A New and Efficient Method for the Selective Olefination of Aldehydes with Ethyl Diazoacetate Catalyzed by an Iron(II) Porphyrin Complex

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A New and Efficient Method for the Selective Olefination of Aldehydes with Ethyl Diazoacetate Catalyzed by an Iron(II) Porphyrin Complex

Abstract
Olefination of aromatic and aliphatic aldehydes with ethyl diazoacetate was achieved in excellent yields with triphenylphosphine and catalytic amounts of iron(II) meso-tetra(p-tolyl)porphyrin. The reaction conditions are mild and the process is efficient and highly selective (>90%) for the synthesis of the trans-olefin isomer. Results of mechanistic studies are discussed.

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A New and Efficient Method for the Selective Olefination of Aldehydes with Ethyl Diazoacetate Catalyzed by an Iron(II) Porphyrin Complex

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Transition metal complexes based on porphyrins and on a variety of ancillary ligands have been used extensively by this group and others to catalyze the cyclopropanation of alkenes with ethyl diazoacetate and other suitable diazo reagents. In this communication, we describe a novel extension of the catalytic activity of metallloporphyrins with the first use of an iron(II) porphyrin complex as a catalyst for the efficient and selective olefination of aldehydes. The generation of a carbon−carbon double bond is one of the important synthetic transformations in organic chemistry, especially in the areas of natural products and polymer synthesis. Although other metal complexes can catalyze this reaction, the iron system is especially proficient and cost-effective.

Olefination of aromatic and aliphatic aldehydes (Table 1) was achieved in excellent yield at ambient temperature using 2 equiv of ethyl diazoacetate, \( N_2 CHCO_2Et \) (EDA), and 1.1 equiv of triphenylphosphine, Ph₃P, in the presence of catalytic amounts of iron(II) porphyrin, Fe(TTP). In the absence of the catalyst, the azine, PhCH=CH(20:1 v/v) afforded a 94% yield for olefination. 

Regeneration of Fe(TTP) would occur by oxidation of phosphine to phosphine oxide. GC and GC-MS analysis confirmed formation of Fe(TTP)-catalyzed reaction of benzaldehyde and EDA was run for the analogous methyltrioxorhenium (MTO) catalyzed reaction involves oxygen atom abstraction from MTO by phosphine. The resultant Re(V) dioxo complex reacts with a diazo reagent to produce a carbene complex that subsequently forms a metallaoxetane species in the presence of aldehydes. Fragmentation of the metallaoxetane produces the new olefin and regenerates MTO. We assume that the active species in the iron porphyrin catalyzed reactions is an iron−carbon complex formed by reaction of the iron(II) porphyrin with EDA. Related complexes prepared from mesityl diazomethane and trimethylsilyldiazomethane are readily observed by \(^1\)H NMR spectroscopy. However, (TTP)Fe=CHCO₂Et is too reactive to isolate or detect spectroscopically. The more electron rich osmium analogue, (TTP)Os=CHCO₂Et, has been isolated and is well characterized. If a metallaoxetane intermediate is involved, the iron−carbon complex may serve as a nucelophile that attacks the carbonyl functional group of aldehydes. This is consistent with the higher reactivity of electron poor aldehydes. Subsequent ring opening of the metallaoxetane would produce an olefin and an oxoiron porphyrin complex. Regeneration of Fe(TTP) would occur by oxidation of phosphine to phosphine oxide.

For this mechanism to be viable, the inner sphere reaction between unencumbered oxoiron(IV) and iron(II) porphyrins, producing a \( \mu \)-oxo Fe(III) dimer, must be minimal. Formation of the Fe(III) dimer would serve to quickly inactivate the catalyst. However, rapid deactivation was not observed and attempts were made to test for the presence of the iron(IV) oxo complex with other oxygen atom acceptors. Olefins were chosen since oxoiron(IV) porphyrin complexes effectively epoxidize the double bond. When an Fe(TTP)-catalyzed reaction of benzaldehyde and EDA was run for the analogous methyltrioxorhenium (MTO) catalyzed reaction involves oxygen atom abstraction from MTO by phosphine.

**Table 1.** Olefination of Aldehydes with EDA/Ph₃P/Fe(TTP)\(^{\text{a}}\)

<table>
<thead>
<tr>
<th>aldehyde</th>
<th>yield (%)</th>
<th>turnover</th>
<th>reaction time (h)</th>
<th>selectivity trans/cis</th>
<th>yield (%)</th>
<th>turnover</th>
<th>reaction time (h)</th>
<th>selectivity trans/cis</th>
</tr>
</thead>
<tbody>
<tr>
<td>PhCH₂CH=CH₂</td>
<td>94</td>
<td>12</td>
<td>93</td>
<td>64</td>
<td>49:1</td>
<td>2</td>
<td>90</td>
<td>80</td>
</tr>
<tr>
<td>PhCHCH₂CH₃</td>
<td>93</td>
<td>12</td>
<td>85</td>
<td>95</td>
<td>10:1</td>
<td>3</td>
<td>95</td>
<td>98</td>
</tr>
</tbody>
</table>

Table 1. Olefination of Aldehydes with EDA/Ph₃P/Fe(TTP)\(^{\text{a}}\)

\(^{\text{a}}\) Typical procedure: To a stirred solution of 1 mol % Fe(TTP), 0.94 mmol (1 equiv) aldehyde, and 1.04 mmol (1.1 equiv) of Ph₃P in 10 mL of toluene at ambient temperature under an inert atmosphere was added dropwise a solution of 1.88 mmol (2 equiv) of EDA in 3 mL of toluene. The progress of reaction was monitored by GC. \(^1\)H NMR analysis showed a \( \delta \) of 15.9 Hz for trans-hydrogens and a \( \delta \) of 12.6 Hz for cis-hydrogens.

**Scheme 1**

RCHO + N₂CHCO₂Et + Ph₃P \( \xrightarrow{\text{Fe(TTP)}} \) RCH=CHCO₂Et + Ph₃PO

R = Ph-, p-CH₂C₆H₄-, p-NO₂C₆H₄-, p-C₆H₄Cl-, PhCH₂-, (Ph₂)CH-

removed by chromatography. Treatment of benzaldehyde, 1, with EDA/Ph₃P/Fe(TTP) in toluene at ambient temperature resulted in 98% conversion to ethyl cinnamate after 6 h of reaction time. Both GC and \(^1\)H NMR analysis confirmed a high selectivity for trans to cis olefin products (24:1). Purification of the trans-olefin product by silica gel column chromatography with hexane:ethyl acetate (20:1 v/v) afforded a 94% yield for olefination of 1 (Table 1). The reaction is catalytic as no olefin formation were formed without Fe(TTP). In the absence of the catalyst, the azine, PhCH=N=N=CHCO₂Et (m/z 204, 131 base, 104, 77), was produced when the reaction mixture was allowed to stir for a period of 2 days. The reaction in the absence of Ph₃P also produced no olefination product. We found that this reaction requires a stoichiometric amount of Ph₃P to that of the aldehydes to give a high conversion to olefination products. The aldehyde oxygen is transferred to Ph₃P, producing 1 equiv of phosphine oxide. GC and GC-MS analysis confirmed formation of Ph₃P=O (m/z 278).

Preliminary studies were undertaken to probe the mechanism for this olefination process. A catalytic cycle (Scheme 1) proposed

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with styrene substituted as the reductant in place of Ph$_3$P, no ethyl cinnamate was observed. The only product was ethyl 2-phenyl-cyclopropycarboxylate (100%), indicating that styrene was much more efficient in reacting with the carbene complex than was the aldehyde. An alternative oxygen atom acceptor, cyclohexene, was subsequently employed. 1,2-Substituted olefins are poor cyclopropanation substrates, but readily undergo epoxidation. However, using cyclohexene in place of Ph$_3$P under catalytic conditions resulted in neither olefination of the aldehyde nor epoxidation of the alkene. The organic products were ethyl maleate and fumarate produced by carbene dimerization. These studies indicated that an iron—carbene complex was involved but that the oxoiron(V) species was an unlikely intermediate.

The reactivity profile of the Fe(TTP)-catalyzed olefination reaction differs significantly from the MoO(S$_2$CNEt$_2$)$_2$-mediated species was an unlikely intermediate. This reaction differed significantly from the MoO(S$_2$CNEt$_2$)$_2$-mediated reaction, with a high trans/cis selectivity of 9:1. The organic products were ethyl maleate and fumarate produced by carbene dimerization. These studies indicated that an iron—carbene complex was involved but that the oxoiron(V) species was an unlikely intermediate.

We also examined two aliphatic aldehyde substrates, phenylacetaldheyde, 5, and diphenylacetaldheyde, 6. Olefination of 5 was slow and required 23 h of reaction time for a 91% conversion and 85% isolated yield after purification. A high trans/cis selectivity (10:1) was also achieved for olefination of 6. Olefination of aliphatic aldehyde, 6, resulted in 95% conversion after 12 h and produced a trans/cis selectivity of 49:1. Purification of the reaction mixture from substrate 6 with column chromatography afforded a 93% isolated yield of the trans-olefin product.

We have reported here the first application of an Fe(II) metalloporphyrin catalyst for the olefination of carbonyl compounds with EDA and Ph$_3$P. Both aromatic and aliphatic aldehydes were efficiently converted to olefin products in excellent yields (>85%) with high selectivity for the trans-olefin isomer (>90%). Further mechanistic studies, application of Fe(II) porphyrin complexes as a catalyst for the olefination of ketones, and the use of other diazo reagents in this system are currently under investigation.

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References

(10) (a) In a control experiment with ethyl cinnamate (trans/cis = 6) and Fe(TTP) in toluene, no change in the trans/cis ratio was observed over 4 days in either the presence or absence of ethyl diazoacetate. Thus, olefin isomerization does not occur under catalytic conditions.

Scheme 2

Toulaldehyde, 2, was converted to olefin after 12 h of reaction time, with a high trans/cis selectivity of 24:1. Purification of the product by silica gel column chromatography gave 99% of the trans-olefin product (Table 1). The reaction is slower for substrate 2 compared to benzaldehyde due to the presence of the electron-donating methyl group.

Olefination of p-Cl and p-NO$_2$ substrates, 3 and 4, both containing electron-withdrawing groups, produced 100% conversion to olefin in much shorter reaction times. Olefination of 3 was complete after 3 h and resulted in a trans/cis ratio of 13:1 in 95% isolated yield after purification. Furthermore, the olefination of 4 was complete after 2 h, producing a high selectivity of trans- cis-olefins (24:1) with an isolated yield of 90% after purification. Electron-poor aldehydes are more susceptible to nucleophilic attack by the phosphate.