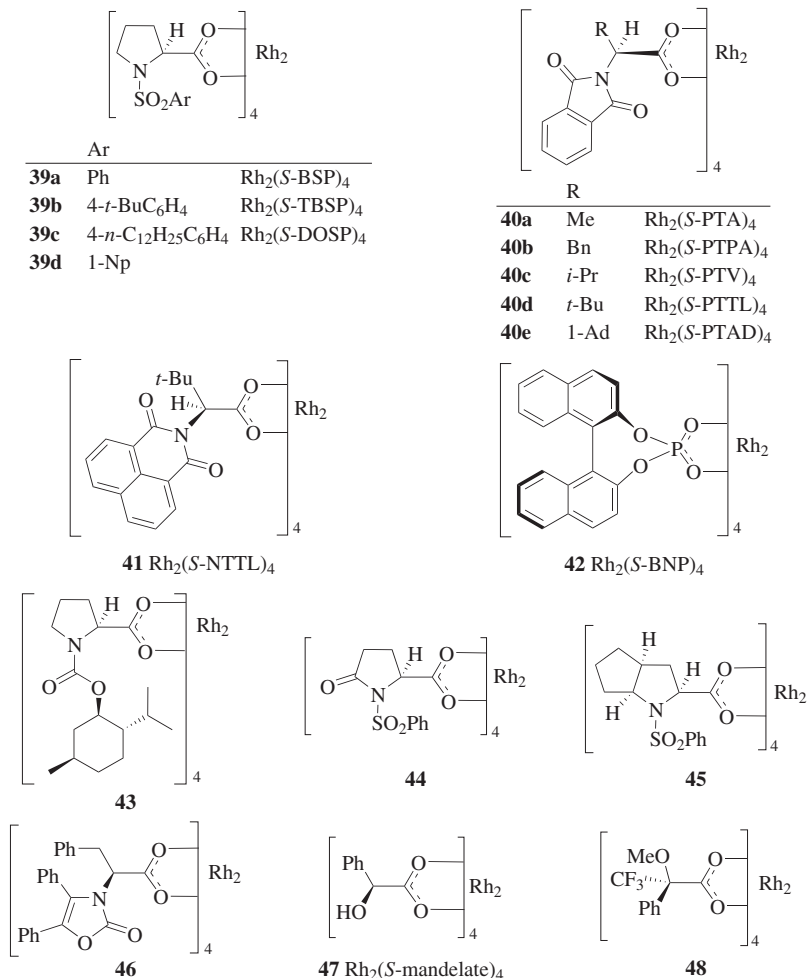
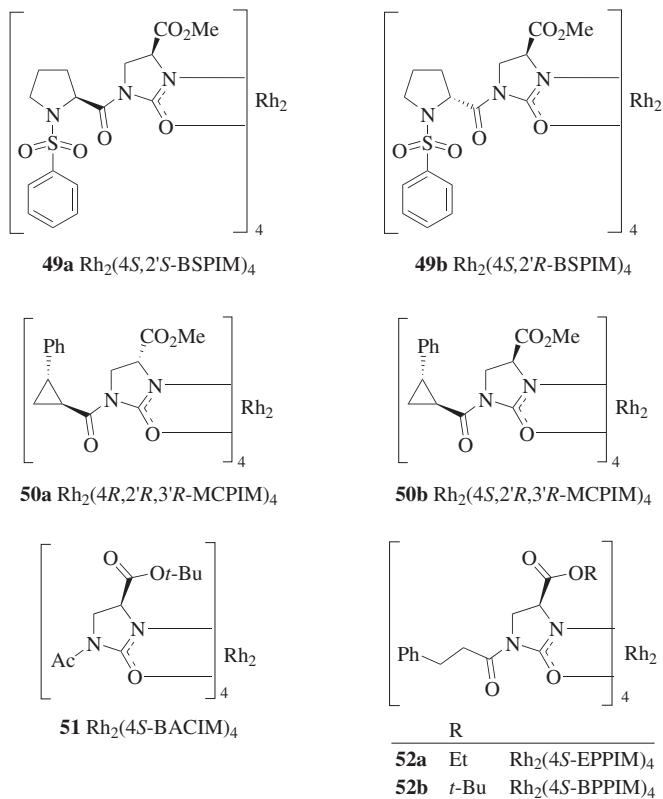
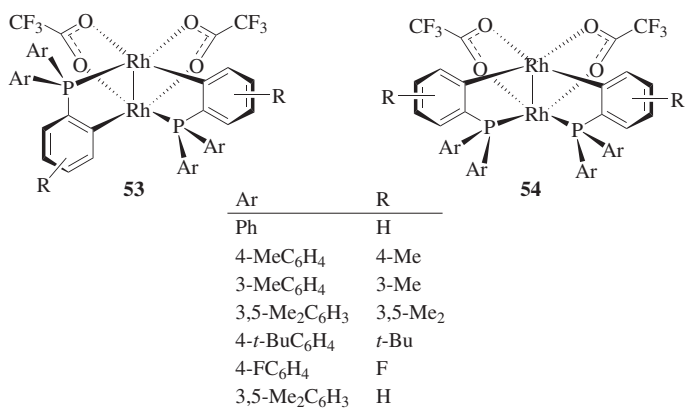


Figure 4. Chiral dirhodium(II) carboxylate catalysts.

Several other dirhodium *N*-acylimidazolidinone-ligated catalysts (Fig. 5) have been evaluated to determine the influence of multiple stereocenters in the ligands on reaction selectivity (**49** and **50**)²⁴⁴ and the influence of size of the carboxylate group on reaction selectivity (**51** and **52**).²⁵¹ *cis*-Orthometalated arylphosphine dirhodium catalysts like **53** and **54**^{252,253} (Fig. 6) appear to have unique capabilities for enantioselective C–H insertion reactions of diazo ketones for which dirhodium carboxamides and carboxylates are unselective, but only a few examples are reported.^{66,253}

These dirhodium(II) complexes have two cisoid bridging carboxylates (O₂CR)²⁵⁴ or imidates²⁵⁵ and two ortho-metalated aryl phosphines (PC) for use as catalysts for C–H insertion reactions of diazo compounds. The *cis*-orthometalated

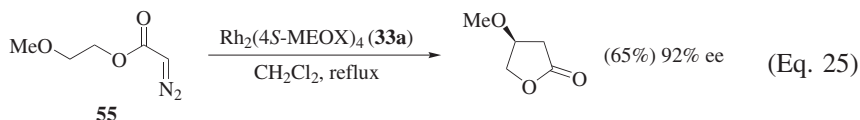
**Figure 5.** Chiral dirhodium(II) *N*-acylimidazolidinone catalysts.**Figure 6.** *cis*-Orthometalated arylphosphine dirhodium catalysts.

phosphines are oriented in a head-to-tail arrangement (**53**, Fig. 6) around the Rh_2^{4+} core or a *cis* head-to-head arrangement (**54**). The *cis*-orthometalated arylphosphine dirhodium catalysts **54** are achiral and show poor reactivity towards C–H insertion, but the isomeric complexes **53**, suitably resolved, can give both high reactivity and enantioselectivity in competitive C–H insertion reactions of selected diazo esters and diazo ketones.⁶⁶ Variation of the substituents on the metalated phenyl ring gives differences in enantioselectivity that are consistent with electronic influences on an electron-deficient carbene species. However, poor site selectivity can be a major drawback when using these catalysts.⁶⁶

Synthesis of Lactones by C–H Insertion

The synthesis of lactones by catalytic, asymmetric, intramolecular C–H insertion performed with diazoacetates generally occurs with high enantiocontrol.^{6,7,13,18,19,31,32,156} However, diazoacetoacetates and diazomalonates give lower enantioselectivities.^{135,143,256,257} In the absence of steric or electronic constraints, γ -lactones are formed exclusively or predominantly. β -Lactone formation, which is facilitated by the electronic influence of the ester oxygen, is more common than is δ -lactone formation.

Monocyclic γ -Butyrolactones. 2-Methoxyethyl diazoacetate (**55**) (Eq. 25)^{242,258} undergoes C–H insertion to give the lactone product in good yield and high enantiomeric excess with dirhodium carboxamidate catalysts **31–38**. Increasing the size of the alkoxy group lowers the enantioselectivity slightly, and steric crowding near the site of insertion does so dramatically. A more typical example is the reaction of 3-substituted-1-propyl diazoacetates²⁵⁹ in which the advantage of chiral imidazolidinone-ligated $\text{Rh}_2(\text{MPPIM})_4$ (**35b** and **36b**) catalysts relative to other chiral carboxamidate-derived dirhodium catalysts is demonstrated.



These catalysts were also applied to the synthesis of lignan lactones (**56**)²⁵⁹ and (*S*)-(+)-imperanene (**57**)²⁶⁰ (Fig. 7). The imidazolidinone-based complexes **35a,b** and **36a,b** are the optimal catalysts for lactone formation, providing the highest levels of enantioselectivity. Without exception, the (*R*)-configured catalyst gives the (*R*)-configured product, and the (*S*)-configured catalyst gives the (*S*)-configured product. The amount of catalyst employed is 0.5 to 1.0 mol %, and yields of C–H insertion products are in the range of 55–80%.

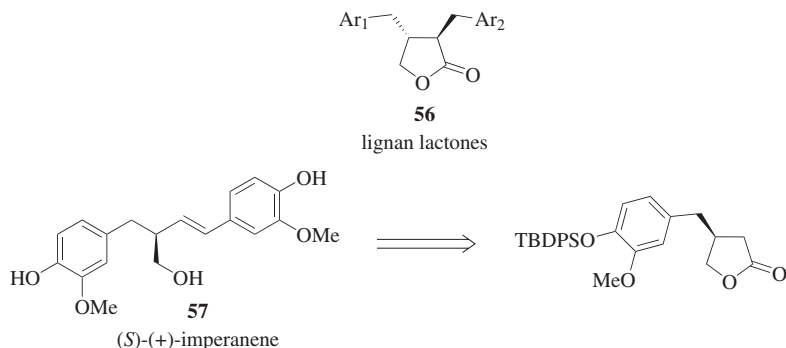
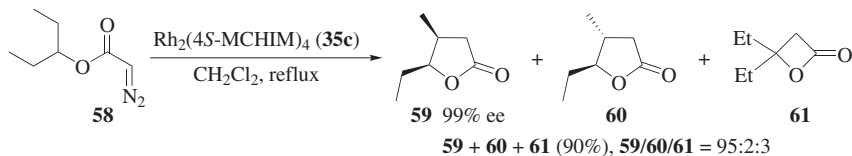


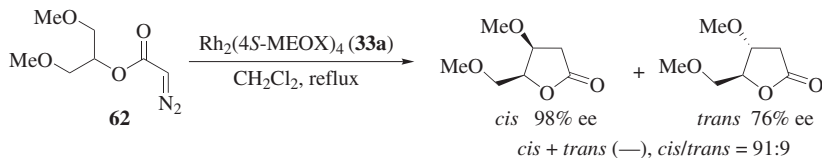
Figure 7. Lignan lactones and (S)-(+)-imperanene.

Desymmetrization of secondary alkyl diazoacetates (Eq. 26)¹⁵² is an efficient strategy to access disubstituted γ -lactones with excellent diastereo- and enantioselectivities. Catalytic diazo decomposition reactions of 3-pentyl diazoacetate (**58**) produce three isomers, the two γ -lactone diastereomers **59** and **60**, and β -lactone **61** (arising from carbene insertion into the ether-oxygen-activated methine C–H bond). Of the catalysts examined, Rh₂(4*S*-MCHIM)₄ (**35c**) gives the highest diastereocontrol and provides the *cis*-disubstituted γ -lactone **59** in 99% ee.

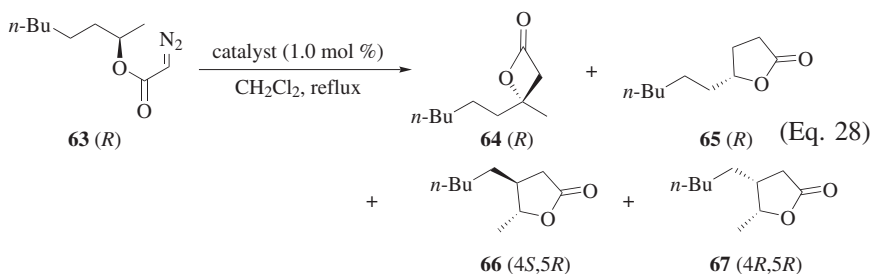


(Eq. 26)

Desymmetrization of 1,3-methoxy-2-propyl diazoacetate (**62**) is applied to the synthesis of deoxyxylolactone derivatives in high yield and with excellent enantio- and stereoselectivity favoring the *cis* isomer (Eq. 27).^{153,154} Reactions of (*R*)-2-octyl diazoacetate (**63**) show match/mismatch catalyst influences with chiral dirhodium carboxamidates (Eq. 28).¹³⁴ The β -lactone product **64** resulting from the mismatch of catalyst and diazoacetate configurations is dominant among the products **64**–**67**.

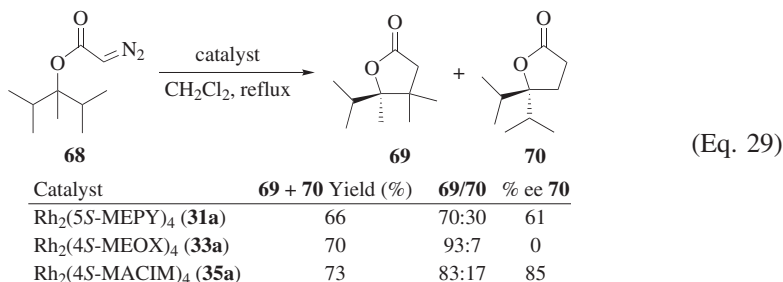


(Eq. 27)

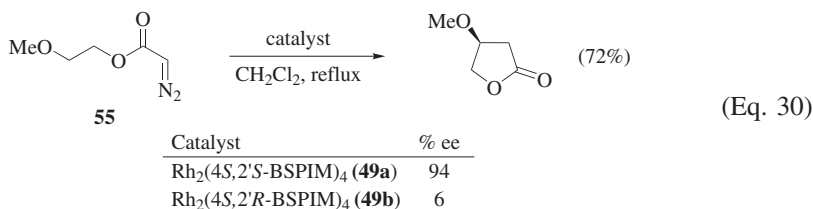


Catalyst	64–67 Yield (%)	64/65/66/67
Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	59	66:14:14:6
Rh ₂ (5 <i>R</i> -MEPY) ₄ (32a)	53	43:1:14:42
Rh ₂ (4 <i>S</i> -MEOX) ₄ (33a)	59	83:10:4:3
Rh ₂ (4 <i>R</i> -MEOX) ₄ (34a)	71	57:2:12:29

With tertiary diazoacetates, such as **68**, where access to a methyl group as well as to a secondary or tertiary C–H bond for insertion is possible, site selectivity becomes an issue.²⁶¹ Not enough data are available to allow the derivation of general rules on such selectivity (Eq. 29).²⁵⁸ Chiral catalysts developed after 1995 (e.g. **35b** and **37**) have not yet been applied to these more complex substrates.

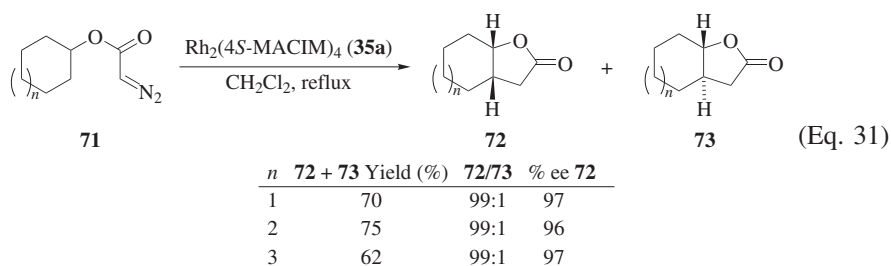


Significant match/mismatch effects on enantioselectivity are often observed in the C–H insertion reactions: substrate **55**, already illustrated in Eq. 25, provides a dramatic example (Eq. 30).²⁴⁴

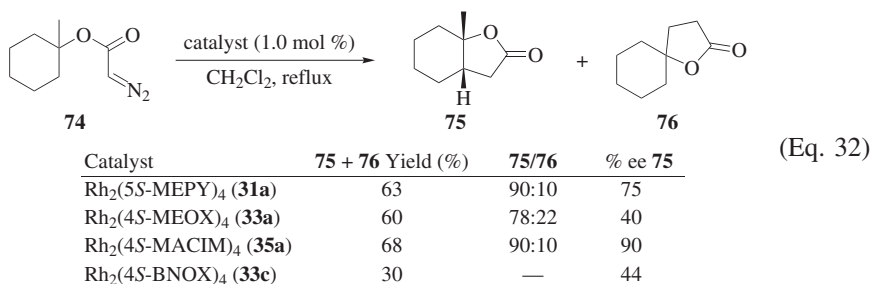


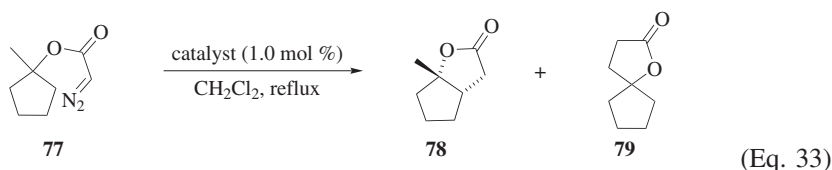
Bicyclic γ -Butyrolactones. Chiral dirhodium(II) carboxamidates exhibit exceptional enantio- and diastereoselectivities for C–H insertion reactions of

cycloalkyl diazoacetates. Cycloalkyl diazoacetates **71** ($n = 1 - 3$) have been used extensively to evaluate diastereo- and enantioselectivities provided by dirhodium catalysts (Eq. 31).^{155,242–244,251,262–264} With the exception of the reactions with cyclopentyl diazoacetate, the catalysts $\text{Rh}_2(4S\text{-MEOX})_4$ (**33a**) and $\text{Rh}_2(5S\text{-MEPY})_4$ (**31a**) show high enantioselectivities, but the lactone products are formed with low diastereoselectivity.^{155,243} Only with the imidazolidinone-ligated catalyst $\text{Rh}_2(4S\text{-MACIM})_4$ (**35a**) were high diastereo- and enantioselectivities first achieved,²⁴³ as illustrated by the predominance of lactone **72** over its isomer **73**. A later report shows that $\text{Rh}_2(4S\text{-MPPIM})_4$ (**35b**) provides comparable or, in some cases, even higher selectivities.²⁴⁴



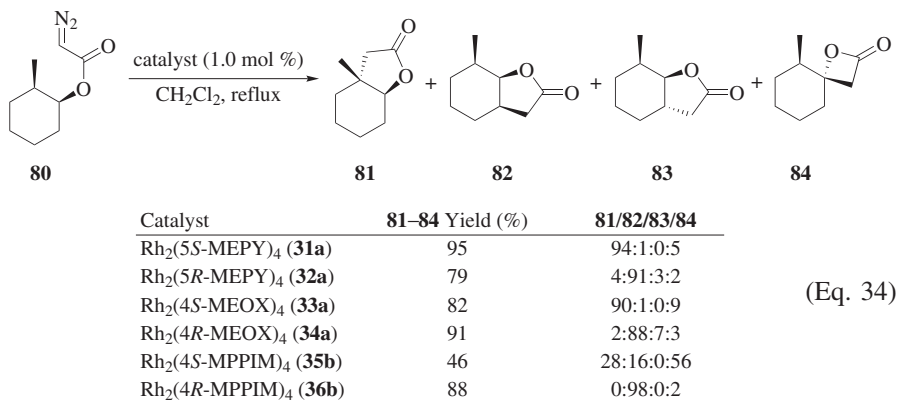
Intramolecular C–H insertion reactions of diazoacetates from cyclic, tertiary alcohols produce bicyclic lactones with lower enantioselectivities than corresponding reactions with their secondary counterparts.²⁶¹ Also, insertion into a methyl C–H bond is competitive with insertion into a secondary C–H bond. Reactions of 1-methylcyclohexyl diazoacetate (**74**) and 1-methylcyclopentyl diazoacetate (**77**) exhibit slightly higher site selectivities with $\text{Rh}_2(4S\text{-MACIM})_4$ (**35a**) and $\text{Rh}_2(5S\text{-MEPY})_4$ (**31a**) than with the more open $\text{Rh}_2(4S\text{-MEOX})_4$ (**33a**) (Eqs. 32 and 33),²⁶⁵ as determined from the ratios of the bicyclic γ -lactone products **75** and **78** to the spiro-products **76** and **79**.



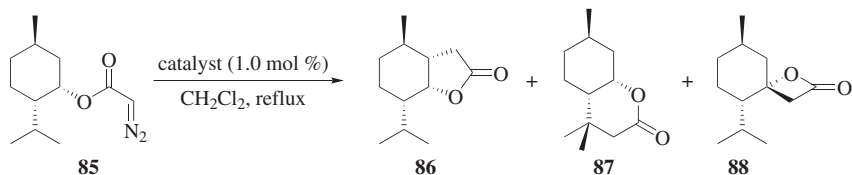


Catalyst	78 + 79 Yield (%)	78/79	% ee 78
Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	52	94:6	36
Rh ₂ (4 <i>S</i> -MEOX) ₄ (33a)	61	83:17	33
Rh ₂ (4 <i>S</i> -MACIM) ₄ (35a)	56	90:10	85
Rh ₂ (4 <i>S</i> -BNOX) ₄ (33c)	17	—	1

Selectivity in C–H insertion reactions of chiral, non-racemic diazoacetates can be maximized using chiral catalysts, and is highly dependent upon the absolute configuration of the catalyst that is used. An excellent example of a match/mismatch effect is provided by the reactions of enantiomerically pure (1*S*,2*R*)-*cis*-2-methylcyclohexyl diazoacetate (**80**) and its enantiomer (1*R*,2*S*)-*cis*-2-methylcyclohexyl diazoacetate catalyzed by each enantiomer of Rh₂(MEPY)₄ (**31a** and **32a**), Rh₂(MEOX)₄ (**33a** and **34a**), and Rh₂(MPPIM)₄ (**35b** and **36b**) species (Eq. 34).¹³⁴ With Rh₂(4*S*-MPPIM)₄ (**35b**), for example, low site selectivity is obtained, and the low yield (46%) suggests severe constraints to C–H insertion. Of the four insertion products **81**–**84**, three are obtained in appreciable amounts. In contrast, with Rh₂(4*R*-MPPIM)₄ (**36b**) C–H insertion of enantiomer **80** provides exceptionally high site selectivity and diastereoselectivity; product **82** is formed almost exclusively. The outcome from reactions of enantiomer **80** with the more open Rh₂(MEOX)₄ catalysts is different: the “mismatched” (4*S*)-catalyst (**33a**) forms product **81** with very high selectivity whereas the “matched” (4*R*)-catalyst (**34a**) forms products **82** and **83** with high site selectivity but, typical for this catalyst, only fair diastereoselectivity (~12:1). Similar results are obtained with the Rh₂(MEPY)₄ catalysts, and mirror image results are obtained with (1*R*,2*S*)-*cis*-2-methylcyclohexyl diazoacetate (*ent*-**80**) with each set of catalysts. The formation of β-lactone **84** is particularly illustrative of the configurational mismatch between catalyst and substrate;



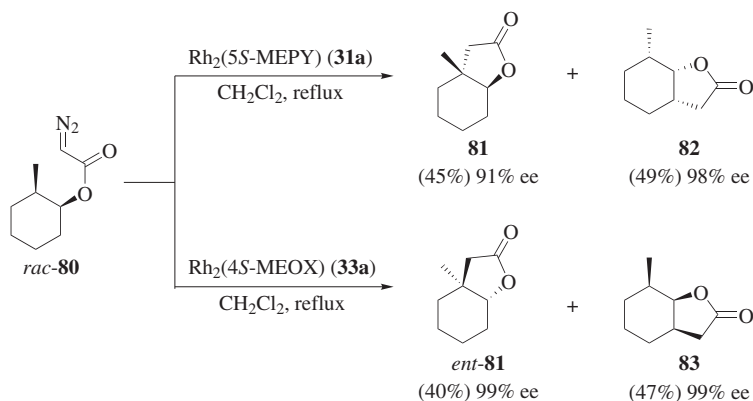
however, β -lactone formation is only rarely observed with diazoacetates.^{40,135,143} The insertion products **86–88** resulting from reactions with the single enantiomer of D-(+)-menthyl diazoacetate **85** also show match/mismatch influences with enantiomeric sets of chiral dirhodium carboxamidate catalysts (Eq. 35).¹³⁴



Catalyst	86–87 Yield (%)	86/87/88
$\text{Rh}_2(5S\text{-MEPY})_4$ (31a)	65	52:45:3
$\text{Rh}_2(5R\text{-MEPY})_4$ (32a)	75	89:11:0
$\text{Rh}_2(4S\text{-MEOX})_4$ (33a)	77	28:39:33
$\text{Rh}_2(4R\text{-MEOX})_4$ (34a)	97	98:2:0

(Eq. 35)

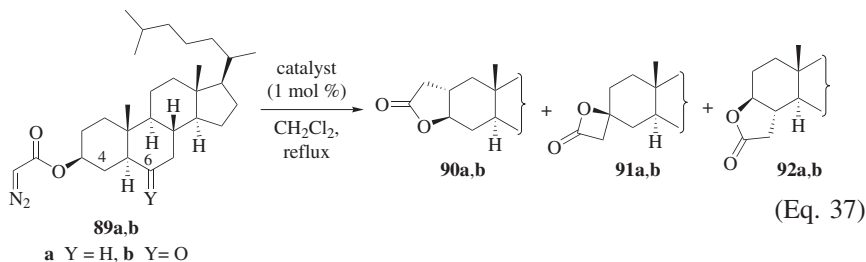
The high degree of control that catalyst configuration has over product distribution of chiral diazoacetates is further illustrated by the kinetic resolution of racemic mixtures of methyl-substituted cyclohexyl diazoacetates.¹³⁴ Results obtained with *rac-cis*-2-methylcyclohexyl diazoacetate (**80**) confirm that $\text{Rh}_2(5S\text{-MEPY})_4$ (**31a**) directs intramolecular C–H insertion of the (1*S*,2*R*)-enantiomer to **81** (91% ee, 45% yield) and the (1*R*,2*S*)-enantiomer to **82** (98% ee, 49% yield) with high selectivity (Eq. 36).²⁶⁶ With catalyst $\text{Rh}_2(4S\text{-MEOX})_4$ (**33a**) *rac-cis*-2-methylcyclohexyl diazoacetate produces instead the (1*R*,2*S*) enantiomer *ent*-**81** whereas the (1*S*,2*R*) enantiomer produces **83** (Eq. 36).



(Eq. 36)

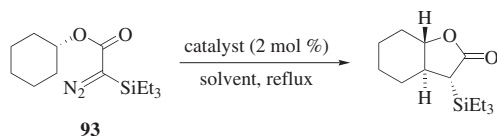
Steroidal Lactones. The conformationally rigid 5 α -cholestan-3 β -yl diazoacetate (**89a**) and 6-keto-5 α -cholestan-3 β -yl diazoacetate (**89b**) undergo catalyst-controlled, intramolecular C–H insertion reactions that are markedly dependent on ligand structure and configuration (Eq. 37).¹³⁵ The (*R*)-configured ligands on dirhodium(II) favor attack at the equatorial C–H bond of the 2-position of the

steroid to give **90a** and much less at the equatorial C–H bond of the 4-position to give **92a**; formation of β -lactone **91a** is a competing process but not the major reaction pathway. In contrast, lactone **91b** is a more significant product in reactions catalyzed by dirhodium carboxamidate catalysts whose ligands are in the (*S*)-configuration. The presence of a keto group in the 6-position of the steroid skeleton prevents C–H insertion at the 4-position.



Y	Catalyst	90–92 Yield (%)	90/91/92
H	Rh ₂ (5 <i>R</i> -MEPY) ₄ (32a)	89	72:20:8
H	Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	87	6:62:32
H	Rh ₂ (4 <i>R</i> -MEOX) ₄ (34a)	86	60:33:7
H	Rh ₂ (4 <i>S</i> -MEOX) ₄ (33a)	91	4:70:26
O	Rh ₂ (5 <i>R</i> -MEPY) ₄ (32a)	85	61:39:0
O	Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	76	8:92:0
O	Rh ₂ (4 <i>R</i> -MEOX) ₄ (34a)	88	43:57:0
O	Rh ₂ (4 <i>S</i> -MEOX) ₄ (33a)	90	3:97:0

Silylated γ -Butyrolactones. α -Silylated 1,4-lactones are produced in good yield and with moderate enantiocontrol when cyclohexyl diazo(triethylsilyl) acetates undergo diazo decomposition, and the highest enantioselectivities are achieved in reactions catalyzed by the modified imido-acid ligated Rh₂(*S*-NTTL)₄ (**41**) and similar chiral dirhodium(II) carboxylate catalysts (Eq. 38).²⁵⁶ In contrast with diazoacetates without the silyl group, only insertion into the equatorial C–H bond is observed. The chiral dirhodium(II) carboxamidate catalysts are much less reactive toward C–H insertion with substrate **93** compared to dirhodium(II) carboxylate catalysts. Chiral prolinates-ligated complexes are also reactive, but provide low enantioselectivities. The chiral BINOL–phosphate ligated complexes Rh₂(BNP)₄ (**42** and its enantiomer) give only modest enantioselectivities. Diastereoselectivity is appreciably lower with the trimethylsilyl or triisopropylsilyl groups in place of triethylsilyl in substrate **93**.

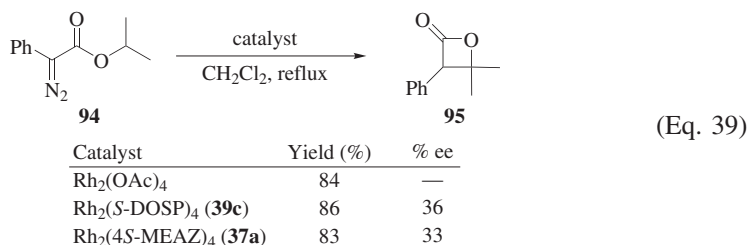


Catalyst	Solvent	Yield (%)	% ee
Rh ₂ (OAc) ₄	C ₆ H ₆	61	—
Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	C ₆ H ₆	16	0
Rh ₂ (<i>S</i> -NTTL) ₄ (41)	CH ₂ Cl ₂	87	56
Rh ₂ (<i>S</i> -BNP) ₄ (42)	C ₆ H ₆	30	40

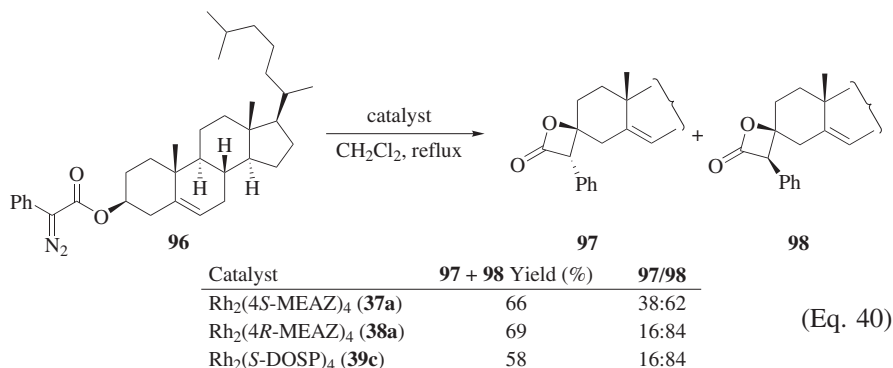
(Eq. 38)

β -Lactones. As is readily apparent from the examples discussed thus far, γ -lactones are nearly always the exclusive C–H insertion products of alkyl diazoacetates. β -Lactones are often minor products, and they are typically not reported. The exception is in C–H insertion reactions of 2-octyl diazoacetate, from which the corresponding β -lactone is the major product (see Eq. 28). When a substantial conformational bias exists, monosubstituted diazoacetates form β -lactones.^{134,135,266} The utility of β -lactones in the synthesis of natural products and biologically active compounds makes them appealing targets.^{268–271}

Alkyl phenyldiazoacetates produce β -lactones as the dominant or sole intramolecular C–H insertion products (Eq. 39).¹⁴³ Catalytic, intramolecular cyclization of isopropyl 2-diazo-2-phenylacetate (**94**) occurs by insertion into the methine C–H bond to yield β -lactone **95** with the γ -lactone arising from insertion into the methyl C–H bond as only a trace component, irrespective of the catalyst used. Enantioselectivities, however, are low (<40% ee). Note that the pyrrolidinone-, oxazolidinone-, or imidazolidinone-ligated dirhodium(II) carboxamate catalysts (**31–36**) are relatively unreactive toward diazo decomposition of phenyldiazoacetates.

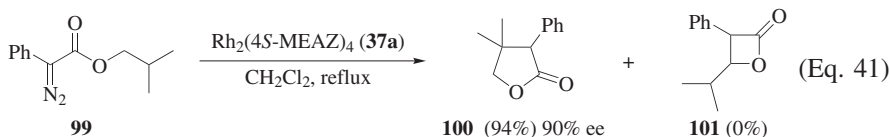


Diastereoselectivities in β -lactone formation are modest in insertion reactions of chiral, non-racemic alkyl phenyldiazoacetates catalyzed by chiral dirhodium carboxamides,^{135,143} which exhibit matched/mismatched configurational effects as evidenced by the ratios of products **97** and **98** from steroid **96** (Eq. 40).



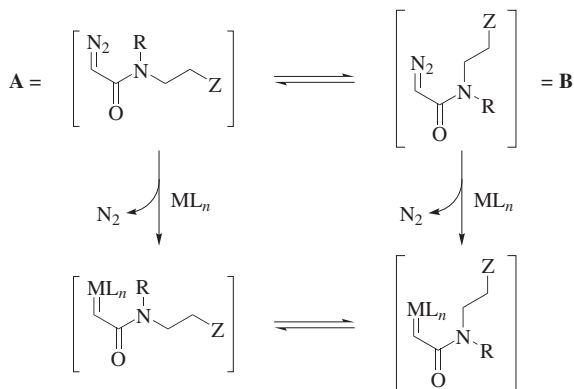
In the phenyldiazoacetate systems that produce β -lactones, the methine C–H bond undergoing insertion^{135,143} is electronically, but not sterically, more predisposed toward insertion than the neighboring methylene and methyl C–H bonds,

leading to γ -lactones.^{120,272} The cyclization of substrate **99**, therefore, provides an interesting test on the limitations of β -lactone formation (Eq. 41).¹⁴³ To form a β -lactone in this case, insertion must occur into an oxygen-activated methylene rather than into an alkyl-group-activated methine C–H bond. Insertion occurs into the methine C–H to provide γ -lactone **100** to the exclusion of β -lactone **101**. This example suggests that β -lactone formation is suppressed if highly activated γ -C–H bonds are available.



Synthesis of Lactams by C–H Insertion

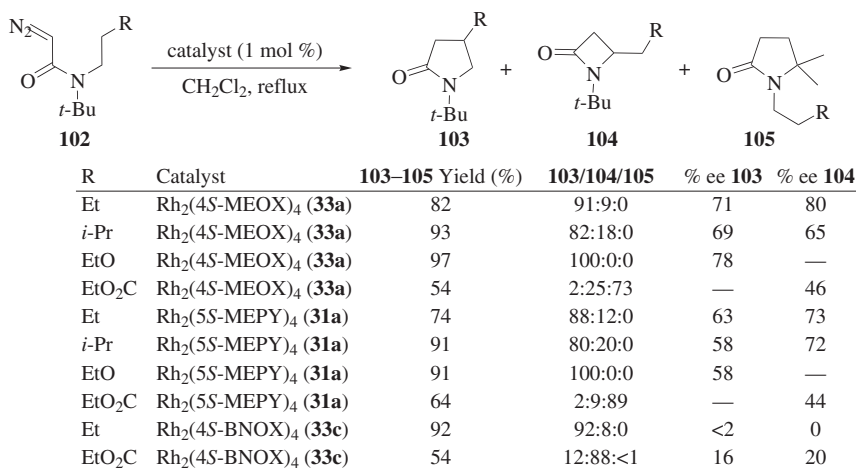
Lactams are obtained by the cyclization of metallo-carbenes generated from diazoacetamides, diazoacetoacetamides, and other functionalized diazoacetamides.⁹⁵ A wide range of carboxamidate- and carboxylate-ligated dirhodium complexes have been used to provide high stereoselectivities. Unlike the cyclization of diazoacetates to lactones, site selectivity in C–H insertion of diazoacetamides and diazoacetoacetamides is often complicated by the competition between the formation of β - and γ -lactams.^{95,273} Whereas diazoacetates almost always produce γ -lactones, the amide nitrogen of diazoacetamides and their substituted counterparts strongly activate the adjacent C–H bond toward carbene insertion, giving rise to β -lactams. A major determinant of the reactivity and selectivity differences between diazoacetates and diazoacetamides is the barrier to rotation around the carbonyl–nitrogen bond, which is 17–22 kcal/mol for amides but only 10–12 kcal/mol for the carbonyl group of esters.^{273a} Conformation **A** (Scheme 4) leads to an intermediate metallo-carbene in which the accessible C–H bond is far removed from the carbene center. Only in conformation **B** are the carbene center and C–H bond favorably disposed for insertion.



Scheme 4

The predominant presence of conformer **A** in diazo compounds derived from secondary amides explains why C–H insertion reactions with this class ($R = H$) are not synthetically viable processes. To promote rotation, and therefore C–H insertion, the nitrogen atom is usually protected with a bulky alkyl group (see below).

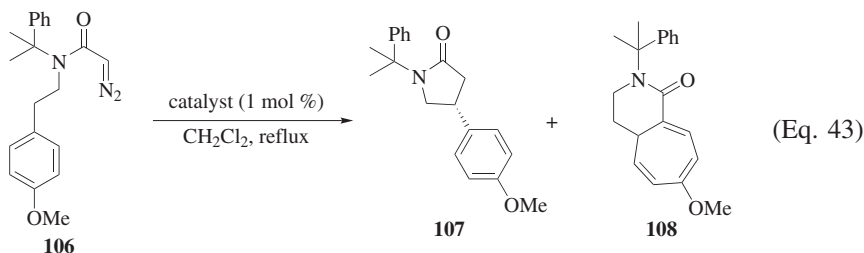
γ -Lactams and β -Lactams. The majority of asymmetric, intramolecular C–H insertion reactions of diazoacetamides use the dirhodium-carboxamidate-based catalysts **31–36**.^{138,274} Modest enantioselectivities are obtained in the cyclization of *N*-*tert*-butyldiazoacetamides **102** (Eq. 42).¹³⁸ γ -Lactam formation (product **103**) is favored over carbene insertion into the C–H bond adjacent to nitrogen leading to β -lactam **104** by the presence of alkyl substituents. When the substituent R is an ethyl ether, β -lactam **104** is not observed. The electron-withdrawing character of an ester ($R = CO_2Et$) significantly inhibits the C–H insertions that lead to γ -lactam **103** and β -lactam **104**. Instead, the predominant cyclization pathway is carbene insertion into a methyl C–H bond of the *tert*-butyl protecting group to yield γ -lactam **105**. However, the use of $Rh_2(4S\text{-BNOX})_4$ (**33c**) as the catalyst nearly completely blocks this side reaction, presumably because of the influence of the benzyl group of **33c** on regioselectivity. The *tert*-butyl protecting group is widely used because its methyl C–H bonds are generally unreactive toward carbene insertion,^{95,273} but, as exemplified by Eq. 42, insertion into the *tert*-butyl group can occur if the *N*-alkyl C–H bonds are sufficiently deactivated.



(Eq. 42)

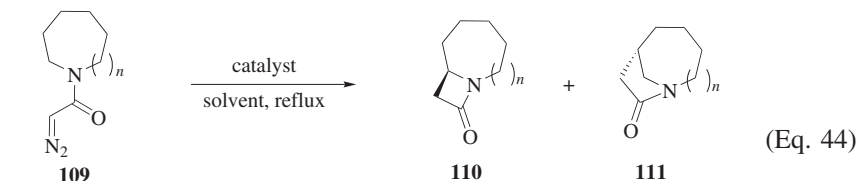
Direct catalytic C–H insertion of diazoacetamide **106** using $Rh_2(4S\text{-MEOX})_4$ (**33a**) as the catalyst produces γ -lactam **107** with high chemoselectivity (Eq. 43) but only modest enantioselectivity.²⁷⁵ With other catalysts, including the more electrophilic chiral dirhodium carboxylates, formation of the product of carbene addition to the benzene ring (**108**) competes with C–H insertion; product yields

are low, and so is enantioselectivity. In this example, the *N*-cumyl group is found to be as effective as the *N*-*tert*-butyl group in establishing the amide conformation most suitable for C–H insertion, and this group can be more easily cleaved using trifluoroacetic acid.²⁷⁶ Solvent and temperature in Rh₂(4*S*-MEOX)₄-catalyzed reactions have negligible influence on yield and enantioselectivity.



Catalyst	107 + 108 Yield (%)	107/108	% ee 107
Rh ₂ (<i>S</i> -DOSP) ₄ (39c)	36	47:53	3
Rh ₂ (<i>S</i> -NTTL) ₄ (41)	25	58:42	2
Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	53	87:13	18
Rh ₂ (4 <i>S</i> -MEOX) ₄ (33a)	72	>98:2	47

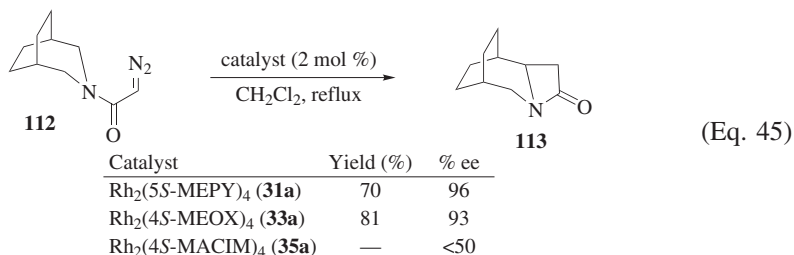
The seven-membered-ring diazoacetamide **109a** undergoes intramolecular C–H insertion with excellent stereo- and site selectivity to provide β-lactam **110a** in 97% ee using the catalyst Rh₂(5*S*-MEPY)₄ (**31a**, Eq. 44).²⁷⁷ β-Lactam formation in diazo decomposition reactions of the eight-membered-ring diazoacetamide **109b** does not occur with high site selectivity, yielding both β- and γ-lactams in ratios that vary with both catalyst and temperature. Results from reactions in refluxing dichloromethane versus 1,2-dichloroethane show increased site selectivity for product **110** at higher temperature, which probably reflects higher conformational freedom. γ-Lactam **111b** is formed with an exceptionally high level of enantiocontrol.



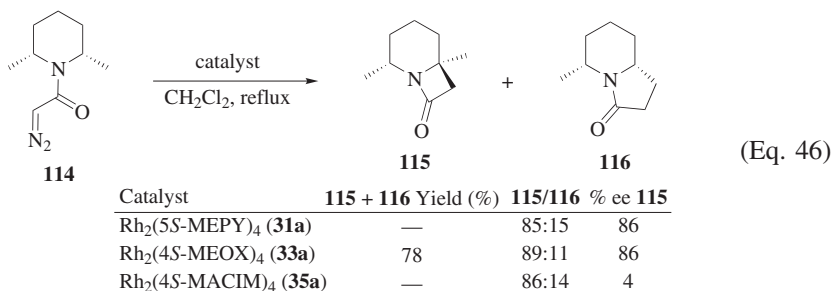
a *n* = 1, **b** *n* = 2

<i>n</i>	Solvent	Catalyst	110 + 111 Yield (%)	110/111	% ee 110	% ee 111
1	CH ₂ Cl ₂	Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	67	>99:1	97	—
1	C ₂ H ₄ Cl ₂	Rh ₂ (4 <i>S</i> -MEOX) ₄ (33a)	68	99:1	92	—
2	CH ₂ Cl ₂	Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	77	40:60	31	97
2	C ₂ H ₄ Cl ₂	Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	67	67:33	30	96
2	CH ₂ Cl ₂	Rh ₂ (4 <i>S</i> -MEOX) ₄ (33a)	95	26:74	15	98
2	C ₂ H ₄ Cl ₂	Rh ₂ (4 <i>S</i> -MEOX) ₄ (33a)	68	49:51	8	96
2	C ₂ H ₄ Cl ₂	Rh ₂ (4 <i>S</i> -MACIM) ₄ (35a)	81	39:61	66 <i>ent</i> - 110	96

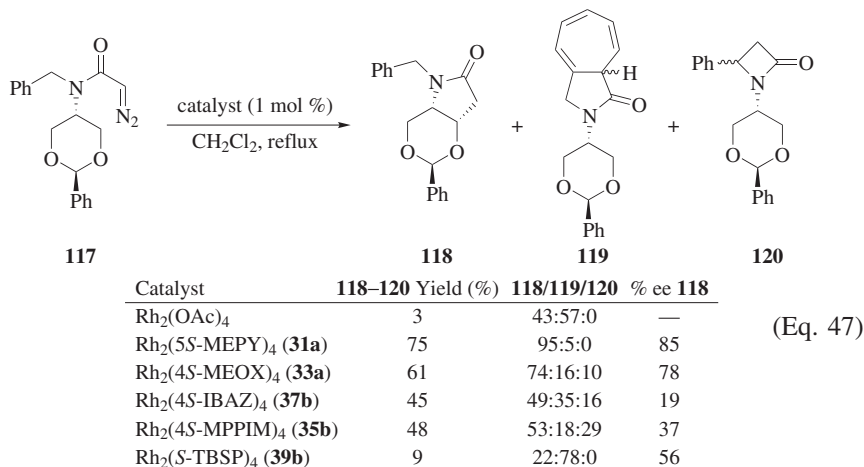
The bicyclic 3-diazoacetyl-3-azabicyclo[3.2.2]nonane (**112**) undergoes C–H insertion to give the β -lactam **113** as the sole insertion product (Eq. 45).²⁷⁷



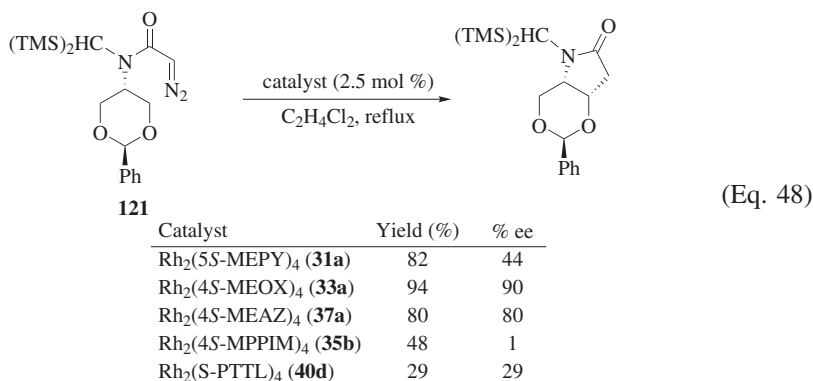
Although 2,6-unsubstituted piperidines do not undergo C–H insertion, the desymmetrization of *cis*-2,6-dimethylpiperidine (**114**) provides the lactams **115** and **116** in good yields (Eq. 46).²⁷⁷ Insertion into the methine C–H bond to form the β -lactam **115** is favored by a factor of $\sim$ 8:1 over the γ -lactam **116**. In addition to the electronic factors favoring β -lactam formation—nitrogen activation of the adjacent C–H bond toward carbene insertion and preference for insertion into a methine over a methyl C–H bond—conformational factors also favor the formation of β -lactam **115**; the methyl substituents of substrate **114** likely occupy axial positions, which are not easily accessible to the metal-stabilized carbene.



Desymmetrization has also been successfully accomplished in C–H insertion reactions of 1,3-dioxan-5-yl diazoacetamide **117** bearing an *N*-benzyl group (Eq. 47).²⁷⁸ In this case C–H insertion into a benzylic C–H bond (product **120**) and cyclization on the aryl group (product **119**) compete with the desired C–H insertion into the oxygen-activated C–H bond of the 1,3-dioxanyl ring (product **118**). The outcome of the dinitrogen extrusion performed with diazoacetamide **117** in refluxing dichloromethane is highly dependent on the catalyst used, and Rh₂(5*S*-MEPY)₄ (**31a**) provides the highest overall selectivities. Reactions performed in refluxing 1,2-dichloroethane are less site-selective. Carboxylate-ligated dirhodium catalysts (e.g. **39b**) favor aromatic substitution over C–H insertion in this case.

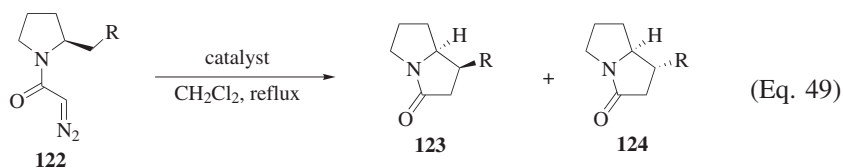


The use of the bis(trimethylsilyl)methyl group (BTMSM) to protect the nitrogen in diazo decomposition reactions of diazoacetamides^{279,280} prevents the formation of byproducts that normally occur on the protective groups for nitrogen. Application to 1,3-dioxan-5-yl diazoacetamide **121** (an analog of **117**) gives the γ -butyrolactam C–H insertion product exclusively and in high yield (Eq. 48).²⁸¹ Although an incorrect rationale was provided for the stereoselectivities observed with enantiomeric catalysts due to impurities in the catalysts,²⁸² the influence of chiral carboxamidate-ligated catalysts is particularly revealing. The facts that Rh₂(MPPIM)₄ (**35b**) exerts no apparent enantiocontrol on reactions conducted in refluxing 1,2-dichloroethane, and that no reaction occurs in refluxing dichloromethane, suggest that a size limit exists in the operation of chiral carboxamidate-ligated dirhodium catalysts. The lack of selectivity in this C–H insertion may be due to reaction of a free carbene rather than a metallo-carbene.



High levels of diastereocontrol have been observed in reactions of chiral diazoacetamides with chiral catalysts. The chiral, non-racemic, proline-derived

diazoacetamide **122** undergoes C–H insertion with low diastereocontrol when achiral catalysts such as $\text{Rh}_2(\text{OAc})_4$ are used. However, use of chiral dirhodium-carboxamidate catalysts provides lactam **123** in excellent yield and selectivity (Eq. 49);²⁸³ β -lactam formation is not observed. Configurational match/mismatch is seen with the use of the two $\text{Rh}_2(\text{MEPY})_4$ (**31a** and **32a**) enantiomers. Of particular significance in these examples is the high level of diastereoselectivity that favors the formation of lactam **123** over its configurationally more stable isomer **124**.



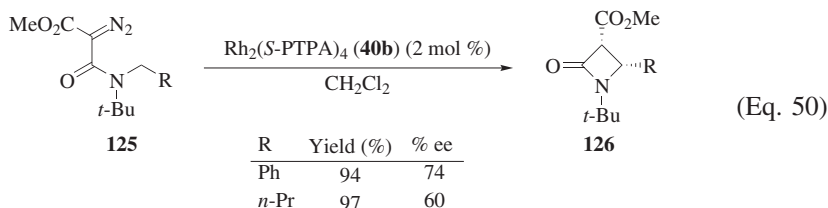
R	Catalyst	122 + 123 Yield (%)	123/124
MeO	$\text{Rh}_2(\text{OAc})_4$	45	53:47
MeO	$\text{Rh}_2(\text{cap})_4$	45	63:37
MeO	$\text{Cu}(\text{OTf})$	55	38:62
MeO	$\text{Rh}_2(5S\text{-MEPY})_4$ (31a)	95	90:10
MeO	$\text{Rh}_2(5R\text{-MEPY})_4$ (32a)	96	73:27
MeO	$\text{Rh}_2(4S\text{-MEOX})_4$ (33a)	99	89:11
MeO	$\text{Rh}_2(4S\text{-MACIM})_4$ (35a)	88	97:3
MeO	$\text{Rh}_2(4S\text{-MPPIM})_4$ (35b)	97	96:4
BnO	$\text{Rh}_2(\text{OAc})_4$	41	49:35 ^a
BnO	$\text{Rh}_2(\text{cap})_4$	27	33:23 ^a
BnO	$\text{Cu}(\text{OTf})$	—	—
BnO	$\text{Rh}_2(5S\text{-MEPY})_4$ (31a)	81	90:9
BnO	$\text{Rh}_2(5R\text{-MEPY})_4$ (32a)	87	55:36 ^a
BnO	$\text{Rh}_2(4S\text{-MEOX})_4$ (33a)	90	89:11
BnO	$\text{Rh}_2(4S\text{-MACIM})_4$ (35a)	94	97:3
BnO	$\text{Rh}_2(4S\text{-MPPIM})_4$ (35b)	93	96:4

^a Deviation from a 100% mass balance is due to formation of the product from C–H insertion at the benzyl carbon.

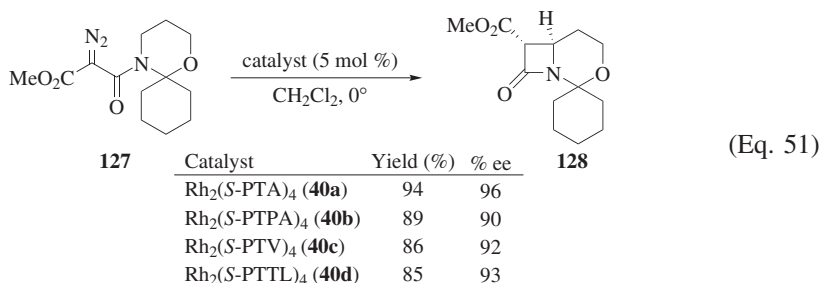
The *N*-phthaloyl-amino-acid-ligated dirhodium catalysts (**40** and **41**) are the most commonly used chiral catalysts in reactions of diazoacetoacetamides.^{249,250} These kinetically active carboxylate-based complexes are required for the efficient dinitrogen extrusion and generation of metallo-carbenes from diazoacetoacetamides, which have the diazo functionality highly stabilized by two adjacent electron-withdrawing groups. Due to their significantly lower reactivity towards dinitrogen extrusion, all dirhodium carboxamidates with the exception of those with azetidinone ligands (**37**) are ineffective with this class of diazo compounds. However, few cyclizations of diazoacetoacetamides using *N*-phthaloyl-amino-acid-ligated dirhodium catalysts have been reported to proceed with high enantioselectivities. The site selectivity of C–H insertion leading to the formation of

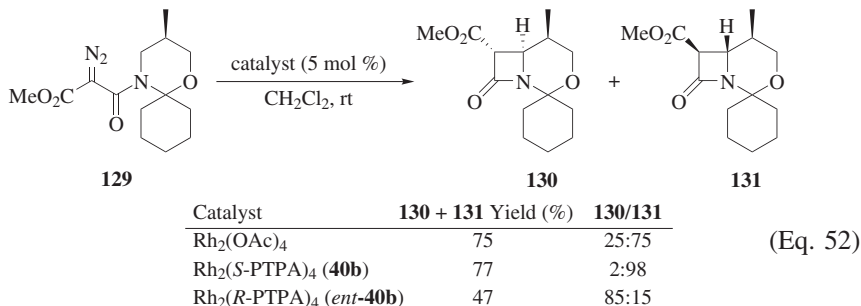
β - or γ -lactams is substrate dependent, so either lactam may be formed. Selectivity is often achieved by using substrates in which the β - or γ -position is biased toward insertion as a result of electronic or conformational effects.

As with diazoacetamides, a typical choice of amide nitrogen protecting group for diazoacetoacetamides and diazomalonamides is the *tert*-butyl group, as its methyl C–H bonds rarely undergo carbene insertion. The cyclization of acetoacetamide **125** produces β -lactam **126** with a high degree of site selectivity, although enantioselectivities are modest (Eq. 50).^{64,249} The *N*-BTMSM group has also been used and gives the γ -lactam product, but enantioselectivities are modest to low.²⁸⁴ Aryl rings have also been employed as nitrogen protecting groups.^{250,273} Those with the *N*-4-nitrophenyl protecting group allow formation of γ -lactam products in good yields and with high diastereoselectivity.²⁸⁵ As an *N*-protecting group, the electron-deficient *N*-4-nitrophenyl does not react with the metal carbene to an appreciable degree and may be removed by a two-step protocol consisting of reduction to the corresponding aniline and oxidative hydrolysis. Electron-rich aryl groups are unsuitable protecting groups because they undergo aromatic cycloaddition.²⁷³ Enantioselectivities are highly variable; insertion into benzylic C–H bonds leads to higher enantioselectivity than insertion into alkyl C–H bonds, as shown in Eq. 50.



The highest levels of enantioselectivity in the C–H insertion reaction of diazoacetoacetamides occur with the reaction of *N,O*-acetals (e.g. Eq. 51).²⁸⁶ Several catalysts with *N*-phthaloyl- and *N*-phenyl-fused phthaloyl-(*S*)-amino acids as bridging ligands provide the β -lactam **128** from substrate **127** in 83–96% ee.^{286,287} With diazoacetoacetamide **129**, which has a methyl group positioned at the 5-position of a tetrahydro-1,3-oxazine ring, match/mismatch effects are seen with the $\text{Rh}_2(\text{PTPA})_4$ (e.g., **40b**) catalysts,²⁸⁸ whereas a natural selectivity toward the *syn* product **131** over the *anti* isomer **130** is seen in the absence of a chiral catalyst (Eq. 52).

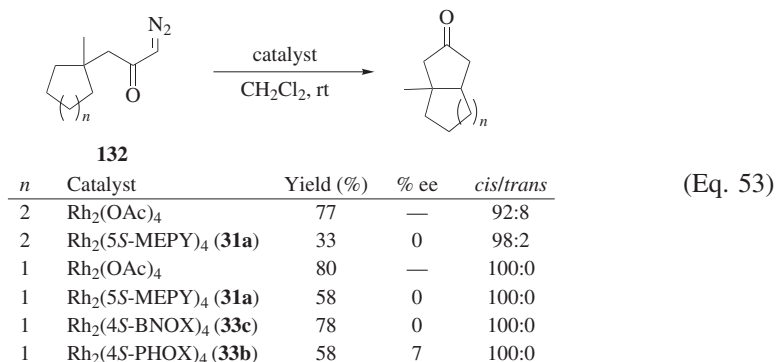




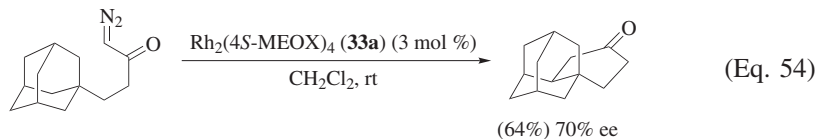
Synthesis of Cycloalkane Derivatives by C–H Insertion

In contrast to C–H insertion reactions using diazoacetates and diazoacetamides and their derivatives, only a few studies report asymmetric induction in reactions of diazoketones. This paucity is due in part to the relative difficulty of their synthesis.⁷¹ However, the principal reason is the low selectivity achieved in catalytic applications, except in special cases. The reactivity of diazoketones and diazoalkanoates toward dinitrogen extrusion are at least as good as those of diazoacetates,³² but catalysts that are effective for high stereocontrol with diazoacetates generally do not provide high stereocontrol in reactions with diazoketones and diazoalkanoates. This dichotomy was observed early and extensively in attempts to achieve enantio-controlled intramolecular cyclopropanation reactions.^{67,289,290} The cause of this considerable change in stereocontrol has been explained by conformational differences in the alignment of the keto carbene on the catalyst face.²⁹¹

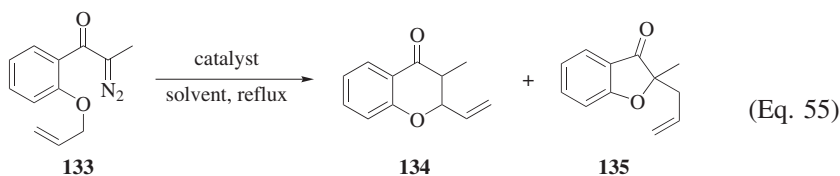
Cyclopentanones. Indicative of the challenges associated with C–H insertion reactions with diazoketones, 3-cycloalkyl-1-diazo-2-propanones **132** undergo C–H insertion catalyzed by dirhodium(II) complexes at room temperature producing the corresponding bicyclic compounds. Although good yields and diastereoselectivities are observed, very low or negligible enantioselectivities are obtained with chiral dirhodium carboxamidates (Eq. 53).¹⁵⁵ Low enantioselectivity is also evident in reactions catalyzed by chiral dirhodium carboxylates.²⁹² Hydride abstraction and subsequent ring closure is reported as a side reaction.²⁹³



Formation of cyclopentanones by intramolecular C–H insertion using chiral dirhodium carboxamidates is thus far poorly stereoselective, but formation of cyclohexanones can be rather enantioselective (Eq. 54).¹⁸³ In this example, only the $\text{Rh}_2(4S\text{-MEOX})_4$ (**33a**) catalyst is effective; the bicyclic cyclohexanone product is not formed when $\text{Rh}_2(\text{MEPY})_4$, $\text{Rh}_2(\text{MPPIM})_4$, or $\text{Rh}_2(\text{MEAZ})_4$ is used.



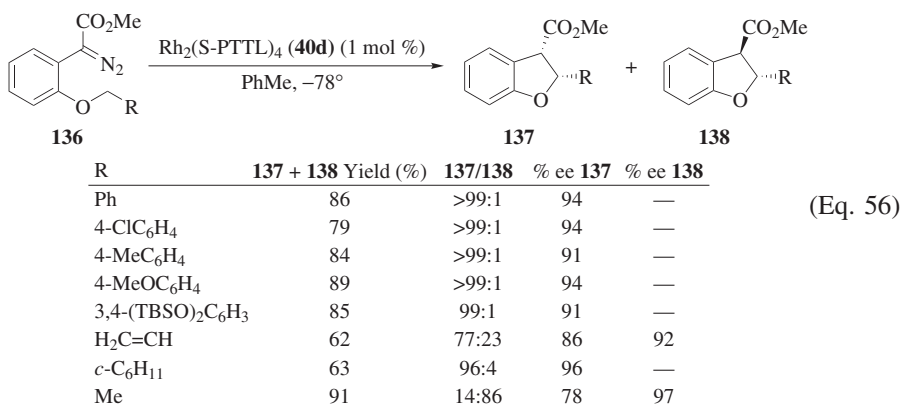
One of the first demonstrations of enantioselectivity in intramolecular C–H insertion reactions of diazoketones was with diazoketone **133** (Eq. 55).^{180,294} The β -hydride elimination reaction to give an α,β -unsaturated ketone (a common competing reaction)³² is not reported in this case, and yields are quantitative. Competition between C–H insertion yielding product **134** with ylide generation and [2,3]-sigmatropic rearrangement yielding product **135** is common and catalyst dependent.^{295–297} Many other examples of highly chemoselective catalytic C–H insertion reactions of diazoketones that have moderate to low enantioselectivities have been reported,^{148,298–304} and they often illustrate the unpredictability of these transformations.^{148,298}



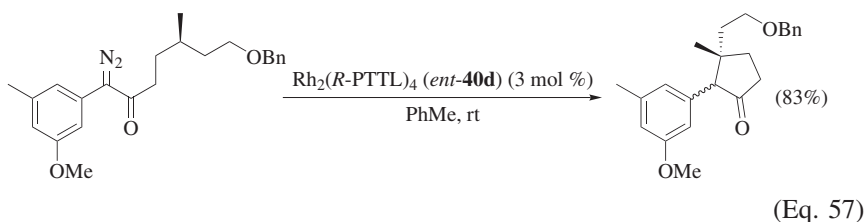
Catalyst	134 Yield (%)	135 Yield (%)	<i>cis</i> - 134 / <i>trans</i> - 134	% ee <i>cis</i> - 134	% ee <i>trans</i> - 134
$\text{Rh}_2(\text{OAc})_4$	93	7	74:26	—	0
$\text{Rh}_2(S\text{-BSP})_4$ (39a)	93	7	93:7	60	—
(39d)	96	4	85:15	31	18
(43)	96	4	83:17	10	7
(44)	82	18	75:25	20	—
(45)	97	3	92:8	40	—
(46)	90	10	92:8	8	—
$\text{Rh}_2(S\text{-mandelate})_4$ (47)	88	12	80:20	20	11
$\text{Rh}_2(5S\text{-MEPY})_4$ (31a)	96	4	74:26	0	0

2-Alkoxy-substituted methyl phenyldiazoacetates such as substrate **136** undergo highly enantioselective C–H insertion (Eq. 56).^{218,305–307} Diastereoselectivity is highest with chiral phthalimido dirhodium catalysts, and with catalyst $\text{Rh}_2(S\text{-PTAD})$ (**40e**) C–H insertion is a key step in the synthesis of the natural product (–)-ephedradine.³⁰⁵ Reactions performed at -78° with $\text{Rh}_2(S\text{-PTTL})_4$ (**40d**) occur with exceptionally high enantio- as well as diastereoselectivity, as

supported by the data for products **137** and **138**.²¹⁸

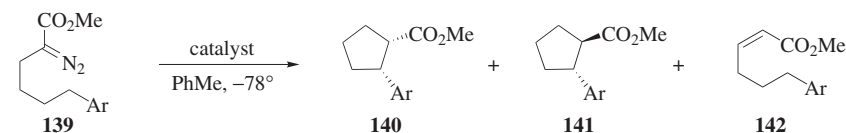


The C–H insertion reaction of diazoketones in which the diazo carbon lies between a carbonyl group and an aromatic ring illustrates the versatility of this method (Eq. 57).³⁰⁸ However, although this example illustrates the effects of match/mismatch between catalyst configuration and diastereoselectivity, the diastereomeric ratio is not reported and experiments using catalyst Rh₂(S-PTTL)₄ (**40d**) are not described.



Cyclopentanes. A suitably functionalized diazoester can give rise to cyclopentane derivatives. Very promising results are obtained using chiral dirhodium(II) phthaloyl-amino acid catalysts, as represented by the cyclization of aryl-substituted substrate **139** yielding products **140–142** (Eq. 58).³⁰⁹ These examples demonstrate not only high enantio- and diastereoselectivities, but also the suppression of a 1,2-hydrogen shift as a side reaction.³² An early report of intramolecular C–H insertion of a phenyldiazoacetate into a methylene group activated by adjacent nitrogen suggests that chiral copper-bisoxazolidine catalysts are more advantageous than Rh₂(5*S*-MEPY)₄ (**31a**) or Rh₂(S-TBSP)₄ (**39b**); but even with the former catalysts both diastereoselectivities and enantioselectivities are low,^{310,311} and an alternative process for introducing enantioselectivity was eventually employed.³¹² The catalyst Rh₂(S-PTTL)₄ (**40d**) affords high enantio- and diastereoselectivity in intramolecular C–H insertion reactions of

phenyldiazoacetates.²¹⁸

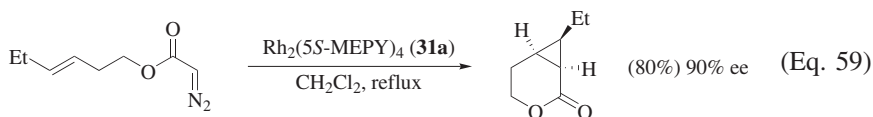


Ar	Catalyst	140–142 Yield (%)	140/141/142	% ee 140	% ee 141
Ph	Rh ₂ (<i>S</i> -PTTL) ₄ (40d)	85	>99:0:0	95	—
Ph	Rh ₂ (<i>S</i> -PTPA) ₄ (40b)	66	56:37:7	89	27
Ph	Rh ₂ (<i>S</i> -PTA) ₄ (40a)	69	73:19:8	90	56
Ph	Rh ₂ (<i>S</i> -PTV) ₄ (40c)	68	77:20:3	95	22
4-MeOC ₆ H ₄	Rh ₂ (<i>S</i> -PTTL) ₄ (40d)	85	>99:0:0	92	—
4-ClC ₆ H ₄	Rh ₂ (<i>S</i> -PTTL) ₄ (40d)	81	>99:0:0	93	—

(Eq. 58)

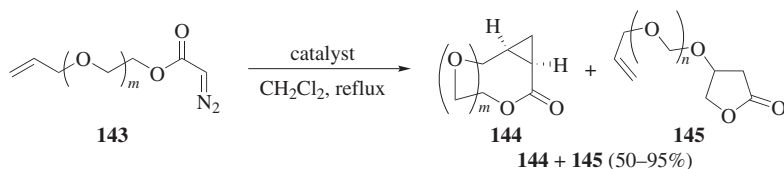
Side Reactions

The competition between intramolecular cyclopropanation and C–H insertion provides an instructive illustration of the effects of catalyst selection on chemoselectivity toward the C–H insertion processes in unsaturated substrates.³¹³ Allylic and homoallylic diazoacetates (Eq. 59) undergo intramolecular cyclopropanation in preference to C–H insertion,³¹⁴ and the enantioselectivities vary dramatically with the chiral catalyst employed.³¹³ In general, rhodium-carboxamidate-ligated complexes favor C–H insertion, whereas copper- and rhodium-carboxylate complexes favor cyclopropanation.



This trend also holds for diazo compounds having longer chains. With dirhodium carboxamidate catalysts substrates **143** undergo nearly exclusive C–H insertion to form γ -butyrolactones **145** with high enantioselectivity, whereas products of intramolecular cyclopropanation **144** are formed preferentially but with low enantioselectivity when more reactive dirhodium carboxylates and Cu(box)PF₆ are employed (Eq. 60).³¹³ That the competition between cyclopropanation and C–H insertion is related to the electronic ligand-controlled bias placed on the metal was first suggested by results from dirhodium catalysts having achiral ligands.^{137,142,316} Results obtained with Rh₂(4*S*-IBAZ)₄ (**37b**), which is electronically more reactive than the other dirhodium carboxamidates, support this interpretation. Preferential C–H insertion to form γ -butyrolactone products with high enantioselectivity is generally reported for chiral dirhodium carboxamidate-catalyzed reactions of diazo compounds that have remote, potentially reactive, functional groups.^{315,317–319} The only exceptions are found

when access to a γ -CH group is sterically prevented.^{320,321}



<i>m</i>	<i>n</i>	Catalyst	144/145	% ee 144
1	0	Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	<1:99	—
1	0	Rh ₂ (4 <i>S</i> -MEOX) ₄ (33a)	<1:99	—
1	0	Rh ₂ (4 <i>S</i> -MPPIM) ₄ (35b)	—	—
1	0	Rh ₂ (4 <i>S</i> -IBAZ) ₄ (37b)	5:95	49
1	0	Rh ₂ (<i>S</i> -TBSP) ₄ (39b)	95:5	28
1	0	Cu(box)PF ₄	—	71
2	1	Rh ₂ (5 <i>S</i> -MEPY) ₄ (31a)	5:95	53
2	1	Rh ₂ (4 <i>S</i> -MEOX) ₄ (33a)	1:99	48
2	1	Rh ₂ (4 <i>S</i> -MPPIM) ₄ (35b)	—	—
2	1	Rh ₂ (4 <i>S</i> -IBAZ) ₄ (37b)	42:58	56
2	1	Rh ₂ (<i>S</i> -TBSP) ₄ (39b)	98:2	11
2	1	Cu(box)PF ₄	100:0	79

(Eq. 60)

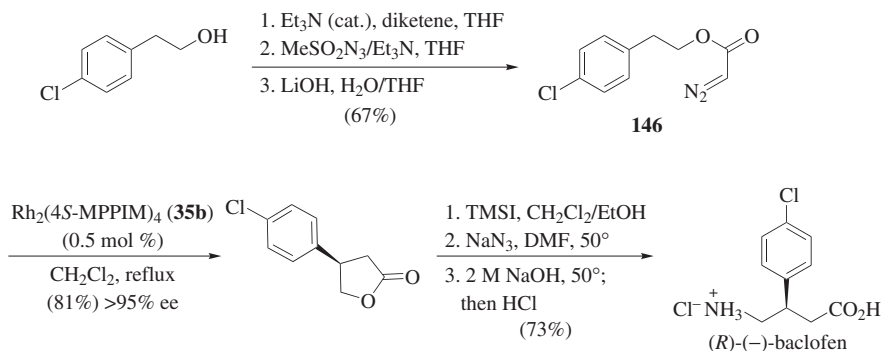
To minimize competing “carbene dimerization,” reactions of diazoacetates are commonly performed by slow, controlled addition of the diazoacetate to the catalyst solution.^{322–325} This competing reaction arises from electrophilic addition of the metal carbene to excess diazoacetate. Thus, limiting the concentration of the diazo compound decreases the rate of formation of the carbene dimer.³²² Maleate and fumarate “carbene dimer” products (RO₂C–CH=CH–CO₂R) can themselves undergo dipolar cycloaddition with the reactant diazoacetate, but these products are rarely identified. The formation of azines (RO₂C–CH=N–N=CH–CO₂R) in these reactions remains poorly understood, but the reaction pathway is not believed to be associated with the catalyst. These basic compounds coordinate with the catalyst and inhibit the reaction.³²²

As exemplified in Eq. 58 (product **142**), the 1,2-hydrogen shift is competitive with other metal carbene transformations of diazoalkanoates and similar diazoketones.^{32,326,327} This reaction is often significant except when hydrogen migration from a methyl group is involved. The catalyst influences the extent of this competing reaction, but its complete suppression has rarely been reported.^{309,326}

APPLICATIONS TO SYNTHESIS

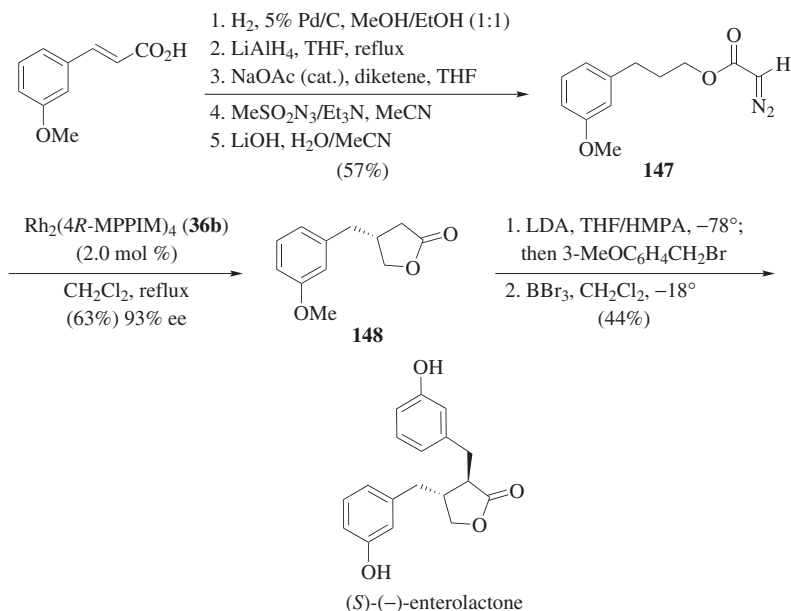
Examples of biologically active compounds that have been prepared in greater than 90% ee by intramolecular C–H insertion include lignan lactones (see Scheme 9 in “Comparison with Other Methods”)^{259,260} and the 2-deoxyxylolactone **25** (Eq. 12).^{153,154} The reaction of 2-(4-chlorophenyl)ethyl diazoacetate (**146**) with only 0.5 mol % Rh₂(4*S*-MPPIM)₄ (**35b**) results in insertion into the benzylic C–H

bond in 81% yield and 95% ee (Scheme 5). This reaction was applied to the synthesis of (*R*)-(-)-baclofen, a therapeutically effective GABA receptor agonist.³²⁸ The related 2-phenyl-1-ethyl diazoacetate gives the corresponding lactone in 42% yield and 46% ee with $\text{Rh}_2(5S\text{-MEPY})_4$ (**31a**) as catalyst.²⁵⁸ The $\text{Rh}_2(\text{MPPIM})_4$ catalysts are thus optimal for high enantiocontrol in the intramolecular C–H insertion reactions of alkyl diazoacetates.



Scheme 5

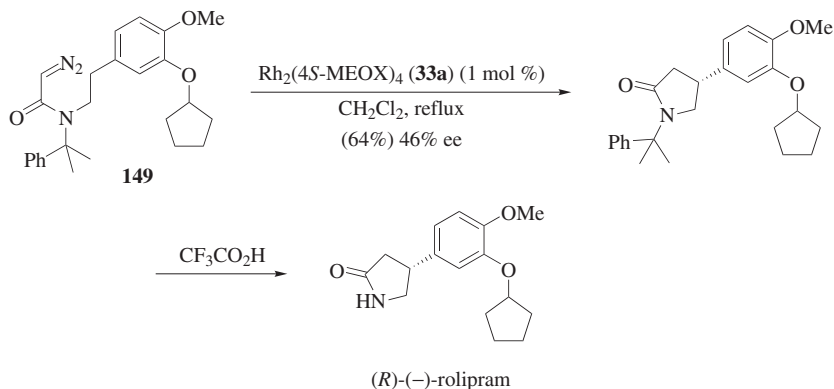
The construction of the natural lignan lactone (*S*)-(-)-enterolactone^{223,259} is also illustrative of the synthetic advantages of this method (Scheme 6). C–H



Scheme 6

insertion on diazoacetate **147** with catalyst $\text{Rh}_2(4R\text{-MPPIM})_4$ (**36b**) results in the formation of β -substituted γ -lactone **148** with the absolute configuration at C-4 established as (*R*). Subsequent alkylation and demethylation forms (*S*)-(-)-enterolactone. Use of $\text{Rh}_2(4S\text{-MPPIM})_4$ (**35b**) forms the product of opposite chirality and provides access to (*R*)-(-)-enterolactone. The predictability of absolute configuration with these catalysts has allowed configurational assignment in the synthesis of imperanene.²⁶⁰

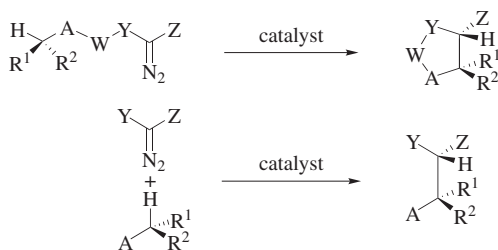
(*R*)-(-)-Rolipram, a selective inhibitor of phosphodiesterase type IV, is prepared in 46% ee by C–H insertion with diazoacetamide **149**, followed by standard transformations (Scheme 7).²⁷⁵



Scheme 7

COMPARISON WITH OTHER METHODS

Catalytic, asymmetric, intramolecular C–H insertion provides convenient access to 5- and 4-membered ring lactones, lactams, and, in selective instances, cyclopentanes with moderate to high selectivities. The method is direct, insertion is stereospecific at the C–H bond undergoing insertion, and stereoselectivity can be controlled. Catalyst loading can be lowered to <1.0 mol %, and catalysts could, in principle, be recovered.³² Although the target compounds can often be prepared by more conventional methods,³²⁹ the catalytic metal carbene approach effects C–H functionalization and stereocontrol in the same reaction process, thereby providing superior efficiency in the number of steps required for the synthesis. Directly comparable alternative methods that incorporate C–H insertion with the construction of a C–C bond are not available, and therefore the following discussion will focus on the advantages and disadvantages of intramolecular versus intermolecular C–H insertion (Scheme 8).



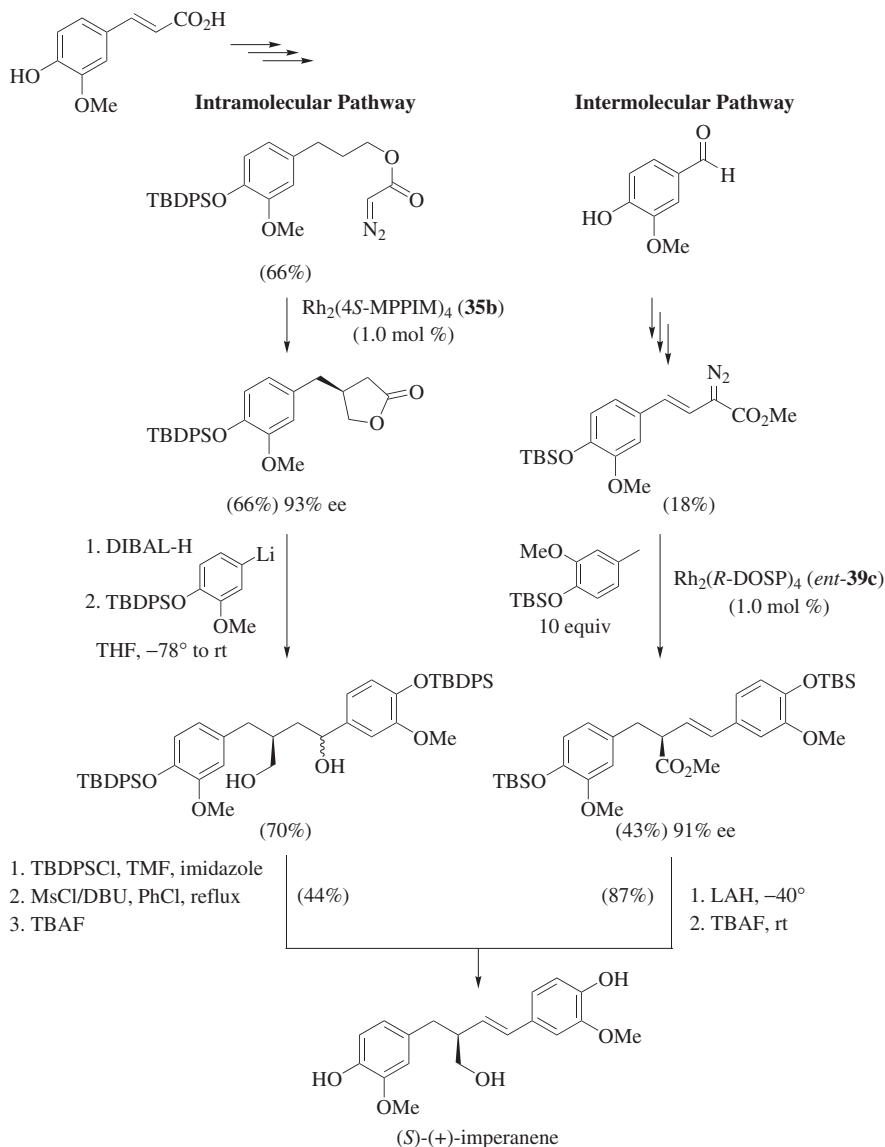
Scheme 8

Intramolecular catalytic C–H insertion was utilized as a synthetic method before intermolecular applications because of the greater ability to control site selectivity with intramolecular reactions.^{39,59} Achievement of high stereo- and site selectivity in intermolecular C–H insertion has been a significant advance in C–H functionalization.⁵⁹ The broad spectrum of substrates for C–H insertion offers unlimited possibilities. However, thus far these reactions are achievable only with donor–acceptor metallo-carbene species such as those derived from aryldiazoacetates or styryldiazoacetates.^{7,19} A direct comparison between inter- and intramolecular C–H insertion approaches to a specific natural product has been made.⁵⁹ The yield-related advantages of the intramolecular approach are evident in an (*S*)-(+)-imperanene synthesis (Scheme 9). On the other hand, the fewer steps and the convenience of the chemistry in the intermolecular version represent a distinctive advantage, at least in this case. Few other direct comparisons exist, and the applications of inter- and intramolecular C–H insertion reactions applied to organic synthesis remain distinct.

EXPERIMENTAL CONDITIONS

The handling of diazocarbonyl compounds should follow the normal precautions used for compounds that are potentially toxic and subject to explosive decomposition. However, because the carbonyl group imparts stability to the adjacent diazo functionality, diazocarbonyl compounds have a much higher thermal stability than do diazomethane and other diazoalkanes. For example, the half life for decomposition of ethyl diazoacetate at 100° in mesitylene is 109 hours, and that for the decomposition of 1-diazo-2-cyclohexanone is 32 minutes, compared to 3 hours for the decomposition of 2-diazopropane at 0° in diethyl ether.³² In fact, ethyl diazoacetate can be purified by distillation at atmospheric pressure (b.p. 140–141°). For those diazocarbonyl compounds that are formed by diazo transfer from sulfonyl azides, care must be taken in the handling of the azide reagent. Studies of their thermal stability, ease of handling, and safety have been reported,^{201,202} and from examination of twelve sulfonyl azides the commonly used methanesulfonyl azide was determined to pose the greatest hazard.

Diazocarbonyl compounds are unstable toward strong Brønsted and Lewis acids, but ethyl diazoacetate and similarly stable diazo esters survive treatment with glacial acetic acid at room temperature. They can also be decomposed



Scheme 9

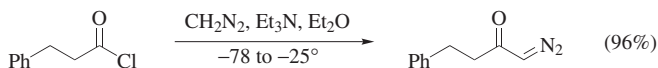
by prolonged exposure to light and, as is the subject of this review, treatment with select transition-metal complexes. Catalyzed reactions are commonly performed under simulated high-dilution conditions, especially with diazoacetates, diazoacetamides, and diazoketones having the structure $\text{RC}(\text{O})\text{CHN}_2$, to minimize “carbene dimerization” that is often the major competing reaction. Dropwise

addition of the dilute diazocarbonyl compound or controlled addition by syringe pump is the commonly used experimental condition.

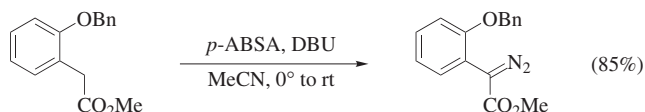
The presence of Lewis bases in the reaction medium, even those that are functional groups on the substrate, can interfere with the desired reaction by either occupying the catalytically active center of the transition metal or by reacting with the intermediate metallo-carbene. Water commonly interferes through catalytic reactions with the diazocarbonyl compound to form the corresponding α -hydroxy compound. The solvents employed for diazo decomposition reactions are hydrocarbons, dichloromethane, 1,2-dichloroethane, or toluene. Benzene, a carcinogen, has been used in some investigations, but it does not offer special advantages that could not be reproduced with an alternative solvent such as toluene.

EXPERIMENTAL PROCEDURES

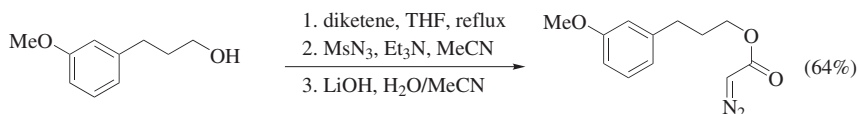
Preparation of Diazo Compounds



1-Diazo-4-phenylbutan-2-one [Arndt–Eistert Reaction].¹⁷⁰ Dry NEt_3 (11.1 mL, 80 mmol) was added to 350 mL of an anhydrous ethereal solution of diazomethane (80 mmol, 200 mL of 0.4 M solution) under N_2 in a dry 1-L Morton flask fitted with a mechanical stirrer, a dropping funnel, and a low-temperature thermometer. The solution was cooled to -78° (dry ice/acetone) and 11.8 mL of 3-phenylpropanoyl chloride (80 mmol) in 40 mL of anhydrous Et_2O was added dropwise with vigorous stirring over 25 min. A thick slurry formed during the addition. The reaction mixture was stirred an additional 15 min at -78° and then for 1 h at -25° to -20° (dry ice/ $\text{H}_2\text{O}/\text{CaCl}_2$). During the course of the reaction, the mixture became more viscous and then thinned out again. After warming to rt, the reaction mixture was diluted with water. The organic layer was separated and washed successively with 10% aqueous acetic acid, water, sat. NaHCO_3 solution, and brine. The resulting solution was dried over CaSO_4 and concentrated under vacuum to give the title compound as a deep yellow oil (12.8–13.5 g, 76–80 mmol, 92–100%), having spectral properties identical to those reported:³³⁰ IR (neat) 3087 (m), 2928 (w), 2105 (s), 1638 (s), 1454 (w), 1376 (s), 1140 (m), 1099 (m), 751 (m), 700 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.36–7.27 (m, 2H), 7.26–7.15 (m, 3H), 5.21 (br s, 1H), 2.98 (t, $J = 7.7$ Hz, 2H), 2.66 (br s, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 193.9 (C), 140.7 (C), 128.6 (2 x CH), 128.4 (2 x CH), 126.3 (CH), 54.6 (CH), 42.4 (CH_2), 31.0 (CH_2); UPLC/MS: $t_R = 2.28$ min (100%, $m/z + 1 = 175$); HRMS– ES^+ (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}$, 175.08659; found, 175.08670.



Methyl 2-(2-(Benzyloxy)phenyl)-2-diazoacetate [Diazo Transfer Reaction].²¹⁸ To a solution of methyl 2-(2-benzyloxy)phenylacetate (2.0 g, 7.8 mmol) and 4-acetamidobenzenesulfonyl azide (*p*-ABSA, 5.6 g, 23.4 mmol) in MeCN (10 mL) at 0° was added dropwise 1,8-diazabicyclo-7-undecene (4.7 mL, 31.2 mmol). The mixture was stirred at rt for 24 h. The resulting orange mixture was partitioned between EtOAc (100 mL) and water (50 mL). The organic layer was washed successively with 10% aq NaOH, water, and brine, and dried over Na₂SO₄. Filtration and evaporation afforded 2.1 g of crude product as an orange oil. The latter was purified by column chromatography on silica gel (hexane/EtOAc = 8 : 1) to provide the title compound (1.9 g, 6.7 mmol, 85%) as an orange oil: IR (film) 2099, 1701, 1254 cm⁻¹; ¹H NMR (270 MHz, C₆D₆) δ 7.82 (m, 1H), 7.17–6.85 (m, 7H), 6.54 (m, 1H), 4.56 (s, 2H), 3.34 (s, 3H); ¹³C NMR (67.8 MHz, C₆D₆) δ 165.9, 154.9, 136.7, 130.7, 128.7, 128.4, 128.2, 127.6, 121.6, 114.6, 112.4, 70.7, 59.8, 51.4; HRMS–EI (*m/z*): M⁺ calcd for C₁₆H₁₄N₂O₃, 282.1004; found, 282.1028. Anal. Calcd for C₁₆H₁₄N₂O₃: C, 61.95; H, 7.80; N, 5.16. Found: C, 61.84; H, 7.72; N, 5.08.

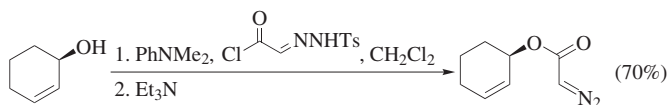


3-(3-Methoxyphenyl)propyl 2-Diazoacetate [Acyl Cleavage Reaction].²²³ To a solution of 3-(3-methoxyphenyl)propan-1-ol (6.2 g, 37 mmol) in anhydrous THF (50 mL) was added NaOAc (80 mg, 1.0 mmol), and then a solution of diketene (4.8 g, 55 mmol, 1.5 equiv) in THF (10 mL) was added dropwise at rt. The resulting solution was continually stirred for 10 h at rt, then was heated to reflux for 1.5 h. After evaporation of the solvent, the residue was purified by column chromatography on silica gel (hexane/EtOAc = 3 : 1 to 2 : 1) to provide a colorless oil (8.8 g, 35 mmol, 95%) identified as 3-(3-methoxyphenyl)propyl acetoacetate: ¹H NMR (300 MHz, CDCl₃) δ 7.21 (td, *J* = 7.4, 1.2 Hz, 1H), 6.77 (d, *J* = 7.4 Hz, 2H), 2.28 (s, 3H), 2.03–1.93 (m, 2H) with the enol form at 5.02 (s, 1H), 2.17 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 167.1, 159.7, 142.6, 129.5, 120.8, 114.2, 111.3, 64.7, 55.2, 50.1, 32.1, 30.2, 30.0.

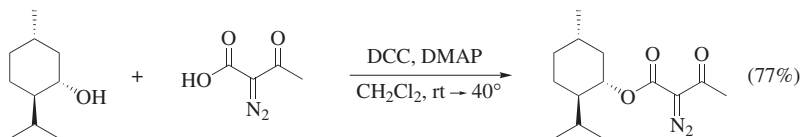
A solution of methanesulfonyl azide (6.6 g, 54 mmol, 1.5 equiv) in anhydrous acetonitrile (70 mL) was added dropwise over 20 min to a solution of 3-(3-methoxyphenyl)propyl acetoacetate (8.8 g, 35 mmol) and NEt₃ (5.5 g, 54 mmol, 1.5 equiv) in anhydrous acetonitrile (60 mL). The resulting yellow solution was stirred for 12 h at rt, after which the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc = 2 : 1 to 1 : 1) to give 3-(3-methoxyphenyl)propyl diazoacetoacetate

(10.3 g, 32 mmol, 90% yield, ~85% pure): ^1H NMR (300 MHz, CDCl_3) δ 7.18 (t, $J = 7.8$ Hz, 1H), 6.76–6.68 (m, 3H), 4.24 (t, $J = 6.5$ Hz, 2H), 3.77 (s, 3H), 2.68–2.63 (m, 2H), 2.44 (s, 3H), 2.05–1.95 (m, 2H).

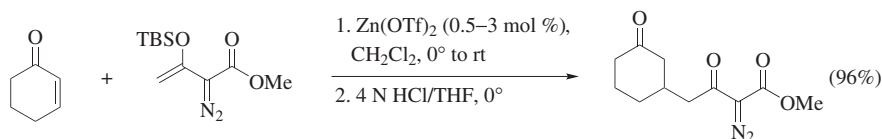
The diazoacetate (10.3 g, 32 mmol) was dissolved in 40 mL of MeCN and added in one portion to a solution of $\text{LiOH}\cdot\text{H}_2\text{O}$ (4.9 g, 117 mmol, 3.7 equiv) in H_2O (100 mL). The reaction mixture was stirred for 1.5 h at rt whereupon the resulting dark-brown solution was extracted with EtOAc (3×75 mL), and the organic extract was then washed with brine (75 mL), sat. aq citric acid (75 mL), and brine (2×75 mL). After drying over anhydrous MgSO_4 , the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel (hexane/EtOAc = 3 : 1) to afford the title compound (5.50 g, 23.5 mmol, 74%) as a yellow oil: IR (film) 2113, 1695 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.19 (dd, $J = 8.7, 7.6$ Hz, 1H), 6.77–6.70 (m, 3H), 4.74 (br s, 1H), 4.16 (t, $J = 6.6$ Hz, 2H), 3.77 (s, 3H), 2.65 (t, $J = 7.8$ Hz, 2H), 1.95 (tt, $J = 7.8, 6.6$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.5, 142.5, 129.2, 120.6, 114.0, 111.1, 63.9, 54.9, 45.9, 31.9, 30.1. Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_3$: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.46; H, 5.99; N, 12.02.



(*R*)-Cyclohex-2-en-1-yl 2-Diazoacetate [Direct Diazoacetylation].²²⁴ Dry *N,N*-dimethylaniline (1.55 g, 12.24 mmol) was added to a cold (0°) and stirred solution of *R*-2-cyclohexen-1-ol (1.0 g, 10.2 mmol) and [(4-toluenesulfonyl)hydrazone]acetyl chloride (3.31 g, 12.75 mmol) in dry CH_2Cl_2 (68 mL). After 20 min at 0° , dry NEt_3 (7.1 mL, 51 mmol) was injected over about 1 min and stirring was continued for 15 min. The cold bath was removed, and, after a further 30 min, the mixture was quenched with water (30 mL) and concentrated. The residue was extracted with EtOAc/hexane (1 : 9, 2×65 mL), and the combined extracts were washed with sat. aq citric acid (2×30 mL). The combined aqueous layers were extracted with EtOAc/hexane (1 : 9, 30 mL), and the organic extract was washed with sat. aq citric acid (5 mL). All the organic extracts were combined, dried over MgSO_4 and evaporated. Flash column chromatography of the residue over silica gel (4×20 cm, EtOAc/hexane = 1 : 12) afforded the title compound (1.19 g, 7.2 mmol, 70%) as a bright yellow oil containing trace impurities. The material was distilled (Kugelrohr, 45° , 0.05 mm Hg) for characterization: FT-IR (CHCl_3 cast) 3120, 2950, 2055, 1690, 1380, 1180 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.96 (ddt, $J = 10.0, 3.8, 1.2$ Hz, 1H), 5.72 (ddt, $J = 10.0, 3.8, 2.1$ Hz, 1H), 5.35 (m, 1H), 4.74 (br s, 1H), 2.18–1.81 (m, 3H), 1.81–1.55 (m, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 132.7, 125.7, 68.6, 28.5, 24.9, 18.6; HRMS (m/z): M^+ calcd for $\text{C}_8\text{H}_{10}\text{N}_2\text{O}_2$, 166.0742; found, 166.0725. Anal. Calcd for $\text{C}_8\text{H}_{10}\text{N}_2\text{O}_2$: C, 57.82; H, 6.06; N, 16.86. Found: C, 57.81; H, 5.98; N, 16.81.



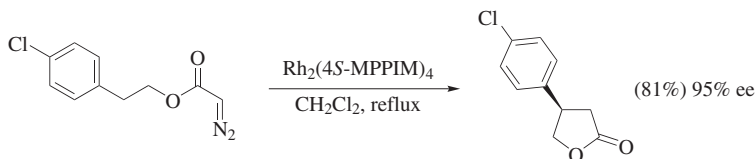
D-(+)-Menthyl Diazoacetoacetate [DCC Coupling Reaction].⁷⁷ To a solution of D-(+)-menthol (78 mg, 0.50 mmol), diazoacetoacetic acid (154 mg, 1.2 mmol) and DMAP (6 mg, 0.05 mmol) in CH₂Cl₂ (3.3 mL) at rt was added in one portion DCC (206 mg, 1.0 mmol). The reaction mixture was heated at 40° until the reaction was complete (60–90 min). The mixture was filtered through a plug of Celite (Et₂O as eluent), and the resulting filtrate was partitioned between H₂O and Et₂O. The aqueous layer was extracted twice with Et₂O. The organic extracts were combined, washed with sat. aq NaHCO₃ and then with brine. The organic layer was dried with anhydrous MgSO₄ and concentrated under vacuum. The crude product was purified by column chromatography (hexane/EtOAc = 9:1) giving the title product (87 mg, 0.39 mmol, 77%) having spectral properties identical to those previously reported:¹²¹ [α]_D²⁵ –88.7 (*c* = 2.15, CHCl₃); IR (thin film) 2139, 1712, 1662 cm^{–1}; ¹H NMR (300 MHz, CDCl₃) δ 4.82 (dt, *J* = 10.9, 4.4 Hz, 1H), 2.48 (s, 3H), 2.10–2.02 (m, 1H), 1.84 (d quin, *J* = 7.0, 2.7 Hz, 1H), 1.76–1.65 (m, 2H), 1.60–1.32 (m, 3H), 1.18–0.98 (m, 2H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.80 (d, *J* = 6.9 Hz, 3H). Anal. Calcd for C₁₄H₂₂N₂O₃: C, 63.18; H, 8.33; N, 10.52. Found: C, 63.26; H, 8.38; N, 10.61.



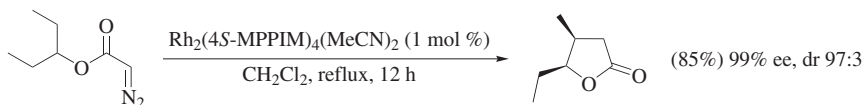
Methyl 2-Diazo-3-oxo-4-(3-oxocyclohexyl)butanoate [Mukaiyama–Michael Reaction].⁷⁵ To a flame-dried, 25-mL, round-bottomed flask under nitrogen was added zinc triflate (5.5 mg, 0.015 mmol), followed by 2-cyclohexen-1-one (49 mg, 0.50 mmol) and dry CH₂Cl₂ (2 mL). The mixture was stirred at 0°. Methyl 3-*tert*-butyldimethylsilyloxy-2-diazobut-3-enoate (202 mg, 0.750 mmol) was added via syringe all at once. The yellow solution was stirred at 0° for 1 h and then was allowed to warm slowly to rt. After 16 h the crude reaction mixture was concentrated under reduced pressure. The residue was dissolved in THF (5 mL) and stirred at 0°, then an aq HCl (4 M, 1.0 mL) solution was added dropwise. After 1 h at 0° the reaction was quenched by slow addition of sat. NaHCO₃ (15 mL) solution until basic to pH paper. The resulting solution was extracted with three 10-mL portions of CH₂Cl₂, and the combined organic layers were dried over anhydrous MgSO₄ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography, eluting with EtOAc/hexane (1:2) to give the title compound (114 mg, 0.48 mmol, 96%) as a light yellow oil: IR

(neat) 2137, 1712, 1652 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 3.75 (s, 3H), 2.86 (dd, $J = 15.7, 6.5$ Hz, 1H), 2.76 (dd, $J = 15.7, 6.5$ Hz, 1H), 2.37–2.13 (mp, 4H), 2.06–1.85 (mp, 3H), 1.65–1.55 (m, 1H), 1.39–1.29 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 210.5, 190.7, 161.6, 76.1, 52.2, 47.4, 46.0, 41.1, 35.0, 31.0, 24.9; HRMS–FAB (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_4$, 239.1032; found, 239.1035.

Catalytic, Asymmetric, Intramolecular C–H Insertions

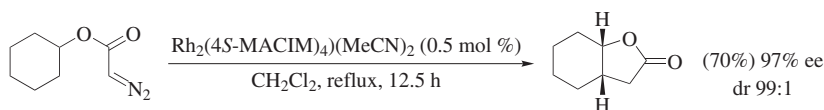


(*R*)-4-(4-Chlorophenyl)dihydrofuran-2(3*H*)-one [Synthesis of a β -Substituted γ -Butyrolactone from an Acyclic Diazoacetate].³²⁹ A solution of 4-chlorophenethyl 2-diazoacetate (708 mg, 3.2 mmol) in dry CH_2Cl_2 (20 mL) was added, over a period of 5 h via a syringe pump, to a refluxing solution of $\text{Rh}_2(4\text{S-MPPIM})_4$ (22 mg, 0.016 mmol) in dry CH_2Cl_2 (80 mL). The solvent was evaporated under vacuum and the crude residue was purified by chromatography on silica gel (hexanes/ $\text{EtOAc} = 4:1$) to afford the title compound (502 mg, 2.56 mmol, 81%) as a white solid: $[\alpha]_{\text{D}}^{26} -50.9$ ($c = 0.7$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.33 (d, $J = 8.5$ Hz, 2H), 7.16 (d, $J = 8.0$ Hz, 2H), 4.65 (dd, $J = 9.0, 7.5$ Hz, 1H), 4.22 (dd, $J = 9.0, 7.5$ Hz, 1H), 3.76 (pent, $J = 9.0$ Hz, 1H), 2.92 (dd, $J = 17.5, 9.0$ Hz, 1H), 2.62 (dd, $J = 17.5, 9.0$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 137.9, 133.5, 129.2, 128.0, 75.9, 73.7, 40.3, 35.5; HRMS (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{10}\text{H}_9\text{O}_2\text{Cl}$, 197.0369; found, 197.0372. The enantioselectivity was determined as follows: a sample of the γ -butyrolactone was reduced with a THF solution of LiAlH_4 to give the corresponding diol, followed by treatment with excess trifluoroacetic anhydride to give the (bis)trifluoroacetate ester. The ee (95%) was determined by GC on a 30-m Chiraldex B-DM column: $t_{\text{R}}(\text{R}) = 99.6$ min, (*S*) = 100.4 min (flow rate: 1.0 mL/min, oven temperature 100° for 20 min, then $0.5^\circ/\text{min}$ to 140°).

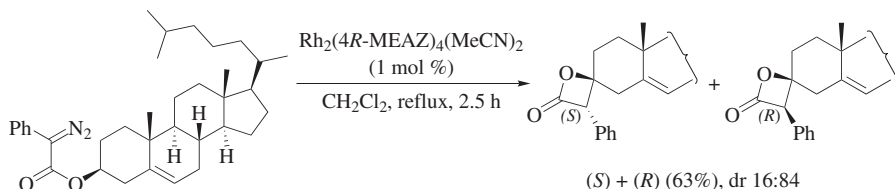


(4*S*,5*S*)-5-Ethyl-4-methyldihydrofuran-2(3*H*)-one [Desymmetrization of a Secondary Alkyl Diazoacetate].¹⁵² To a refluxing solution of $\text{Rh}_2(4\text{S-MPPIM})_4$

(MeCN)₂ (14 mg, 0.010 mmol) in anhydrous CH₂Cl₂ (20 mL) was added pentan-3-yl 2-diazoacetate (156 mg, 1.0 mmol) in CH₂Cl₂ (5 mL) over a 12 h period. The solvent was removed on a rotary evaporator. The product was purified by distillation (12 mm Hg, 105°) to yield the γ -lactone product (109 mg, 0.85 mmol, 85%) as a colorless oil in 99% ee. The enantiomeric composition was determined by CSP–GC with baseline separation on a B-PH column. The spectral properties were identical to those previously reported:³³¹ [α]_D²⁵ –34.4 (*c* = 2.0, CHCl₃); IR (neat) 1777, 1466, 1223, 1128, 811 cm^{–1}; ¹H NMR (300 MHz, CDCl₃) δ 3.64–3.55 (m, 1H), 2.70 (dd, *J* = 16.8, 7.6 Hz, 1H), 2.60–2.40 (m, 1H), 2.2 (dd, *J* = 16.8, 3.0 Hz, 1H), 2.00–1.85 (m, 2H), 1.12 (d, *J* = 7.5 Hz, 3H), 0.92 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.3, 111.7, 37.5, 34.5, 26.6, 14.3, 13.5; EIMS (70 eV) *m/z*: 128, 99, 71, 59, 42.

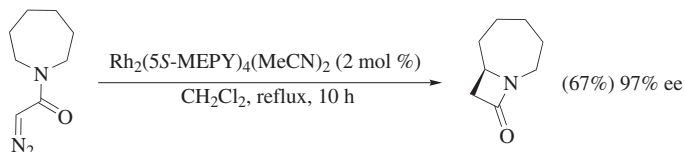


(3a*S*,7a*S*)-Hexahydrobenzofuran-2(3*H*)-one [Formation of a Bicyclic γ -Lactone from a Cyclic Diazoacetate].²⁴³ To a light-blue solution of Rh₂(4*S*-MACIM)₄(MeCN)₂ (5.1 mg, 0.0050 mmol) in refluxing anhydrous CH₂Cl₂ (50 mL) was added a solution of cyclohexyl 2-diazoacetate (168 mg, 1.0 mmol) in CH₂Cl₂ (10 mL) through a syringe pump at a rate of 0.8 mL/h (12.5 h). After addition was complete, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (hexane/EtOAc = 9 : 1) to give the title compound (98 mg, 0.70 mmol, 70%) as a colorless oil in 97% ee: [α]_D²⁶ –34.4 (*c* 0.41, MeOH); IR (film) 1776 (C=O) cm^{–1}; ¹H NMR (300 MHz, CDCl₃) δ 4.51 (q, *J* = 4.1 Hz, 1H), 2.61 (dd, *J* = 16.8, 6.7 Hz, 1H), 2.45–2.33 (m, 1H), 2.24 (dd, *J* = 16.8, 2.5 Hz, 1H), 2.14–2.02 (m, 1H), 2.01–1.18 (m, 7H). Enantiomeric separations were performed on a Chiraldex G-TA column with baseline separation at 130°: *t*_R (1*R*,6*R*) = 50.2 min, *t*_R (1*S*,6*S*) = 50.9 min.

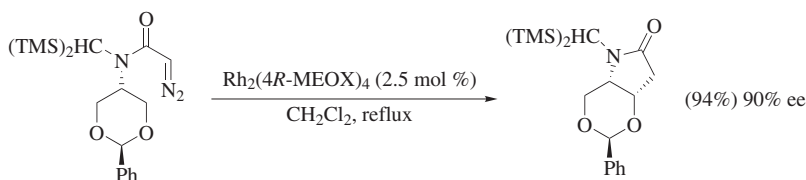


(2*S*) and (2*R*)-3-(3 β -Hydroxy-5-cholesten-3 α -yl)phenylacetic Acid Lactones [β -Lactone Formation from a Phenyldiazoacetate].¹³⁵ To a stirred

solution of $\text{Rh}_2(4S\text{-MEAZ})_4(\text{MeCN})_2$ (3.8 mg, 0.0047 mmol) in dry CH_2Cl_2 (5.0 mL) heated at reflux under an argon atmosphere was added the steroidal phenyl diazoacetate substrate (250 mg, 0.47 mmol) in dry CH_2Cl_2 (3.0 mL) over 2 h via syringe pump. The reaction mixture was heated at reflux for an additional 30 min upon completion of the addition. After cooling to rt, the mixture was filtered through a short silica plug, which was subsequently washed with EtOAc/hexanes (1 : 4, 25 mL). The solvent was removed under reduced pressure to afford 239 mg of the crude product as an off-white crystalline solid. ^1H NMR analysis of the reaction mixture showed the presence of (2*S*)- and (2*R*)-3-(3 β -hydroxy-5-cholesten-3 α -yl)phenylacetic acid lactones in 69% yield. Column chromatography on silica gel (hexanes/EtOAc = 19 : 1) afforded a mixture of the isomeric (*S*) and (*R*) title products (149 mg 0.30 mmol, 63%) as white crystals, dr = 16 : 84 as determined by ^1H NMR (600 MHz). Analytical separation of these two products was achieved by column chromatography (silica gel, β -lactones loading ratio 100 : 1, EtOAc/hexanes = 1 : 100 to 1 : 50) to afford each as a white solid film. (2*S*)-3-(3 β -Hydroxy-5-cholesten-3 α -yl)phenylacetic Acid Lactone: IR (CDCl_3) 1816 ($\text{C}=\text{O}$) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 7.37–7.30 (m, 3H), 7.16 (dd, J = 8.0, 1.7 Hz, 2H), 5.63–5.59 (m, 1H), 4.46 (s, 1H, α -H β -lactone), 3.05 (dddd, J = 13.3, 2.7, 2.6, 2.4 Hz, 1H, C4-H_{ax}), 2.15 (dd, J = 13.3, 2.8 Hz, 1H, C4-H_{eq}), 2.12–2.04 (m, 1H), 1.98 (ddd, J = 18.5, 13.9, 4.7 Hz, 1H, C2-H_{ax}), 1.96–1.91 (m, 1H), 1.88–1.80 (m, 1H), 1.80–1.74 (m, 1H, C2-H_{eq}), 1.70–0.95 (m, 19H), 1.01 (s, 3H), 0.89 (d, J = 6.6 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.73 (ddd, J = 16.0, 12.2, 4.7 Hz, 1H), 0.66 (s, 3H), 0.40 (ddd, J = 18.3, 14.0, 4.3 Hz, 1H); ^{13}C NMR (150 MHz, CDCl_3) δ 169.7, 138.7, 130.9, 129.5, 128.6, 128.2, 124.2, 83.8, 63.6, 56.6, 56.2, 50.4, 44.6, 42.3, 39.5, 36.2, 35.7, 35.2, 32.1, 31.9, 29.7, 28.2, 28.0, 27.9, 24.3, 23.8, 22.8, 22.6, 21.0, 19.2, 18.7, 11.8; HRMS–FAB $^+$ (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{50}\text{O}_2$, 503.3889; found, 503.3889. (2*R*)-3-(3 β -Hydroxy-5-cholesten-3 α -yl)phenylacetic Acid Lactone: IR (CDCl_3) 1817 ($\text{C}=\text{O}$) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 7.33–7.25 (m, 3H), 7.15 (dd, J = 8.3, 1.5 Hz, 2H), 4.48 (s, 1H, α -H β -lactone), 4.13–4.09 (m, 1H), 2.66 (dddd, J = 13.8, 2.9, 2.8, 2.5 Hz, 1H, C4-H_{ax}), 2.30 (dddd, J = 17.1, 14.2, 3.9, 1.0 Hz, 1H, C2-H_{ax}), 2.15 (dd, J = 13.8, 2.8 Hz, 1H, C4-H_{eq}), 2.07–1.99 (m, 2H), 1.96 (dddd, J = 12.9, 3.3, 3.2, 3.1 Hz, 1H, C2-H_{eq}), 1.85–1.76 (m, 1H), 1.70–1.63 (m, 1H), 1.56–1.05 (m, 18H), 1.04–0.85 (m, 3H), 0.99 (s, 3H), 0.92 (d, J = 6.6 Hz, 3H), 0.87 (d, J = 6.7 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.81 (ddd, J = 16.6, 11.9, 5.2 Hz, 1H), 0.64 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 169.6, 135.7, 130.8, 129.6, 128.1, 128.0, 124.0, 82.8, 63.8, 56.6, 56.2, 50.2, 42.3, 39.7, 39.5, 38.1, 36.4, 36.2, 36.1, 35.7, 33.8, 31.9, 31.7, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.1, 19.2, 18.7, 11.8; HRMS–FAB $^+$ (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{50}\text{O}_2$, 503.3889; found, 503.3889.

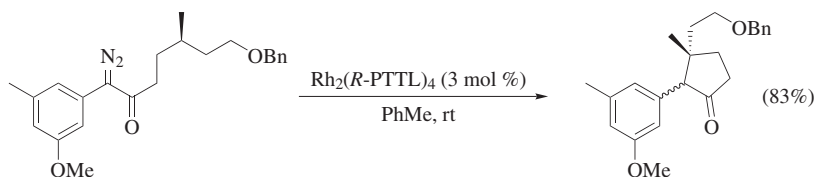


(*R*)-1-Azabicyclo[5.2.0]nonan-9-one [β -Lactam Formation from a Diazoacetamide].²⁷⁷ To a solution of $\text{Rh}_2(5S\text{-MEPY})_4(\text{MeCN})_2$ (17.2 mg, 0.020 mmol) in refluxing anhydrous CH_2Cl_2 (50 mL), 1-(azepan-1-yl)-2-diazoethanone (167 mg, 1.0 mmol) in CH_2Cl_2 (10 mL) was added by syringe pump at a rate of 1.0 mL/h (10 h). After addition was complete, the reaction mixture was concentrated under reduced pressure, and the catalyst was removed by passing the chloroform solution through a silica gel plug. The solvent was removed under reduced pressure and the residue was distilled. Fractions with boiling points of 90–100° at 0.07 mm Hg were collected to yield the title β -lactam (93 mg, 0.67 mmol, 67%) as an oil in 97% ee. Enantiomer separation was achieved on a 30-m Chiraldex B-PH column at 120°: t_R (minor) = 87.2 min, t_R (major) = 88.2 min; $[\alpha]_D^{21} + 55.0$ (c 1.93, CHCl_3). The spectral properties were identical to those previously reported:³³² IR (film) 1745 cm^{-1} ; ^1H NMR (60 MHz, CDCl_3) δ 3.61 (br s, 1H), 2.85 (dd, J = 14, 5 Hz, 1H), 2.30 (dd, J = 14, 3 Hz, 1H); MS (m/z): 139 (100).



(2*S*,4*aS*,7*aS*)-5-(bis(trimethylsilyl)methyl)-2-phenyltetrahydro-[1,3]dioxino[5,4-*b*]pyrrol-6(4*H*)-one [γ -Lactam Formation from a Diazoacetamide].²⁸¹ A solution of *N*-(bis(trimethylsilyl)methyl)-2-diazo-*N*-((2*r*,5*r*)-2-phenyl-1,3-dioxan-5-yl)acetamide (40 mg, 0.10 mmol) in dry CH_2Cl_2 (4 mL) was added via cannula to a solution of $\text{Rh}_2(4R\text{-MEOX})_4$ (2.5 mol %) in dry CH_2Cl_2 (4 mL). After the addition was complete, the reaction mixture was heated at reflux for 20 min. The solvent was removed under reduced pressure to yield the title compound (35 mg, 0.094 mmol, 94%) as a white solid in 90% ee: mp 135–136°; IR (CH_2Cl_2) 3017, 2955, 1680, 1215, 849, 758 cm^{-1} ; ^1H NMR (200 MHz, CDCl_3) δ 7.52–7.36 (m, 5H), 5.84 (s, 1H), 4.67 (dd, J = 14.0, 6.3 Hz, 1H), 4.26 (dd, J = 11.7, 5.3 Hz, 1H), 3.86 (dd, J = 11.7, 7.6 Hz, 1H), 3.70–3.66 (m, 1H), 2.77 (dd, J = 16.9, 6.5 Hz, 1H), 2.56 (dd, J = 16.9, 7.8 Hz, 1H), 2.10 (s, 1H), 0.18 (s, 9H), 0.12 (s, 9H); ^{13}C NMR (50.3 MHz, CDCl_3) δ 171.3, 137.5,

129.0, 128.5, 126.2, 95.6, 90.2, 67.1, 63.7, 34.1, 0.8, 0.2; HRMS (m/z): M^+ calcd for $C_{19}H_{31}NO_3Si_2$, 377.1843; found, 377.1847.



(S)-3-(2-(Benzyloxy)ethyl)-2-(3-methoxy-5-methylphenyl)-3-methylcyclopentanone [Synthesis of a Cyclopentanone from a Diazoketone].³⁰⁸ $Rh_2(R-PTTL)_4$ (5 mg) was dissolved in toluene (2 mL). To this solution was added a solution of (*R*)-7-(benzyloxy)-1-diazo-1-(3-methoxy-5-methylphenyl)-5-methyl heptan-2-one (140 mg, 0.368 mmol) in toluene (2.0 mL) at rt within 1 min. The reaction was continued for an additional 15 min at rt. Then the reaction mixture was concentrated and the residue chromatographed to afford the title compound (108 mg, 0.305 mmol, 83%) as a mixture of two diastereomers: TLC R_f (PE/MTBE, 8:2) 0.22; IR (film) 2959, 1724, 1173, 1068 cm^{-1} ; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (m, 5H), 6.62 (s, 1H), 6.43 (m, 2H), 4.49 (s, 0.8H), 4.41 (s, 1.2H), 3.75 (s, 1.8H), 3.74 (s, 1.2H), 3.6–3.4 (m, 2H), 3.24 (s, 0.4H), 3.11 (s, 0.6H), 2.42 (m, 1H), 2.34 (s, 3H), 2.31 (m, 1H), 1.94 (m, 1H), 1.83 (m, 1H), 1.67 (m, 1H), 1.50 (m, 1H), 1.18 (s, 1.8H), 0.79 (s, 1.2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 217.9, 217.6, 159.4, 159.3, 139.1, 139.0, 138.3, 136.2, 135.9, 73.3, 73.2, 67.2, 67.0, 43.3, 43.2, 40.8, 36.1, 35.9, 33.8, 33.2, 32.3; d 128.5, 127.7, 123.9, 123.5, 113.6, 113.4, 113.3, 113.2, 68.9, 67.4, 55.2, 26.1, 21.8, 21.7, 20.7; HRMS (m/z): M^+ calcd for $C_{23}H_{28}O_3$, 352.2038; found, 352.2023.



(1S,2R)-cis-2-phenylcyclopentane-1-carboxylate [Synthesis of a Cyclopentane from a Methyl Diazoester].³⁰⁹ $Rh_2(S-PTTL)_4 \cdot 2EtOAc$ (2.8 mg, 0.002 mmol, 0.01 equiv) was added to a solution of methyl 2-diazo-6-phenylhexanoate (46.5 mg, 0.20 mmol) in toluene (1.0 mL) at -78° . After 30 min, the mixture was concentrated at rt and the residue purified by column chromatography (silica gel, hexane/EtOAc = 15:1) to give the title compound (34.7 mg, 85%) as a colorless oil: R_f (hexane/EtOAc, 5:1) 0.39; $[\alpha]_D^{19} +98.88$ (c 1.12, $CHCl_3$); IR (neat) 1732, 1200, 1171, 700 cm^{-1} ; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28–7.15 (m, 5H, ArH), 3.41 (ddd, $J = 7.1, 9.0, 9.0$ Hz, 1H, C1-H), 3.22 (s, 3H, CO_2CH_3), 3.16 (ddd, $J = 6.2, 9.0, 9.0$ Hz, 1H, C2-H), 2.15–1.95 (m, 5H), 1.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9 (C), 141.5 (C), 127.9 (CH), 127.8 (CH), 126.3 (CH), 50.9 (CH_3), 49.8 (CH), 49.2 (CH), 31.2 (CH_2), 28.6 (CH_2), 24.8

(CH₂); HRMS–EI (m/z): M⁺ calcd for C₁₃H₁₆O₂, 204.1150; found, 204.1151. Anal. Calcd for C₁₃H₁₆O₂: C, 76.44; H, 7.90. Found: C, 76.33; H, 7.98. The ee (95%) was determined by HPLC using a connected series of a Daicel Chiralcel OJ-H column and a Daicel Chiralpak AS-H column (hexanes/*i*-PrOH = 100 : 1, 1.0 mL/min): t_R [minor, (1*R*,2*S*)] = 12.9 min; t_R [major, (1*S*,2*R*)] = 14.7 min.

TABULAR SURVEY

The following tables are intended to include all reported examples of catalytic, asymmetric, intramolecular C–H insertion reactions reported up through and including 2009. The charts preceding the tables show the catalyst structures together with the bold numbers assigned to them. These numbers are used throughout the tables to reference the catalyst structures; note that the numbers differ from those used in the text portion of this chapter. Charts 1–4 provide a guide to the chiral dirhodium catalysts used in these reactions, and Chart 5 shows the chiral copper catalysts.

The arrangement of the Tabular Survey parallels that of the “Scope and Limitations” section. The organization of the entries in all of the tables is by ascending order of the carbon count of the substrate with the exclusion of protecting groups, esters (except for the carboxy carbon), and ethers, unless directly involved in the reaction. Isolated yields of the products are included in parentheses and a dash (–) indicates that no yield was reported.

The following abbreviations and acronyms (excluding those listed in “The *Journal of Organic Chemistry* Standard Abbreviations and Acronyms”) are used in the Tabular Survey:

abs.	absolute
avg	average
BACIM	<i>tert</i> -butyl 1-acetyl-2-oxoimidazolidinate-4-carboxylate
BNAZ	benzyl 4-oxoazetidine-2-carboxylate
BNOX	4-benzyl-1,3-oxazolidin-2-onate
BNP	1,1'-binaphthalene-2,2'-diyl hydrogen phosphate
BPPIM	isobutyl 2-oxo-1-(3-phenylpropanoyl)imidazolidinate-4-carboxylate
BPTA	2-(1,3-dioxo-1,3-dihydro-2 <i>H</i> -benzo[<i>f</i>]isoindol-2-yl)propanoate
BPTPA	2-(1,3-dioxo-1,3-dihydro-2 <i>H</i> -benzo[<i>f</i>]isoindol-2-yl)-3-phenylpropanoate
BPTTL	2-(1,3-dioxo-1,3-dihydro-2 <i>H</i> -benzo[<i>f</i>]isoindol-2-yl)-3,3-dimethylbutanoate
BPTV	2-(1,3-dioxo-1,3-dihydro-2 <i>H</i> -benzo[<i>f</i>]isoindol-2-yl)-3-methylbutanoate
BSP	1-(phenylsulfonyl)prolinate
BSPIM	methyl 2-oxo-1-[1-(phenylsulfonyl)propyl]imidazolidinate-4-carboxylate

cap	caprolactamate
CHAZ	cyclohexyl 4-oxoazetidine-2-carboxylate
dFIBAZ	<i>iso</i> -butyl 3,3-difluoro-4-oxoazetidine-2-carboxylate
DOSP	(<i>p</i> -dodecylphenylsulfonyl)prolinate
ee	enantiomeric excess
EPPIM	ethyl 2-oxo-1-(3-phenylpropanoyl)imidazolidinate-4-carboxylate
IBAZ	isobutyl 4-oxoazetidine-2-carboxylate
MACIM	methyl 1-acetyl-2-oxoimidazolidinate-4-carboxylate
MANIM	methyl 1-[methoxy(phenyl)acetyl]-2-oxoimidazolidinate-4-carboxylate
MBOIM	methyl 1-benzoyl-2-oxoimidazolidinate-4-carboxylate
MCHIM	methyl 1-(cyclohexylacetyl)-2-oxoimidazolidinate-4-carboxylate
MCPIIM	methyl 2-oxo-1-[(2- <i>trans</i> -phenylcyclopropyl)carbonyl]imidazolidinate-4-carboxylate
MEAZ	methyl 4-oxoazetidine-2-carboxylate
MEOX	methyl 2-oxo-1,3-oxazolidinate-4-carboxylate
MEPY	methyl 5-oxoprolinate
MNACIM	1-menthyl 4-methyl 2-oxoimidazolidinate-1,4-dicarboxylate
MPMT	2-([[(1 <i>R</i> ,2 <i>S</i> ,5 <i>R</i>)-2-isopropyl-5-methylcyclohexyl]oxy]carbonyl)benzoate
MPPIM	methyl 2-oxo-1-(3-phenylpropanoyl)imidazolidinate-4-carboxylate
NEPAZ	2,2-dimethylpropyl 4-oxoazetidine-2-carboxylate
NEPY	2,2-dimethylpropyl 5-oxoprolinate
NTPA	2-(1,3-dioxo-1 <i>H</i> -benzo[de]isoquinolin-2(3 <i>H</i>)-yl)-3-phenylpropanoate
NTTL	2-(1,3-dioxo-1 <i>H</i> -benzo[de]isoquinolin-2(3 <i>H</i>)-yl)-3,3-dimethylbutanoate
ODPY	<i>n</i> -octadecyl 5-oxoprolinate
<i>p</i> -ABSA	<i>p</i> -acetamidobenzenesulfonyl azide
pfb	perfluorobutyrate
PCC	3-phenylcholestane-2-carboxylate
PHOX	4-phenyl-1,3-oxazolidin-2-onate
protos	1-[(4-methylphenyl)sulfonyl]prolinate
PTA	2-(1,3-dioxo-1,3-dihydro-2 <i>H</i> -isoindol-2-yl)propanoate
PTAD	1-adamantyl(1,3-dioxo-1,3-dihydro-2 <i>H</i> -isoindol-2-yl)acetate
PTPA	2-(1,3-dioxo-1,3-dihydro-2 <i>H</i> -isoindol-2-yl)-3-phenylpropanoate
PTPG	(1,3-dioxo-1,3-dihydro-2 <i>H</i> -isoindol-2-yl)(phenyl)acetate
PTTL	2-(1,3-dioxo-1,3-dihydro-2 <i>H</i> -isoindol-2-yl)-3,3-dimethylbutanoate
PTV	2-(1,3-dioxo-1,3-dihydro-2 <i>H</i> -isoindol-2-yl)-3-methylbutanoate
TBDPS	<i>tert</i> -butyldiphenylsilyl
TBPRO	1-(<i>tert</i> -butylsulfonyl)prolinate
TBSP	1-[(4- <i>tert</i> -butylphenyl)sulfonyl]prolinate
TFEA	2,2,2-trifluoroethyl trifluoroacetate
THREOX	methyl (4 <i>S</i> ,5 <i>R</i>)-5-methyl-2-oxo-1,3-oxazolidinate-4-carboxylate

CHART 1. CHIRAL DIRHODIUM CARBOXYAMIDATE CATALYSTS

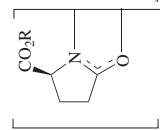
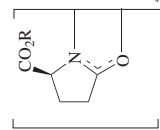
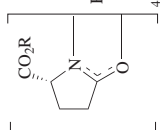
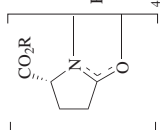
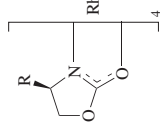
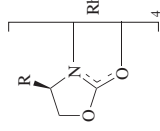
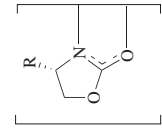
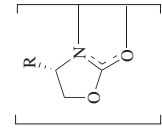
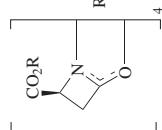
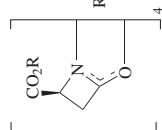
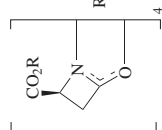
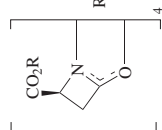
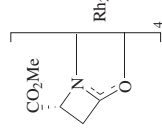
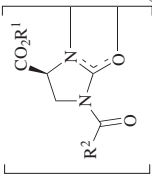
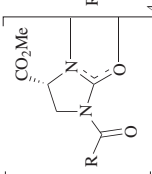
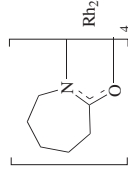
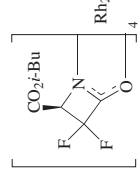
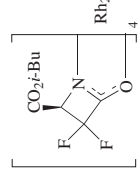
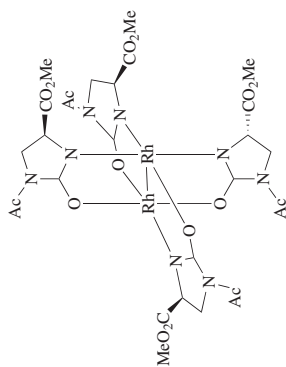
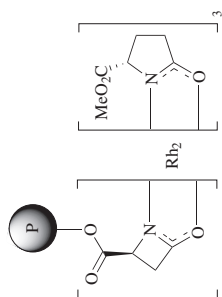
	R		
	1a	Me	Rh ₂ (5S-MEPY) ₄
		<i>n</i> -C ₁₈ H ₃₇	Rh ₂ (5S-ODPY) ₄
	1b		
	R	Me	Rh ₂ (5R-MEPY) ₄
	2a		
		<i>t</i> -BuCH ₂	Rh ₂ (5R-NEPY) ₄
	2b		
	R	MeO ₂ C	Rh ₂ (4S-MEOX) ₄
	3a	Ph	Rh ₂ (4R-PHOX) ₄
		Bn	Rh ₂ (4R-BNOX) ₄
	3c		
	R	MeO ₂ C	Rh ₂ (4R-MEOX) ₄
	4a	Bn	Rh ₂ (4R-BNOX) ₄
			
	4b		
	R	Me	Rh ₂ (4S-MEAZ) ₄
	5a	<i>i</i> -Bu	Rh ₂ (4S-IBAZ) ₄
		<i>c</i> -C ₆ H ₁₁	Rh ₂ (4S-CHAZ) ₄
	5c		
		Bn	Rh ₂ (4S-BNAZ) ₄
	5d		
		<i>t</i> -BuCH ₂	Rh ₂ (4S-NEPAZ) ₄
	5e		
			
6 Rh ₂ (4R-MEAZ) ₄			

CHART 1. CHIRAL DIRHODIUM CARBOXYAMIDATE CATALYSTS (Continued)

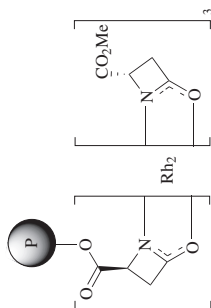
			
R ¹	R ²	R	
7a	Me	Me	8a Rh ₂ (4 <i>S</i> -MACIM) ₄
7b	Me	Ph	Rh ₂ (4 <i>S</i> -MBOIM) ₄
7c	Me	PhCH ₂ CH ₂	Rh ₂ (4 <i>S</i> -MPPIM) ₄
7d	Me	<i>c</i> -C ₆ H ₁₁ CH ₂	Rh ₂ (4 <i>S</i> -MCHIM) ₄
7e	Et	PhCH ₂ CH ₂	Rh ₂ (4 <i>S</i> -EPPIM) ₄
7f	<i>i</i> -Bu	PhCH ₂ CH ₂	Rh ₂ (4 <i>S</i> -BPPIM) ₄
7g	Me	(<i>S</i>)-Ph(OMe)CH	Rh ₂ (2' <i>S</i> ,4 <i>S</i> -MANIM) ₄
7h	Me	(<i>R</i>)-Ph(OMe)CH	Rh ₂ (2' <i>R</i> ,4 <i>S</i> -MANIM) ₄
7i	Me	(+)-menthyl	Rh ₂ (1' <i>S</i> ,2' <i>R</i> ,5' <i>S</i> ,4 <i>S</i> -MNACIM) ₄
7j	Me	(-)-menthyl	Rh ₂ (1' <i>R</i> ,2' <i>S</i> ,5' <i>R</i> ,4 <i>S</i> -MNACIM) ₄
7k	Me		Rh ₂ (2' <i>S</i> ,3' <i>S</i> ,4 <i>S</i> -MCPIM) ₄
7l	Me		Rh ₂ (2' <i>R</i> ,3' <i>R</i> ,4 <i>S</i> -MCPIM) ₄
7m	Me		Rh ₂ (2' <i>S</i> ,4 <i>S</i> -BSPIM) ₄
7n	Me		Rh ₂ (2' <i>R</i> ,4 <i>S</i> -BSPIM) ₄
7o	<i>t</i> -Bu	Me	Rh ₂ (4 <i>S</i> -BACIM) ₄
			
11 Rh ₂ (cap) ₄			
			
9 Rh ₂ (4 <i>S</i> ,5 <i>R</i> -THREOX) ₄			
			
10 Rh ₂ (5- <i>q</i> FIBAZ) ₄			



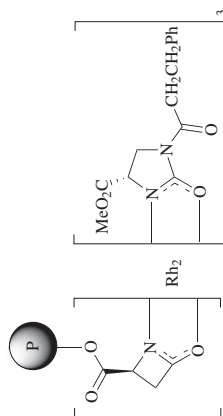
7a = 12 (1,3)-Rh₂(4S-MACIM)₄



13 N-AZ-Rh₂(5S-MEPY)₃

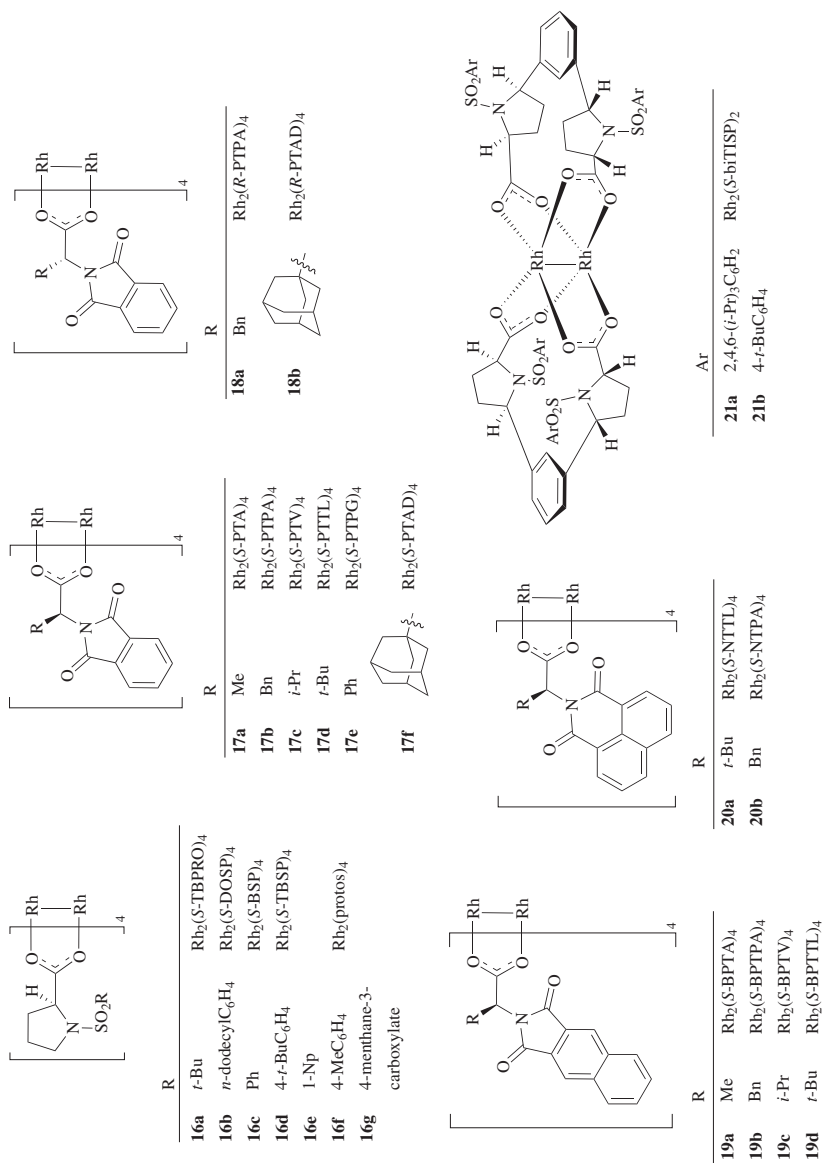


14 N-AZ-Rh₂(4S-MEAZ)₃



15 N-AZ-Rh₂(4S-MPPIM)₃

CHART 2. CHIRAL DIRHODIUM CARBOXYLATE CATALYSTS



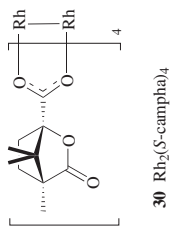
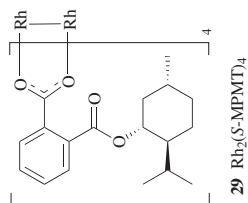
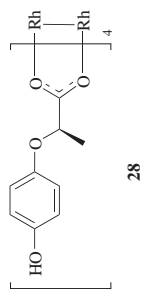
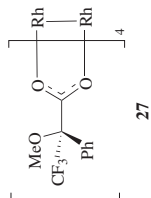
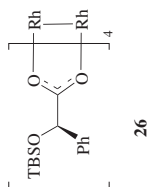
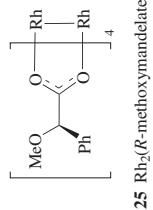
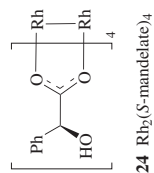
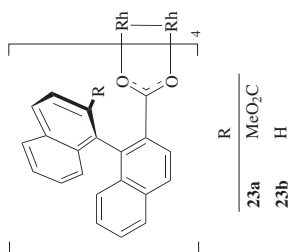
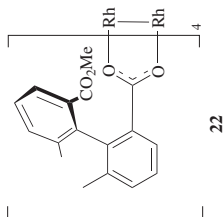


CHART 2. CHIRAL DIRHODIUM CARBOXYLATE CATALYSTS (Continued)

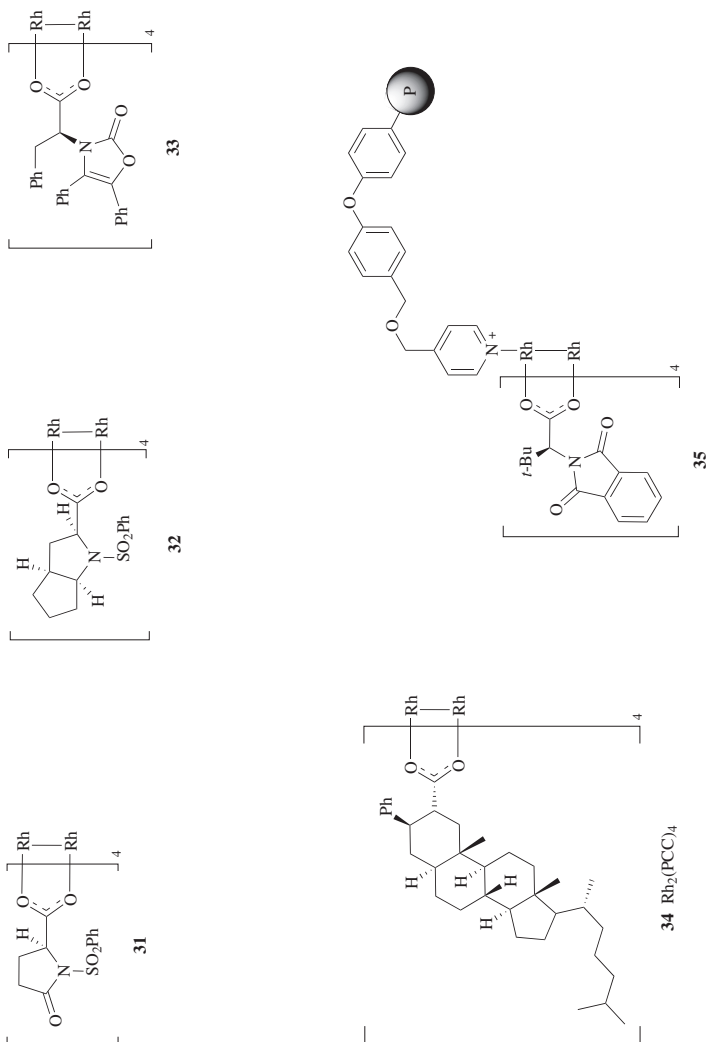


CHART 3. CHIRAL ARYLPHOSPHATE DIRHODIUM CATALYSTS

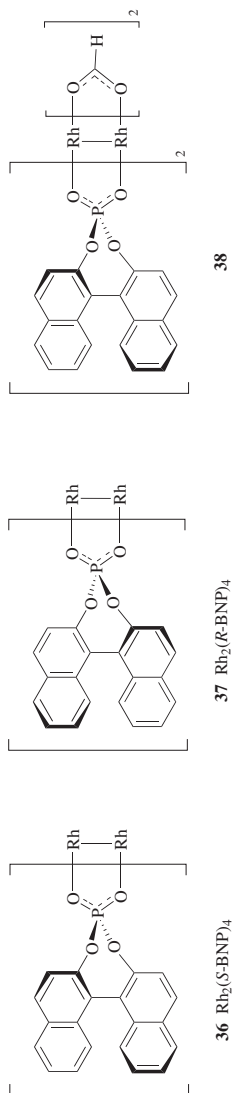


CHART 4. CHIRAL *cis*-ORTHOMETALATED ARYLPHOSPHINE DIRHODIUM CATALYSTS

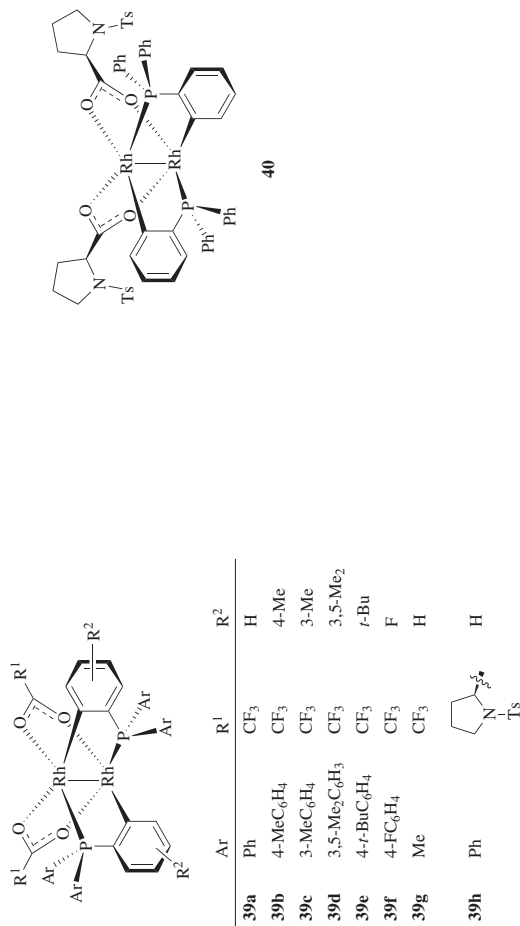
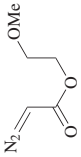
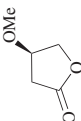
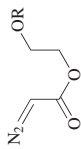
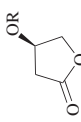


TABLE 1. MONOCYCLIC γ -LACTONES FROM DIAZOACETATES

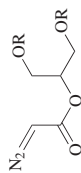
C₄

Please refer to the charts preceding the tables, not to the text discussion, for structures indicated by the **bold** numbers.

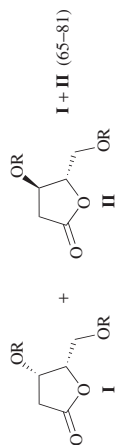
Diazoacetate	Conditions	Product(s) and Yield(s) (%)	Refs.																																																																				
	Catalyst, DCM																																																																						
		<table> <tr> <th>Cat.</th><th>Temp</th><th>Time (h)</th><th>% ee</th></tr> <tr> <td>1a</td><td>reflux</td><td>6</td><td>(62) 91 (S)</td></tr> <tr> <td>1a</td><td>reflux</td><td>24</td><td>(—) 91 (S)</td></tr> <tr> <td>2a</td><td>reflux</td><td>6</td><td>(73) 91 (R)</td></tr> <tr> <td>3a</td><td>reflux</td><td>6</td><td>(65) 92 —</td></tr> <tr> <td>3c</td><td>reflux</td><td>24</td><td>(78) 55 (R)</td></tr> <tr> <td>4b</td><td>reflux</td><td>24</td><td>(—) 11 (S)</td></tr> <tr> <td>7a</td><td>reflux</td><td>6</td><td>(58) 58 —</td></tr> <tr> <td>7b</td><td>reflux</td><td>6</td><td>(56) 56 —</td></tr> <tr> <td>7c</td><td>reflux</td><td>6</td><td>(50) 50 —</td></tr> <tr> <td>7d</td><td>reflux</td><td>6</td><td>(63) 63 —</td></tr> <tr> <td>7k</td><td>reflux</td><td>6</td><td>(69) 91 —</td></tr> <tr> <td>7l</td><td>reflux</td><td>6</td><td>(64) 46 —</td></tr> <tr> <td>7m</td><td>reflux</td><td>6</td><td>(72) 94 —</td></tr> <tr> <td>7n</td><td>reflux</td><td>6</td><td>(72) 6 —</td></tr> <tr> <td>7i</td><td>35°</td><td>2</td><td>(66) 93 —</td></tr> <tr> <td>7j</td><td>35°</td><td>2</td><td>(75) 55 —</td></tr> </table>	Cat.	Temp	Time (h)	% ee	1a	reflux	6	(62) 91 (S)	1a	reflux	24	(—) 91 (S)	2a	reflux	6	(73) 91 (R)	3a	reflux	6	(65) 92 —	3c	reflux	24	(78) 55 (R)	4b	reflux	24	(—) 11 (S)	7a	reflux	6	(58) 58 —	7b	reflux	6	(56) 56 —	7c	reflux	6	(50) 50 —	7d	reflux	6	(63) 63 —	7k	reflux	6	(69) 91 —	7l	reflux	6	(64) 46 —	7m	reflux	6	(72) 94 —	7n	reflux	6	(72) 6 —	7i	35°	2	(66) 93 —	7j	35°	2	(75) 55 —	258 274 258 242 274 274 242 242 242 242 244 244 244 244 264 264
Cat.	Temp	Time (h)	% ee																																																																				
1a	reflux	6	(62) 91 (S)																																																																				
1a	reflux	24	(—) 91 (S)																																																																				
2a	reflux	6	(73) 91 (R)																																																																				
3a	reflux	6	(65) 92 —																																																																				
3c	reflux	24	(78) 55 (R)																																																																				
4b	reflux	24	(—) 11 (S)																																																																				
7a	reflux	6	(58) 58 —																																																																				
7b	reflux	6	(56) 56 —																																																																				
7c	reflux	6	(50) 50 —																																																																				
7d	reflux	6	(63) 63 —																																																																				
7k	reflux	6	(69) 91 —																																																																				
7l	reflux	6	(64) 46 —																																																																				
7m	reflux	6	(72) 94 —																																																																				
7n	reflux	6	(72) 6 —																																																																				
7i	35°	2	(66) 93 —																																																																				
7j	35°	2	(75) 55 —																																																																				
	Catalyst, DCM, reflux, 6 h																																																																						
		<table> <tr> <th>R</th><th>Cat.</th><th>% ee</th></tr> <tr> <td>Et</td><td>1a</td><td>(64) 89 (S)</td></tr> <tr> <td>Et</td><td>2a</td><td>(63) 89 (R)</td></tr> <tr> <td>Bn</td><td>1a</td><td>(64) 87 (S)</td></tr> <tr> <td>Bn</td><td>2a</td><td>(69) 87 (R)</td></tr> </table>	R	Cat.	% ee	Et	1a	(64) 89 (S)	Et	2a	(63) 89 (R)	Bn	1a	(64) 87 (S)	Bn	2a	(69) 87 (R)	258																																																					
R	Cat.	% ee																																																																					
Et	1a	(64) 89 (S)																																																																					
Et	2a	(63) 89 (R)																																																																					
Bn	1a	(64) 87 (S)																																																																					
Bn	2a	(69) 87 (R)																																																																					

Please refer to the charts preceding the tables, not to the text discussion, for structures indicated by the **bold** numbers.

C₄

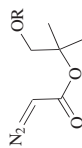
C₅

Catalyst, DCM, reflux, 10 h

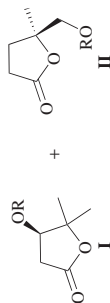


153, 154

R	Cat.	I/II	% ee I	% ee II
Me	2a	93:7	97 (3 <i>R</i> ,4 <i>R</i>)	50 (3 <i>S</i> ,4 <i>R</i>)
Me	1a	94:6	97 (3 <i>S</i> ,4 <i>S</i>)	45 (3 <i>R</i> ,4 <i>S</i>)
Me	3a	91:9	98 (3 <i>S</i> ,4 <i>S</i>)	76 (3 <i>R</i> ,4 <i>S</i>)
Et	2a	93:7	89 (3 <i>R</i> ,4 <i>R</i>)	50 (3 <i>S</i> ,4 <i>R</i>)
Et	1a	94:6	90 (3 <i>S</i> ,4 <i>S</i>)	45 (3 <i>R</i> ,4 <i>S</i>)
Et	3a	91:9	96 (3 <i>S</i> ,4 <i>S</i>)	85 (3 <i>R</i> ,4 <i>S</i>)
Bn	2a	93:7	94 (3 <i>R</i> ,4 <i>R</i>)	50 (3 <i>S</i> ,4 <i>R</i>)
Bn	1a	93:7	94 (3 <i>S</i> ,4 <i>S</i>)	— (3 <i>R</i> ,4 <i>S</i>)
Bn	3a	90:10	94 (3 <i>S</i> ,4 <i>S</i>)	— (3 <i>R</i> ,4 <i>S</i>)

C₆

Catalyst, DCM, reflux, 6 h



R	Cat.	I + II	I/II	% ee I
Me	1a	(68)	—	56 (S)
Me	2a	(70)	—	57 (R)
Me	7a	(85)	87:13	56 (S)
Bn	1a	(85)	—	51 (S)
Bn	7a	(74)	84:16	58 (S)

258

258

261

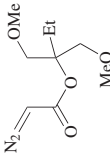
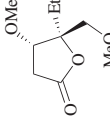
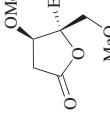
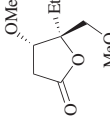
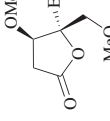
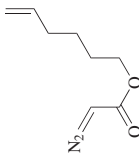
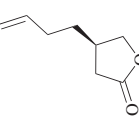
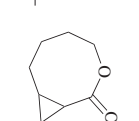
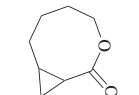
258

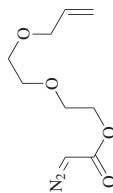
261

TABLE 1. MONOCYCLIC γ -LACTONES FROM DIAZOACETATES (Continued)

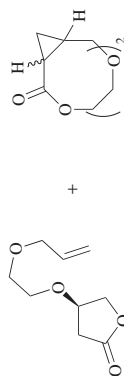
Diazoacetate	Conditions	Product(s) and Yield(s) (%)					Refs.				
C ₆₋₈	Catalyst 7c , DCM, reflux, 10 h					I	II				
						R	% ee I	% ee II			
						Me	(52)	96	(4)		
						<i>i</i> -Pr	(60)	95	(5)	(5)	259
C ₇	Catalyst, DCM, reflux					I	II				
						R	% ee I	% ee II			
						Me	(52)	96	(4)		
						<i>i</i> -Pr	(60)	95	(5)	(5)	259
C ₇	Catalyst, DCM, reflux, 12 h					I	II				
						R	% ee I	% ee II			
						Me	(52)	96	(4)		
						<i>i</i> -Pr	(60)	95	(5)	(5)	259

TABLE 1. MONOCYCLIC γ -LACTONES FROM DIAZOACETATES (*Continued*)

Diazoacetate	Conditions	Product(s) and Yield(s) (%)	Refs.	
	Catalyst, DCM, reflux, 10 h	 I  II +  I  II 34–72% ee 34–72% ee	Cat. $\text{Rh}_2(\text{OAc})_4$ 2a 3a 7a (86) (79) (61) (82) 76:24 60:40 64:36 55:45	154
	Catalyst, DCM, reflux	 I  II +  34–72% ee 34–72% ee	Cat. $\text{Rh}_2(\text{OAc})_4$ 16a 5b 1a 7c 3a 41b 16:84 18:82 50:50 86:14 87:13 19:81 <1:99 — 10 50 95 >97 97 74	313

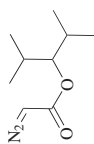
C₉

Catalyst, DCM, reflux, 2.5 h

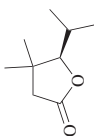


315

Cat.	I + II	I/II	II	<i>cis/trans</i>	% ee I	% ee <i>cis</i> - II	% ee <i>trans</i> - II
Rh ₂ (OAc) ₄	(83)	4:96		87:13	—	—	—
Cu(MeCN) ₄ PF ₆	(64)	0:100		91:9	—	—	—
41b	(58)	0:100		86:14	—	79	85
16a	(80)	2:98		87:13	14	11	12
10	(67)	15:85		84:16	75	33	67
5b	(69)	58:42		88:12	90	56	64
1a	(77)	95:5		88:12	92	53	65
3a	(73)	99:1		88:12	92	48	67

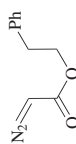


Catalyst, DCM, rt, 20 h

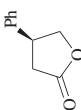


155

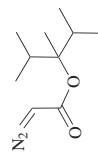
Cat.	% ee
1a	(42)
2a	(42)
	95

C₁₀

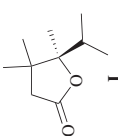
Catalyst, DCM, reflux, 6 h



258



Catalyst, DCM, reflux, 6 h



Cat.	I + II	I/II	% ee I
1a	(77)	93:7	61
2a	(77)	—	60
2b	(82)	—	70
3a	(70)	70:30	0
7a	(73)	83:17	85

258

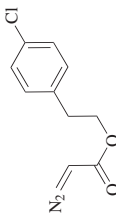
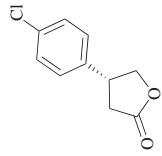
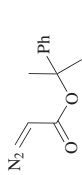
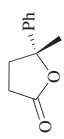
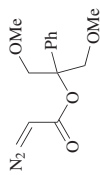
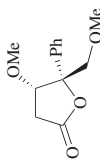
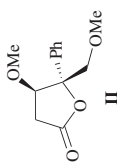
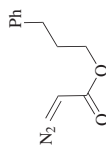
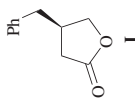
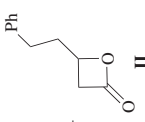
258

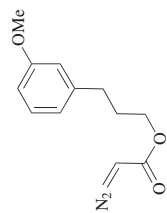
258

261

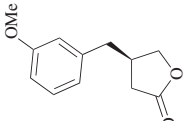
261

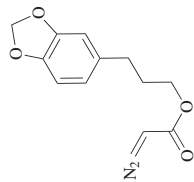
TABLE 1. MONOCYCLIC γ -LACTONES FROM DIAZOACETATES (Continued)

Diazoacetate	Conditions	Product(s) and Yield(s) (%)	Refs.																				
C₁₀ 	Catalyst, DCM, reflux, 5 h	 <table><tr><th>Cat.</th><th>% ee</th></tr><tr><td>7c</td><td>(81) 95 (R)</td></tr><tr><td>2a</td><td>(13) 51 (S)</td></tr><tr><td>3a</td><td>(67) 45 (S)</td></tr></table>	Cat.	% ee	7c	(81) 95 (R)	2a	(13) 51 (S)	3a	(67) 45 (S)	328												
Cat.	% ee																						
7c	(81) 95 (R)																						
2a	(13) 51 (S)																						
3a	(67) 45 (S)																						
C₁₁ 	Catalyst, DCM, reflux, 6 h	 <table><tr><th>Cat.</th><th>% ee</th></tr><tr><td>1a</td><td>(30) 76 (R)</td></tr><tr><td>2a</td><td>(39) 79 (S)</td></tr></table>	Cat.	% ee	1a	(30) 76 (R)	2a	(39) 79 (S)	258														
Cat.	% ee																						
1a	(30) 76 (R)																						
2a	(39) 79 (S)																						
	Catalyst, DCM, reflux, 10 h	 I +  II	154																				
	Catalyst, DCM, reflux, 13 h	 I +  II <table><tr><th>Cat.</th><th>I + II</th><th>I/II</th><th>% ee I</th></tr><tr><td>2a</td><td>(49)</td><td>93:7</td><td>72 (R)</td></tr><tr><td>3a</td><td>(76)</td><td>94:6</td><td>51 (S)</td></tr><tr><td>7c</td><td>(59)</td><td>93:7</td><td>87 (S)</td></tr><tr><td>8b</td><td>(76)</td><td>93:7</td><td>91 (R)</td></tr></table>	Cat.	I + II	I/II	% ee I	2a	(49)	93:7	72 (R)	3a	(76)	94:6	51 (S)	7c	(59)	93:7	87 (S)	8b	(76)	93:7	91 (R)	259
Cat.	I + II	I/II	% ee I																				
2a	(49)	93:7	72 (R)																				
3a	(76)	94:6	51 (S)																				
7c	(59)	93:7	87 (S)																				
8b	(76)	93:7	91 (R)																				

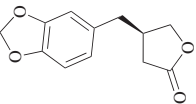


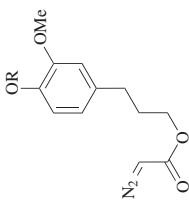
Catalyst, DCM, reflux, 10 h

	Cat.	% ee	
	3a (56)	45 (<i>R</i>)	259
	2a (66)	68 (<i>S</i>)	223
	7a (25)	84 (<i>S</i>)	223
	7c (66)	91 (<i>S</i>)	223
	8b (63)	93 (<i>R</i>)	223



Catalyst, DCM, reflux, 13 h

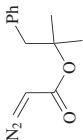
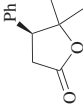
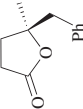
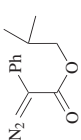
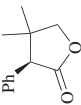
	Cat.	% ee	
	7c (67)	95 (<i>S</i>)	259
	8b (57)	95 (<i>R</i>)	



Catalyst, DCM, reflux, 10 h

R	Cat.	Time (h)	% ee	
Me	7c	10	(62)	94 (<i>S</i>)
Me	8b	10	(61)	94 (<i>R</i>)
Bn	8b	10	(59)	96.5 (<i>R</i>)
TBDPS	7c	5	(68)	93 (<i>S</i>)
TBDPS	2a	5	(51)	67 (<i>R</i>)
TBDPS	3a	5	(37)	36 (<i>S</i>)
TBDPS	5b	5	(40)	42 (<i>S</i>)

TABLE 1. MONOCYCLIC γ -LACTONES FROM DIAZOACETATES (Continued)

Diazoacetate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12} 	 I +  II Catalyst, DCM, reflux, 6 h	1a 3a 7a (62) (75) (74) 30:70 20:80 32:68 53 34 77 70 10 83	261
	 Catalyst, reflux	6 5b 16b 16b Rh₂(OAc)₄ DCM DCM DCM DCM pentane (79) (94) (89) (95) (89) — 90 84 56 86	143

^a The catalyst was diluted by a factor of 20.

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES

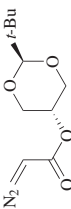
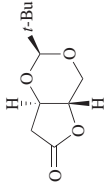
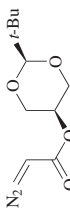
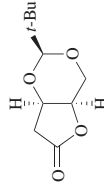
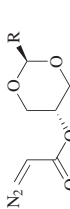
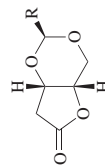
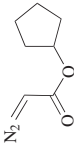
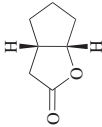
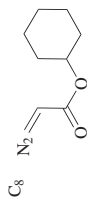
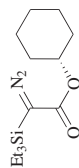
Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
<i>Please refer to the charts preceding the tables, not to the text discussion, for structures indicated by the bold numbers.</i>			
	Catalyst, DCM, reflux, 6 h	 Cat. 5b (35) 81 3a (42) 59 1a (49) 52	154
	Catalyst, DCM, reflux, 6 h	 Cat. 5b (32) 85 3a (57) 96 4a (55) 96 7c (59) 91	154
	Catalyst, DCM, reflux, 6 h	 R Cat. 5b (85) 88 Ph 3a (48) 67 Ph 1a (71) 94 Ph 2a (75) 94 2-Np 3a (68) 83 2-Np 1a (72) 95	154

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

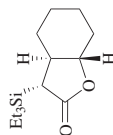
Cyclic Ketone	Conditions		Product(s) and Yield(s) (%)				Refs.
	Cat.	Temp	Time (h)	% ee			
							
	1a	rt	20	(25)	38	(3S,6S)	155
	1a	reflux	12	(54)	40	—	152
	2a	rt	20	(25)	38	(3R,6R)	155
	3c	rt	20	(15)	3	—	155
	7a	reflux	12	(40)	89	—	152
	7c	reflux	6	(67)	93	—	244
	7k	reflux	6	(81)	88	—	244
	7l	reflux	6	(75)	40	—	244
	7m	reflux	6	(78)	98	—	244
	7n	reflux	6	(62)	22	—	244
	7i	reflux	2	(84)	33	—	264
	7j	reflux	2	(79)	77	—	264



Cat.	Temp	Time (h)			I/II		% ee I				% ee II	
			I + II									
Rh ₂ (OAc) ₄	rt	20	(46)	40:60	—	—	—	—	—	—	—	155
Rh ₂ (OAc) ₄	reflux	10	(70)	40:60	—	—	—	—	—	—	—	243
1a	rt	20	(30)	75:25	95	(35,7S)	90	(35,7R)	90	(35,7R)	155	243
1a	—	—	(68–80)	86:14	>99	—	—	—	—	—	—	263
1b	—	—	(68–80)	74:26	99	—	—	—	—	—	—	263
2a	rt	20	(30)	75:25	97	(3R,7R)	—	(3R,7S)	—	(3R,7S)	155	243
2a	reflux	10	(65)	75:25	97	—	—	—	—	—	—	243
3a	reflux	10	(50)	55:45	96	—	—	—	—	—	—	243
3b	rt	20	(5)	—	—	—	—	(3R,7S)	—	(3R,7S)	155	243
3c	rt	20	(30)	33:67	60	(3R,7R)	60	(3R,7S)	60	(3R,7S)	155	243
7a	reflux	10	(70)	99:1	97	(3S,7S)	63	(3S,7R)	63	(3S,7R)	243	244
7c	reflux	6	(71)	100:0	92	—	—	—	—	—	—	251
7e	reflux	—	(57)	84:16	88	—	—	—	—	—	—	251
7f	reflux	—	(69)	78:22	88	—	—	—	—	—	—	251
7g	reflux	16	(60)	87:13	82	(3S,7S)	56	(3S,7R)	56	(3S,7R)	262	262
7h	reflux	16	(68)	72:28	80	(3S,7S)	72	(3S,7R)	72	(3S,7R)	262	264
7i	35°	2	(80)	100:0	95	—	—	—	—	—	—	264
7j	35°	2	(71)	79:21	84	—	—	—	—	—	—	264
7k	reflux	6	(78)	99:1	97	—	—	—	—	—	—	244
7l	reflux	6	(63)	80:20	72	—	—	—	—	—	—	244
7m	reflux	6	(88)	97:3	>99	—	—	—	—	—	—	244
7n	reflux	6	(89)	98:2	74	—	—	—	—	—	—	244
7o	reflux	—	(82)	99:1	99	—	—	—	—	—	—	251
13	—	—	(68–80)	54:46	97	—	—	—	—	—	—	263
15	—	—	(68–80)	60:40	95	—	—	—	—	—	—	263



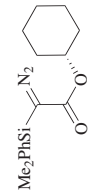
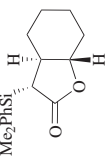
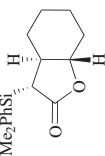
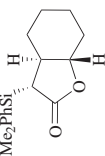
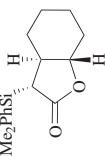
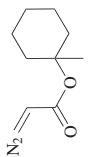
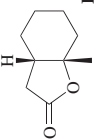
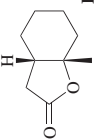
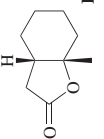
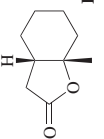
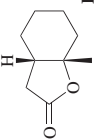
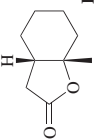
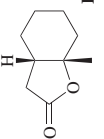
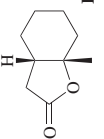
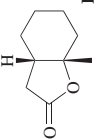
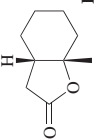
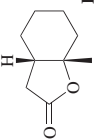
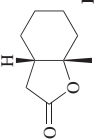
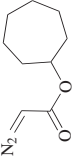
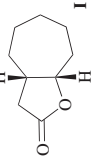
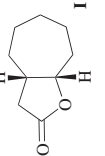
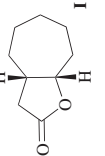
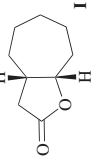
Catalyst, Solvent

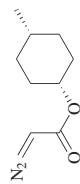


256

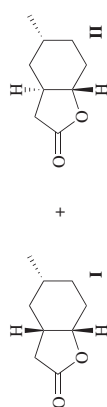
	Cat.	Solvent	Temp	Time (h)	% ee
	Rh ₂ (OAc) ₄	benzene	reflux	15	(42) —
	Rh ₂ (OAc) ₄	toluene	rt	96	(33) —
	Rh ₂ (OAc) ₄	DCM	rt	24	(61) —
<i>enr</i> - 22		benzene	reflux	21	(21) 39
1a		benzene	reflux	48	(16) 0
3a		benzene	reflux	6	(0) —
5d		benzene	reflux	5	(10) 71
5d		DCE	reflux	20	(11) 74
5d		toluene	reflux	4	(4) 79
5d		PhCF ₃	reflux	3	(7) 62
16b		benzene	reflux	1.5	(49) 13
16d		benzene	reflux	1.5	(45) 13
17b		benzene	reflux	2	(50) 19
17b		PhCF ₃	reflux	3	(48) 16
17d		benzene	60°	1	(67) 60
17d		toluene	rt	1.5	(75) 64
19d		toluene	rt	1	(74) 66
20a		benzene	reflux	15	(68) 59
20a		benzene	rt	2.5	(82) 62
20a		DCM	reflux	1	(87) 56
20a		DCM	rt	2	(90) 56
20a		toluene	rt	1.5	(76) 61
36		benzene	reflux	2.5	(30) 40
29		benzene	40°	2.5	(34) 7
30		benzene	reflux	15	(62) 2

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (Continued)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)				Refs.
		Cat.	Temp	Time (h)	% ee	
C₈ 	Catalyst, toluene		Rh ₂ (OAc) ₄	reflux	2 (29)	—
			20a	rt	48 (34)	41
			17d	reflux	2 (27)	42
			19d	reflux	2.5 (4)	43
C₉ 	Catalyst, DCM					
						
						
						
						
						
						
						
						
						
						
						
	Catalyst, DCM, reflux, 10 h					
						
						
						

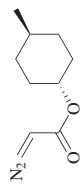


Catalyst, DCM, reflux, 10 h

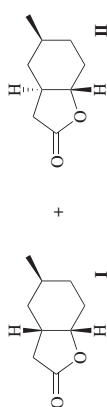


243

Cat.	I + II	I/II	% ee I	% ee II
2a	(—)	98:2	98	84
3a	(—)	>99:1	98	—
7a	(—)	>99:1	95	—



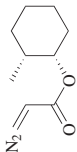
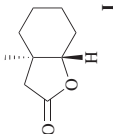
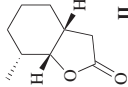
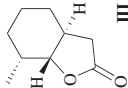
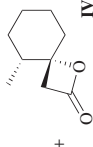
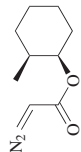
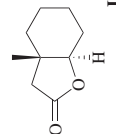
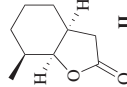
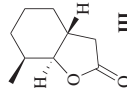
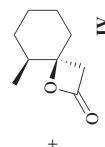
Catalyst, DCM, reflux, 10 h

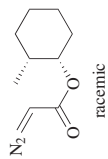


243

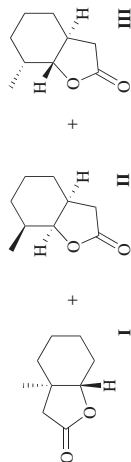
Cat.	I + II	I/II	% ee I	% ee II
2a	(—)	15:85	82	91
3a	(—)	10:90	68	95
7a	(—)	63:37	93	57

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (Continued)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)		Refs.																					
	Catalyst, DCM, reflux, 11 h		 + 	134																					
																									
		<table><tr><th>Cat.</th><th>I + II + III + IV</th><th>I/II/III/IV</th></tr><tr><td>1a</td><td>(95)</td><td>94:1:0:5</td></tr><tr><td>2a</td><td>(79)</td><td>4:91:3:2</td></tr><tr><td>3a</td><td>(82)</td><td>90:1:0:9</td></tr><tr><td>4a</td><td>(91)</td><td>2:88:7:3</td></tr><tr><td>7c</td><td>(46)</td><td>28:16:0:56</td></tr><tr><td>8b</td><td>(88)</td><td>0:98:0:2</td></tr></table>		Cat.	I + II + III + IV	I/II/III/IV	1a	(95)	94:1:0:5	2a	(79)	4:91:3:2	3a	(82)	90:1:0:9	4a	(91)	2:88:7:3	7c	(46)	28:16:0:56	8b	(88)	0:98:0:2	
Cat.	I + II + III + IV	I/II/III/IV																							
1a	(95)	94:1:0:5																							
2a	(79)	4:91:3:2																							
3a	(82)	90:1:0:9																							
4a	(91)	2:88:7:3																							
7c	(46)	28:16:0:56																							
8b	(88)	0:98:0:2																							
	Catalyst, DCM, reflux, 11 h		 + 	134																					
																									
		<table><tr><th>Cat.</th><th>I + II + III + IV</th><th>I/II/III/IV</th></tr><tr><td>1a</td><td>(86)</td><td>5:90:3:2</td></tr><tr><td>2a</td><td>(74)</td><td>92:3:0:5</td></tr><tr><td>3a</td><td>(89)</td><td>2:88:7:3</td></tr><tr><td>4a</td><td>(86)</td><td>88:3:0:9</td></tr><tr><td>7a</td><td>(90)</td><td>1:96:1:2</td></tr><tr><td>7c</td><td>(91)</td><td>0:98:0:2</td></tr></table>		Cat.	I + II + III + IV	I/II/III/IV	1a	(86)	5:90:3:2	2a	(74)	92:3:0:5	3a	(89)	2:88:7:3	4a	(86)	88:3:0:9	7a	(90)	1:96:1:2	7c	(91)	0:98:0:2	
Cat.	I + II + III + IV	I/II/III/IV																							
1a	(86)	5:90:3:2																							
2a	(74)	92:3:0:5																							
3a	(89)	2:88:7:3																							
4a	(86)	88:3:0:9																							
7a	(90)	1:96:1:2																							
7c	(91)	0:98:0:2																							

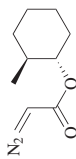


Catalyst, DCM, reflux, 11 h

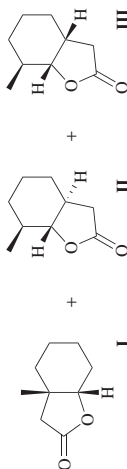


266

Cat.	I + II + III + IV	I/II/III/IV	% ee I	% ee II	% ee IV
1a	(75)	45:49:2:4	91	98	4
2a	(62)	44:49:2:5	92	98	5
3a	(86)	40:47:4:9	99	99	9
7a	(77)	11:66:1:22	87	77	22



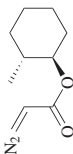
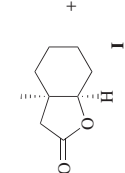
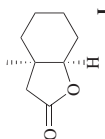
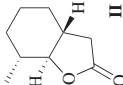
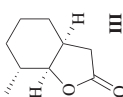
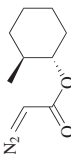
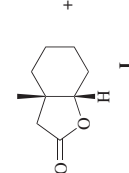
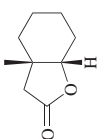
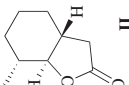
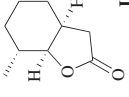
Catalyst, DCM, reflux, 11 h



134

Cat.	I + II + III + IV	I/II/III/IV
1a	(71)	92:3:2:3
2a	(64)	10:74:1:60
3a	(77)	87:3:1:9
4a	(86)	2:87:9:2
7c	(69)	58:9:7:26
11	(12)	56:38:6:0

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (Continued)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.																														
	Catalyst, DCM, reflux, 11 h	    <table> <tr> <th>Cat.</th><th>I + II + III + IV</th><th>I/II/III/IV</th></tr> <tr> <td>1a</td><td>(75)</td><td>13:72:15:0</td></tr> <tr> <td>2a</td><td>(56)</td><td>88:6:3:3</td></tr> <tr> <td>3a</td><td>(92)</td><td>4:85:9:2</td></tr> <tr> <td>4a</td><td>(74)</td><td>84:4:3:9</td></tr> <tr> <td>7c</td><td>(81)</td><td>3:21:76:0</td></tr> </table>	Cat.	I + II + III + IV	I/II/III/IV	1a	(75)	13:72:15:0	2a	(56)	88:6:3:3	3a	(92)	4:85:9:2	4a	(74)	84:4:3:9	7c	(81)	3:21:76:0	134												
Cat.	I + II + III + IV	I/II/III/IV																															
1a	(75)	13:72:15:0																															
2a	(56)	88:6:3:3																															
3a	(92)	4:85:9:2																															
4a	(74)	84:4:3:9																															
7c	(81)	3:21:76:0																															
 racemic	Catalyst, DCM, reflux, 11 h	    <table> <tr> <th>Cat.</th><th>I + II + III + IV</th><th>I/II/III/IV</th><th>% ee I</th><th>% ee II</th><th>% ee III</th></tr> <tr> <td>1a</td><td>(65)</td><td>49:40:9:2</td><td>80</td><td>93</td><td>78</td></tr> <tr> <td>2a</td><td>(57)</td><td>47:41:9:3</td><td>79</td><td>93</td><td>82</td></tr> <tr> <td>3a</td><td>(75)</td><td>39:50:6:5</td><td>96</td><td>95</td><td>79</td></tr> <tr> <td>7a</td><td>(57)</td><td>18:19:51:12</td><td>87</td><td>49</td><td>86</td></tr> </table>	Cat.	I + II + III + IV	I/II/III/IV	% ee I	% ee II	% ee III	1a	(65)	49:40:9:2	80	93	78	2a	(57)	47:41:9:3	79	93	82	3a	(75)	39:50:6:5	96	95	79	7a	(57)	18:19:51:12	87	49	86	266
Cat.	I + II + III + IV	I/II/III/IV	% ee I	% ee II	% ee III																												
1a	(65)	49:40:9:2	80	93	78																												
2a	(57)	47:41:9:3	79	93	82																												
3a	(75)	39:50:6:5	96	95	79																												
7a	(57)	18:19:51:12	87	49	86																												

C₉

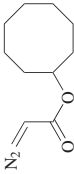
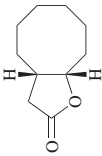
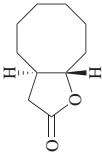
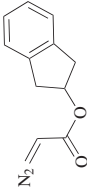
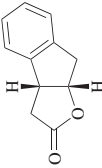
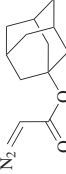
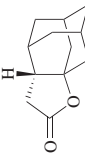
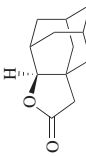
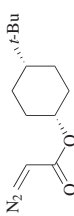
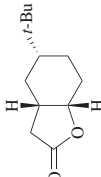
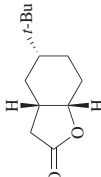
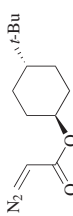
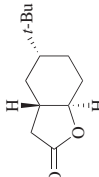
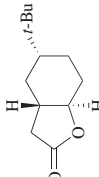
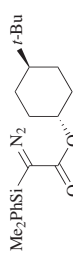
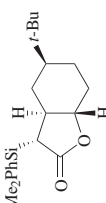
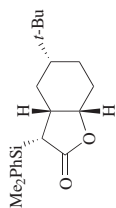
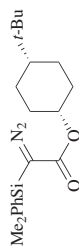
C ₁₀		Catalyst, DCM, reflux, 10 h		+		243																									
			<table> <tr> <th>Cat.</th><th>I + II</th><th>I/II</th><th>% ee I</th><th>% ee II</th></tr> <tr> <td>Rh₂(OAc)₄</td><td>(33)</td><td>29:71</td><td>—</td><td>—</td></tr> <tr> <td>2a</td><td>(80)</td><td>72:28</td><td>97</td><td>59</td></tr> <tr> <td>3a</td><td>(60)</td><td>57:43</td><td>99</td><td>95</td></tr> <tr> <td>7a</td><td>(62)</td><td>99:1</td><td>97</td><td>95</td></tr> </table>	Cat.	I + II	I/II	% ee I	% ee II	Rh ₂ (OAc) ₄	(33)	29:71	—	—	2a	(80)	72:28	97	59	3a	(60)	57:43	99	95	7a	(62)	99:1	97	95			
Cat.	I + II	I/II	% ee I	% ee II																											
Rh ₂ (OAc) ₄	(33)	29:71	—	—																											
2a	(80)	72:28	97	59																											
3a	(60)	57:43	99	95																											
7a	(62)	99:1	97	95																											
C ₁₁		Catalyst, DCM, reflux, 12 h				152																									
			<table> <tr> <th>Cat.</th><th>% ee</th></tr> <tr> <td>1a</td><td>(35) 36</td></tr> <tr> <td>7a</td><td>(20) 79</td></tr> <tr> <td>7c</td><td>(75) 92</td></tr> </table>	Cat.	% ee	1a	(35) 36	7a	(20) 79	7c	(75) 92																				
Cat.	% ee																														
1a	(35) 36																														
7a	(20) 79																														
7c	(75) 92																														
C ₁₂		Catalyst 3a , DCM, reflux, 10 h		(86)	90% ee	247																									
						247																									
			<table> <tr> <th>Cat.</th><th>% ee</th></tr> <tr> <td>3a</td><td>(82) 98</td></tr> <tr> <td>1a</td><td>— 88</td></tr> </table>	Cat.	% ee	3a	(82) 98	1a	— 88																						
Cat.	% ee																														
3a	(82) 98																														
1a	— 88																														

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (Continued)

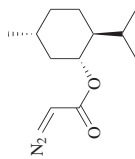
Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)			Refs.																																								
C_{12} 	Catalyst, DCM, reflux, 20 h		Cat. 1a	% ee (40)	155																																								
			2a	(40)																																									
	Catalyst, DCM, reflux, 20 h		Cat. 1a	% ee (30)	155																																								
			2a	(30)																																									
	Catalyst, Solvent				256																																								
<table><tr><th>Cat.</th><th>Solvent</th><th>Temp</th><th>Time (h)</th><th>% ee</th></tr><tr><td>$Rh_2(OAc)_4$</td><td>benzene</td><td>reflux</td><td>15</td><td>(34)</td></tr><tr><td>5d</td><td>benzene</td><td>reflux</td><td>2</td><td>(16)</td></tr><tr><td>37</td><td>benzene</td><td>reflux</td><td>2</td><td>(18)</td></tr><tr><td>17b</td><td>benzene</td><td>reflux</td><td>2</td><td>(7)</td></tr><tr><td>17d</td><td>toluene</td><td>rt</td><td>2</td><td>(73)</td></tr><tr><td>20a</td><td>toluene</td><td>rt</td><td>2</td><td>(73)</td></tr><tr><td>19d</td><td>toluene</td><td>rt</td><td>2</td><td>(63)</td></tr></table>						Cat.	Solvent	Temp	Time (h)	% ee	$Rh_2(OAc)_4$	benzene	reflux	15	(34)	5d	benzene	reflux	2	(16)	37	benzene	reflux	2	(18)	17b	benzene	reflux	2	(7)	17d	toluene	rt	2	(73)	20a	toluene	rt	2	(73)	19d	toluene	rt	2	(63)
Cat.	Solvent	Temp	Time (h)	% ee																																									
$Rh_2(OAc)_4$	benzene	reflux	15	(34)																																									
5d	benzene	reflux	2	(16)																																									
37	benzene	reflux	2	(18)																																									
17b	benzene	reflux	2	(7)																																									
17d	toluene	rt	2	(73)																																									
20a	toluene	rt	2	(73)																																									
19d	toluene	rt	2	(63)																																									



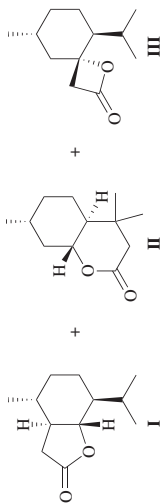
Catalyst, Solvent

256

Cat.	Solvent	Temp	Time (h)	% ee
Rh ₂ (OAc) ₄	benzene	reflux	15	(21)
5d	benzene	reflux	2	(5)
17b	benzene	reflux	2	(23)
17d	toluene	rt	2	(50)
20a	toluene	rt	2	(28)
19d	toluene	rt	2	(42)
				8



Catalyst, DCM, reflux, 11 h



134

Cat.	I + II + III	I/II/III
Rh ₂ (OAc) ₄	(17)	56:44:0
11	(33)	56:44:0
1a	(85)	73:27:0
2a	(84)	42:58:0
3a	(87)	100:0:0
4a	(84)	28:50:22
7c	(72)	73:27:0
5d	(63)	93:7:0
5b	(61)	95:5:0
41b	(15)	93:7:0

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (Continued)

Refs.

Product(s) and Yield(s) (%)

Conditions

Cyclic Ketone

C₁₂

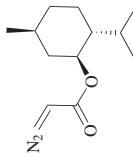
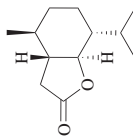
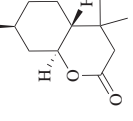
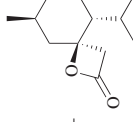
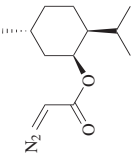
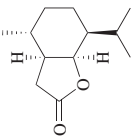
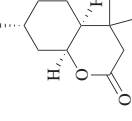
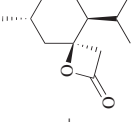
	Catalyst, DCM, reflux, 11 h	 I  II  III	134	Refs.																								
		<table> <tr> <th>Cat.</th><th>I + II + III</th><th>I/II/III</th></tr> <tr> <td>1a</td><td>(70)</td><td>44:56:0</td></tr> <tr> <td>2a</td><td>(92)</td><td>75:25:0</td></tr> <tr> <td>3a</td><td>(61)</td><td>29:53:18</td></tr> <tr> <td>4a</td><td>(75)</td><td>100:0:0</td></tr> <tr> <td>7c</td><td>(50)</td><td>77:23:0</td></tr> <tr> <td>41b</td><td>(28)</td><td>97:3:0</td></tr> </table>	Cat.	I + II + III	I/II/III	1a	(70)	44:56:0	2a	(92)	75:25:0	3a	(61)	29:53:18	4a	(75)	100:0:0	7c	(50)	77:23:0	41b	(28)	97:3:0					
Cat.	I + II + III	I/II/III																										
1a	(70)	44:56:0																										
2a	(92)	75:25:0																										
3a	(61)	29:53:18																										
4a	(75)	100:0:0																										
7c	(50)	77:23:0																										
41b	(28)	97:3:0																										
	Catalyst, DCM, reflux, 11 h	 I  II  III	134																									
		<table> <tr> <th>Cat.</th><th>I + II + III</th><th>I/II/III</th></tr> <tr> <td>Rh₂(OAc)₄</td><td>(16)</td><td>51:49:0</td></tr> <tr> <td>11</td><td>(26)</td><td>55:45:0</td></tr> <tr> <td>1a</td><td>(65)</td><td>52:45:3</td></tr> <tr> <td>2a</td><td>(75)</td><td>89:11:0</td></tr> <tr> <td>3a</td><td>(77)</td><td>28:39:33</td></tr> <tr> <td>4a</td><td>(97)</td><td>98:2:0</td></tr> <tr> <td>41b</td><td>(84)</td><td>94:6:0</td></tr> </table>	Cat.	I + II + III	I/II/III	Rh ₂ (OAc) ₄	(16)	51:49:0	11	(26)	55:45:0	1a	(65)	52:45:3	2a	(75)	89:11:0	3a	(77)	28:39:33	4a	(97)	98:2:0	41b	(84)	94:6:0		
Cat.	I + II + III	I/II/III																										
Rh ₂ (OAc) ₄	(16)	51:49:0																										
11	(26)	55:45:0																										
1a	(65)	52:45:3																										
2a	(75)	89:11:0																										
3a	(77)	28:39:33																										
4a	(97)	98:2:0																										
41b	(84)	94:6:0																										

TABLE 3. β -LACTONES FROM DIAZOACETATES

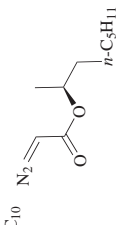
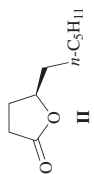
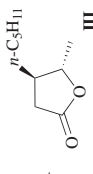
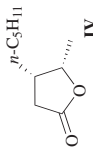
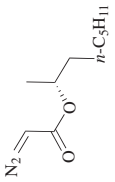
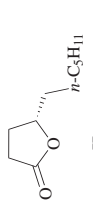
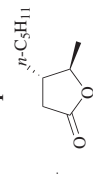
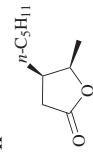
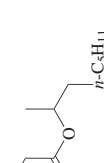
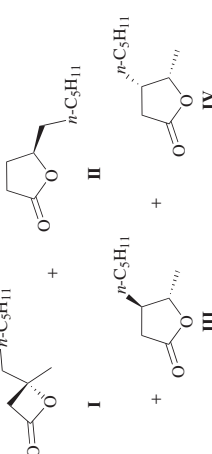
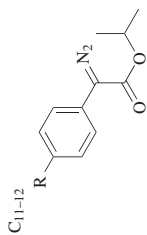
Diazoacetate	Conditions	Product(s) and Yield(s) (%)	Refs.
Please refer to the charts preceding the tables, not to the text discussion, for structures indicated by the bold numbers .			
	Catalyst, DCM, reflux, 11 h	  	266 266 266 134
	Catalyst, DCM, reflux, 11 h	  	266 266 266 134

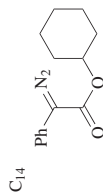
TABLE 3. β -LACTONES FROM DIAZOACETATES (Continued)

Diazoacetate	Conditions	Product(s) and Yield(s) (%)	Refs.							
	Catalyst, DCM, reflux, 11 h		266							
Cat.	I + II + III + IV	I/II/III/IV	% ee I	I	% ee II	II	% ee III	III	% ee IV	IV
1a	(50)	49:7:17:27	16	(R)	88	(R)	6	(4R,5S)	74	(4S,5S)
2a	(45)	85:9:4:2	17	(S)	87	(S)	5	(4S,5R)	77	(4R,5R)
3a	(59)	22:0:2:76	10	(R)	93	(R)	51	(4R,5S)	88	(4S,5S)
7a	(65)	16:0:0:84	15	(R)	98	(R)	64	(4R,5S)	80	(4S,5S)

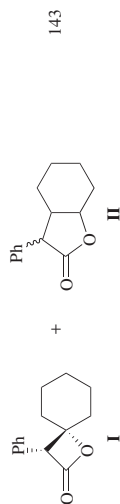


Catalyst, Solvent, reflux

R	Cat.	Solvent	% ee
	Rh ₂ (OAc) ₄	DCM	(84) — 143
H	1a	DCM	(0) — 263
H	13	DCM	(71) 42 263
H	7c	DCM	(0) — 263
H	15	DCM	(74) 39 263
H	5a	DCM	(83) 33 143
H	14	DCM	(83) 28 263
H	5b	DCM	(79) 26 143
H	5d	DCM	(66) 30 143
H	5c	DCM	(85) 35 143
H	5e	DCM	(84) 24 143
H	16b	DCM	(86) 36 143
H	16b	pentane	(78) 41 143
MeO	16b	pentane	— 33 143
Me	5a	DCM	(74) 48 143
Me	16b	pentane	(34) 27 143



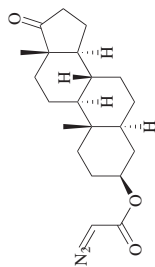
Catalyst, Solvent, reflux



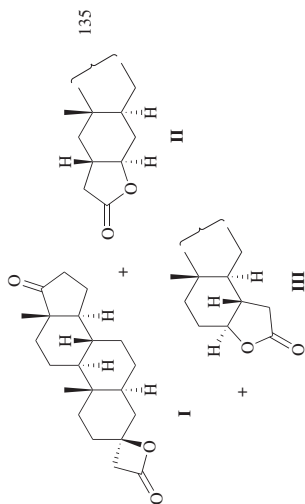
Cat.	Solvent	I + II	I/II	% ee I
Rh ₂ (OAc) ₄	DCM	(55)	98:2	—
5a	DCM	(67)	98:2	50
5b	DCM	(66)	97:3	51
5e	DCM	(65)	97:3	42
16b	DCM	(52)	98:2	49
16b	pentane	(69)	98:2	63

TABLE 3. β -LACTONES FROM DIAZOACETATES (Continued)

	Diazoacetate	Conditions	Product(s) and Yield(s) (%)				Refs.	
C ₁₅		Catalyst, Solvent, reflux		Cat.	Solvent	% ee		
				5a	DCM	(74)	44	143
				16b	pentane	(56)	44	
C ₁₆		Catalyst, Solvent, reflux		+				143
			Cat.	Solvent	I + II		I/II	
			Rh ₂ (OAc) ₄	DCM	(91)	37:63		
			5a	DCM	(79)	22:78		
			6	DCM	(60)	53:47		
			5b	DCM	(68)	36:64		
			16b	pentane	(56)	69:31		

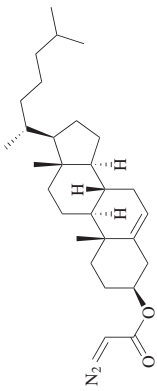
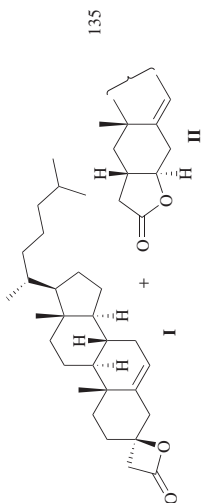


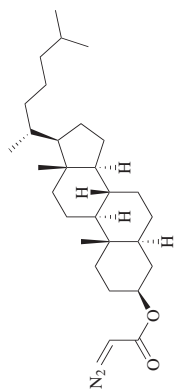
Catalyst, DCM, reflux



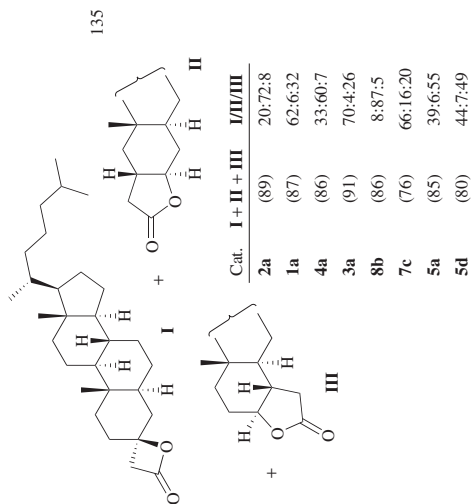
Cat.	Time (h)	I + II + III	I/II/III
Rh ₂ (OAc) ₄	2.5	(62)	32:22:46
2a	5.5	(84)	23:73:4
1a	5.5	(83)	65:3:32
4a	5.5	(89)	37:60:3
3a	5.5	(86)	87:3:10
5a	5.5	(76)	42:1:57

TABLE 3. β -LACTONES FROM DIAZOACETATES (Continued)

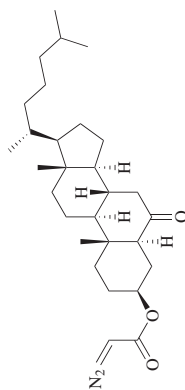
Diazoacetate	Conditions	Product(s) and Yield(s) (%)	Refs.																																												
	Catalyst, DCM, reflux																																														
<table border="1"> <thead> <tr> <th>Cat.</th><th>Time (h)</th><th>I + II</th><th>I/II</th></tr> </thead> <tbody> <tr> <td>Rh₂(OAc)₄</td><td>2.5</td><td>(<5)</td><td>—</td></tr> <tr> <td>2a</td><td>5.5</td><td>(81)</td><td>6:94</td></tr> <tr> <td>1a</td><td>5.5</td><td>(74)</td><td>67:33</td></tr> <tr> <td>4a</td><td>5.5</td><td>(81)</td><td>11:89</td></tr> <tr> <td>3a</td><td>5.5</td><td>(80)</td><td>90:10</td></tr> <tr> <td>5a</td><td>5.5</td><td>(69)</td><td>73:27</td></tr> <tr> <td>5b</td><td>5.5</td><td>(31)</td><td>68:32</td></tr> <tr> <td>7c</td><td>5.5</td><td>(54)</td><td>80:20</td></tr> <tr> <td>41c</td><td>5.5</td><td>—</td><td>28:72</td></tr> <tr> <td>42b</td><td>5.5</td><td>—</td><td>63:37</td></tr> </tbody> </table>				Cat.	Time (h)	I + II	I/II	Rh ₂ (OAc) ₄	2.5	(<5)	—	2a	5.5	(81)	6:94	1a	5.5	(74)	67:33	4a	5.5	(81)	11:89	3a	5.5	(80)	90:10	5a	5.5	(69)	73:27	5b	5.5	(31)	68:32	7c	5.5	(54)	80:20	41c	5.5	—	28:72	42b	5.5	—	63:37
Cat.	Time (h)	I + II	I/II																																												
Rh ₂ (OAc) ₄	2.5	(<5)	—																																												
2a	5.5	(81)	6:94																																												
1a	5.5	(74)	67:33																																												
4a	5.5	(81)	11:89																																												
3a	5.5	(80)	90:10																																												
5a	5.5	(69)	73:27																																												
5b	5.5	(31)	68:32																																												
7c	5.5	(54)	80:20																																												
41c	5.5	—	28:72																																												
42b	5.5	—	63:37																																												



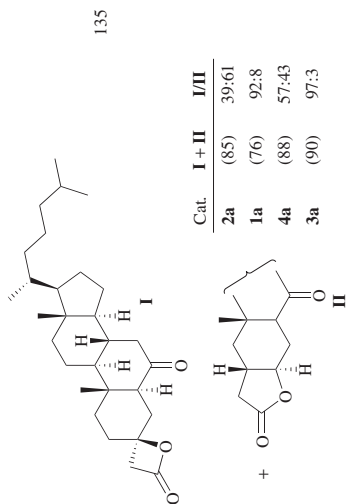
Catalyst, DCM, reflux, 5.5 h



135



Catalyst, DCM, reflux, 5.5 h



135

TABLE 3. β -LACTONES FROM DIAZOACETATES (Continued)

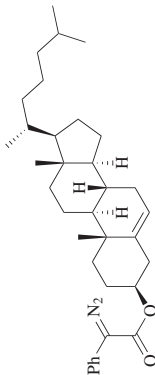
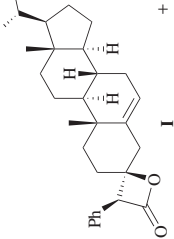
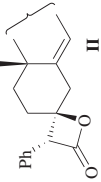
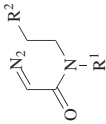
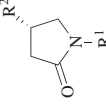
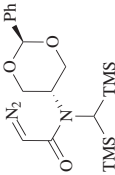
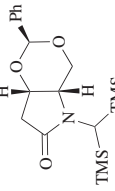
Diazoacetate	Conditions	Product(s) and Yield(s) (%)	Refs.																														
	Catalyst, Solvent, reflux	 +  	135																														
<table><tr><th>Cat.</th><th>Solvent</th><th>Time (h)</th><th>I + II</th><th>I/II</th></tr><tr><td>Rh₂(OAc)₄</td><td>DCM</td><td>2.5</td><td>(69)</td><td>22:78</td></tr><tr><td>6</td><td>DCM</td><td>5.5</td><td>(69)</td><td>16:84</td></tr><tr><td>5a</td><td>DCM</td><td>5.5</td><td>(66)</td><td>38:62</td></tr><tr><td>16b</td><td>DCM</td><td>5.5</td><td>(58)</td><td>16:84</td></tr><tr><td>16b</td><td>pentane</td><td>5.5</td><td>(69)</td><td>10:90</td></tr></table>				Cat.	Solvent	Time (h)	I + II	I/II	Rh ₂ (OAc) ₄	DCM	2.5	(69)	22:78	6	DCM	5.5	(69)	16:84	5a	DCM	5.5	(66)	38:62	16b	DCM	5.5	(58)	16:84	16b	pentane	5.5	(69)	10:90
Cat.	Solvent	Time (h)	I + II	I/II																													
Rh ₂ (OAc) ₄	DCM	2.5	(69)	22:78																													
6	DCM	5.5	(69)	16:84																													
5a	DCM	5.5	(66)	38:62																													
16b	DCM	5.5	(58)	16:84																													
16b	pentane	5.5	(69)	10:90																													

TABLE 4. γ -LACTAMS FROM DIAZOACETAMIDES

Diazoacetamide	Conditions	Product(s) and Yield(s) (%)					Refs.
 C ₆₋₈	Catalyst, DCM, reflux, 6 h	R ²	R ¹	R ²	Cat.	% ee	138
		MeOCH ₂ CH ₂	MeO	1a	(72)	80	
		MeOCH ₂ CH ₂	MeO	3a	(78)	77	
		<i>i</i> -Bu	EtO	1a	(95)	58	
		<i>i</i> -Bu	EtO	3a	(97)	78	
 C ₆	Catalyst, DCM						281, 282
							
	Cat.	Temp	Time (min)	% ee			
2a	rt	40	(72)	66	(4S,7S)		
1a	rt	40	(82)	50	(4R,7R)		
2a	reflux	20	(80)	44	(4S,7S)		
1a	reflux	20	(84)	43	(4R,7R)		
4a	rt	40	(72)	84	(4R,7S)		
3a	rt	40	(76)	70	(4R,7R)		
4a	reflux	20	(95)	90	(4S,7S)		
3a	reflux	20	(92)	68	(4R,7R)		
8b	reflux	180	(62)	1	—		
7c	reflux	180	(88)	4	—		
6	rt	20	(81)	78	(4S,7S)		
5a	rt	20	(69)	66	(4R,7R)		
6	reflux	20	(77)	77	(4S,7S)		
5a	reflux	20	(80)	70	(4R,7R)		
17d	reflux	180	(71)	29	(4R,7R)		

Please refer to the charts preceding the tables, not to the text discussion, for structures indicated by the **bold** numbers.

TABLE 4. γ -LACTAMS FROM DIAZOACETAMIDES (Continued)

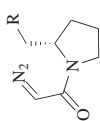
C₇₋₈

Diazoacetamide

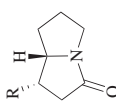
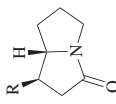
Conditions

Product(s) and Yield(s) (%)

Refs.



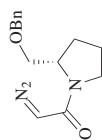
Catalyst, DCM, reflux

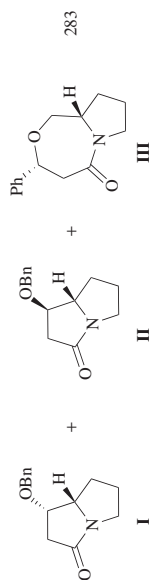
283

R	Cat.	I + II	I/II
MeO	Rh ₂ (OAc) ₄	(45)	53:47
MeO	11	(45)	63:37
MeO	1a	(95)	90:10
MeO	2a	(96)	73:27
MeO	3a	(99)	89:11
MeO	7a	(88)	97:3
MeO	7c	(97)	97:3
MeO	CuOTf	(55)	38:62
MeO	CuPF ₆	(61)	36:64
MeO	41b	(83)	50:50
MeO	42a	(91)	47:53

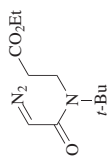
Me	Rh ₂ (OAc) ₄	(32)	18:82
Me	11	(20)	29:71
Me	3a	(98)	71:29
Me	7a	(86)	98:2
Me	7c	(95)	96:4
Me	CuOTf	(30)	20:80
Me	41b	(77)	29:71
Me	42a	(55)	35:65

C₇

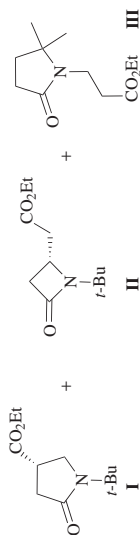
Catalyst, DCM, reflux



283

C₉

Catalyst, DCM, reflux



Cat.	Time (h)	I + II + III	I/II/III	% ee I	% ee II
2a	10	(64)	2:9:89	—	44
3a	10	(54)	2:25:73	—	46
3c	10	(60)	12:88:<1	16	20
3b	8	(60)	16:82:2	8	43

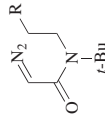
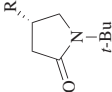
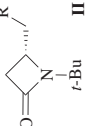
138

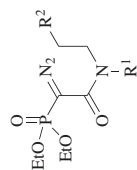
138

138

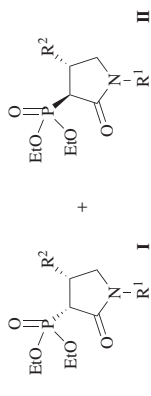
274

TABLE 4. γ -LACTAMS FROM DIAZOACETAMIDES (Continued)

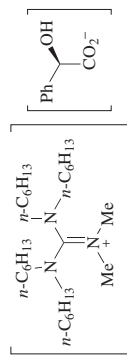
Diazoacetamide	Conditions	Product(s) and Yield(s) (%)						Refs.
 C ₁₀₋₁₁	Catalyst, DCM, reflux	 I	+	 II				
R	Cat.	Time (h)	I + II	I/II	% ee I	% ee II		
Et	1a	6	(74)	88:12	63	73	138	
Et	3a	6	(82)	91:9	71	80	138	
Et	9	6	(78)	90:10	64	71	138	
Et	3c	10	(92)	92:8	<2	0	138	
Et	3b	12.5	(78)	93:7	<4	40	274	
<i>i</i> -Pr	1a	10	(91)	80:20	58	72	138	
<i>i</i> -Pr	3a	10	(93)	82:18	69	65	138	



Catalyst, DCE

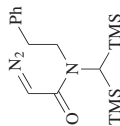
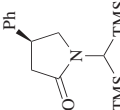
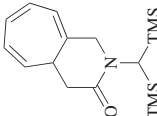
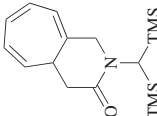
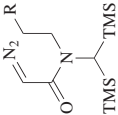
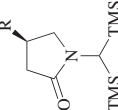


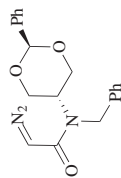
R ¹	R ²	Cat.	Temp	Time (h)	I + II	I/II	% ee II
<i>n</i> -Bu	Et	3a	reflux	24	(72)	0:100	14
<i>n</i> -Bu	Et	16b	reflux	4	(91)	14:86	7
<i>n</i> -Bu	Et	16d	reflux	4	(90)	14:86	1
<i>n</i> -Bu	Et	17b	reflux	4	(73)	17:83	12
<i>n</i> -Bu	Et	24	reflux	4	(87)	10:90	14
<i>n</i> -Bu	Et	25	reflux	4	(89)	15:85	10
<i>n</i> -Bu	Ph	17b	reflux	4	(70)	7:93	15
<i>t</i> -Bu	Ph	24	reflux	4	(76)	12:88	18
<i>t</i> -Bu	Ph	24	60°	24	(97)	11:89	22
<i>t</i> -Bu	Ph	25	reflux	4	(86)	17:83	40
<i>t</i> -Bu	Ph	26	reflux	4	(70)	7:93	21
<i>t</i> -Bu	Ph	27	reflux	4	(81)	7:93	16
<i>t</i> -Bu	Ph	28	reflux	4	(76)	6:94	24
<i>t</i> -Bu	Ph	Rh ₂ (OAc) ₄	110°	3	(84)	33:67	27



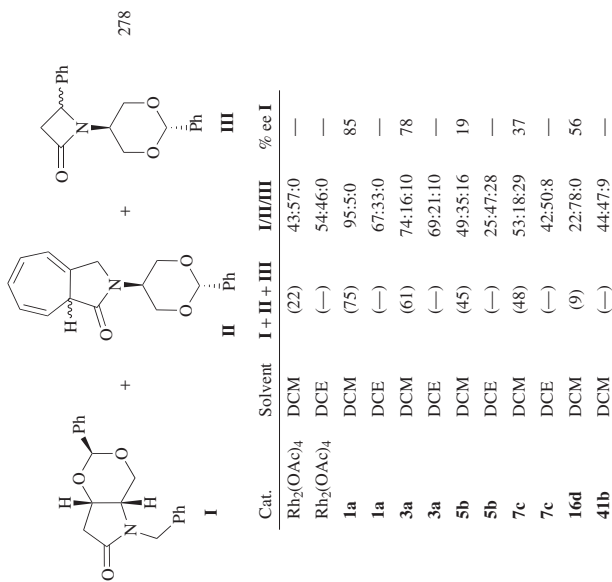
chiral ionic liquid used in the last entry of the sub-table

TABLE 4. γ -LACTAMS FROM DIAZOACETAMIDES (Continued)

Diazoacetamide	Conditions	Product(s) and Yield(s) (%)	Refs.												
 I  2a <td>Catalyst, DCM, reflux</td> <td>  4a 284 </td> <td></td>	Catalyst, DCM, reflux	 4a 284													
 I  2a <td>Catalyst, DCM, reflux</td> <td><table><thead><tr><th>R</th><th>Cat.</th><th>% ee</th></tr></thead><tbody><tr><td>4-MeOC₆H₄</td><td>4a</td><td>(83) 69 (R)</td></tr><tr><td>Bn</td><td>2a</td><td>(90) 32 (R)</td></tr><tr><td>Bn</td><td>4a</td><td>(92) 43 (R)</td></tr></tbody></table> 284 </td> <td></td>	Catalyst, DCM, reflux	<table><thead><tr><th>R</th><th>Cat.</th><th>% ee</th></tr></thead><tbody><tr><td>4-MeOC₆H₄</td><td>4a</td><td>(83) 69 (R)</td></tr><tr><td>Bn</td><td>2a</td><td>(90) 32 (R)</td></tr><tr><td>Bn</td><td>4a</td><td>(92) 43 (R)</td></tr></tbody></table> 284	R	Cat.	% ee	4-MeOC ₆ H ₄	4a	(83) 69 (R)	Bn	2a	(90) 32 (R)	Bn	4a	(92) 43 (R)	
R	Cat.	% ee													
4-MeOC ₆ H ₄	4a	(83) 69 (R)													
Bn	2a	(90) 32 (R)													
Bn	4a	(92) 43 (R)													



Catalyst, reflux, 2.5 h



Cat.	Solvent	I + II + III	I/II/III	% ee I
Rh ₂ (OAc) ₄	DCM	(22)	43:57:0	—
Rh ₂ (OAc) ₄	DCE	(—)	54:46:0	—
1a	DCM	(75)	95:5:0	85
1a	DCE	(—)	67:33:0	—
3a	DCM	(61)	74:16:10	78
3a	DCE	(—)	69:21:10	—
5b	DCM	(45)	49:35:16	19
5b	DCE	(—)	25:47:28	—
7c	DCM	(48)	53:18:29	37
7c	DCE	(—)	42:50:8	—
16d	DCM	(9)	22:78:0	56
41b	DCM	(—)	44:47:9	—

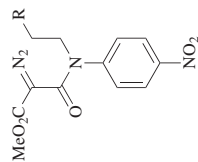
TABLE 4. γ -LACTAMS FROM DIAZOACETAMIDES (Continued)

C₁₂-13

Catalyst

284

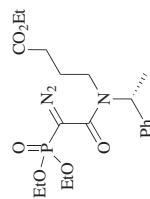
Diazoacetamide	Conditions	Product(s) and Yield(s) (%)	Refs.				
R ¹	R ²	Cat.	Solvent	Temp	I + II	I/II	% ee I
Me	Ph	17b	DCM	reflux	(92)	100:0	5 (3 <i>R</i> ,4 <i>R</i>)
Me	Ph	17c	DCM	reflux	(87)	100:0	7 (3 <i>R</i> ,4 <i>R</i>)
Me	Ph	17d	DCM	reflux	(80)	71:29	65 (3 <i>R</i> ,4 <i>R</i>)
Me	Ph	17d	toluene	50°	(80)	50:50	75 (3 <i>R</i> ,4 <i>R</i>)
Me	Ph	16b	DCM	reflux	(77)	100:0	9 —
Me	Ph	5a	DCM	reflux	(89)	100:0	35 (3 <i>S</i> ,4 <i>S</i>)
Et	Ph	17b	DCM	reflux	(92)	100:0	—
Et	Ph	17c	DCM	reflux	(87)	100:0	—
Et	Ph	17d	DCM	reflux	(80)	55:45	—
Et	4-MeOC ₆ H ₄	17d	DCM	reflux	(82)	90:10	51 (3 <i>R</i> ,4 <i>R</i>)
Et	Bn	17b	DCM	reflux	(73)	100:0	24 —
Et	Bn	17c	DCM	reflux	(90)	85:15	44 —
Et	Bn	17d	DCM	reflux	(75)	56:44	64 —

C₁₂₋₁₇

Catalyst

250

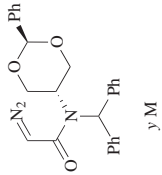
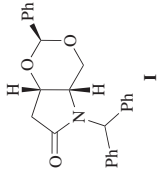
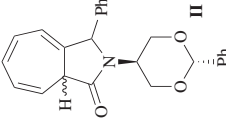
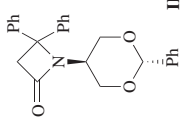
R	Cat.	Solvent	Temp (°)	Time (h)	% ee	
Me	17d	DCM	20	3	(82)	33 (3S,4S)
Et	17d	DCM	20	4	(84)	34 (3S,4S)
Ph	17b	DCM	20	4	(82)	47 (3S,4R)
Ph	17b	Et ₂ O	20	4	(—)	45 (3S,4R)
Ph	17b	toluene	20	4	(—)	37 (3S,4R)
Ph	17a	DCM	20	5	(83)	47 (3S,4R)
Ph	17c	DCM	20	3	(82)	26 (3S,4R)
Ph	17d	DCM	20	5	(80)	73 (3S,4R)
Ph	16d	DCM	20	4	(87)	6 (3S,4R)
4-ClC ₆ H ₄	17d	DCM	23	6	(83)	82 (3S,4R)
4-O ₂ NC ₆ H ₄	17d	DCM	20	8	(81)	73 (3S,4R)
4-MeOC ₆ H ₄	17d	DCM	20	4	(72)	81 (3S,4R)

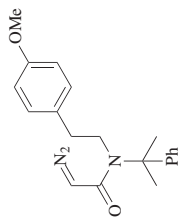
C₁₄Catalyst **24**, DCE, reflux, 4 h

(40) dr 1.7:1

334

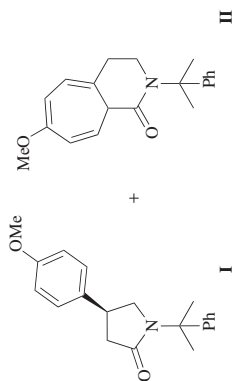
TABLE 4. γ -LACTAMS FROM DIAZOACETAMIDES (Continued)

Diazoacetamide	Conditions	Product(s) and Yield(s) (%)	Refs.					
 y M	Catalyst (x mol %), Solvent, reflux	 I +  II +  III	281, 282					
y	Cat.	x	Solvent	Time (min)	I + II + III	I/II/III	% ee I	% ee II
0.009	2a	10	DCM	5	(98)	1.96:3	—	3
0.009	1a	10	DCM	5	(52)	35:35:30	94	28
0.009	2a	1	DCM	5	(81)	10:81:9	88	50
0.009	1a	1	DCM	5	(52)	34:38:28	95	22
0.009	2a	0.1	DCM	60	(87)	12:78:10	78	32
0.009	1a	0.1	DCM	60	(66)	18:50:32	>95	33
0.27	2a	0.1	DCM	60	(75)	9:75:16	81	34
0.009	1a	0.1	DCE	60	(74)	19:66:15	75	7
0.009	4a	1	DCM	5	(48)	35:23:42	86	62
0.009	3a	1	DCM	5	(61)	32:35:33	87	38
0.009	4a	0.1	DCM	60	(55)	18:47:35	82	13
0.009	8b	1	DCM	5	(85)	10:69:21	29	20
0.009	7c	1	DCM	5	(82)	8:55:37	64	5



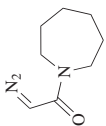
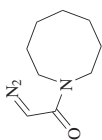
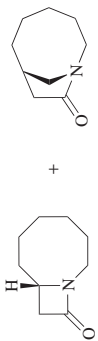
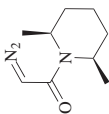
Catalyst, Solvent

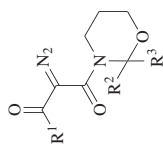
275



Cat.	Solvent	Temp	Time (h)	I + II	I/II	% ee I
16b	DCM	reflux	1.5	(36)	47:53	3 (R)
20a	DCM	reflux	1.5	(25)	58:42	2 (R)
20b	DCM	reflux	1.5	(36)	53:47	13 (R)
1a	DCM	reflux	1.5	(53)	87:13	18 (S)
3a	DCM	reflux	1.5	(72)	>98:2	47 (S)
3a	DCM	20°	—	(76)	>98:2	52 (S)
3a	DCM	0°	—	(69)	>98:2	52 (S)
3a	DCE	20°	—	(74)	>98:2	37 (S)
3a	toluene	20°	—	(71)	>98:2	47 (S)
3a	THF	40°	—	(69)	>98:2	41 (S)
3a	Et ₂ O	reflux	—	(73)	>98:2	46 (S)
3a	dioxane	40°	—	(70)	>98:2	54 (S)

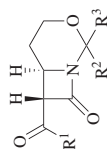
TABLE 5. β -LACTAMS FROM DIAZOACETAMIDES

Diazoacetamide	Conditions	Product(s) and Yield(s) (%)	Refs.																																	
Please refer to the charts preceding the tables, not to the text discussion, for structures indicated by the bold numbers.																																				
 C₈	Catalyst, DCM, reflux		277																																	
		<table><tr><th>Cat.</th><th>I + II</th><th>I/II</th><th>% ee I</th></tr><tr><td>1a</td><td>(67)</td><td>100:0</td><td>97</td></tr><tr><td>3a</td><td>(68)</td><td>99:1</td><td>92</td></tr><tr><td>7a</td><td>(—)</td><td>—</td><td><50</td></tr></table>		Cat.	I + II	I/II	% ee I	1a	(67)	100:0	97	3a	(68)	99:1	92	7a	(—)	—	<50																	
Cat.	I + II	I/II	% ee I																																	
1a	(67)	100:0	97																																	
3a	(68)	99:1	92																																	
7a	(—)	—	<50																																	
 C₉	Catalyst, Solvent, reflux		277																																	
		<table><tr><th>Cat.</th><th>Solvent</th><th>I + II</th><th>I/II</th><th>% ee I</th><th>% ee II</th></tr><tr><td>1a</td><td>DCM</td><td>(77)</td><td>40:60</td><td>31</td><td>97</td></tr><tr><td>1a</td><td>DCE</td><td>(67)</td><td>67:33</td><td>30</td><td>96</td></tr><tr><td>3a</td><td>DCM</td><td>(95)</td><td>26:74</td><td>15</td><td>98</td></tr><tr><td>3a</td><td>DCE</td><td>(68)</td><td>49:51</td><td>8</td><td>96</td></tr><tr><td>7a</td><td>DCE</td><td>(81)</td><td>39:61</td><td>66</td><td>96</td></tr></table>		Cat.	Solvent	I + II	I/II	% ee I	% ee II	1a	DCM	(77)	40:60	31	97	1a	DCE	(67)	67:33	30	96	3a	DCM	(95)	26:74	15	98	3a	DCE	(68)	49:51	8	96	7a	DCE	(81)
Cat.	Solvent	I + II	I/II	% ee I	% ee II																															
1a	DCM	(77)	40:60	31	97																															
1a	DCE	(67)	67:33	30	96																															
3a	DCM	(95)	26:74	15	98																															
3a	DCE	(68)	49:51	8	96																															
7a	DCE	(81)	39:61	66	96																															
	Catalyst, DCM, reflux		277																																	
		<table><tr><th>Cat.</th><th>I + II</th><th>I/II</th><th>% ee I</th></tr><tr><td>1a</td><td>(78)</td><td>89:11</td><td>86</td></tr><tr><td>3a</td><td>(—)</td><td>85:15</td><td>86</td></tr><tr><td>7a</td><td>(—)</td><td>86:14</td><td>4</td></tr></table>		Cat.	I + II	I/II	% ee I	1a	(78)	89:11	86	3a	(—)	85:15	86	7a	(—)	86:14	4																	
Cat.	I + II	I/II	% ee I																																	
1a	(78)	89:11	86																																	
3a	(—)	85:15	86																																	
7a	(—)	86:14	4																																	

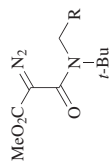
C₉₋₁₁

Catalyst, DCM

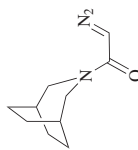
333



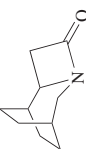
R ¹	R ²	R ³	Cat.	Temp (°)	Time (h)	% ee
MeO	Me	Me	17a	0	6	(89) 93
Me	Me	Me	17b	rt	6	(84) 0
MeO	Et	Et	17a	0	8	(89) 83

C₁₀₋₁₄Catalyst **17b**, DCM

R	Temp (°)	Time (h)	% ee
MeO ₂ CCH ₂	22	8	(98) 56 (3 <i>R</i> ,4 <i>S</i>)
<i>n</i> -Pr	16	5	(97) 60 (3 <i>R</i> ,4 <i>S</i>)
Ph	22	6	(94) 74 (3 <i>R</i> ,4 <i>R</i>)

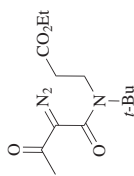
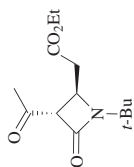
C₁₀

Catalyst, DCM, reflux



Cat.	% ee
1a	(70) 96
3a	(80) 93
7a	(—) <50

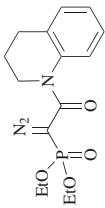
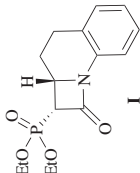
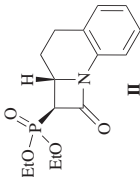
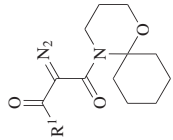
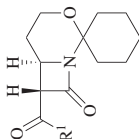
277

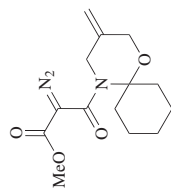
C₁₁Catalyst **38**, DCM, rt, 8 h

(93) 26% ee

64

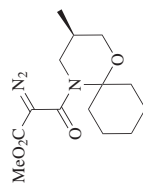
TABLE 5. β -LACTAMS FROM DIAZOACETAMIDES (Continued)

	Diazoacetamide	Conditions	Product(s) and Yield(s) (%)				Refs.		
C ₁₁		Catalyst, DCE, reflux, 4 h			I + II	I/II	% ee II	334	
			Cat.						
			Rh ₂ (OAc) ₄	(73)	21:79	—			
			17b	(80)	25:75	10			
			24	(65)	25:75	2			
			25	(75)	17:83	5			
			26	(65)	28:72	16			
			27	(73)	7:93	15			
			28	(67)	22:78	6			
C ₁₃		Catalyst, DCM							
			R ¹	Cat.	Temp	Time (h)	% ee		
			MeO	17a	0°	2	(94)	(6 <i>R</i> ,7 <i>R</i>)	333
			MeO	17b	0°	3	(89)	(6 <i>R</i> ,7 <i>R</i>)	333
			MeO	17c	0°	3	(86)	(6 <i>R</i> ,7 <i>R</i>)	333
			MeO	17d	0°	4	(85)	(6 <i>R</i> ,7 <i>R</i>)	333
			MeO	17e	0°	3	(85)	(6 <i>R</i> ,7 <i>R</i>)	333
			MeO	22	rt	24	(58)	(6 <i>R</i> ,7 <i>R</i>)	287
			MeO	23a	rt	36	(62)	(6 <i>R</i> ,7 <i>R</i>)	287
			MeO	23b	rt	18	(71)	(6 <i>R</i> ,7 <i>R</i>)	287
			Me	17b	rt	6	(84)	0	333

Catalyst **17a**, DCM, rt, 13 h

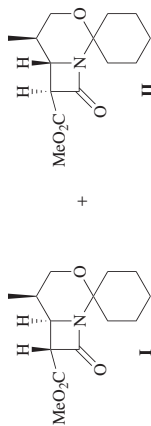
(83) 88% ee

333



Catalyst, DCM, rt

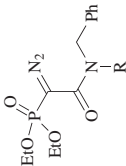
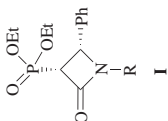
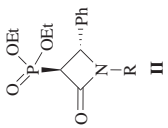
288

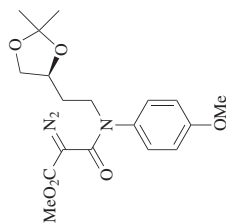


Cat.	Time (h)	I + II	I/II
Rh ₂ (OAc) ₄	18	(75)	25:75
18a	18	(77)	2:98
17b	24	(47)	85:15

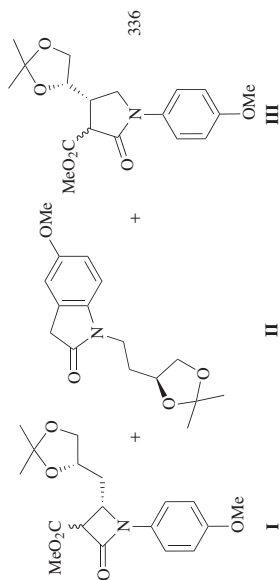
TABLE 5. β -LACTAMS FROM DIAZOACETAMIDES (Continued)

C₃–16

Diazoacetamide	Conditions	Product(s) and Yield(s) (%)	Refs.			
	Catalyst, DCE	 	334			
R	Cat.	Temp	Time (h)	I + II	I/II	% ee II
<i>t</i> -Bu	17b	reflux	4	(83)	83:17	20
<i>t</i> -Bu	24	reflux	4	(81)	70:30	11
<i>t</i> -Bu	24	60°	48	(91)	80:20	16
<i>t</i> -Bu	25	reflux	4	(90)	80:20	15
<i>t</i> -Bu	26	reflux	4	(76)	91:9	15
<i>t</i> -Bu	27	reflux	4	(94)	82:18	6
<i>t</i> -Bu	28	reflux	4	(88)	94:6	15
Bn	3a	reflux	48	(52)	29:71	1
Bn	16b	reflux	4	(80)	20:80	10
Bn	16d	reflux	4	(65)	20:80	8
Bn	17b	reflux	4	(72)	17:83	28
Bn	24	reflux	4	(60)	19:81	26
Bn	25	reflux	4	(70)	25:75	40

C₁₃

Catalyst, Solvent



Cat.	Solvent	Temp (°)	I + II + III	I/II/III
Rh ₂ (OAc) ₄	DCM	30	(75)	50:0:50
Rh ₂ (OAc) ₄	DCM	45	(64)	60:0:40
Rh ₂ (OAc) ₄	benzene	rt	(82)	55:0:45
Rh ₂ (OAc) ₄	benzene	80	(60)	71:0:29
Rh ₂ (OOct) ₄	DCM	rt	(65)	63:0:37
Rh ₂ (OPiv) ₄	benzene	80	(56)	83:0:17
17b	DCM	30	(47)	40:60:0
Rh ₂ (acam) ₄	benzene	80	(17)	0:100:0

TABLE 5. β -LACTAMS FROM DIAZOACETAMIDES (Continued)

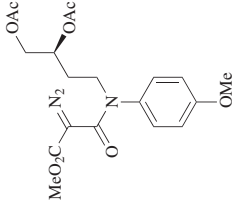
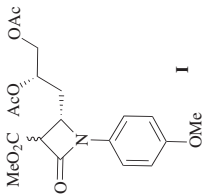
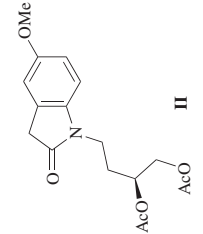
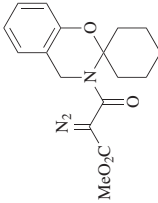
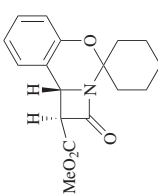
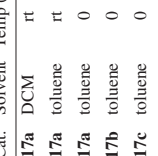
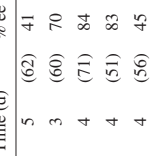
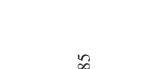
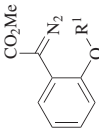
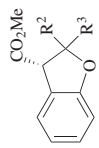
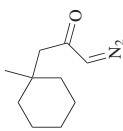
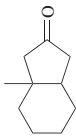
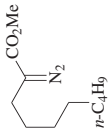
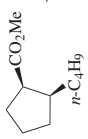
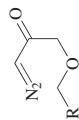
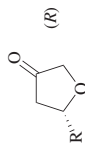
	Diazoacetamide	Conditions	Product(s) and Yield(s) (%)	Refs.																																								
C ₁₃		Catalyst 17h , DCE	 I +  II 336																																									
		Temp (°)	I + II																																									
		30	(77)	71:29																																								
		60	(78)	57:43																																								
C ₁₆		Catalyst, Solvent	 17a  17b  17c  17d	<table><tr><th>Cat.</th><th>Solvent</th><th>Temp (°)</th><th>Time (d)</th><th>% ee</th></tr><tr><td>17a</td><td>DCM</td><td>rt</td><td>5</td><td>(62) 41</td></tr><tr><td>17a</td><td>toluene</td><td>rt</td><td>3</td><td>(60) 70</td></tr><tr><td>17a</td><td>toluene</td><td>0</td><td>4</td><td>(71) 84</td></tr><tr><td>17b</td><td>toluene</td><td>0</td><td>4</td><td>(51) 83</td></tr><tr><td>17c</td><td>toluene</td><td>0</td><td>4</td><td>(56) 45</td></tr><tr><td>17e</td><td>toluene</td><td>0</td><td>3</td><td>(78) 10</td></tr><tr><td>17d</td><td>toluene</td><td>0</td><td>4</td><td>(66) 84</td></tr></table>	Cat.	Solvent	Temp (°)	Time (d)	% ee	17a	DCM	rt	5	(62) 41	17a	toluene	rt	3	(60) 70	17a	toluene	0	4	(71) 84	17b	toluene	0	4	(51) 83	17c	toluene	0	4	(56) 45	17e	toluene	0	3	(78) 10	17d	toluene	0	4	(66) 84
Cat.	Solvent	Temp (°)	Time (d)	% ee																																								
17a	DCM	rt	5	(62) 41																																								
17a	toluene	rt	3	(60) 70																																								
17a	toluene	0	4	(71) 84																																								
17b	toluene	0	4	(51) 83																																								
17c	toluene	0	4	(56) 45																																								
17e	toluene	0	3	(78) 10																																								
17d	toluene	0	4	(66) 84																																								

TABLE 6. SYNTHESIS OF CYCLOALKANE DERIVATIVES (Continued)

Substrate	Conditions	Product(s) and Yield(s) (%)				Refs.					
	Catalyst, Solvent										
		R ¹	R ²	R ³	Cat.	Solvent	Temp (°)	Time (h)	% ee		
		Me	H	H	16b	hexanes	-50	72	(98)	<5	307
		Me	H	H	21a	DCM	-50	72	(70)	43	307
		Me	H	H	21b	DCM	-50	72	(70)	68	307
		Me	H	H	17d	toluene	-23	1	(69)	44	218
		<i>i</i> -Pr	Me	Me	17d	toluene	-78	1.5	(88)	22	218
		<i>i</i> -Pr	Me	Me	16b	hexanes	-50	72	(98)	94	307
		<i>i</i> -Pr	Me	Me	21a	DCM	-50	72	(48)	60	307
		<i>i</i> -Pr	Me	Me	21b	DCM	-50	72	(57)	65	307
	Catalyst, DCM, rt										
						Cat.	% ee				
						Rh ₂ (OAc) ₄	(77)	—			155
						1a	(33)	0			
	Catalyst 17d , toluene, -78°, 1.5 h										
										I + II (90) II = 10:90, 94% ee II	309

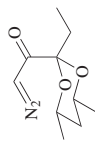
C₁₀-11

Catalyst, Solvent, 6 h

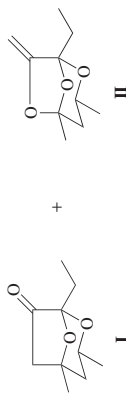


337

R	Cat.	Solvent	Temp	% ee
<i>c</i> -C ₆ H ₁₁	34	pentane	-78°	(52) 67
<i>n</i> -C ₇ H ₁₅	16b	DCM	rt	(28) 13
<i>n</i> -C ₇ H ₁₅	16d	DCM	rt	(31) 14
<i>n</i> -C ₇ H ₁₅	1a	DCM	reflux	(84) 8
<i>n</i> -C ₇ H ₁₅	34	DCM	rt	(80) 37
<i>n</i> -C ₇ H ₁₅	34	pentane/DCM (10:1)	-78°	(87) 36
<i>n</i> -C ₇ H ₁₅	34	PhF	-40°	(65) 30
<i>n</i> -C ₇ H ₁₅	34	pentane	rt	(79) 33
<i>n</i> -C ₇ H ₁₅	34	pentane	-45°	(72) 71

C₁₀

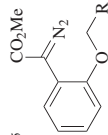
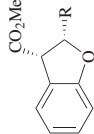
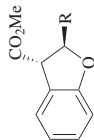
Catalyst, DCM, reflux

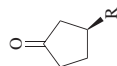
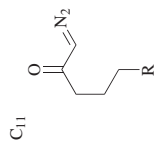


292

Cat.	I	% ee I	II	% ee II
Rh ₂ (OAc) ₄	(58)	—	(28)	—
17b	(36)	20	(10)	10
16b	(31)	7	(0)	—
16d	(17)	<5	(5)	<5
1a	(11)	<5	(8)	7

TABLE 6. SYNTHESIS OF CYCLOALKANE DERIVATIVES (Continued)

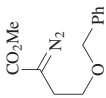
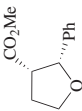
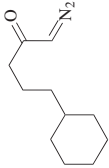
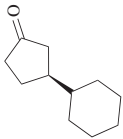
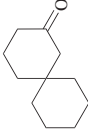
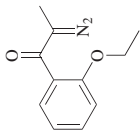
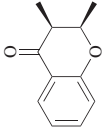
Substrate	Conditions	Product(s) and Yield(s) (%)				Refs.			
 C ₁₀₋₁₅	Catalyst, Solvent	 I	+	 II					
R	Cat.	Solvent	Temp (°)	Time (h)	I + II	I/II	% ee I	% ee II	
Me	16b	hexanes	-50	72	(85)	80:20	60	—	307
Me	21a	DCM	-50	72	(50)	85:15	53	—	307
Me	21b	DCM	-50	72	(70)	88:12	45	—	307
Me	17d	toluene	-78	0.5	(91)	14:86	78	97	218
vinyl	17d	toluene	-23	2	(62)	77:23	86	92	218
<i>c</i> -C ₆ H ₁₁	16b	hexanes	-50	72	(72)	95:5	63	—	307
<i>c</i> -C ₆ H ₁₁	21a	DCM	-50	72	(22)	60:40	22	—	307
<i>c</i> -C ₆ H ₁₁	21b	DCM	-50	72	(35)	75:25	35	—	307
<i>c</i> -C ₆ H ₁₁	17d	toluene	-78	7	(63)	96:4	96	—	218
Ph	16b	hexanes	rt	0.5	(60)	60:40	38	—	338
Ph	17f	hexanes	rt	0.5	(83)	>30:1	87	—	338
Ph	18b	hexanes	-60	—	(79)	>30:1	95	—	338
Ph	35a	toluene	rt	5	(68)	95:5	78	—	306
Ph	17b	toluene	-60	0.5	(86)	70:30	70	80	218
Ph	17a	toluene	-60	0.5	(84)	81:19	61	79	218
Ph	17c	toluene	-60	0.5	(86)	89:11	61	69	218
Ph	17e	toluene	-60	0.5	(83)	99:1	71	—	218
Ph	17d	toluene	-60	0.5	(87)	100:0	90	—	218
Ph	19b	toluene	-60	1	(57)	68:32	65	77	218
Ph	19a	toluene	-60	1	(69)	82:18	63	80	218
Ph	19c	toluene	-60	0.5	(73)	89:11	61	57	218
Ph	19d	toluene	-60	0.5	(84)	100:0	86	—	218
Ph	17d	DCM	-45	0.5	(63)	100:0	90	—	218
Ph	17d	Et ₂ O	-10	0.5	(78)	100:0	88	—	218
Ph	17d	hexanes	rt	0.2	(78)	100:0	70	—	218
Ph	17d	toluene	-78	1	(86)	100:0	94	—	218
Ph	19d	toluene	-78	12	(70)	100:0	91	—	218
3,4-(TBSO) ₂ C ₆ H ₃	17d	toluene	-78	2	(85)	99:1	91	—	218

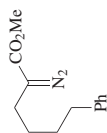


Catalyst, DCM, reflux

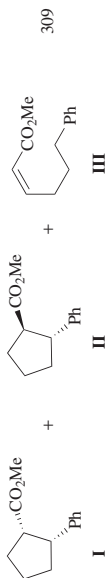
R	Cat.	Time (h)	% ee
Ph	39a	1 (80)	45 (S)
Ph	39b	1 (73)	54 (S)
Ph	39c	1 (78)	40 (S)
Ph	39d	48 (65)	17 (S)
Ph	39e	48 (68)	48 (S)
Ph	39f	1 (64)	32 (S)
Ph	39g	1 (68)	51 (R)
Ph	39h	1 (0)	—
Ph	40	1 (0)	—
Ph	16f	1 (0)	—
4-FC ₆ H ₄	39a	1 (68)	60 (S)
4-FC ₆ H ₄	39b	1 (61)	58 (S)
4-FC ₆ H ₄	39d	48 (44)	40 (S)
4-FC ₆ H ₄	39e	48 (18)	60 (S)
4-FC ₆ H ₄	39f	1 (61)	36 (S)
4-FC ₆ H ₄	39g	1 (70)	36 (R)
4-ClC ₆ H ₄	39a	1 (87)	65 (S)
4-ClC ₆ H ₄	39b	1 (74)	59 (S)
4-ClC ₆ H ₄	39c	1 (87)	73 (S)
4-ClC ₆ H ₄	39d	48 (63)	57 (S)
4-ClC ₆ H ₄	39e	48 (0)	—
4-ClC ₆ H ₄	39f	1 (54)	46 (S)
4-ClC ₆ H ₄	39g	1 (54)	33 (R)
4-MeOC ₆ H ₄	39a	1 (86)	22 (S)
4-MeOC ₆ H ₄	39b	1 (75)	7 (S)
4-MeOC ₆ H ₄	39c	1 (74)	28 (S)
4-MeOC ₆ H ₄	39d	48 (87)	3 (S)
4-MeOC ₆ H ₄	39e	48 (78)	30 (S)
4-MeOC ₆ H ₄	39f	1 (78)	36 (S)
4-MeOC ₆ H ₄	39g	1 (95)	56 (R)

TABLE 6. SYNTHESIS OF CYCLOALKANE DERIVATIVES (Continued)

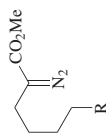
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	Catalyst 17d , toluene, -78°, 1 h	 (91) 41% ee	218
	Catalyst, DCM, reflux	 + 	254
	Catalyst 16c , DCM, reflux, 14 h	 (89) 82% ee	180

C₁₂

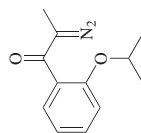
Catalyst



Cat.	Solvent	Temp (°)	Time (h)	I + II + III	I/II/III	% ee I	% ee II
17d	toluene	-78	0.5	(85)	100:0:0	95	—
17d	toluene	-45	0.2	(85)	91:0:9	90	—
17d	toluene	0	0.1	(80)	82:0:18	81	—
17d	DCM	-78	0.5	(76)	93:0:7	95	—
17d	Et ₂ O	-78	0.5	(73)	97:0:3	94	—
17b	toluene	-78	7	(73)	56:37:7	89	27
17a	toluene	-78	30	(69)	73:19:8	90	56
17c	toluene	-78	6	(80)	77:20:3	95	22
19d	toluene	-78	0.5	(76)	100:0:0	67	—
17d	toluene	-78	9	(82)	100:0:0	95	—

Catalyst **17d**, toluene,
-78°, 0.5 h

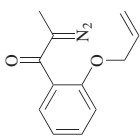
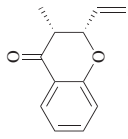
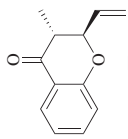
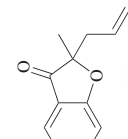
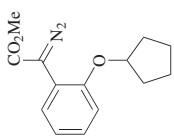
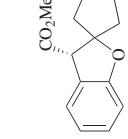
R	% ee
4-ClC ₆ H ₄	(81) 93
4-MeOC ₆ H ₄	(85) 92

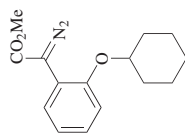


Catalyst, DCM, reflux, 12 h

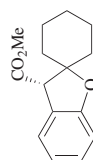
Cat.	% ee
Rh ₂ (OAc) ₄	—
16c	50
16e	23
16g	18
32	30
24	10

TABLE 6. SYNTHESIS OF CYCLOALKANE DERIVATIVES (Continued)

Substrate	Conditions	Product(s) and Yield(s) (%)					Refs.
	Catalyst, DCM, 12 h						
	Catalyst 16b , hexanes, -50°, 72h						

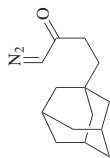
C₁₄

Catalyst **16b**, hexanes,
-50°, 72 h

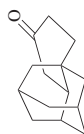


(12) 80% ee

307

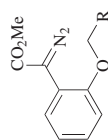
C₁₅₋₁₆

Catalyst **3a**, DCM, rt

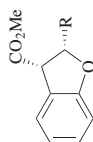


(64) 70% ee

183

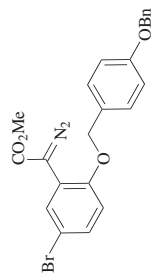
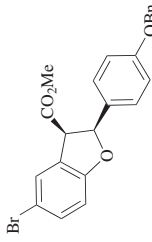
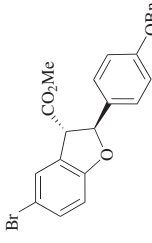
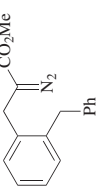
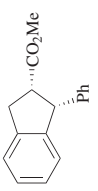
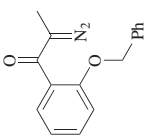
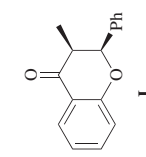
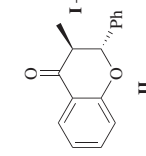


Catalyst **17d**, toluene, -78°



R	Time (h)	% ee	
4-ClC ₆ H ₄	1.5	(79)	94
4-MeOC ₆ H ₄	1	(89)	94
4-MeC ₆ H ₄	1.5	(84)	91
			—
			218

TABLE 6. SYNTHESIS OF CYCLOALKANE DERIVATIVES (Continued)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	Catalyst, DCM, 0.5 h	 	338
	Catalyst 17d , toluene, -78°, 1.5 h		(85) 92% ee 309
	Catalyst 16c , DCM, reflux, 12 h	 	I + II (100) I/II = 80:20, 62% ee I 180, 294

REFERENCES

- ¹ Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, 97, 2879.
- ² Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, 417, 507.
- ³ Arndtsen, B. A.; Bergman, R. G.; Mobley, T. A.; Peterson, T. H. *Acc. Chem. Res.* **1995**, 28, 154.
- ⁴ Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, 102, 1731.
- ⁵ Dick, A. R.; Sanford, M. S. *Tetrahedron* **2006**, 62, 2439.
- ⁶ Godula, K.; Sames, D. *Science* **2006**, 312, 67.
- ⁷ Davies, H. M. L.; Manning, J. R. *Nature* **2008**, 451, 417.
- ⁸ Lewis, J. C.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2008**, 41, 1013.
- ⁹ Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, 36, 1173.
- ¹⁰ Vedernikov, A. N. *Curr. Org. Chem.* **2007**, 11, 1401.
- ¹¹ Kalyani, D.; Sanford, M. S. *Top. Organomet. Chem.* **2007**, 24, 85.
- ¹² Diaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Perez, P. J. *Dalton Trans.* **2006**, 5559.
- ¹³ Ferreira, V. F. *Curr. Org. Chem.* **2007**, 11, 177.
- ¹⁴ Diaz-Requejo, M. M.; Perez, P. J. *Chem. Rev.* **2008**, 108, 3379.
- ¹⁵ Jones, W. D. *Science* **2000**, 287, 1942.
- ¹⁶ Davies, H. M. L.; Long, M. S. *Angew. Chem., Int. Ed.* **2005**, 44, 3518.
- ¹⁷ Müller, P.; Fruit, C. *Chem. Rev.* **2003**, 103, 2905.
- ¹⁸ Davies, H. M. L.; Beckwith, R. E. J. *Chem. Rev.* **2003**, 103, 2861.
- ¹⁹ Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. *Chem. Rev.* **2010**, 110, 704.
- ²⁰ Biermann, U.; Friedt, W.; Lang, S.; Luehs, W.; Machmueller, G.; Metzger, J. O.; Rüschi, M.G.K.; Schaefer, H. J.; Schneider, M. P. In *Biorefineries—Industrial Processes and Products*; Kamm, B., Gruber, P. R., Kamm, M., Eds.; Wiley-VCH: Weinheim, 2006; Vol. 2, Chapter 8.
- ²¹ Oku, A.; Harada, T. *Adv. Carbene Chem.* **2001**, 3, 287.
- ²² Davies, H. M. L.; Antoulinakis, E. G. *J. Organomet. Chem.* **2001**, 617–618, 47.
- ²³ Davies, H. M. L. *J. Mol. Catal. A: Chem.* **2002**, 189, 125.
- ²⁴ Li, Z.; He, C. *Eur. J. Org. Chem.* **2006**, 4313.
- ²⁵ Davies, H. M. L. *Eur. J. Org. Chem.* **1999**, 2459.
- ²⁶ Davies, H. M. L.; Walji, A. M. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, 2005; pp 301–340.
- ²⁷ Davies, H. M. L. *Angew. Chem., Int. Ed.* **2006**, 45, 6422.
- ²⁸ Davies, H. M. L.; Nikolai, J. *Org. Biomol. Chem.* **2005**, 3, 4176.
- ²⁹ Davies, H. M. L. In *Comprehensive Asymmetric Catalysis: Supplement, Volume 1*; Jacobsen, E.; Platz, A.; Yamamoto, H., Eds.; Springer: New York, 2004; Chapter 16.4.
- ³⁰ Davies, H. M. L.; Loe, O. *Synthesis* **2004**, 2595.
- ³¹ Doyle, M. P. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: New York, 2000; Chapter 5.5.
- ³² Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*; Wiley-Interscience: New York, 1998.
- ³³ Demonceau, A.; Noels, A. F.; Hubert, A. J.; Teyssie, P. J. *Chem. Soc., Chem. Commun.* **1981**, 688.
- ³⁴ Wenkert, E.; Davis, L. L.; Mylari, B. L.; Solomon, M. F.; Da Silva, R. R.; Shulman, S.; Warnet, R. J.; Ceccherelli, P.; Curini, M.; Pellicciari, R. *J. Org. Chem.* **1982**, 47, 3242.
- ³⁵ Taber, D. F.; Petty, E. H. *J. Org. Chem.* **1982**, 47, 4808.
- ³⁶ Pfaltz, A. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; Vol. 2, Chapter 16.1.
- ³⁷ Lydon, K. M.; McKervey, M. A. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; Vol. 2; Chapter 16.2.
- ³⁸ Charette, A. B.; Lebel, H. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; Vol. 2; Chapter 16.3.
- ³⁹ Burke, S. D.; Grieco, P. A. *Org. React.* **1979**, 26, 361.
- ⁴⁰ Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, 94, 1091.
- ⁴¹ Yates, P. *J. Am. Chem. Soc.* **1952**, 74, 5376.
- ⁴² Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, 98, 911.

- 43 Doyle, M. P. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, 2005; Chapter 15.
- 44 Diaz-Requejo, M. M.; Perez, P. J. *J. Organomet. Chem.* **2005**, *690*, 5441.
- 45 Müller, P. *Acc. Chem. Res.* **2004**, *37*, 243.
- 46 Grohmann, M.; Maas, G. *Tetrahedron* **2007**, *63*, 12172.
- 47 Grohmann, M.; Buck, S.; Schaeffler, L.; Maas, G. *Adv. Synth. Catal.* **2006**, *348*, 2203.
- 48 Choi, M. K.-W.; Yu, W.-Y.; Che, C.-M. *Org. Lett.* **2005**, *7*, 1081.
- 49 Wang, S. R.; Zhu, C.-Y.; Sun, X.-L.; Tang, Y. J. *Am. Chem. Soc.* **2009**, *131*, 4192.
- 50 Mbuvi, H. M.; Woo, L. K. *Organometallics* **2008**, *27*, 637.
- 51 Li, Y.; Huang, J.-S.; Zhou, Z.-Y.; Che, C.-M.; You, X.-Z. *J. Am. Chem. Soc.* **2002**, *124*, 13185.
- 52 Kennedy, M.; McKervey, M. A.; Maguire, A. R.; Roos, G. H. P. *J. Chem. Soc., Chem. Commun.* **1990**, 361.
- 53 Hashimoto, S.; Watanabe, N.; Ikegami, S. *Tetrahedron Lett.* **1990**, *31*, 5173.
- 54 Davies, H. M. L.; Hutcheson, D. K. *Tetrahedron Lett.* **1993**, *34*, 7243.
- 55 Doyle, M. P.; Brandes, B. D.; Kazala, A. P.; Pieters, R. J.; Jarstfer, M. B.; Watkins, L. M.; Eagle, C. T. *Tetrahedron Lett.* **1990**, *31*, 6613.
- 56 Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919.
- 57 Davies, H. M. L.; Hansen, T. *J. Am. Chem. Soc.* **1997**, *119*, 9075.
- 58 Davies, H. M. L.; Hansen, T.; Churchill, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 3063.
- 59 Davies, H. M. L.; Pelphrey, P. M. *Org. React.* **2011**, *75*, 75.
- 60 Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977.
- 61 Davies, H. M. L.; Antoulinakis, E. G. *Org. React.* **2001**, *57*, 1.
- 62 Doyle, M. P. *Angew. Chem., Int. Ed.* **2009**, *48*, 850.
- 63 Pirrung, M. C.; Zhang, J. *Tetrahedron Lett.* **1992**, *33*, 5987.
- 64 McCarthy, N.; McKervey, M. A.; Ye, T.; McCann, M.; Murphy, E.; Doyle, M. P. *Tetrahedron Lett.* **1992**, *33*, 5983.
- 65 Taber, D. F.; Malcolm, S. C.; Bieger, K.; Lahuerta, P.; Sanau, M.; Stiriba, S.-E.; Perez-Prieto, J.; Monge, M. A. *J. Am. Chem. Soc.* **1999**, *121*, 860.
- 66 Estevan, F.; Herbst, K.; Lahuerta, P.; Barberis, M.; Perez-Prieto, J. *Organometallics* **2001**, *20*, 950.
- 67 Barberis, M.; Perez-Prieto, J.; Stiriba, S.-E.; Lahuerta, P. *Org. Lett.* **2001**, *3*, 3317.
- 68 Barberis, M.; Perez-Prieto, J.; Herbst, K.; Lahuerta, P. *Organometallics* **2002**, *21*, 1667.
- 69 Doyle, M. P. *Aldrichimica Acta* **1996**, *29*, 3.
- 70 Timmons, D. J.; Doyle, M. P. *J. Organomet. Chem.* **2001**, *617–618*, 98.
- 71 Regitz, M.; Maas, G. *Diazo Compounds. Properties and Synthesis*; Academic Press: Orlando, 1986.
- 72 Regitz, M. *Synthesis* **1972**, 351.
- 73 Regitz, M. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 733.
- 74 Myers, E. L.; Raines, R. T. *Angew. Chem., Int. Ed.* **2009**, *48*, 2359.
- 75 Liu, Y.; Zhang, Y.; Jee, N.; Doyle, M. P. *Org. Lett.* **2008**, *10*, 1605.
- 76 Javed, M. I.; Brewer, M. *Org. Lett.* **2007**, *9*, 1789.
- 77 Meyer, M. E.; Ferreira, E. M.; Stoltz, B. M. *Chem. Commun.* **2006**, 1316.
- 78 Zhao, Y.; Wang, J. *Synlett* **2005**, 2886.
- 79 Doyle, M. P.; Kundu, K.; Russell, A. E. *Org. Lett.* **2005**, *7*, 5171.
- 80 Sa, M. M.; Silveira, G. P.; Bortoluzzi, A. J.; Padwa, A. *Tetrahedron* **2003**, *59*, 5441.
- 81 Wurz, R. P.; Charette, A. B. *Org. Lett.* **2002**, *4*, 4531.
- 82 Maas, G. *Top. Curr. Chem.* **1987**, *137*, 75.
- 83 Müller, P.; Fernandez, D. *Helv. Chim. Acta* **1995**, *78*, 947.
- 84 Müller, P.; Bolea, C. *Molecules* **2001**, *6*, 258.
- 85 Müller, P.; Bolea, C. *Helv. Chim. Acta* **2002**, *85*, 483.
- 86 Wolckenhauer, S. A.; Devlin, A. S.; Du Bois, J. *Org. Lett.* **2007**, *9*, 4363.
- 87 Park, S. B.; Nishiyama, H.; Itoh, Y.; Itoh, K. *J. Chem. Soc., Chem. Commun.* **1994**, 1315.
- 88 Nishiyama, H. *Top. Organomet. Chem.* **2004**, *11*, 81.
- 89 Doyle, M. P.; Griffin, J. H.; Bagheri, V.; Dorow, R. L. *Organometallics* **1984**, *3*, 53.

- ⁹⁰ Doyle, M. P.; Griffin, J. H.; Da Conceicao, J. *J. Chem. Soc., Chem. Commun.* **1985**, 328.
- ⁹¹ Closs, G. L.; Moss, R. A. *J. Am. Chem. Soc.* **1964**, 86, 4042.
- ⁹² Watanabe, N.; Ogawa, T.; Ohtake, Y.; Ikegami, S.; Hashimoto, S.-i. *Synlett* **1996**, 85.
- ⁹³ Watanabe, N.; Ohtake, Y.; Hashimoto, S.; Shiro, M.; Ikdgami, S. *Tetrahedron Lett.* **1995**, 36, 1491.
- ⁹⁴ Wood, J. L.; Holubec, A. A.; Stoltz, B. M.; Weiss, M. M.; Dixon, J. A.; Doan, B. D.; Shamji, M. F.; Chen, J. M.; Heffron, T. P. *J. Am. Chem. Soc.* **1999**, 121, 6326.
- ⁹⁵ Gois, P. M. P.; Afonso, C. A. M. *Eur. J. Org. Chem.* **2004**, 3773.
- ⁹⁶ Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon Press: New York, 1995; Vol. 12; Chapter 5.2.
- ⁹⁷ Drago, R. S.; Tanner, S. P.; Richman, R. M.; Long, J. R. *J. Am. Chem. Soc.* **1979**, 101, 2897.
- ⁹⁸ Drago, R. S.; Long, J. R.; Cosmano, R. *Inorg. Chem.* **1981**, 20, 2920.
- ⁹⁹ Drago, R. S. *Inorg. Chem.* **1982**, 21, 1697.
- ¹⁰⁰ Drago, R. S.; Long, J. R.; Cosmano, R. *Inorg. Chem.* **1982**, 21, 2196.
- ¹⁰¹ Telser, J.; Drago, R. S. *Inorg. Chem.* **1984**, 23, 2599.
- ¹⁰² Bilgrien, C.; Drago, R. S.; Stahlbush, J. R.; Kuechler, T. C. *Inorg. Chem.* **1985**, 24, 4268.
- ¹⁰³ Telser, J.; Drago, R. S. *Inorg. Chem.* **1986**, 25, 2989.
- ¹⁰⁴ Chifotides, H. T.; Dunbar, K. R. In *Multiple Bonds between Metal Atoms*, 3rd ed.; Cotton, F. A., Murillo, C. A., Walton, R. A., Eds.; Springer: New York, 2005; Chapter 12.
- ¹⁰⁵ Pirrung, M. C.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **1994**, 116, 8991.
- ¹⁰⁶ Pirrung, M. C.; Liu, H.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **2002**, 124, 1014.
- ¹⁰⁷ Nakamura, E.; Yoshikai, N.; Yamanaka, M. *J. Am. Chem. Soc.* **2002**, 124, 7181.
- ¹⁰⁸ Pirrung, M. C.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **1996**, 118, 8162.
- ¹⁰⁹ Maxwell, J. L.; Brown, K. C.; Bartley, D. W.; Kodadek, T. *Science* **1992**, 256, 1544.
- ¹¹⁰ Wong, F. M.; Wang, J.; Hengge, A. C.; Wu, W. *Org. Lett.* **2007**, 9, 1663.
- ¹¹¹ Barluenga, J.; Santamaria, J.; Tomas, M. *Chem. Rev.* **2004**, 104, 2259.
- ¹¹² Gomez-Gallego, M.; Mancheno, M. J.; Sierra, M. A. *Acc. Chem. Res.* **2005**, 38, 44.
- ¹¹³ Mindiola, D. J. *Acc. Chem. Res.* **2006**, 39, 813.
- ¹¹⁴ Doetz, K. H.; Stendel, J. *Chem. Rev.* **2009**, 109, 3227.
- ¹¹⁵ Ofele, K.; Tosh, E.; Taubmann, C.; Herrmann, W. A. *Chem. Rev.* **2009**, 109, 3408.
- ¹¹⁶ Whited, M. T.; Grubbs, R. H. *Acc. Chem. Res.* **2009**, 42, 1607.
- ¹¹⁷ Taber, D. F.; Joshi, P. V. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, 2005; Chapter 16.
- ¹¹⁸ Chuprakov, S.; Malik, J. A.; Zibinsky, M.; Fokin, V. V. *J. Am. Chem. Soc.* **2011**, 133, 10352.
- ¹¹⁹ Taber, D. F.; Petty, E. H.; Raman, K. *J. Am. Chem. Soc.* **1985**, 107, 196.
- ¹²⁰ Taber, D. F.; Ruckle, R. E., Jr. *J. Am. Chem. Soc.* **1986**, 108, 7686.
- ¹²¹ Doyle, M. P.; Westrum, L. J.; Wolthuis, W. N. E.; See, M. M.; Boone, W. P.; Bagheri, V.; Pearson, M. M. *J. Am. Chem. Soc.* **1993**, 115, 958.
- ¹²² Taber, D. F.; Song, Y. *J. Org. Chem.* **1996**, 61, 6706.
- ¹²³ Taber, D. F.; You, K. K.; Rheingold, A. L. *J. Am. Chem. Soc.* **1996**, 118, 547.
- ¹²⁴ Taber, D. F.; Malcolm, S. C. *J. Org. Chem.* **1998**, 63, 3717.
- ¹²⁵ Taber, D. F.; Joshi, P. V. *J. Org. Chem.* **2004**, 69, 4276.
- ¹²⁶ Yoshikai, N.; Nakamura, E. *Adv. Synth. Catal.* **2003**, 345, 1159.
- ¹²⁷ Spero, D. M.; Adams, J. *Tetrahedron Lett.* **1992**, 33, 1143.
- ¹²⁸ Wang, P.; Adams, J. *J. Am. Chem. Soc.* **1994**, 116, 3296.
- ¹²⁹ Stork, G.; Nakatani, K. *Tetrahedron Lett.* **1988**, 29, 2283.
- ¹³⁰ Doyle, M. P.; Taunton, J.; Pho, H. Q. *Tetrahedron Lett.* **1989**, 30, 5397.
- ¹³¹ Müller, P.; Tohill, S. *Tetrahedron* **2000**, 56, 1725.
- ¹³² Davies, H. M. L.; Ren, P.; Jin, Q. *Org. Lett.* **2001**, 3, 3587.
- ¹³³ Ceccherelli, P.; Curini, M.; Marcotullio, M. C.; Rosati, O. *Tetrahedron* **1991**, 47, 7403.
- ¹³⁴ Doyle, M. P.; Kalinin, A. V.; Ene, D. G. *J. Am. Chem. Soc.* **1996**, 118, 8837.
- ¹³⁵ Doyle, M. P.; Davies, S. B.; May, E. J. *J. Org. Chem.* **2001**, 66, 8112.
- ¹³⁶ Sonawane, H. R.; Bellur, N. S.; Ahuja, J. R.; Kulkarni, D. G. *J. Org. Chem.* **1991**, 56, 1434.

- ¹³⁷ Padwa, A.; Austin, D. J.; Hornbuckle, S. F.; Semones, M. A.; Doyle, M. P.; Protopopova, M. *N. J. Am. Chem. Soc.* **1992**, *114*, 1874.
- ¹³⁸ Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Daniel, K. L. *Tetrahedron Lett.* **1992**, *33*, 7819.
- ¹³⁹ Hashimoto, S.; Watanabe, N.; Ikegami, S. *Tetrahedron Lett.* **1992**, *33*, 2709.
- ¹⁴⁰ Moody, C. J.; Miah, S.; Slawin, A. M. Z.; Mansfield, D. J.; Richards, I. C. *Tetrahedron* **1998**, *54*, 9689.
- ¹⁴¹ Miah, S.; Slawin, A. M. Z.; Moody, C. J.; Sheehan, S. M.; Marino, J. P., Jr.; Semones, M. A.; Padwa, A.; Richards, I. C. *Tetrahedron* **1996**, *52*, 2489.
- ¹⁴² Padwa, A.; Austin, D. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1797.
- ¹⁴³ Doyle, M. P.; May, E. J. *Synlett* **2001**, 967.
- ¹⁴⁴ Doyle, M. P.; Wang, Y.; Ghorbani, P.; Bappert, E. *Org. Lett.* **2005**, *7*, 5035.
- ¹⁴⁵ Shi, W.; Zhang, B.; Zhang, J.; Liu, B.; Zhang, S.; Wang, J. *Org. Lett.* **2005**, *7*, 3103.
- ¹⁴⁶ Kennedy, M.; McKerver, M. A.; Maguire, A. R.; Roos, G. H. P. *J. Chem. Soc., Chem. Commun.* **1990**, 361.
- ¹⁴⁷ Cane, D. E.; Thomas, P. J. *J. Am. Chem. Soc.* **1984**, *106*, 5295.
- ¹⁴⁸ Hinman, A.; Du Bois, J. *J. Am. Chem. Soc.* **2003**, *125*, 11510.
- ¹⁴⁹ Doyle, M. P.; Protopopova, M. N.; Poulter, C. D.; Rogers, D. H. *J. Am. Chem. Soc.* **1995**, *117*, 7281.
- ¹⁵⁰ Yates, P.; Danishefsky, S. *J. Am. Chem. Soc.* **1962**, *84*, 879.
- ¹⁵¹ Wrobel, J.; Takahashi, K.; Honkan, V.; Lannoye, G.; Cook, J. M.; Bertz, S. H. *J. Org. Chem.* **1983**, *48*, 139.
- ¹⁵² Doyle, M. P.; Zhou, Q.-L.; Dyatkin, A. B.; Ruppar, D. A. *Tetrahedron Lett.* **1995**, *36*, 7579.
- ¹⁵³ Doyle, M. P.; Dyatkin, A. B.; Tedrow, J. S. *Tetrahedron Lett.* **1994**, *35*, 3853.
- ¹⁵⁴ Doyle, M. P.; Tedrow, J. S.; Dyatkin, A. B.; Spaans, C. J.; Ene, D. G. *J. Org. Chem.* **1999**, *64*, 8907.
- ¹⁵⁵ Müller, P.; Polleux, P. *Helv. Chim. Acta* **1994**, *77*, 645.
- ¹⁵⁶ Zhang, Z.; Wang, J. *Tetrahedron* **2008**, *64*, 6577.
- ¹⁵⁷ Clapham, B. *Curr. Opin. Drug Discovery Dev.* **2004**, *7*, 813.
- ¹⁵⁸ Maas, G. *Angew. Chem., Int. Ed.* **2009**, *48*, 8186.
- ¹⁵⁹ Fulton, J. R.; Aggarwal, V. K.; de Vicente, J. *Eur. J. Org. Chem.* **2005**, 1479.
- ¹⁶⁰ Sales, Z. S.; Mani, N. S. *J. Org. Chem.* **2009**, *74*, 891.
- ¹⁶¹ Chuprakov, S.; Kwok, S. W.; Zhang, L.; Lercher, L.; Fokin, V. V. *J. Am. Chem. Soc.* **2009**, *131*, 18034.
- ¹⁶² Grimster, N.; Zhang, L.; Fokin, V. V. *J. Am. Chem. Soc.* **2010**, *132*, 2510.
- ¹⁶³ Müller, P.; Fernandez, D.; Nury, P.; Rossier, J.-C. *J. Phys. Org. Chem.* **1998**, *11*, 321.
- ¹⁶⁴ Goudreau, S. R.; Marcoux, D.; Charette, A. B. *J. Org. Chem.* **2009**, *74*, 470.
- ¹⁶⁵ Müller, P.; Allenbach, Y. F.; Chappellet, S.; Ghanem, A. *Synthesis* **2006**, 1689.
- ¹⁶⁶ Ghanem, A.; Lacrampe, F.; Schurig, V. *Helv. Chim. Acta* **2005**, *88*, 216.
- ¹⁶⁷ Moriarty, R. M.; Kim, J.; Guo, L. *Tetrahedron Lett.* **1993**, *34*, 4129.
- ¹⁶⁸ Moriarty, R. M.; Bailey, B. R., III; Prakash, O.; Prakash, I. *J. Am. Chem. Soc.* **1985**, *107*, 1375.
- ¹⁶⁹ Bequette, J. P.; Jungong, C. S.; Novikov, A. V. *Tetrahedron Lett.* **2009**, *50*, 6963.
- ¹⁷⁰ Scott, L. T.; Minton, M. A. *J. Org. Chem.* **1977**, *42*, 3757.
- ¹⁷¹ Arndt, F. *Org. Synth.* **1943**, *2*, 461.
- ¹⁷² DeBoer, T. J.; Backer, H. J. *Org. Synth.* **1956**, *36*, 16.
- ¹⁷³ Moore, J. A.; Reed, D. E. *Org. Synth.* **1961**, *41*, 16.
- ¹⁷⁴ Aoyama, T.; Shioiri, T. *Tetrahedron Lett.* **1980**, *21*, 4461.
- ¹⁷⁵ Aoyama, T.; Shioiri, T. *Chem. Pharm. Bull.* **1981**, *29*, 3249.
- ¹⁷⁶ Shioiri, T.; Aoyama, T.; Mori, S. *Org. Synth.* **1990**, *68*, 1.
- ¹⁷⁷ Burtoloso, A. C. B.; Correia, C. R. D. *J. Organomet. Chem.* **2005**, *690*, 5636.
- ¹⁷⁸ Maguire, A. R.; O'Leary, P.; Harrington, F.; Lawrence, S. E.; Blake, A. J. *J. Org. Chem.* **2001**, *66*, 7166.
- ¹⁷⁹ Nakatani, K.; Adachi, K.; Tanabe, K.; Saito, I. *J. Am. Chem. Soc.* **1999**, *121*, 8221.
- ¹⁸⁰ Ye, T.; Fernandez Garcia, C.; McKerver, M. A. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1373.

- ¹⁸¹ Padwa, A.; Kassir, J. M.; Semones, M. A.; Weingarten, M. D. *J. Org. Chem.* **1995**, *60*, 53.
- ¹⁸² Wenkert, E.; Decorzant, R.; Naef, F. *Helv. Chim. Acta* **1989**, *72*, 756.
- ¹⁸³ Nicolaou, K. C.; Stepan, A. F.; Lister, T.; Li, A.; Montero, A.; Tria, G. S.; Turner, C. I.; Tang, Y.; Wang, J.; Denton, R. M.; Edmonds, D. J. *J. Am. Chem. Soc.* **2008**, *130*, 13110.
- ¹⁸⁴ Nicolaou, K. C.; Lister, T.; Denton, R. M.; Montero, A.; Edmonds, D. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 4712.
- ¹⁸⁵ Hodgson, D. M.; Le Strat, F.; Avery, T. D.; Donohue, A. C.; Brueckl, T. *J. Org. Chem.* **2004**, *69*, 8796.
- ¹⁸⁶ Nakatani, K.; Isoe, S.; Maekawa, S.; Saito, I. *Tetrahedron Lett.* **1994**, *35*, 605.
- ¹⁸⁷ Padwa, A.; Chiacchio, U.; Fairfax, D. J.; Kassir, J. M.; Litrico, A.; Semones, M. A.; Xu, S. L. *J. Org. Chem.* **1993**, *58*, 6429.
- ¹⁸⁸ Flowers, W. T.; Holt, G.; Poulos, C. P.; Poulos, K. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1757.
- ¹⁸⁹ Nerdel, F.; Pawlowski, K. H. *Chem. Ber.* **1954**, *87*, 215.
- ¹⁹⁰ Kennedy, M.; McKervey, M. A.; Maguire, A. R.; Tuladhar, S. M.; Twohig, M. F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1047.
- ¹⁹¹ Duddeck, H.; Ferguson, G.; Kaitner, B.; Kennedy, M.; McKervey, M. A.; Maguire, A. R. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1055.
- ¹⁹² Kennedy, M.; McKervey, M. A. *J. Chem. Soc., Chem. Commun.* **1988**, 1028.
- ¹⁹³ Agarwal, R.; Bahadur, P. *Rev. Roum. Chim.* **1986**, *31*, 297.
- ¹⁹⁴ Hudlicky, T.; Kwart, L. D.; Tiedje, M. H.; Ranu, B. C.; Short, R. P.; Frazier, J. O.; Rigby, H. L. *Synthesis* **1986**, 716.
- ¹⁹⁵ Hudlicky, T.; Koszyk, F. J.; Dochwat, D. M.; Cantrell, G. L. *J. Org. Chem.* **1981**, *46*, 2911.
- ¹⁹⁶ Flowers, W. T.; Holt, G.; Hope, M. A.; Poulos, C. P. *J. Chem. Soc., Perkin Trans. 1* **1975**, 286.
- ¹⁹⁷ Yates, P.; Farnum, D. G.; Wiley, D. W. *Tetrahedron* **1962**, *18*, 881.
- ¹⁹⁸ Franzen, V. *Justus Liebigs Ann. Chem.* **1957**, 602, 199.
- ¹⁹⁹ Taber, D. F.; Ruckle, R. E., Jr.; Hennessy, M. J. *J. Org. Chem.* **1986**, *51*, 4077.
- ²⁰⁰ Baum, J. S.; Shook, D. A.; Davies, H. M. L.; Smith, H. D. *Synth. Commun.* **1987**, *17*, 1709.
- ²⁰¹ Hazen, G. G.; Weinstock, L. M.; Connell, R.; Bollinger, F. W. *Synth. Commun.* **1981**, *11*, 947.
- ²⁰² Bollinger, F. W.; Tuma, L. D. *Synlett* **1996**, 407.
- ²⁰³ Taber, D. F.; Tian, W. *J. Org. Chem.* **2007**, *72*, 3207.
- ²⁰⁴ Hasegawa, K.; Arai, S.; Nishida, A. *Tetrahedron* **2006**, *62*, 1390.
- ²⁰⁵ de S. Rianelli, R.; de Souza, M. C.; Ferreira, V. F. *Synth. Commun.* **2004**, *34*, 951.
- ²⁰⁶ Wurz, R. P.; Lin, W.; Charette, A. B. *Tetrahedron Lett.* **2003**, *44*, 8845.
- ²⁰⁷ Xu, Y.; Wang, Y.; Zhu, S. *J. Fluorine Chem.* **2000**, *105*, 25.
- ²⁰⁸ Charette, A. B.; Wurz, R. P.; Ollevier, T. *J. Org. Chem.* **2000**, *65*, 9252.
- ²⁰⁹ Lee, J. C.; Yuk, J. Y. *Synth. Commun.* **1995**, *25*, 1511.
- ²¹⁰ Davies, H. M. L.; Cantrell, W. R., Jr.; Romines, K. R.; Baum, J. S. *Org. Synth.* **1992**, *70*, 93.
- ²¹¹ Kumar, S. M. *Synth. Commun.* **1991**, *21*, 2121.
- ²¹² Ghosh, S.; Datta, I. *Synth. Commun.* **1991**, *21*, 191.
- ²¹³ Ben Alloum, A.; Villemain, D. *Synth. Commun.* **1989**, *19*, 2567.
- ²¹⁴ Doyle, M. P.; Shanklin, M. S.; Pho, H. Q.; Mahapatro, S. N. *J. Org. Chem.* **1988**, *53*, 1017.
- ²¹⁵ Ledon, H. *J. Org. Synth.* **1980**, *59*, 66.
- ²¹⁶ Ledon, H. *Synthesis* **1974**, 347.
- ²¹⁷ Regitz, M.; Menz, F.; Rueter, J. *Tetrahedron Lett.* **1967**, 739.
- ²¹⁸ Saito, H.; Oishi, H.; Kitagaki, S.; Nakamura, S.; Anada, M.; Hashimoto, S. *Org. Lett.* **2002**, *4*, 3887.
- ²¹⁹ Doyle, M. P.; Dorow, R. L.; Terpstra, J. W.; Rodenhouse, R. A. *J. Org. Chem.* **1985**, *50*, 1663.
- ²²⁰ Danheiser, R. L.; Miller, R. F.; Brisbois, R. G.; Park, S. Z. *J. Org. Chem.* **1990**, *55*, 1959.
- ²²¹ Danheiser, R. L.; Miller, R. F.; Brisbois, R. G. *Org. Synth.* **1996**, *73*, 134.
- ²²² Taber, D. F.; Sheth, R. B.; Joshi, P. V. *J. Org. Chem.* **2005**, *70*, 2851.
- ²²³ Doyle, M. P.; Protodopova, M. N.; Zhou, Q.-L.; Bode, J. W.; Simonsen, S. H.; Lynch, V. J. *Org. Chem.* **1995**, *60*, 6654.
- ²²⁴ Clive, D. L. J.; Daigneault, S. *J. Org. Chem.* **1991**, *56*, 3801.
- ²²⁵ Ouhiha, A.; Rene, L.; Guilhem, J.; Pascard, C.; Badet, B. *J. Org. Chem.* **1993**, *58*, 1641.

- Blankley, C. J.; Sauter, F. J.; House, H. O. *Org. Synth.* **1969**, 49, 22.
- Corey, E. J.; Myers, A. G. *Tetrahedron Lett.* **1984**, 25, 3559.
- Doyle, M. P.; Kalinin, A. V. *J. Org. Chem.* **1996**, 61, 2179.
- Zhou, L.; Doyle, M. P. *Org. Lett.* **2010**, 12, 796.
- Schwartz, B. D.; Denton, J. R.; Lian, Y.; Davies, H. M. L.; Williams, C. M. *J. Am. Chem. Soc.* **2009**, 131, 8329.
- Davies, H. M. L.; Ahmed, G.; Churchill, M. R. *J. Am. Chem. Soc.* **1996**, 118, 10774.
- Kundu, D.; Doyle, M. P. *Tetrahedron: Asymmetry* **2006**, 17, 574.
- Taber, D. F.; Jiang, Q. *J. Org. Chem.* **2001**, 66, 1876.
- Garcia, F. S.; Cebrian, G. M. P.; Lopez, A. H.; Herrera, F. J. L. *Tetrahedron* **1998**, 54, 6867.
- Wenkert, E.; McPherson, C. A. *J. Am. Chem. Soc.* **1972**, 94, 8084.
- Jiang, N.; Wang, J. *Tetrahedron Lett.* **2002**, 43, 1285.
- Kanemasa, S.; Araki, T.; Kanai, T.; Wada, E. *Tetrahedron Lett.* **1999**, 40, 5059.
- Moody, C. J.; Morfitt, C. N. *Synthesis* **1998**, 1039.
- Calter, M. A.; Sugathapala, P. M.; Zhu, C. *Tetrahedron Lett.* **1997**, 38, 3837.
- Calter, M. A.; Zhu, C. *J. Org. Chem.* **1999**, 64, 1415.
- Deng, G.; Tian, X.; Qu, Z.; Wang, J. *Angew. Chem., Int. Ed.* **2002**, 41, 2773.
- Doyle, M. P.; Zhou, Q.-L.; Raab, C. E.; Roos, G. H. P.; Simonsen, S. H.; Lynch, V. *Inorg. Chem.* **1996**, 35, 6064.
- Doyle, M. P.; Dyatkin, A. B.; Roos, G. H. P.; Canas, F.; Pierson, D. A.; van Basten, A.; Müller, P.; Polleux, P. *J. Am. Chem. Soc.* **1994**, 116, 4507.
- Doyle, M. P.; Morgan, J. P.; Fettingner, J. C.; Zavalij, P. Y.; Colyer, J. T.; Timmons, D. J.; Carducci, M. D. *J. Org. Chem.* **2005**, 70, 5291.
- Doyle, M. P.; Zhou, Q. L.; Simonsen, S. H.; Lynch, V. *Synlett* **1996**, 697.
- Doyle, M. P.; Davies, S. B.; Hu, W. *Org. Lett.* **2000**, 2, 1145.
- Doyle, M. P.; Dyatkin, A. B.; Protopopova, M. N.; Yang, C. I.; Miertschin, C. S.; Winchester, W. R.; Simonsen, S. H.; Lynch, V.; Ghosh, R. *Recl. Trav. Chim. Pays-Bas* **1995**, 114, 163.
- Davies, H. M. L.; Bruzinski, P.; Hutcheson, D. K.; Kong, N.; Fall, M. J. *J. Am. Chem. Soc.* **1996**, 118, 6897.
- Watanabe, N.; Anada, M.; Hashimoto, S.-i.; Ikegami, S. *Synlett* **1994**, 1031.
- Anada, M.; Hashimoto, S.-i. *Tetrahedron Lett.* **1998**, 39, 79.
- Doyle, M. P.; Colyer, J. *J. Mol. Catal. A: Chem.* **2003**, 196, 93.
- Estevan, F.; Lahuerta, P.; Perez-Prieto, J.; Sanau, M.; Stiriba, S.-E.; Ubeda, M. A. *Organometallics* **1997**, 16, 880.
- Estevan, F.; Lahuerta, P.; Perez-Prieto, J.; Pereira, I.; Stiriba, S.-E. *Organometallics* **1998**, 17, 3442.
- Estevan, F.; Herbst, K.; Lahuerta, P.; Barberis, M.; Perez-Prieto, J. *Organometallics* **2001**, 20, 950.
- Barberis, M.; Estevan, F.; Lahuerta, P.; Perez-Prieto, J.; Sanau, M. *Inorg. Chem.* **2001**, 40, 4226.
- Müller, P.; Lacrampe, F.; Bernardinelli, G. *Tetrahedron: Asymmetry* **2003**, 14, 1503.
- Marsden, S. P.; Pang, W.-K. *Tetrahedron Lett.* **1998**, 39, 6077.
- Doyle, M. P.; Van Oeveren, A.; Westrum, L. J.; Protopopova, M. N.; Clayton, T. W., Jr. *J. Am. Chem. Soc.* **1991**, 113, 8982.
- Bode, J. W.; Doyle, M. P.; Protopopova, M. N.; Zhou, Q.-L. *J. Org. Chem.* **1996**, 61, 9146.
- Doyle, M. P.; Hu, W.; Valenzuela, M. V. *J. Org. Chem.* **2002**, 67, 2954.
- Doyle, M. P.; Zhou, Q.-L.; Raab, C. E.; Roos, G. H. P. *Tetrahedron Lett.* **1995**, 36, 4745.
- Roos, G. H. P.; Raab, C. E.; Emslie, N. D.; Doyle, M. P.; Lynch, V. *Aust. J. Chem.* **1998**, 51, 1.
- Doyle, M. P.; Yan, M.; Gau, H.-M.; Blossey, E. C. *Org. Lett.* **2003**, 5, 561.
- Doyle, M. P.; Morgan, J. P.; Colyer, J. T. *J. Organomet. Chem.* **2005**, 690, 5525.
- Doyle, M. P.; Dyatkin, A. B. *J. Org. Chem.* **1995**, 60, 3035.
- Doyle, M. P.; Kalinin, A. V. *Russ. Chem. Bull.* **1995**, 44, 1729.
- Doyle, M. P.; Dyatkin, A. B.; Kalinin, A. V.; Ruppar, D. A.; Martin, S. F.; Spaller, M. R.; Liras, S. *J. Am. Chem. Soc.* **1995**, 117, 11021.
- Yang, H. W.; Romo, D. *Tetrahedron* **1999**, 55, 6403.

- 269 Schneider, C. *Angew. Chem., Int. Ed.* **2002**, 41, 744.
- 270 Robin, S.; Rousseau, G. *Eur. J. Org. Chem.* **2002**, 3099.
- 271 Tidwell, T. T. *Eur. J. Org. Chem.* **2006**, 563.
- 272 Doyle, M. P.; Bagheri, V.; Pearson, M. M.; Edwards, J. D. *Tetrahedron Lett.* **1989**, 30, 7001.
- 273 Wee, A. G. H.; Liu, B.; Zhang, L. *J. Org. Chem.* **1992**, 57, 4404.
- 273a Liebman, J. L. *Biophys. Chem.* **1974**, 1, 222.
- 274 Doyle, M. P.; Winchester, W. R.; Protopopova, M. N. *Helv. Chim. Acta* **1993**, 76, 2227.
- 275 Liu, W.-J.; Chen, Z.-L.; Chen, Z.-Y.; Hu, W.-H. *Tetrahedron: Asymmetry* **2005**, 16, 1693.
- 276 Chen, Z.; Chen, Z.; Jiang, Y.; Hu, W. *Synlett* **2004**, 1763.
- 277 Doyle, M. P.; Kalinin, A. V. *Synlett* **1995**, 1075.
- 278 Doyle, M. P.; Yan, M.; Phillips, I. M.; Timmons, D. J. *Adv. Synth. Catal.* **2002**, 344, 91.
- 279 Wee, A. G. H.; Duncan, S. C. *Tetrahedron Lett.* **2002**, 43, 6173.
- 280 Wee, A. G. H.; Duncan, S. C. *J. Org. Chem.* **2005**, 70, 8372.
- 281 Doyle, M. P.; Hu, W.; Wee, A. G. H.; Wang, Z.; Duncan, S. C. *Org. Lett.* **2003**, 5, 407.
- 282 Doyle, M. P.; Hu, W.; Wee, A. G. H.; Wang, Z.; Duncan, S. C. *Org. Lett.* **2003**, 5, 2371.
- 283 Doyle, M. P.; Kalinin, A. V. *Tetrahedron Lett.* **1996**, 37, 1371.
- 284 Wee, A. G. H.; Duncan, S. C.; Fan, G.-j. *Tetrahedron: Asymmetry* **2006**, 17, 297.
- 285 Anada, M.; Hashimoto, S.-I. *Tetrahedron Lett.* **1998**, 39, 9063.
- 286 Anada, M.; Watanabe, N. *Chem. Commun.* **1998**, 1517.
- 287 Hikichi, K.; Kitagaki, S.; Anada, M.; Nakamura, S.; Nakajima, M.; Shiro, M.; Hashimoto, S. *Heterocycles* **2003**, 61, 391.
- 288 Anada, M.; Kitagaki, S.; Hashimoto, S. *Heterocycles* **2000**, 52, 875.
- 289 Pique, C.; Fahndrich, B.; Pfaltz, A. *Synlett* **1995**, 491.
- 290 Tokunoh, R.; Tomiyama, H.; Sodeoka, M.; Shibasaki, M. *Tetrahedron Lett.* **1996**, 37, 2449.
- 291 Doyle, M. P.; Eismont, M. Y.; Zhou, Q. L. *Russ. Chem. Bull.* **1997**, 46, 955.
- 292 Wardrop, D. J.; Forslund, R. E.; Landrie, C. L.; Velter, A. I.; Wink, D.; Surve, B. *Tetrahedron: Asymmetry* **2003**, 14, 929.
- 293 Doyle, M. P.; Dyatkin, A. B.; Autry, C. L. *J. Chem. Soc., Perkin Trans. 1* **1995**, 619.
- 294 McKervey, M. A.; Ye, T. *J. Chem. Soc., Chem. Commun.* **1992**, 823.
- 295 Marmsaeter, F. P.; Vanecko, J. A.; West, F. G. *Org. Lett.* **2004**, 6, 1657.
- 296 Marmsaeter, F. P.; Vanecko, J. A.; West, F. G. *Tetrahedron* **2002**, 58, 2027.
- 297 Marmsaeter, F. P.; West, F. G. *J. Am. Chem. Soc.* **2001**, 123, 5144.
- 298 White, J. D.; Hrciar, P.; Stappenbeck, F. J. *Org. Chem.* **1999**, 64, 7871.
- 299 Sonawane, H. R.; Bellur, N. S.; Ahuja, J. R.; Kulkarni, D. G. *J. Org. Chem.* **1991**, 56, 1434.
- 300 Srikrishna, A.; Beeraiah, B.; Satyanarayana, G. *Tetrahedron: Asymmetry* **2006**, 17, 1544.
- 301 Srikrishna, A.; Satyanarayana, G. *Tetrahedron* **2005**, 61, 8855.
- 302 Yakura, T.; Ueki, A.; Kitamura, T.; Tanaka, K.; Nameki, M.; Ikeda, M. *Tetrahedron* **1999**, 55, 7461.
- 303 White, J. D.; Hrciar, P.; Stappenbeck, F. J. *Org. Chem.* **1997**, 62, 5250.
- 304 Yakura, T.; Tanaka, T.; Ikeda, M.; Uenishi, J. i. *Chem. Pharm. Bull.* **2003**, 51, 471.
- 305 Reddy, R. P.; Lee, G. H.; Davies, H. M. L. *Org. Lett.* **2006**, 8, 3437.
- 306 Davies, H. M. L.; Walji, A. M. *Org. Lett.* **2005**, 7, 2941.
- 307 Davies, H. M. L.; Grazini, M. V. A.; Aouad, E. *Org. Lett.* **2001**, 3, 1475.
- 308 Taber, D. F.; Tian, W. *J. Org. Chem.* **2008**, 73, 7560.
- 309 Minami, K.; Saito, H.; Tsutsui, H.; Nambu, H.; Anada, M.; Hashimoto, S. *Adv. Synth. Catal.* **2005**, 347, 1483.
- 310 Lim, H.-J.; Sulikowski, G. A. *J. Org. Chem.* **1995**, 60, 2326.
- 311 Lee, S.; Lim, H.-J.; Cha, K. L.; Sulikowski, G. A. *Tetrahedron* **1997**, 53, 16521.
- 312 Lee, S.; Lee, W.-M.; Sulikowski, G. A. *J. Org. Chem.* **1999**, 64, 4224.
- 313 Doyle, M. P.; Phillips, I. M. *Tetrahedron Lett.* **2001**, 42, 3155.
- 314 Doyle, M. P.; Austin, R. E.; Bailey, A. S.; Dwyer, M. P.; Dyatkin, A. B.; Kalinin, A. V.; Kwan, M. M. Y.; Liras, S.; Oalman, C. J.; Pieters, R. J.; Protopopova, M. N.; Raab, C. E.; Roos, G. H. P.; Zhou, Q.-L.; Martin, S. F. *J. Am. Chem. Soc.* **1995**, 117, 5763.
- 315 Doyle, M. P.; Hu, W. *J. Org. Chem.* **2000**, 65, 8839.

- ³¹⁶ Padwa, A.; Austin, D. J.; Price, A. T.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Tran, A. *J. Am. Chem. Soc.* **1993**, *115*, 8669.
- ³¹⁷ Doyle, M. P.; Chapman, B. J.; Hu, W.; Peterson, C. S.; McKervey, M. A.; Garcia, C. F. *Org. Lett.* **1999**, *1*, 1327.
- ³¹⁸ Doyle, M. P.; Hu, W. *Tetrahedron Lett.* **2000**, *41*, 6265.
- ³¹⁹ Doyle, M. P.; Hu, W. *Synlett* **2001**, 1364.
- ³²⁰ Doyle, M. P.; Hu, W.; Chapman, B.; Marnett, A. B.; Peterson, C. S.; Vitale, J. P.; Stanley, S. A. *J. Am. Chem. Soc.* **2000**, *122*, 5718.
- ³²¹ Weathers, T. M., Jr.; Wang, Y.; Doyle, M. P. *J. Org. Chem.* **2006**, *71*, 8183.
- ³²² Doyle, M. P.; Devia, A. H.; Bassett, K. E.; Terpstra, J. W.; Mahapatro, S. N. *J. Org. Chem.* **1987**, *52*, 1619.
- ³²³ Baratta, W.; Del Zotto, A.; Rigo, P. *Organometallics* **1999**, *18*, 5091.
- ³²⁴ Graban, E.; Lemke, F. R. *Organometallics* **2002**, *21*, 3823.
- ³²⁵ Shankar, B. K. R.; Shechter, H. *Tetrahedron Lett.* **1982**, *23*, 2277.
- ³²⁶ Taber, D. F.; Hennessy, M. J.; Louey, J. P. *J. Org. Chem.* **1992**, *57*, 436.
- ³²⁷ Taber, D. F.; Song, Y. *Tetrahedron Lett.* **1995**, *36*, 2587.
- ³²⁸ Doyle, M. P.; Hu, W. *Chirality* **2002**, *14*, 169.
- ³²⁹ Doyle, M. P.; Ratnikov, M.; Liu, Y. *Org. Biomol. Chem.* **2011**, *9*, 4007.
- ³³⁰ Martin, L. J.; Marzinzik, A. L.; Ley, S. V.; Baxendale, I. R. *Org. Lett.* **2011**, *13*, 320.
- ³³¹ Ferreira, J. T. B.; Marques, J. A.; Marino, J. P. *Tetrahedron: Asymmetry* **1994**, *5*, 641.
- ³³² Edwards, O. E.; Paton, J. M.; Benn, M. H.; Mitchell, R. E.; Watanatada, C.; Vohra, K. N. *Can. J. Chem.* **1971**, *49*, 1648.
- ³³³ Anada, M.; Watanabe, N. *Chem. Commun.* **1998**, 1517.
- ³³⁴ Gois, P. M. P.; Candeias, N. R.; Afonso, C. A. M. *J. Mol. Catal. A: Chem.* **2005**, *227*, 17.
- ³³⁵ Branco, L. C.; Gois, P. M. P.; Lourenco, N. M. T.; Kurteva, V. B.; Afonso, C. A. M. *Chem. Commun.* **2006**, 2371.
- ³³⁶ Wee, A. G. H.; McLeod, D. D. *Heterocycles* **2000**, *53*, 637.
- ³³⁷ Hwang, C. H.; Chong, Y. H.; Song, S. Y.; Kwak, H. S.; Lee, E. *Chem. Commun.* **2004**, 816.
- ³³⁸ Reddy, R. P.; Lee, G. H.; Davies, H. M. L. *Org. Lett.* **2006**, *8*, 3437.

