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Efficient aldehyde olefination reactions catalyzed by an iron porphyrin complex in an ionic liquid

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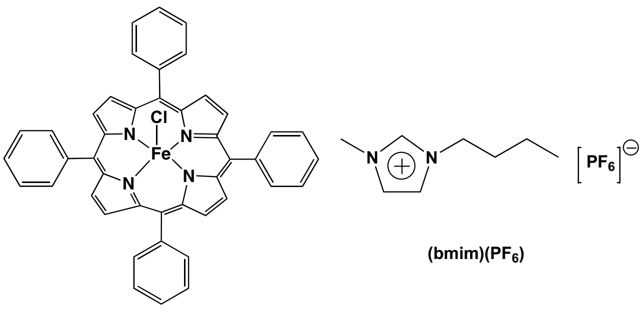
Abstract—The commercially available complex Fe(TPP)Cl is an active and highly (*E*)-selective catalyst for the olefination of a variety of aldehydes in the presence of PPh_3 and diazoacetate in the ionic liquid (bmim)(PF_6). Dependent on the reactivity of the applied aldehyde, the reaction can be carried out at a reaction temperature of 50–80 °C. After 0.5–24 h quantitative olefin yields are reached with a broad variety of different aldehydes. Due to the application of an ionic liquid as reaction medium the products can be easily removed from the catalyst by a simple extraction and the catalyst is conveniently reusable without significant activity loss. Spectroscopic investigations indicate that the reaction mechanism includes the quantitative formation of a phosphorus ylide, which then reacts further in a Wittig reaction under formation of an olefin.

One of the classic approaches for constructing carbon–carbon double bonds in organic synthesis involves the Wittig reaction and its numerous variants.[1] Despite being broadly applicable methods, they still have some noteworthy drawbacks, most prominently the requirement of stepwise synthesis of ylide precursors under basic conditions.[1] Accordingly, growing research interest arose in the development of new methods that can directly use easily accessible diazo compounds for in situ generation of ylides under neutral conditions.[2] Several transition metal complexes, among them Mo, Re, Rh, Fe, Co and Cu have been shown to catalyze the olefination of aldehydes with diazo compounds in the presence of tertiary phosphines (Eq. 1).[3]

Usually the catalysts are employed in ratios between 1 and 5 mol%, sometimes even 10 mol% (with respect to diazo compound) in order to avoid unwanted side reactions such as the formation of azines.[4] The reactions are usually performed in toluene or tetrahydrofurane (THF). The (necessary) excess of tertiary phosphines as well as the increasing amount of the reaction product phosphine oxide are able to slow down the reaction velocity due to blocking of the active site of the catalyst in several cases.[4] Even more importantly, the separation procedures necessary to obtain the products often lead to significant catalyst losses.[3] In order to minimize these problems we applied the iron porphyrin complex Fe(TPP)Cl, which does not directly bind phosphines and the PF_6^--salt of 1-butyl,3-methylimide ((bmim)(PF_6))[5] as reaction medium. Fe(TPP)Cl (formula see Chart 1) has been shown to be one of the most active aldehyde olefination catalysts,[3n] particularly in low catalyst concentrations in THF and toluene. (Bmim)(PF_6) (formula see Chart 1) is a room temperature ionic liquid, which should allow an extraction of the olefins without (significant) catalyst loss.[5,6]



(bmim)(PF_6)

Fe(TPP)Cl

Chart 1.

Keywords: Aldehyde olefination; Catalysis; Diazo compounds; Iron porphyrin.

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In this work we present our finding that the commercially available, stable compound Fe(TPP)Cl can be successfully applied as catalyst together with the commercially available (as well as easy to synthesize)[5] room temperature ionic liquid (bmim)(PF_6). The combination Fe(TPP)Cl/(bmim)(PF_6) fulfils the demand described above for a commercially available, active, stable and reusable catalyst/solvent system.

The catalyst Fe(TPP)Cl was applied in 1:100 molar relationship (1 mol%) to all examined aldehydes. Triphenylphosphine was applied in a 1.2-fold molar excess with respect to the aldehyde and ethyl diazoacetate (EDA) was used as diazo compound (for more details see Table 1 and Ref. 7). The products can be separated from the catalyst/ionic liquid system by simple extraction with diethyl ether in all examined cases. When the ionic liquid containing the catalyst is reused for several runs, the activity of the reaction system does not decrease to a significant extent. It is not necessary to re-isolate the catalyst after each run. Spectroscopic examinations confirm a complete separation of the reaction products from the catalyst containing system by extraction. This is a clear and remarkable advantage of the reaction system described here in comparison to the application of Fe(TPP)Cl in conventional organic solvents, such as the previously applied toluene and THF, where the workup procedure (to obtain the olefin) does not often allow an easy reuse of the catalyst.[3] Furthermore, in the case of other catalysts such as $ReO(Cl)_3(PPh_3)_2$, which can react with $O{=}PPh_3$, the reaction in conventional organic solvents, which do not allow easy product/by-product removal is increasingly slowed down due to by-product ($O{=}PPh_3$) formation, particularly when several catalytic runs are performed with the same solvent/catalyst system.[3]

Benzaldehyde needs 2 h to be transformed quantitatively to the corresponding olefin. Among the methylbenzaldehydes, the *para* derivative is the easiest one to be olefinated, the *ortho* derivative the most difficult one. This shows that the olefination is strongly influenced by the steric bulk of the aldehyde. If electronic reasons would dominate, the *meta* derivative should be the easiest of the three methylbenzaldehydes to be transformed to the olefin. The deactivated *p*-methoxybenzaldehyde and *p*-(dimethyl)aminobenzaldehyde require higher reaction temperatures to be quantitatively transformed to olefins. The reaction with the least activated aldehyde, *p*-(dimethyl)aminobenzaldehyde is completed after 1 day at 80 °C.

Aliphatic aldehydes as well as aromatic aldehydes can be used as substrates. In the case of aliphatic aldehydes, higher reaction temperatures (80 °C) are recommended to shorten the reaction time. The (*E*)-selectivities are quite good in all examined cases, ranging from ca. 11-fold to 30-fold excess of the (*E*)-product (see Table 1). Reduction of the reaction temperature to 20 °C leads to very similar (*E*)-selectivities but significantly prolonged reaction times.

These results, summarized in Table 1 clearly indicate that not only activated (electron poor) but also deactivated (electron rich) aldehydes as well as sterically hindered aldehydes can be transferred in good to quantitative yields to the corresponding olefins. Not unexpectedly, the isolated yields are usually somewhat lower than the GC-yields due to losses in the workup procedure. These losses decrease, however, when the reactions are performed in larger scale. Scaling up the reaction, for example, from 0.5 to 5 mmol *p*-methylbenzaldehyde (see Table 1, all other reactants are, of course, also used in a larger scale) leads to approximately the same isolated yield, while further increase leads to higher isolated yields. Furthermore, the selectivity towards olefins in ionic liquids seems to be even higher than in common organic solvents, where azines are usually formed as by-products in amounts mainly dependent on the applied catalyst, the reaction velocity and the catalyst:substrate ratio.

The reaction mechanism (Scheme 1) presumably consists—as it does in common organic solvents—of the

Table 1. Aldehyde olefination catalyzed by 1 mol% Fe(TPP)Cl in (bmim)(BF_6)[7]

Aldehyde	*T* (°C)	*t* (h)	GC-yield (%)	Isolated yield (%)	*E*/*Z*-ratio
Benzaldehyde	80	1	95	91	18.9
Benzaldehyde	80	1	95[a]	88[a]	18.8[a,b]
Benzaldehyde	50	2	100	[c]	18.9
o-Methylbenzaldehyde	50	3	100	[c]	13.2
m-Methylbenzaldehyde	50	2	100	[c]	17.7
p-Methylbenzaldehyde	50	1	100	80	18.3
p-Methylbenzaldehyde[d]	50[d]	1[d]	[e]	81[d]	18.4[d]
p-Methoxybenzaldehyde	80	1	100	92	16.6
1-Naphthyl aldehyde	80	1	[e]	89	15.8
3-Benzyl propionaldehyde	80	1	[e]	88	10.6
Cyclohexyl aldehyde	80	1	[e]	80	29.6
p-(Dimethyl)amino benzaldehyde	80	20	100	95	12.5

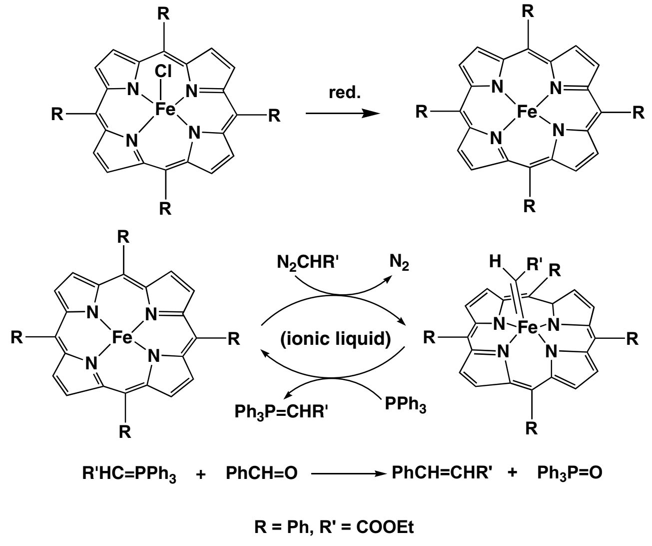
[a] Second run (reuse of the catalyst).

[b] The *E*/*Z*-ratio may vary slightly.

[c] No isolated yield determined.

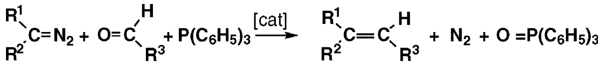
[d] 5 mmol *p*-methylbenzaldehyde, 6 mmol PPh_3 and EDA, 2 mol% cat., 5 mL $BmimPF_6$ and CH_2Cl_2.

[e] No GC-yield determined.



Scheme 1.

reaction of EDA with the catalyst under formation of a metal carbene species and nitrogen extrusion, which successively reacts with triphenylphosphine under ylide formation. The ylide then reacts with aldehyde in a classical Wittig reaction. If no aldehyde is present, ylide is the only reaction product and can be easily identified by ^{31}P NMR spectroscopy. We did, however, not attempt to observe the carbene intermediate by NMR spectroscopy. As the postulated reduction of iron(III) to iron(II) in common organic solvents[3n] this still hypothetic reaction needs closer examination. Anyway, the main advantage of the aldehyde olefination described here is the straightforward and clean ylide formation without the involvement of multistep syntheses or the application of basic reaction conditions.



$$R^1R^2C{=}N_2 + O{=}C(H)R^3 + P(C_6H_5)_3 \xrightarrow{[cat]} R^1R^2C{=}C(H)R^3 + N_2 + O{=}P(C_6H_5)_3 \quad (1)$$

Ylides, however, which do not undergo the Wittig reaction, such as ylides derived from diazomalonate are not activated under the reaction conditions described here. Other types of catalysts would have to be applied.[4]

In summary the application of Fe(TPP)Cl as catalyst for the aldehyde olefination in the ionic liquid (bmim)(PF_6) leads to a particularly easy, clean and selective way of synthesizing olefins starting from aldehydes, triphenylphosphine and ethyl diazoacetate (EDA). The application of an ionic liquid as reaction medium for the catalytic aldehyde olefination, here reported for the first time, obviously is a convenient way to obtain the desired olefins in quantitative yields and to preserve the catalyst for further catalytic runs. We are currently examining other, even more (*E*)-selective aldehyde olefination catalysts under similar reaction conditions and with other ionic liquids.

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7. Typical procedure for the aldehyde olefination: To a solution of Fe(TPP)Cl (3.5mg, 0.005mmol) and PPh_3 (157.4mg, 0.6mmol) in 1mL of (bmim)(PF_6) the corresponding amount of aldehyde (0.5mmol) and ethyl diazoacetate (0.6mmol) in 1mL of CH_2Cl_2 is added. The

reaction mixture is stirred at a constant reaction temperature in an oil bath until the reaction is completed, according to the GC/MS results. After the reaction is finished, the mixture is cooled to room temperature and extracted with diethyl ether in order to separate the products from the catalyst containing ionic liquid. The catalyst stays in the ionic liquid and can be used for the next reaction. The yield and the *E*/*Z*-ratio where determined by GC. In the case of the determination of isolated yields the products were purified by flash silica gel chromatography.