Iron-catalyzed transformations of diazo compounds

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ABSTRACT

Although iron-promoted diazo transformations were only discovered during the 1990s, iron can undergo facile changes in its oxidation state and possesses distinct Lewis acid character, and these properties have afforded iron a privileged position as a catalyst in the transformations of diazo compounds. In this review, we have provided an overview of the iron-catalyzed diazo transformation reactions reported in the literature by the end of 2013 with the aim of stimulating further interest in this area of research.

Keywords: iron, catalysis, diazo compounds, synthesis

INTRODUCTION

Catalysis can be used to enhance the reactivity and selectivity of specific chemical transformations, as well as decreasing the amount of energy consumed by these processes. Most catalytic reactions fulfill the criteria for a sustainable transformation on the macroscopic scale, and a wide variety of efficient catalytic systems have been developed in both industry and academia that are capable of affecting a broad range of chemical transformations. Unfortunately, however, most of the popular and frequently used catalysts are based on precious metals such as palladium, rhodium, ruthenium, iridium, and osmium, which are becoming increasingly expensive because they are derived from dwindling resources [1]. Similarly, the use of heavy metals as catalysts in the pharmaceutical and agricultural industries has been limited by their toxicity. In the interests of developing a long-term strategy towards sustainable development, there is an urgent need to develop effective and abundant replacements for the rare and toxic metals currently used in catalysis. Iron is a readily available, inexpensive, and environmentally benign metal, which represents an ideal alternative to the use of precious metals. Iron, however, has not been developed as a catalyst to the same extent as other transition metals with regard to usage in organic transformations especially asymmetric processes [2].

The transition-metal-catalyzed transformations of diazo compounds are widely used in organic synthesis [3]. The catalysts used in reactions of diazo compounds are generally derived from rhodium, ruthenium, and copper. Iron can undergo facile changes in its oxidation state and exhibit distinct Lewis acid character, and could therefore be used to activate diazo compounds in a variety of different ways. With this in mind, iron may be used as an effective catalyst for transformations of diazo compounds (Scheme 1). For example, the iron catalyst could attack the α-carbon of diazo compound 1, and the subsequent loss of nitrogen can lead to the formation of an iron carbene and carbenoid species 3 and 3′, respectively (processes a and b). The iron carbene and carbenoid species may readily undergo carbene transfer reactions, including the cyclopropanation of olefins I (process c), C–H insertion into hydrocarbons II (process d), or ylide formation with heteroatom-containing compounds bearing a lone pair III (process e). The iron-activated diazo compounds 2 and 2′ could also form ylides by undergoing a substitution reaction with heteroatom-containing compounds bearing a lone pair III (process f). Furthermore, iron may act as a Lewis acid catalyst and activate electrophiles, such as imines and aldehydes, which could then react with diazo compound 1 (process g). In this review, we have provided an overview of the iron-catalyzed diazo transformation reactions reported in the literature by the end of 2013 with the aim of stimulating further interest in this area of research.
Scheme 1. Outline of the iron-catalyzed transformations of diazo compounds.

Scheme 2. Cyclopropanation of olefins with EDA catalyzed by \([\eta^5\text{C}_5\text{Me}_6]\text{Fe} (\text{CO})_2\text{BF}_4\) (4).

Table 1. Iron porphyrin-catalyzed cyclopropanation of styrene with EDA.

| Entry | Catalyst | Time (h) | TON | trans/cis |
|-------|----------|----------|-----|-----------|
| 1     | Fe(6b)   | 1        | 1300| 8.8       |
| 2     | Fe(6a)C/CoCP_1 | 2  | 910 | 8.7       |
| 3     | Fe(6a)C/CoCP_1 | 10 | 400 | 5.5       |
| 4     | Fe(6c)C/CoCP_1 | 3  | 730 | 9.0       |
| 5     | Fe(6e)C/CoCP_1 | 2  | 890 | 13        |
| 6     | Fe(6f)Cl | 6        | 4200| 6.0       |
| 7^b   | Fe(6g)C/CoCP_1 | 1.5| 970 | 30        |
| 8     | Fe(6h)C/CoCP_1 | 4  | 300 | 10        |

^a All of these data have been taken from [7], except entry 7, which was taken from [8].^b Performed in CHCl_3.

**CYCLOPROPANATION**

**Cyclopropanation of alkenes**

The cyclopropane subunit is the smallest of the cycloalkanes and exists as a basic structural element in a wide range of naturally occurring compounds. Cyclopropanes have also been used as versatile synthetic intermediates for the construction of functionalized cyclic and acyclic compounds. The cyclopropanation of olefins via the transition-metal-catalyzed decomposition of diazo compounds has been studied extensively [4]. Although the cyclopropanation of olefins with stoichiometric iron carbones was first documented over 40 years ago [5], the iron-catalyzed cyclopropanation of olefins with diazo compounds was not reported until the 1990s, and several other iron complexes have subsequently been developed as efficient catalysts for this important transformation.

Hossain et al. [6] reported the first iron-catalyzed cyclopropanation reaction using \([(\eta^5\text{C}_5\text{Me}_6)\text{Fe} (\text{CO})_2]\text{BF}_4\) (4) as a catalyst. According to this report, styrene and α-methylstyrene were reacted smoothly with ethyl diazoacetate (EDA) in the presence of the iron Lewis acid 4 to give the corresponding cyclopropanes with moderate to good cis-selectivity. Unfortunately, however, the use of aliphatic olefins such as 2-methyl-2-butene and cyclohexene under these conditions did not afford the desired cyclopropanation products (Scheme 2). Vinyl ethers could also be used as substrates in this reaction, with the corresponding cyclopropanes being formed in good yields, albeit with lower levels of diastereoselectivity. Attempts to characterize the iron carbene complex using variable-temperature H NMR measurements were...
unsuccesful. However, the formation of carbene dimerization products (i.e. diethyl fumarate and diethyl maleate) and the selectivity exhibited by the cyclopropanation reaction suggested that the iron carbene 5 was involved as an intermediate in the reaction.

Kodadek and Woo [7] revealed that iron porphyrin complexes can be used as highly active catalysts for the cyclopropanation of alkenes with EDA to afford trans-enriched cyclopropyl esters (Table 1). The isolated iron(II) porphyrin complex Fe(6b) was identified as the active catalyst in this particular transformation (Table 1, entry 1). The iron(III) porphyrin complexes can be reduced in situ by EDA or cobaltocene (CoCp2) to afford the active catalysts (Table 1, entries 2–8). Moderate to good levels of trans-selectivity were obtained for all of the iron porphyrin catalysts evaluated in this study, with the halogenated FeIII(6g)Cl catalyst [8] affording the best results in this regard. It is noteworthy that the electron-deficient FeIII(6f)Cl catalyst could be readily reduced to FeII(6f) by EDA, even at ambient temperature, and that this catalyst exhibited remarkably high turnover numbers (TONs, up to 4300) for the cyclopropanation of various terminal olefins with EDA (Table 2). These reactions were also determined to be selective for monosubstituted and 1,1-disubstituted alkenes, especially those bearing aryl substituents (Table 3).

Table 2. The Fe(6f)Cl-catalyzed cyclopropanation of terminal olefins with EDA.

| Entry | R¹ | Time (h) | TON | trans/cis |
|-------|----|----------|-----|-----------|
| 1     | Ph | 3        | 4300| 1.1       |
| 2     | 4-MeOCH₂ | 7   | 2000| 5.8       |
| 3     | OEt| 4        | 1800| 3.3       |
| 4     | Et | 2        | 390 | --        |

Table 3. Competition experiments for the iron porphyrin-catalyzed cyclopropanation reactions of olefins.

| Entry | Catalyst | Olefin A | Olefin B | Ratio of products derived from A/B |
|-------|----------|----------|----------|-----------------------------------|
| 1     | Fe(6b)   | Ph       | PhMe     | Only reaction of A observed       |
| 2     | Fe(6f)Cl | Ph       | benzene  | 26                                |
| 3     | Fe(6f)Cl | Ph       | n-C₄H₉   | 74                                |
| 4     | Fe(6b)   | Ph       | PhMe     | 3.0                               |

A secondary kinetic isotope effect (KIE) was observed in a competitive reaction between styrene and styrene-⁵⁸ using Fe(6f)Cl as the catalyst. It was proposed that these cyclopropanation reactions proceeded via the formation of a key iron(II) carbene intermediate. The transition states of the carbene transfer step were also proposed to rationalize the trans-selectivity of this reaction (Fig. 1).

The iron porphyrin Fe(6b) has also been reported as an efficient catalyst for the cyclopropanation of styrenes with aryl diazomethanes.
Table 4. Iron porphyrin-catalyzed intramolecular cyclopropanation reactions.

| Entry | R1 | R2 | Yield (%) |
|-------|----|----|-----------|
| 1     | Ph | H  | 76        |
| 2     | Me | Me | 92        |
| 3     | Et | H  | 62        |
| 4*    | MeC=CH(CH3)2 | Me | 73        |
| 5     | MeC=CH(CH3)2 | Me | 58        |

*0.1 mol% Fe(6f)(CPh2) and 0.1 mol% 2,6-Cl2Py (2,6-dichloropyridine) were used, with 84% conversion.

Table 5. Iron porphyrin-catalyzed cyclopropanation reactions using diazo compounds generated in situ from benzaldehyde N-tosylhydrazone sodium salt.

| Entry | Alkene | Yield (%) | trans/cis |
|-------|--------|-----------|-----------|
| 1     | Ph     | 73 (48)   | 91:9 (23:77) |
| 2     | Me     | 73 (44)   | 90:10 (50:50) |
| 3     | MeO     | 86 (46)   | 59:41 (9:91) |
| 4     | Me     | 39 (24)   | 88:12 (79:23) |
| 5     | n-Bu   | 43 (49)   | 68:32 (23:77) |

*The data in parentheses were obtained using 1 mol% Rh2(OAc)4 as the catalyst.

Table 6. Catalytic cyclopropanation of trifluoroethylamine hydrochloride and styrene under aqueous conditions.

| Entry | Catal. | Additive | Yield (%) | trans/cis |
|-------|--------|----------|-----------|-----------|
| 1     | Fe(6a)Cl (3 mol%) | DMAP (9 mol%) | 89 | > 95:5 |
| 2     | Fe(6a)Cl (1 mol%) | DMAP (3 mol%) | 70 | > 95:5 |
| 3     | Co(6a) (3 mol%) | DMAP (9 mol%) | 50 | > 95:5 |
| 4     | Ru(6a)CO (3 mol%) | none | 56 | 86:14 |

Scheme 4. The Fe6aCl-catalyzed cyclopropanation reactions of hydrazones and N-vinylphthalimide.

Che et al. [10] reported the isolation and characterization of the stable iron porphyrin carbenic complex [Fe(6f)(CPh2)] and its N-methylimidazole (MeIm) adduct [Fe(6f)(CPh2)-(MeIm)] (Fig. 2). X-ray crystallographic analysis of these compounds allowed for their structures to be determined and provided a direct measure of the trans influence of the MeIm ligand on the Fe=CPh2 bond. These complexes were reported to be reactive towards styrene, affording the corresponding cyclopropane with 82 and 53% yields, respectively. Furthermore, the first iron-catalyzed intramolecular cyclopropanation of allyl diazoacetates was also realized using Fe(6f)(CPh2) as a catalyst (Table 4).

Aggarwal et al. [11] reported the development of a practical one-pot process for the catalytic cyclopropanation of alkenes with diazo compounds, which could be generated in situ from the sodium salts of toslyhydrazones or toslyhydrazones themselves (Table 5). These cyclopropanation reactions avoided the direct use of unstable aryldiazomethane and afforded moderate to good yields as well as high level of trans-selectivity for the cyclopropanation of various terminal olefins. The iron porphyrin Fe6aCl generally afforded higher yields of the cyclopropane products than the traditional superior catalyst Rh2(OAc)4. Furthermore, the iron porphyrin catalysts afforded complementary diastereoselectivity to that of Rh2(OAc)4 in most cases.

Furthermore, a much simpler route to cis-arylcyclopropanamines was established through the cyclopropanation of toslyhydrazones and N-vinylphthalimide, which provided the desired cyclopropane products in moderate to good yields (Scheme 4).

Carreira and Morandi [12] reported a method for the iron-catalyzed cyclopropanation of styrenes with trifluoroethyl amine hydrochloride in aqueous media using N,N-dimethylpyridin-4-amine (DMAP) as an axial ligand (Table 6). Trifluoromethyl diazomethane exists as a gas at room temperature.
Scheme 5. The Fe(6a)Cl-catalyzed cyclopropanation of olefins with trifluoroethyamine hydrochloride.

| X  | Yield (%) |
|----|-----------|
| H  | 86%       |
| Cl | 85%       |
| Br | 95%       |
| CF<sub>3</sub> | 77% |
| Me | 99%       |
| MeO | 89% |

Scheme 6. The Fe(6a)Cl-catalyzed cyclopropanation of dienes and enynes with trifluoroethylamine hydrochloride.

| Ar                      | Yield (%) |
|-------------------------|-----------|
| Ph                      | 74%       |
| 4-BrC<sub>6</sub>H<sub>4</sub> | 60%     |
| 2-BrC<sub>6</sub>H<sub>4</sub> | 69%     |
| 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub> | 76% |
| furan-2-yl             | 81%       |

Scheme 7. The Fe(6a)Cl-catalyzed cyclopropanation of styrenes with glycine ethyl ester hydrochloride.

| Ar                      | Yield (%) |
|-------------------------|-----------|
| Ph                      | 55-79%    |
| 4-MeOC<sub>6</sub>H<sub>4</sub> | 60% |

Scheme 8. The in situ generation of diazomethane for the cyclopropanation of olefins.
Table 7. Chiral iron porphyrin-catalyzed cyclopropanation reaction of styrene with EDA.

| Entry | [Fe]  | Solvent | Yield (%) | trans/cis | ee % (trans) | ee % (cis) | Ref. |
|-------|-------|---------|-----------|-----------|-------------|------------|------|
| 1     | 8 (0.05 mol%) | CH₂Cl₂ | 72        | 6.6:1     | 15 (1R,2R)  | 23 (1R,2S) | [16]|
| 2     | 9a (0.1–0.4 mol%) | toluene | 99        | 21:1      | 45 (1S,2S)  | 21 (1R,2S) | [17]|
| 3     | 9b (0.05 mol%) | CH₂Cl₂ | 70        | 23:1      | 86          | 6          | [19]|
| 4     | 10 (0.1–0.4 mol%) | toluene | 94.8      | 5.8:1     | 27 (1R,2R)  | 25 (1R,2S) | [17]|
| 5     | 11 (1 mol%) | toluene | 77        | 11.5:1    | 4           | --         | [20]|

The chiral iron porphyrin 9b exhibited high levels of reactivity, good to excellent diastereoselectivities and good enantioselectivities towards various substituted terminal styrenes (Table 8) [19].

The air-stable iron(III) porphyrin complex Fe(6a)Cl was determined to be the best catalyst under these strongly alkaline conditions, with the rhodium, ruthenium, cobalt, palladium, and copper complexes showing much lower levels of activity. An investigation of the scope of this reaction showed that electron-rich and electron-deficient styrene, diene, and enyne were suitable substrates for this reaction (Scheme 8).

Mechanistic studies of this reaction revealed that the bi-phasic model depicted in Scheme 8 provided the optimum reaction conditions. The use of a hydrophilic substrate or a water-soluble catalyst resulted in a sharp decrease in the yield of the reaction. Furthermore, the addition of ethanol to form a homogeneous mixture led to poor conversion under otherwise identical conditions.

Several studies have been conducted towards the development of an asymmetric version of the iron porphyrin-catalyzed cyclopropanation reaction using a variety of chiral iron porphyrin complexes (Fig. 3).

Gross et al. [16] evaluated the use of the Halterman catalyst 8 (derived from tartaric acid) in the cyclopropanation of styrene with EDA, but reported only low enantioselectivities for the trans- and cis-cyclopropane products (Table 7, entry 1). Woo et al. [17] reported the use of the two chiral iron porphyrin complexes 9a and 10 as catalysts in this model reaction (Table 7, entries 2 and 4). Although these catalysts afforded the corresponding cyclopropyl esters in good yields with high diastereoselectivities, the enantioselectivities were poor. Increasing the size of the ester moiety of the diazoacetates from an ethyl to a tert-butyl or even menthyl ester had only a minor effect on the enantioselectivities of the trans-products, whereas the enantioselectivities for cis-isomers increased up to 78% ee.

**Figure 3.** Chiral iron porphyrins used in asymmetric cyclopropanation reactions.

**Scheme 9.** Iron-catalyzed cyclopropanation via the *in situ* generation of diazomethane from diazald 7.
Simonneaux et al. [18] investigated the use of the different C₄ symmetric Halterman catalyst 9b in the asymmetric cyclopropanation reaction. This catalyst provided a high trans/cis ratio (i.e., 95:5) and moderate enantioselectivity (75% ee) for the trans-isomer using only a low loading of the catalyst under mild reaction conditions. At the same time, Lai et al. [19] reported their own investigation of the same reaction using 9b and obtained a higher enantioselectivity (86% ee) for the trans-isomer using slightly different reaction conditions (Table 7, entry 3). A prominent axial ligand effect on the cis/trans ratio was also described in this paper for the cyclopropanation of styrene, and the axially ligated iron monocarbene complex of the chiral porphyrin 9b was observed by ESI-MS. This result therefore suggested that a hexacoordinate iron monocarbene complex was the catalytically active species in this reaction. Zhang and Chen [20] reported that the use of the iron catalyst 11 in the cyclopropanation of styrene with EDA gave low yields of the desired cyclopropane products with low levels of enantioselectivity. In contrast, the corresponding cobalt catalyst gave excellent enantioselectivity together with a high level of catalytic activity, which implied that the iron catalyst activated the diazo compound by association with its terminal nitrogen (as shown in Scheme 1, 2′) rather than forming an iron carbene complex.

The chiral iron porphyrin 9b exhibited high levels of reactivity, good to excellent diastereoselectivities, and good enantioselectivities towards various substituted terminal styrenes (Table 8) [19].

Simonneaux et al. [18,21] achieved the asymmetric cyclopropanation reactions of a series of styrenes with 2,2,2-trifluorodiazoethane and diazoacetophenone to give the optically active trifluoromethylphenyl cyclopropanes (up to 69% ee) and cyclopropyl ketones (up to 80% ee), respectively, using the chiral iron porphyrin 9b as the catalyst (Scheme 10). The same authors also reported the construction of macroporous iron porphyrin polymers [18] and water-soluble iron porphyrins [22] by making modifications to the benzene rings of complex 9b.

The asymmetric cyclopropanation of styrene with the polyfunctionalized diazoketone 6-diazo-5-oxo-L-norleucine (DON, which is an antibiotic isolated from Streptomyces) was accomplished in both high yield and diastereoselectivity with good enantioselectivity using catalyst 9b (Scheme 11) [23]. This chiral iron porphyrin catalyst also exhibited good functional group tolerance and could potentially be used to achieve similar transformations in biological systems.

Although nature has evolved cytochrome P450 enzymes as a diverse toolbox for oxene transfer
processes, the isoelectronic transfer of a carbene species to an olefin (i.e. the cyclopropanation reaction) has no biological counterpart. Arnold et al. [24] reported the use of an engineered variant of cytochrome P450BM3 (variant of cytochrome P450 from *Bacillus megaterium*) that catalyzed the cyclopropanation of styrenes with diazoesters with high levels of diastereo- and enantioselectivity via a putative carbene transfer process (Table 9). It is noteworthy that although the natural hemes only afforded modest enantioselectivity for the model reaction of styrene with EDA, the systematic engineering of P450BM3 led to high levels of diastereo- and enantioselectivity (up to 97% ee). This work effectively highlights the possibility of adapting existing enzymes for the catalysis of important synthetic transformation that are not represented in nature.

In addition to iron porphyrins, several other iron complexes with planar structures have also been used as catalysts in the cyclopropanation reaction of olefins (Fig. 4).

![Figure 4](image-url)

**Figure 4.** Iron porphyrin-related complexes and other ligands used in the iron-catalyzed cyclopropanation of olefins.

**Table 10.** Iron-catalyzed cyclopropanation of styrene with EDA.

| Entry | [Fe] | R   | Conditions | Yield (%) | trans/cis | Ref. |
|-------|------|-----|------------|-----------|-----------|------|
| 1     | 12a  | CO₂Et | CH₂Cl₂, rt | 71        | 1.8:1     | [25] |
| 2     | 13   | CO₂Et | Xylene, reflux | 55       | Not given | [26] |
| 3     | 13   | TMS   | Xylene, reflux | 65       | Not given | [26] |
| 4     | 14   | CO₂Et | Toluene, rt | 87        | 7.4:1     | [17] |
| 5     | 14   | CO₂Bu | Toluene, rt | 15        | 4.5:1     | [17] |
| 6     | 14   | CO₂Men | Toluene, rt | 95        | 13.3:1    | [17] |
| 7     | [Fe(15)₂]O | CO₂Et | Benzene, reflux | 85       | 2.5:1     | [27a] |
| 8     | [Fe(15)₂]O | CO₂Bu | Benzene, reflux | 83       | 4.0:1     | [27b] |
| 9     | Fe(16)Cl₂ | CO₂Et | CH₂Cl₂, reflux | 65       | 1.9:1     | [28] |

*Ar = 4-MeC₆H₄, Men = L-menthyl.

**Scheme 12.** Iron-catalyzed cyclopropanation of benzene with 2-aryldiazoacetates.
the reaction. Kwong et al. [28] prepared several iron complexes based on chiral C₁- and C₂-terpyridines and evaluated their performances as catalysts towards the cyclopropanation of styrene with EDA. Among the complexes examined, [Fe(16)Cl₂] gave the highest levels of enantiomeric excess for the trans- (65% ee) and cis-cyclopropanes (67% ee) (Table 10, entry 9).

Cyclopropanation reactions of arenes (Büchner reaction)

Woo and Mbuvi [29] reported the iron-catalyzed cyclopropanation reaction of para-substituted methyl 2-phenyldiazoacetates with arenes using Fe(6a)Cl as a catalyst. The resulting cyclopropanation products existed as rapidly equilibrating mixtures of norcaradiene-cycloheptatriene valence isomers, which were formed in greater than 70% yield at temperatures in the range of 60–100°C (Scheme 12).

The treatment of chlorobenzene, toluene, or anisole with methyl 2-phenyldiazoacetate led to the formation of a regioisomeric mixture. The reaction of 1,4-disubstituted benzenes under these conditions led to the formation of fused cyclopropane structures.

Cyclopropanation in tandem reactions

Tang et al. [30] developed an iron-catalyzed intermolecular insertion reaction for the formal insertion of a carbenoid species into the olefinic C–H bonds of allylic phosphoranes (Scheme 13). Subsequent investigation of the mechanism showed that the insertion involved the cyclopropanation of an allylic ylide with the iron carbenoid followed by the ring-opening reaction of the resulting cyclopropaneylide 17, which could be readily isolated from the reaction mixture. Based on this observation, a one-pot reaction was developed for the facile construction of 1,1,4-trisubstituted 1,3-butadienes via the reaction of a trialkylphosphine-derived salt with tert-butyl diazoacetate and an aldehyde under mild conditions.

Tang et al. [31] further extended this reaction to allylic phosphonium salts bearing a trisubstituted olefin moiety (Scheme 14, eq 1). The reaction with methyl diazoacetate proceeded via a formal sp² C–H insertion to the double bond and delivered multisubstituted 1,3-butadienes in moderate to excellent yields with excellent Z/E-selectivity. The use of diazo arylethanone as a substrate under these conditions led to the formation of the corresponding cyclopentadiene derivatives via the intramolecular Wittig reaction of intermediate 18 (Scheme 14, eq 2). This result demonstrated that the low reactivity or inactivity of di- and trisubstituted alkenes towards electrophilic iron carbenes could be partially overcome by increasing the electron density of the double bond.
C–H INSERTION REACTIONS

The transition-metal-catalyzed insertion of a carbene species into a C–H bond represents one of the most efficient approaches currently available for the activation of a C–H bond [33], and recent advances in the development of dirhodium(II) catalysts mean that C–H insertion reactions can now be reliably conducted on a wide variety of sp³ hybrid C–H bonds. Although iron porphyrins can also be used to promote C–H insertion reactions, they are much less efficient than dirhodium(II) catalysts.

sp³ C–H insertion

Che et al. [10] examined the stoichiometric reactions of the iron carbene complexes Fe(6f)(CPhR) with the saturated C–H bonds of various hydrocarbons, including cyclohexene, cumene, and tetrahydrofuran (which can be considered as an activated hydrocarbon). All of these reactions proceeded smoothly at temperatures in the range of 60–80°C to give the desired C–H insertion products in moderate to high yields with good levels of regioselectivity (Scheme 16).

Woo and Mbuvi [34] reported the development of the iron porphyrin Fe(6a)Cl-catalyzed insertion of carbene fragments into aromatic and aliphatic C–H bonds with moderate to high yields (Scheme 17). These reactions were conducted in one pot with a low catalyst loading (1–2 mol%) and performed most effectively with tertiary C–H bonds. The use of mesitylene under these reaction conditions afforded a mixture of sp³ and sp³ C–H insertion products.

Mechanistic studies of this reaction revealed that the C–H activation step involved an electrophilic carbene complex and occurred via a concerted process (Fig. 5). It is important to mention, however, that it was not possible to rule out the occurrence of an electron transfer process involving hydrogen abstraction during the C–H insertion reaction.
Scheme 17. Iron porphyrin-catalyzed sp³ C–H insertion reactions of methyl α-aryldiazoacetates.

Scheme 18. Iron-catalyzed C–H insertion of indoles. TMEDA = N,N,N',N'-tetramethylethane-1,2-diamine; NaBARF = sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate.

Table 11. N–H insertion reaction of 4-chloroaniline with EDA catalyzed by iron corrole and iron porphyrin complexes.

| Entry | Catal. | Time | Yield (%) |
|-------|--------|------|-----------|
| 1     | 12a    | 3 min | 92        |
| 2     | 12b    | 3 min | 92        |
| 3     | Fe(6a)Cl | 3 min | 95        |
| 4     | Fe(6h)Cl | 3 min | 94        |
| 5     | Rh₂(OAc)₆ | 24 h | 25        |

sp² C–H insertion

Although methods allowing for the insertion of reactive species into sp² hybrid C–H bonds represent a powerful tool for the functionalization of aromatic compounds, only a few asymmetric sp² C–H insertion reactions have been described in the literature. The insertion of α-aryl-α-diazoester into the sp² C–H bonds of indoles is a useful reaction for the construction of α-aryl-α-indolylacetates, which are key intermediates in the synthesis of a wide range of bioactive compounds. However, when rhodium(II) (S)-N-(dodecylbenzenesulfonyl)prolinate was used to catalyze the sp² C–H insertion reaction of methyl α-phenyl-α-diazoacetate with 1,2-dimethylindole, the desired product was formed with only negligible enantioselectivity (<5% ee) [35]. Zhou et al. [36] developed an efficient iron-catalyzed C–H insertion reaction for indoles, which provided rapid access to a series of α-aryl-α-indolylacetate derivatives under mild reaction conditions (Scheme 18, eq 1). The asymmetric C–H insertion of indoles was also achieved with up to 78% ee using the iron complex of the chiral spiro bisoxazoline ligand (R₉,S,S)-22a (Scheme 18, eq 2).

A plausible mechanism for this iron-catalyzed C–H insertion reaction was proposed in the literature, and featured a metal-associated zwitterionic intermediate (I) as the key intermediate (Scheme 19). A significant first-order KIE (k_H/k_D = 5.06) was observed in this reaction, indicating that the proton transfer (step c) was most likely the rate-determining step. Several alternative mechanisms have been proposed for this reaction, including those involving a cyclopropanation-ring-opening sequence and a concerted C–H insertion process [36]. Furthermore, the role of iron as a Lewis acid catalyst for the activation of the diazo compounds cannot be excluded.

REACTIONS INVOLVING YLIDES

X–H insertion reaction

Transition-metal-catalyzed heteroatom–hydrogen bond (X–H, X = N, O, S, P, etc.) insertion reactions that occur via a metal carbene or carbenoid intermediate represent one of the most efficient approaches currently available in organic synthesis for the construction of C–X bonds. Owing to readily available substrates, neutral and mild reaction conditions, and high levels of reactivity, transition-metal-catalyzed X–H insertion reactions have been widely applied in organic synthesis [3]. In contrast to reactions involving the insertion of a reactive
species into a C–H bond, which is a concerted process (Scheme 20, 1), reactions involving the insertion of reactive species into X–H bonds bearing a lone pair occur in a stepwise manner, and involve the formation of a ylide and a 1,2-proton transfer step (Scheme 20, 2).

Iron corroles and porphyrins have been reported to exhibit excellent levels of activity and selectivity in the N–H insertion reactions of primary or secondary amines with diazoacetates [37]. It is noteworthy that the activities of iron corroles and porphyrins are much higher than that of the traditional carbene transfer catalyst Rh$_2$(OAc)$_4$ under identical reaction conditions (Table 11).

Iron catalysts exhibit excellent selectivity towards N–H insertion reactions, and a competition reaction between an N–H insertion reaction and a cyclopropanation reaction led to exclusive formation of the N–H insertion product (Scheme 21).

In addition to anilines, the aliphatic amines also afforded excellent outcomes with EDA by using iron porphyrin as a catalyst (Scheme 22).

The use of α-substituted diazoacetates in this reaction proved to be much less efficient than the use of EDA, and an increase in the catalyst loading was required together with higher reaction temperatures and longer reaction times for the N–H insertion of α-methyl and α-phenyl diazoacetate with aniline (Scheme 23).

Ammonia has also been reported as a suitable substrate for this iron-catalyzed N–H insertion reaction, where it was used to prepare non-protected amino acid esters (Scheme 24)[38]. The high level of tolerance exhibited by iron porphyrins towards amines enabled this transformation to run smoothly with high reactivity.

Gross and Aviv [37c] conducted a thorough mechanistic investigation of iron (III) corrole and porphyrin-catalyzed N–H insertion reactions and found two major differences in relation to other metal-based catalysts, including (1) the iron complexes in these reactions were not poisoned by the presence of excess amine and (2) the iron carbene intermediates did not appear to be involved in the reaction pathway. These results instead pointed to the importance of the ammonium ylide intermediates formed by the nucleophilic attack of the amines on the diazoacetate-coordinated iron complexes (Scheme 25).

Woo et al. [39] developed an iron porphyrin-catalyzed tandem N–H insertion/cyclization reaction for the preparation of 2-piperazinone (Scheme 26). This reaction began with an N–H insertion reaction and afforded the heterocycle in high yield under very mild reaction conditions.
Table 12. Iron porphyrin-catalyzed N–H insertion reactions of α-diazoacetones.

| Entry | R   | Catal. | T (°C) | Time (h) | Yield (%) | ee (%) |
|-------|-----|--------|--------|----------|-----------|--------|
| 1     | H   | Fe(6a)Cl | 20     | 0.25     | 90        | --     |
| 2     | H   | Fe(6a)OTf | 20     | 0.25     | 92        | --     |
| 3     | Me  | Fe(6a)Cl | 40     | 2        | 66        | --     |
| 4     | Me  | 9b     | 40     | 2        | 51        | 0      |

Scheme 22. Iron porphyrin-catalyzed N–H insertion reactions of aliphatic amines with EDA.

Scheme 23. Iron porphyrin-catalyzed N–H insertion of aniline with α-substituted diazoacetates.

In addition to α-diazoacetates, iron porphyrin catalysts can also be used to promote the N–H insertion reactions of α-diazoacetones (Table 12) [21]. The chiral iron porphyrin 9b, which exhibited good levels of enantioselectivity in cyclopropanation reactions, was also tested in the N–H insertion reaction, but gave no chiral induction.

Arnold et al. [40] reported the development of an N–H bond insertion reaction which was mediated by a variant of the cytochrome P450 enzyme from *B. megaterium*. This enzyme exhibited several attractive properties in the N–H insertion reaction, including high TON (up to 473) and high selectivity values, which were similar to those achieved by the iron porphyrin catalysts in the same reaction.

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Plietker et al. [41] accomplished the N–H insertion of a secondary amine into EDA using the electron-rich ferrate complex Bu4N[Fe(CO)3(NO)] (TBAFe). The metal center in TBAFe has a formal oxidation state of −2 and has been proposed to activate the diazo compounds through a nucleophilic addition reaction followed by nitrogen extrusion to generate a metal carbene (Scheme 27).
The O–H insertion reaction exhibits much lower reactivity than the corresponding N–H insertion reaction because of the lower nucleophilicity of alcohols compared with amines. A few iron-catalyzed O–H insertion reactions have been reported using only FeCl₃ [42] or simple iron porphyrins [37a,39]. The iron porphyrin Fe(6a)Cl was used to catalyze the O–H insertion of α-aryl-α-diazoacetates with alcohols and phenols in good yields (Scheme 28). The same catalyst was also used to catalyze the N–H insertion of EDA into amines with a much lower loading of the catalyst (0.1 mol%) [37–39].

Zhou et al. [43] reported that the iron catalysts prepared in situ from FeCl₃·4H₂O and the chiral spiro bisoxazoline ligand 22 exhibited excellent levels of enantioselectivity and reactivity towards the insertion of the O–H bonds of alcohols with methyl α-diazophenylacetates (Table 13). When ligand (S,S,S)-22b bearing iso-propyl moieties on its oxazoline rings was used in the iron-catalyzed O–H insertion of methyl α-diazophenylacetate with 1-butanol, the reaction proceeded smoothly at 40°C to afford (R)-methyl 2-butoxy-2-phenylacetate in good yield (93%) with high enantioselectivity (98% ee). Several other transition metals, including copper, cobalt, nickel, gold, silver, rhodium, and ruthenium, gave much lower levels of enantioselectivity under identical reaction conditions. Since the previously reported iron catalysts were less reactive than the other transition-metal catalysts and gave lower levels of enantioselectivity in asymmetric reactions, the unambiguous superiority of the chiral spiro iron catalysts in the asymmetric O–H insertion reaction was significant for encouraging the use of environmentally benign iron catalysts in the development of catalytic asymmetric syntheses.

The iron-catalyzed O–H insertion reaction has a wide substrate scope. As shown in Schemes 29 and 30, a variety of different saturated and allylic alcohols underwent the O–H insertion reaction to afford the corresponding α-alkoxy esters in high yields with excellent levels of enantioselectivity (89–99% ee). The enantioselectivities of the iron-catalyzed O–H insertion reactions remarkably surpassed those achieved by any of the previously reported catalysts for this reaction (see the data in parentheses) [44].

The transition-metal-catalyzed asymmetric insertion of α-diazoesters into the O–H bond of water represents an extremely simple approach to chiral α-hydroxyesters, which are versatile building blocks in organic synthesis. Transition-metal catalysts are generally sensitive to water, and the small molecular structure of water makes chiral discrimination quite difficult. For these reasons, asymmetric insertion into O–H bonds of water represents a significant challenge to organic chemistry, and considerable research efforts have been devoted to the development of synthetic methods in this area. Zhou et al. [43,45] reported the development of a highly enantioselective method for the O–H
insertion of water, which was catalyzed by chiral spiro copper and iron catalysts (Scheme 31). Under mild reaction conditions, the copper and iron complexes of \((\text{Sa,S,S})-22\) exhibited high levels of enantioselectivity towards the O–H insertion reactions of water. Notably, during the insertion reactions of \(\alpha\)-aryl-\(\alpha\)-diazoacetates bearing a coordinating group at their \textit{ortho} position, the iron catalyst gave a much high level of enantioselectivity than the corresponding copper catalyst. For example, in the insertion reaction of methyl \(\alpha\)-diazo-2-chlorophenylacetate with water, the iron catalyst \(\text{Fe-}(\text{Sa,S,S})-22\) produced methyl (R)-o-chloromandelate with 95% ee, whereas the analogous copper catalyst gave the same product with only 36% ee.

The facile conversion of methyl (R)-o-chloromandelate to the platelet aggregation inhibitor clopidogrel provided an effective demonstration of the significant potential of this iron-catalyzed asymmetric insertion reaction for the synthesis of chiral drugs (Scheme 32).

The iron porphyrin \(\text{Fe-}(\text{6f})\) is a highly efficient catalyst for S–H insertion reactions, and has been reported to give fast reaction rates and excellent yields for the reactions of mercaptans and thiophenols (Table 14, entries 1 and 2) \[37\text{c}\]. TBAFe has also been applied to the S–H insertion reaction with PhSH, but only provided a moderate yield of the desired product (Table 14, entry 3) \[41\].

**[2,3]-sigmatropic rearrangement of allyl sulfides (Doyle–Kirmse reaction)**

The Doyle–Kirmse reaction of allyl sulfides and diazo compounds is a powerful method for the formation of C–C bonds, and presumably involves a metal carbenoid intermediate (Scheme 33) \[46\]. A variety of metals have been reported to catalyze the Doyle–Kirmse reaction, including rhodium, copper, and cobalt.

Van Vranken and Carter \[47\] reported that several commercially available iron complexes, including \(\text{FeBr}_2\), \(\text{FeCl}_3\), \(\text{FeBr}_3\), \(\text{Fe(acac)}_3\), and \(\text{FeCl}_2/\text{dppe}\), could be used as efficient catalysts for the Doyle–Kirmse reaction of allyl sulfides with (trimethylsilyl)diazomethane (Scheme 34). Given that the diastereoselectivity of this reaction was unaffected by the addition of different phosphine ligands, and the fact that the addition of (R)-BINAP did not result in any enantioselectivity, it seemed unlikely that the iron catalyst for this reaction was involved in the step responsible for determining the stereochemistry of the product.

Gross and Aviv \[37\text{c}\] reported that iron(III) corrole and porphyrin complexes were excellent catalysts for the Doyle–Kirmse reaction of EDA with allylic sulfides. According to the results of this particular study, the Doyle–Kirmse reaction afforded the expected products in excellent yields over very short reaction times with low catalyst loadings (Table 15).
TBAFe can also be used to promote the rearrangement reactions of allylic sulfides with a high level of functional group compatibility, with borate, ether, amine, furan, hydroxyl, and persulfide groups being well tolerated (Scheme 35) [41].

FeCl2/dppe has also been used as a suitable catalyst in the analogous reaction of propargyl sulfides [48]. The yields of the desired allenyldiallsulfide products were generally high for this reaction, except for the propynoate bearing a terminal ester group, which gave a low yield (Scheme 36).

Various propargylic thioethers have been transformed into the corresponding allenes in moderate to good yields using TBAFe as a catalyst (Scheme 37) [41].

Iron porphyrin has been reported as a highly efficient catalyst for the Doyle–Kirmse reaction of propargyl sulfides with EDA (Scheme 38), where it gave very fast reaction rates and excellent yields of the desired products at low catalyst loadings under mild reaction conditions [37c].

The iron(III) corrole and porphyrin complexes also exhibited high levels of reactivity towards the reactions of allylic and propargylic amines with EDA (Scheme 39) [37c]. These reactions involve the generation of an ammonium ylide (e.g. 23 or 24) through the iron-catalyzed reaction of a diazo compound with an allylic or propargylic amine, followed by a [2,3]-sigmatropic rearrangement, which occurs in a similar manner to that of the Doyle–Kirmse reaction (Scheme 33).

**Olefination reaction with carbonyl compounds**

The reaction of diazo compounds with carbonyl compounds in the presence of a metal catalyst and phosphorus produces olefins, and can therefore be defined as an olefination reaction. The proposed mechanism for the iron porphyrin-catalyzed olefination reaction is shown in Scheme 40. The reaction would be initiated by the generation of an iron carbene intermediate. The attack of PPh3 on the electron-deficient iron carbene would then lead to a phosphonium ylide, which would undergo a Wittig reaction with an aldehyde to generate the olefin product.

Iron porphyrins have been proven to be efficient catalysts for the olefination reactions of aldehydes with EDA. Woo et al. [49] reported that Fe(6a) could be used as an efficient catalyst to promote the olefination of aldehydes with EDA with a good TON and excellent E-selectivity under mild reaction conditions (Table 16, entry 1). The PEG-supported catalyst exhibited similar levels of reactivity and
Table 16. Iron-catalyzed olefination reaction of benzaldehyde with EDA.

| Entry | Catal.  | Solvent | T (°C) | Time (h) | TON  | E/Z | Ref. |
|-------|---------|---------|--------|----------|------|-----|-----|
| 1     | Fe(6a)  | toluene | rt     | 6        | 128  | 24:1| [49]|
| 2     | PEG-Fe(6)| toluene | 80     | 1        | 92   | 13.3:1| [50]|
| 3     | Fe(6a)Cl| toluene | 80     | 0.5      | 8900 | 11.5:1| [51]|
| 4     | Fe(6a)Cl| (bmm)BF₄ | 1     | 1        | 91   | 18.9:1| [52]|
| 5     | 13      | toluene | rt     | 3.5      | 18.4 | E-isomer | [53]|
| 6     | TBAFe   | DCE     | 60     | 18       | 6.1  | E-isomer | [41]|

a PEG = poly(ethylene glycol). b AsPh₃ was used instead of PPh₃.

Scheme 35. Functional group compatibility of the TBAFe-catalyzed Doyle–Kirmse reaction.

Scheme 36. FeCl₂/dppe-catalyzed Doyle–Kirmse reaction of propargyl sulfides with (trimethylsilyl)diazomethane. PMB = 4-MeOC₆H₄CH₂; PMP = 4-MeOC₆H₄, Xyl = 2,5-Me₂C₆H₃.

Scheme 37. The TBAFe-catalyzed Doyle–Kirmse reaction of propargyl sulfides with EDA.

Scheme 38. The Fe[6f]Cl-catalyzed Doyle–Kirmse reaction of propargyl sulfide with EDA.

selectivity to the parent complex Fe(6) and could be recycled at least 10 times without any discernible loss in its activity (Table 16, entry 2) [50]. Zhang et al. [51] used Fe(6a)Cl, which is an analog of Fe(6a) bearing an Fe(III) center, in the olefination reaction and achieved a very high TON (8900) (Table 16, entry 3). The Fe(6a)Cl-catalyzed olefination reaction of aldehydes with EDA can also be performed in the ionic liquid (bmim)(PF₆) [52]. The use of an ionic liquid allows for the products to be readily removed from the catalyst using a simple extraction process, and the catalyst can also be reused without any loss in its activity. Iron(II) phthalocyanine [53] and TBAFe [41] can also be used to promote the olefinations of aldehydes with diazoacetate, although the TONs were much lower in these particular cases than they were with the iron porphyrin catalysts (Table 16, entries 5 and 6).

The iron porphyrin-catalyzed olefination reaction has a broad substrate scope, with various aromatic and aliphatic aldehydes reacting smoothly with diazoacetates under the mild reaction conditions to afford the corresponding products in good to excellent yields with excellent E-selectivities (Scheme 41) [51].

Aggarwal et al. [54] reported the olefination of phenyldiazo methane, which was generated in situ from the corresponding sodium tosylhydrazone salt, with aldehydes using iron porphyrin as a catalyst (Scheme 42). The semi-stabilizing phosphorus ylides bearing an oxygen substituent were generated by the reaction of P(OMe)₃ with an iron carbene intermediate. This reaction proceeded with high levels
of reactivity and excellent E-selectivity for both aromatic and aliphatic aldehydes.

The iron-catalyzed olefination reactions of ketones with diazoacetates were explored almost simultaneously by Zhang [55] and Woo [56]. The iron porphyrin Fe(6a)Cl was used as a catalyst in this transformation to prepare trisubstituted olefins. Compared with the olefination of aldehydes [51], the olefination of ketones required longer reaction times and gave lower levels of stereoselectivity (Scheme 43) [55], and these differences were attributed to ketones being less electrophilic than aldehydes.

Zhang et al. [57] also applied this methodology to the synthesis of β-trifluoromethyl α,β-unsaturated esters (Scheme 44). Trifluoromethyl ketones behaved in a similar manner to aldehydes, in that they reacted at a much faster rate and produced higher yields of the products. Trifluoromethyl ketones also gave higher levels of E-selectivity than the corresponding acetoephones, which was attributed to the fluoride effect.

Sun and Tang [58] developed an iron and polyethylene-supported arsine (PE-1) that co-catalyzed the olefination reactions of aldehydes and ketones with diazo compounds (Scheme 45). Polymethylhydrosiloxane was used as a reducing agent to restart the catalytic cycle for PE-1. Various ketones afforded good to excellent yields in this reaction, but excellent E-selectivity was only observed for trifluoromethyl ketone.

Tang and Zhou [59] used the olefination of ketenes to synthesize allenes in the presence of Ph₃P and catalytic Fe(6d)Cl (Scheme 46). An asymmetric version of this reaction was also developed using a chiral phosphine instead of PPh₃, which allowed for the synthesis of chiral allenes in good yields with high enantioselectivities (93–98% ee) (Scheme 47). A competition reaction clearly confirmed that monoylide 25a was the key intermediate in this reaction. Although a stoichiometric amount of a chiral phosphine ligand was required in this reaction, the material could be recovered and reused, making this methodology practically useful.

Reactions of diazoacetates with tertiary amines

The treatment of tertiary amines with diazoacetate in the presence of a catalytic amount of FeCl₃ in ethanol gave the corresponding glycine derivatives in good to excellent yields (Scheme 48, eq 1) [60] via the cleavage of one of the carbon–nitrogen bonds of the tertiary amine. The treatment of
**Scheme 43.** Olefination of ketones with EDA.

**Scheme 44.** Olefination of trifluoromethyl ketones with EDA.

**Scheme 45.** Iron porphyrin and PE-1 co-catalyzed olefination of ketones with EDA.

1-phenylpyrrolidine with EDA under the same reaction conditions led to the formation of an ethyl ether (Scheme 48, eq 2). This result demonstrated that the alkyl chain being cleaved from the nitrogen atom of the amine was being trapped by ethanol. A mechanism was proposed for this reaction involving a metal-associated ammonium ylide (Scheme 49). The nucleophilic addition of a tertiary amine to an iron-activated diazoacetate would result in the formation of the ammonium ylide 26, which would be protonated by EtOH to give the iron catalyst and the ammonium salt 27 simultaneously. One of the methyl groups from the nitrogen atom would then be trapped by EtO\(^-\) (C–N bond cleavage) to give the glycine derivative.

**Trapping ammonium ylides with electrophiles**

Xing and Hu [61] reported the development of an iron porphyrin-catalyzed three-component reaction involving the reaction of EDA with aliphatic amines and \(\alpha,\beta\)-unsaturated esters (Scheme 50). This reaction proceeded via the iron-catalyzed formation of an ammonium ylide, which was trapped with an \(\alpha,\beta\)-unsaturated ester. The use of an iron porphyrin catalyst allowed for aliphatic amines to be used as substrates in the reaction without encountering any catalyst poisoning issues, and this method was used to successfully generate a series of \(\beta\)-hydroxy-\(\alpha\)-amino esters in high yields with excellent regioselectivities.

**REACTIONS WITH IMINES AND ALDEHYDES**

**Reactions with imines**

The aziridine functionality has become increasingly attractive as a versatile intermediate in organic synthesis, and many biologically important compounds have been derived from aziridines, including amino acids, \(\beta\)-lactam antibiotics, and alkaloids. The reaction of diazo compounds with imines represents a useful method for the preparation of aziridine compounds. Hossain et al. [62] reported that the iron Lewis acid 4 was an effective catalyst for the aziridination reaction of diazo compounds with \(N\)-benzylidene imines (Scheme 51, eq 1). This method provided a facile access to cis-aziridines in a single step with yields up to 95%. The cis-selectivity of this reaction with EDA was partially attributed to the catalytic decomposition of the trans-isomer during the reaction (Scheme 51, eq 2) [63]. Mechanistic
studies revealed that the reaction proceeded through an electrophilic iminium ion intermediate rather than an electrophilic carbenoid intermediate, as has often been proposed (Scheme S2).

The enantioselective aziridination reaction of N-benzylidenaniline and EDA was also investigated using the chiral iron–pybox complex (S,S)-28 as a catalyst with AgSbF6 as an initiator (Scheme S3) \[64\]. This reaction afforded the expected cis-aziridine products in yields of up to 47% with an enantioselectivity of up to 49% ee when 'Bu-pybox was used as the chiral ligand.

**Reaction with aldehydes**

Iron complexes can be used to promote the reactions of aldehydes with diazo compounds, and the activation model for these reactions was generally believed to be similar to that of imines (Scheme S4). According to this model, the iron would activate the aldehyde as a Lewis acid and facilitate the nucleophilic attack of the diazo compounds. The activated intermediate \( \text{29} \) could then progress down one of three possible pathways, including a \([1,2]-\text{H shift}\), \([1,2]-\text{Ph shift}\), or \(\text{O-substitution}\).

The iron Lewis acid \( \text{4} \) was also found to catalyze the reaction of phenyldiazomethane with aromatic aldehydes to give epoxides together with the corresponding ketones (Scheme S5) \[65\]. The yield of the epoxide increased with the inclusion of electron-withdrawing substituents on the aldehyde, whereas aldehydes bearing electron-donating substituents gave very little or even none of the desired epoxide product.

The reaction of aromatic aldehydes with EDA in the presence of the Lewis acid iron catalyst \( \text{4} \) yielded 3-hydroxyacrylates and \(\alpha\)-keto esters (Table 17, entry 1) \[66\]. The yield of the enol esters increased as the electron-rich nature of the aldehydes increased. Kirchner et al. \[67\] developed the iron(II) complexes \( \text{30} \), which contained a tridentate PNP pincer-type ligand, and applied it as a catalyst for the coupling of aromatic aldehydes with EDA to give 3-hydroxyacrylates. These reactions were highly chemoselective and proceeded under mild conditions to give the desired products in good yields (Table 17, entry 2).

**CONCLUSIONS**

The transition-metal-catalyzed transformations of diazo compounds have been studied extensively...
and represent an important series of transformations that widely used in organic synthesis. Although catalysts derived from rhodium, ruthenium, and copper have been well established for these transformations, there are still several limitations associated with the use of these catalysts in terms of their substrate scope, reaction efficiency, selectivity, and overall economy. Iron-promoted diazo transformations were only discovered during the 1990s and remain unfamiliar to many synthetic chemists. Iron can undergo facile changes in its oxidation state and possesses distinct Lewis acid character, and these properties have afforded iron a privileged position as a catalyst in the transformations of diazo compounds. For example, the iron porphyrins are among the most efficient catalysts for the cyclopropanation reaction of olefins. Furthermore, iron porphyrin catalysts exhibit unique levels of tolerance towards water, as well as several acids and bases, making them one of the most suitable catalysts for reactions involving the transformation of unstable diazo compounds generated \textit{in situ}. Another example of the overall utility of these catalysts is the X–H bond insertion reaction, where iron porphyrins exhibit the highest level of reactivity towards primary and secondary amines as well as ammonia. Moreover, the iron complexes of chiral spiro bisoxazolines afforded best level of enantioselectivity in the analogous O–H insertion reactions. Several other examples from the literature have provided further indication that iron catalysts have distinct advantages over other catalytic systems in diazo transformations involving the formation of ylide intermediates, such as olefination reactions, the [2,3]-sigmatropic rearrangement reactions of allyl sulfides, and the rearrangement reactions of ammonium ylides. Based on these examples, it is clear that the potential of iron-catalyzed diazo transformations is huge, although there is still a long way to go, and further work is required to develop a deeper understanding of the mechanisms of these iron-catalyzed diazo transformation reactions, as well as determining the active structures of the catalytic species involved in these processes. Furthermore, the development of new and readily tunable iron catalysts will undoubtedly advance research in this exciting field of chemistry.

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Table 17. The iron-catalyzed reactions of aldehydes with EDA.

| Entry | Catal. | Solvent | T (°C) | Yield of A (%) | Yield of B (%) | Ref. |
|-------|--------|---------|--------|---------------|---------------|------|
| 1     | 4      | CH₂Cl₂  | 0      | 32–80         | 0–56          | [66] |
| 2     | 30     | MeNO₂   | rt     | 58–91         | < 3           | [67] |

Scheme 54. The three possible pathways for the iron-catalyzed reactions of aldehydes with diazo compounds.

Scheme 55. The iron-catalyzed reaction of aldehydes with phenyldiazomethane.

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