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[1] and others[2] 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 metalloporphyrins 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,[3] 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_2CHCO_2Et (EDA), and 1.1 equiv of triphenylphosphine, Ph_3P, in the presence of catalytic amounts of iron(II) *meso*-tetra(*p*-tolyl)porphyrin, $Fe^{II}(TTP)$ (1−2 mol %), in toluene (eq 1). Ratios of reagents were selected for convenient reaction times, high yields, and ease of purification. Ethyl maleate and fumarate were also observed as side products, but were readily

$$RCHO + N_2CHCO_2Et + Ph_3P \xrightarrow[-N_2]{Fe^{II}(TTP)} RCH{=}CHCO_2Et + Ph_3P{=}O \quad (1)$$
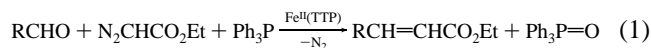
R = Ph-, *p*-CH$_3$C$_6$H$_4$-, *p*-NO$_2$C$_6$H$_4$-, *p*-ClC$_6$H$_4$-, PhCH$_2$-, (Ph)$_2$CH-

removed by chromatography. Treatment of benzaldehyde, **1**, with EDA/Ph$_3$P/Fe^{II}(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).[4] 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 olefination products were formed without Fe^{II}(TTP). In the absence of the catalyst, the azine, PhCH=N−N=CHCO$_2$Et (*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 Ph$_3$P also produced no olefination product. We found that this reaction requires a stoichiometric amount of Ph$_3$P to that of the aldehydes to give a high conversion to olefination products. The aldehyde oxygen is transferred to Ph$_3$P, producing 1 equiv of phosphine oxide. GC and GC-MS analysis confirmed formation of Ph$_3$P=O (*m/z* 278).
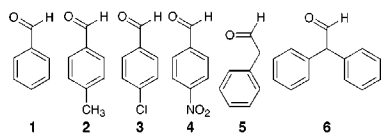

Preliminary studies were undertaken to probe the mechanism for this olefination process. A catalytic cycle (Scheme 1) proposed

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Table 1. Olefination of Aldehydes with EDA/Ph$_3$P/Fe^{II}(TTP)^a

alde-hyde	reaction time (h)	yield (%)^b	turnover no.	*trans/cis* selectivity^c	alde-hyde	reaction time (h)	yield (%)^b	turnover no.	*trans/cis* selectivity^c
1	6	94	128	24:1	**4**	2	90	80	24:1
2	12	99	119	24:1	**5**	23	85	95	10:1
3	3	95	98	13:1	**6**	12	93	64	49:1

^{a} Typical procedure: To a stirred solution of 1−2 mol % Fe^{II}(TTP), 0.94 mmol (1 equiv) aldehyde, and 1.04 mmol (1.1 equiv) of Ph$_3$P 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. ^{b} Isolated yield. ^{c} *Trans/cis* selectivity was determined by GC and ^{1}H NMR. In our GC analysis, the *cis* isomer appeared at a shorter retention time versus the *trans* isomer. ^{1}H NMR analysis showed a $^3J_{HH}$ of 15.9 Hz for *trans*-hydrogens and a $^3J_{HH}$ of 12.6 Hz for *cis*-hydrogens.

Scheme 1
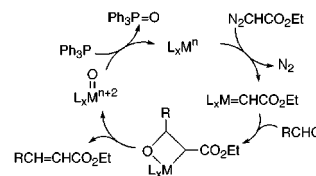
for the analogous methyltrioxorhenium (MTO) catalyzed reaction[3e,5] involves oxygen atom abstraction from MTO by phosphine. The resultant Re(V) dioxo complex reacts with a diazo reagent to produce a carbene complex that subsequently forms a metalla-oxetane species in the presence of aldehydes. Fragmentation of the metallaoxetane produces the new olefin and regenerates MTO. We presume that the active species in the iron porphyrin catalyzed reactions is an iron−carbene complex formed by reaction of the iron(II) porphyrin with EDA. Related complexes prepared from mesityl diazomethane and trimethylsilyl diazomethane are readily observed by ^{1}H NMR spectroscopy.[1c,d] However, (TTP)Fe=CHCO$_2$Et is too reactive to isolate or detect spectroscopically. The more electron rich osmium analogue, (TTP)Os=CHCO$_2$Et, has been isolated and is well characterized.[1a,b] If a metallaoxetane intermediate is involved, the iron−carbene complex may serve as a nucleophile[6] that attacks the carbonyl functional group of aldehydes. This is consistent with the higher reactivity of electron poor aldehydes (vide infra). Subsequent ring opening of the metalla-oxetane 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 μ-oxo Fe(III) dimer,[7] must be minimal. Formation of the Fe(III) dimer would serve to quickly inactivate the catalyst. However, rapid deactivation was not observed[8] 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.[9] When an Fe(TTP)-catalyzed reaction of benzaldehyde and EDA was run

with styrene substituted as the reductant in place of Ph$_3$P, no ethyl cinnamate was observed. The only product was ethyl 2-phenyl-cyclopropylcarboxylate (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,[1c] but readily undergo epoxidation.[9] 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(IV) 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 process.[3h] The catalytic cycle for the Mo system purportedly involves metalloazines,[10] (Et$_2$NCS$_2$)$_2$OMo=N−N=CHCO$_2$Et, and phosphazines, Ph$_3$P=N−N=CHCO$_2$Et.[3h] The phosphazine is presumably responsible for the formation of large amounts of azines with electron-poor aldehydes in this system.

On the basis of the above data, the most likely mechanism for the Fe(TTP) olefination reaction is shown in Scheme 2. In this process, the Fe complex serves to catalytically convert the diazo reagent and phosphine to phosphorane. The phosphorane in turn produces a new olefin and phosphine oxide on reaction with the aldehyde. Evidence for this mechanism is derived from two key control experiments. The production of phosphorane, Ph$_3$P=CHCO$_2$Et, was independently established in a reaction of Ph$_3$P, EDA, and Fe(TTP) (1 mol %). The phosphorane was clearly identified by ^{1}H and ^{31}P NMR spectroscopy.[11,12] Particularly diagnostic is the coupling constant $J = 21$ Hz between the phosphorus and the methine proton.[12a] In addition, the stoichiometric reaction of Ph$_3$P=CHCO$_2$Et and benzaldehyde produced ethyl cinnamate in high yields and high stereoselectivity.

The proposed catalytic cycle in Scheme 2 suggests that an increased phosphine concentration should enhance the rate of reaction. However, phosphine can bind to Fe(TTP)[13] and may inhibit the formation of the carbene complex. These competing factors were observed. Qualitatively, the rate of reaction with 2 equiv of Ph$_3$P was faster than when 1 equiv was used, with no noticeable change in yields. Above 2 equiv of Ph$_3$P, the rate appeared to saturate.

Scheme 2

$$\text{Ph}_3\text{P=CHCO}_2\text{Et} + \text{RCH=O} \longrightarrow \text{RCH=CHCO}_2\text{Et} + \text{Ph}_3\text{P=O}$$
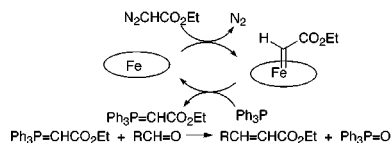
Tolualdehyde, **2**, was converted to olefin after 12 h of reaction time, with a high *trans/cis* selectivity of 24:1. Purification of the product by silica gel column chromatography gave 99% of the *trans*-olefin product (Table 1). The reaction is slower for substrate **2** compared to benzaldehyde 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*- to *cis*-olefins (24:1) with an isolated yield of 90% after purification. Electron-poor aldehydes are more susceptible to nucleophilic attack by the phosphorane.

We also examined two aliphatic aldehyde substrates, phenyl-acetaldehyde, **5**, and diphenylacetaldehyde, **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* to *cis* selectivity (10:1) was also achieved for olefination of **5**. Olefination of aliphatic aldehyde, **6**, resulted in 95% conversion after 12 h and produced a *trans* to *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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(4) 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.

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(11) ^{1}H NMR (400 MHz, CDCl$_3$, −30 °C) cisoid isomer: δ 7.59 (m, C$_6$H$_5$), 7.38 (m, C$_6$H$_5$), 3.99 (2H, q, $J = 7.1$ Hz, CH$_2$), 2.94 (1H, d, $J_{P-H} = 21.3$ Hz, P=CH), 1.19 (3H, t, $J = 7.1$ Hz, CH$_3$); transoid isomer: δ 7.47 (m, C$_6$H$_5$), 7.38 (m, C$_6$H$_5$), 3.78 (2H, q, $J = 7.1$ Hz, CH$_2$), 2.76 (1H, d, $J_{P-H} = 21.9$ Hz, P=CH), 0.60 (3H, t, $J = 7.1$ Hz, CH$_3$). ^{31}P NMR (162 MHz, CDCl$_3$) cisoid isomer: δ 18.0; transoid isomer: δ 16.6.

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