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An Efficient Synthesis of Poly(ethylene glycol)-Supported Iron(II) Porphyrin using a Click Reaction and its Application for the Catalytic Olefination of Aldehydes

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Abstract: The first successful synthesis of poly(ethylene glycol) (PEG) immobilized iron(II) porphyrin using a copper-catalyzed azide-alkyne [3+2] cycloaddition is reported. In contrast to the existing methods for the synthesis of PEG-immobilized metalloporphyrins, the click method offers better catalyst loading under comparatively mild reaction conditions. The prepared complex **5** (PEG-$C_{51}H_{39}FeN_7O$) was found to be an efficient catalyst for the selective olefination of aldehydes with ethyl diazoacetate in the presence of triphenylphosphine and afforded excellent olefin yields with high (*E*) selectivities. The PEG-supported catalyst **5** was readily recovered by precipitation and filtration and was recycled for up to ten runs without significant loss of activity.

Keywords: click chemistry; iron; olefination; poly(ethylene glycol) (PEG); porphyrins; supported catalysts

Introduction

The need to improve both the efficiency and environmental acceptability of catalytic processes has created considerable interest in the development of supported metal catalysts and reagents that maintain high selectivity and reactivity in organic synthesis.[1] Since transition metal complexes are often expensive and difficult to prepare, immobilization on polymeric supports provides a means to handle them more easily and to facilitate recycling from the reaction mixtures. Soluble organic polymers have recently emerged as most promising and convenient supports for the immobilization of transition metal complexes. Reactions promoted by a soluble, polymer-supported catalyst can consequently be run under homogeneous conditions while the catalyst itself can be easily recovered from the reaction mixture by precipitation and filtration upon completion. Among the various polymeric matrices, poly(ethylene) glycols hold a prominent position due to their ease of accessibility, facile functionalization, inexpensive nature and their unique property of being soluble in most common organic solvents but also being insoluble in some such as diethyl ether.[2]

Metalloporphyrins, owing to their high reactivity and remarkable stability, have been recognized as efficient yet versatile catalysts, which find a broad spectrum of applications in organic synthesis.[3] However, the homogeneous nature of these catalysts render their recovery and recycling difficult, which can be overcome by anchoring them to poly(ethylene) glycol *via* a covalent attachment.[4]

The copper-catalyzed [3+2][5] azide-alkyne cycloaddition (CuAAC)[6] termed 'click reaction' is becoming an indispensable tool for ligating functionalized molecule fragments and has been well acknowledged for the preparation of functionalized polymers, dendrimers, diverse scaffolds and immobilized catalysts and reagents.[7] Apart from the few reports on the CuAAC for directly immobilizing metal complexes on polymer supports,[8] its potential for immobilizing metalloporphyrins to polymer supports remains unexplored.

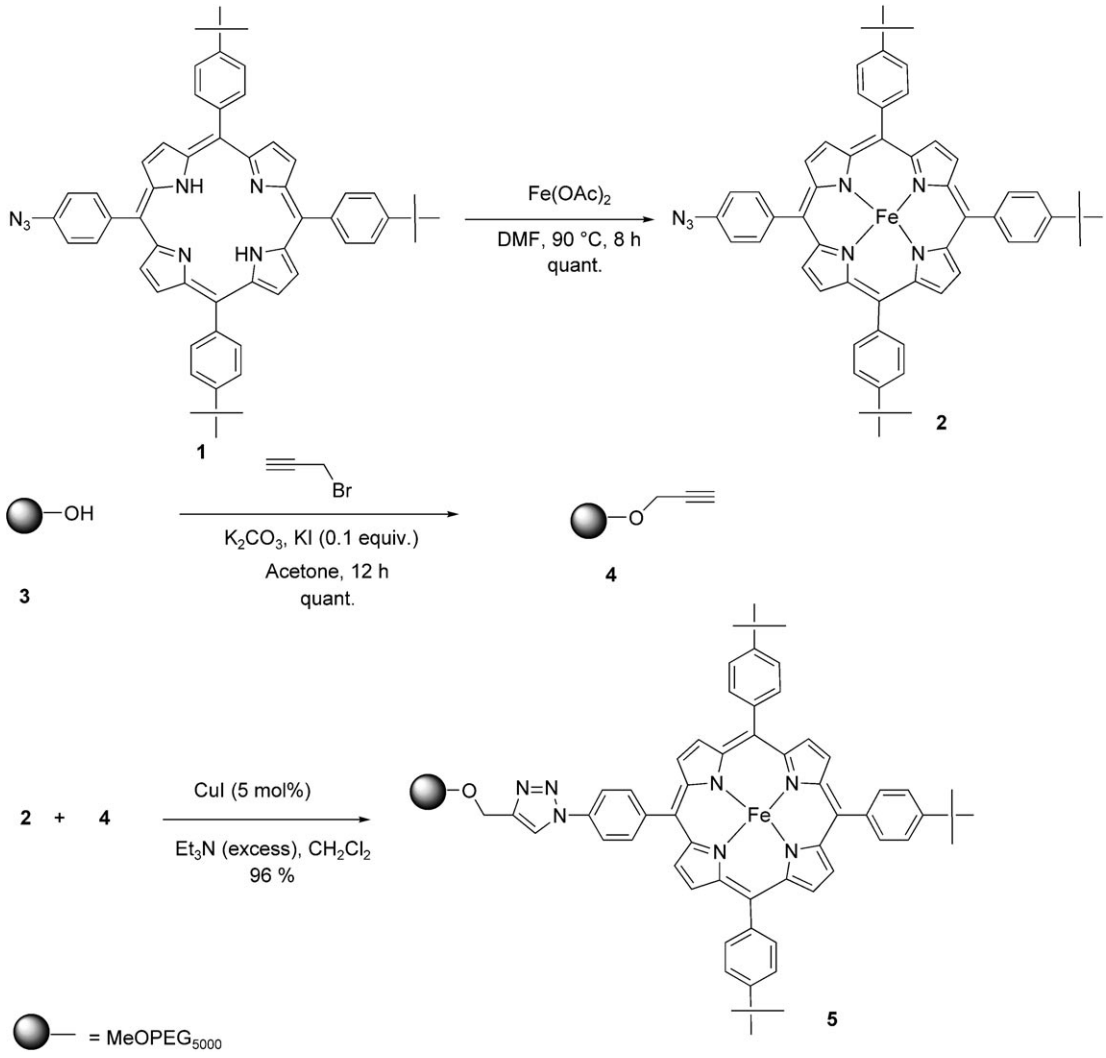
Results and Discussion

We report here the first successful synthesis of a PEG-immobilized iron(II) porphyrin using a copper-catalyzed azide-alkyne [3+2]cycloaddition 'click reaction' and its catalytic activity for the olefination of aldehydes using ethyl diazoacetate in the presence of triphenylphosphine.

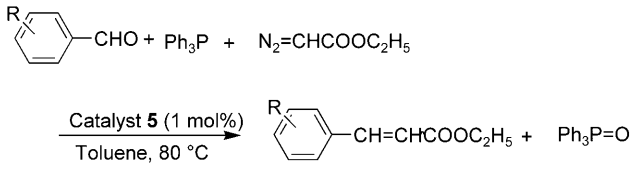
The unsymmetrically substituted azidoporphyrin **1**, accompanied by some tetra-*p*-*tert*-butylphenylprophyrin, was readily prepared according to a literature procedure.[9] As noted before,[9] the free porphyrin **1** is only moderately stable and was therefore directly metallated with ferrous acetate in DMF at 90 °C to give **2** in nearly quantitative yield (Scheme 1). Attachment of iron porphyrin **2** to $MeOPEG_{5000}$ **3** could easily be achieved in an easy two-step sequence: Propargylation of **3** gave rise to **4**, which, on subsequent copper(I) iodide-catalyzed cycloaddition with azidoporphyrin **2** resulted in covalently attached, PEG-immobilized iron(II) porphyrin **5** in a virtually quantitative reaction as evidenced by complete disappearance of the typical azide band (2219 cm^{-1}). The obtained black coloured, PEG-bound catalyst **5** was precipitated with diethyl ether and separated by filtration, washed with 2-propanol and diethyl ether, and dried under vacuum (96% yield). The complex loading was found to be 0.15 mmol g^{-1} as estimated from the nitrogen content, being determined by elemental analysis.[10]

The catalytic potential of catalyst **5** was tested for the olefination of aldehydes with ethyl diazoacetate in presence of triphenylphosphine as a reducing agent (Scheme 2).[11]

In a typical experiment, a 10-mL Schlenk tube placed in a preheated oil bath at 80 °C was charged with benzaldehyde (1 mmol), ethyl diazoacetate (1.2 mmol), triphenylphosphine (1.2 mmol) and catalyst (1 mol%) in toluene under a nitrogen atmosphere. The homogeneous mixture was vigorously



Scheme 1. Synthetic route to PEG-immobilized iron porphyrin using a click reaction.



Scheme 2. Olefination of aldehydes.

stirred under nitrogen at the same temperature. Complete conversion was achieved within 3 h, upon which the catalyst could easily be recovered from the reaction mixture in quantitative yield by precipitation with diethyl ether and filtration, and was then reusable as such for subsequent runs. The cinnamate was obtained upon purification in 96% isolated yield with an *E*/*Z* ratio of 24.

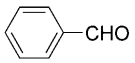
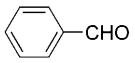
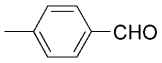
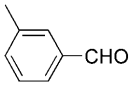
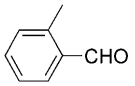
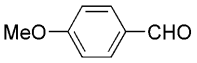
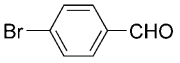
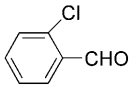
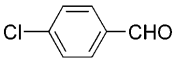
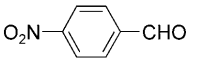
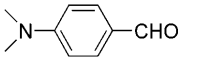
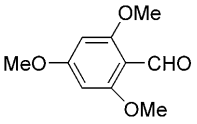
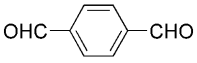
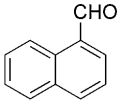
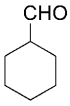
To evaluate the scope of this catalytic system, we studied the olefination of a variety of aldehydes both aromatic and aliphatic types under the described reaction conditions (Table 1). In all cases, almost quantitative conversion, high yields and (*E*) selectivity were achieved, being comparable to those reported for the homogeneous iron porphyrins with the added advantages of facile recovery of the catalyst **5** from the reaction mixture and its reusability.

Among the various aromatic aldehydes studied, in general those substituted with electron-withdrawing groups (Table 1, entries 8–11) were found to be more reactive and required shorter reaction times than benzaldehyde. However, *p*-methoxybenzaldehyde (Table 1, entry 7) and *p*-(dimethyl)aminobenzaldehyde (Table 1, entry 12) were found to be the least reactive and the reactions could be only completed after prolonged reaction times. In case of the three methylbenzaldehydes, the *para*-isomer was found to react faster than the *ortho*- and *meta*-derivatives (Table 1, entries 4–6).

To evaluate the effect of catalyst loading, we studied the olefination of benzaldehyde by using different catalyst concentrations (Table 1, entries 1 and 2) under similar reaction conditions. With increasing catalyst concentration (from 1 to 5 mol%), there was a marginal decrease in the reaction time although the selectivity remained almost the same, indicating the effectiveness of the PEG-supported catalyst even at low concentrations.

To check the recyclability and reusability of the prepared catalyst **5** we studied the olefination of benzaldehyde as a representative example. After completion, the catalyst separated from the reaction mixture by precipitation with diethyl ether and subsequent filtration was reused as such in up to ten runs under identical reaction conditions (Table 2). In the recycling experiments there was only a small decrease in catalytic efficiency in each cycle within ten runs, moreover, the selectivity of the product remained high and almost unchanged during these recyclability experiments.

Table 1. Olefination of aldehydes using PEG-immobilized iron(II) porphyrin (PEG-$C_{51}H_{39}FeN_7O$) **5** as catalyst.[a]

Entry	Substrate	Catalyst Loading [mol%]	Reaction Time [h]	Yield[b] [%]	*E/Z* ratio[c]
1		1	3.0	96	24
2		5	2.5	97	26
3		1	3.5	98	18
4		1	4.0	96	16
5		1	5.0	96	12.5
6		1	6.5	97	13.4
7		1	1.5	98	15
8		1	2.0	97	13
9		1	1.5	96	15
10		1	1.5	98	16
11		1	10.0	94	18.5
12		1	8.0	85	10.5
13		1	2.5	97	12.5
14		1	3.5	97	15
15		1	6.0	92	10
16	CH_3-$(CH_2)_6$CHO	1	7.5	85	8.5

[a] *Reaction conditions:* aldehyde (1 mmol), ethyl diazoacetate (1.2 mmol), Ph_3P (1.2 mmol), catalyst (1 mol%, 0.01 mmol), toluene (2 mL) at 80 °C under N_2 atm.
[b] Isolated yields.
[c] *E/Z* ratio determined by ^{1}H NMR.

The exact mechanism of the reaction is not clear at this stage. The reaction mechanism for the olefination of aldehydes with diazoacetate in the presence of triphenylphosphine by using Fe(II) porphyrin has been

Table 2. Results of recyclability experiments.[a]

Run	Substrate	Hours at r.t.	Yield[b] [%]	*E/Z* ratio
1	Benzaldehyde	3.0	96	24
2	Benzaldehyde	3.0	96	24
3	Benzaldehyde	3.0	95	24
4	Benzaldehyde	3.5	95	24
5	Benzaldehyde	3.5	95	23.5
6	Benzaldehyde	3.5	92	23.5
7	Benzaldehyde	4.5	85	23.5
8	Benzaldehyde	4.5	80	23
9	Benzaldehyde	5.5	78	23
10	Benzaldehyde	6.5	75	23

[a] Benzaldehyde (1 mmol), ethyl diazoacetate (1.2 mmol), triphenylphosphine (1.2 mmol) and catalyst **5** (1 mol%), 80 °C in toluene. Recovery of the catalyst by precipitation with diethyl ether.

[b] Isolated yields.

studied in detail by Woo et al.[12] They reported that iron(II) complexes catalytically convert diazo esters in the presence of phosphines to phosphoranes which in turn on reaction with aldehydes yield olefins and phosphine oxide. We assume an analogous mechanism for our catalytic system.

Conclusions

In summary, the first successful synthesis of a soluble PEG-immobilized iron porphyrin by using a copper-catalyzed azide-alkyne [3+2]cycloaddition 'click reaction' is reported. The click method offers the advantages of being simple as well as allowing a high catalyst loading and mild reaction conditions, when compared to the previously known methods for immobilization of metalloporphyrins. The PEG-immobilized iron porphyrin catalyst can be conveniently used as a recoverable and recyclable catalyst in the olefination of aldehydes with ethyldiazoacetate in the presence of triphenylphosphine. The PEG-immobilized Fe(II) porphyrin catalyst afforded yields and selectivities comparable to those obtained with homogeneous iron porphyrins for the olefination of aldehydes but with the added advantages of facile recovery and recyclability of the catalyst.

Experimental Section

Synthesis of PEG-Immobilized Iron(II) Porphyrin (5)

Propargylation of MeOPEG$_{5000}$: Into a stirred solution of MeOPEG$_{5000}$ **3** (4 mmol, 20.0 g) in acetone (60 mL), K_2CO_3 (7 mmol, 1.0 g) and KI (0.6 mmol, 0.1 equiv., 0.1 g) were added at room temperature. Propargyl bromide (80 wt% solution in toluene, 1.0 mL, 7.5 mmol) was added dropwise and the resulting mixture was refluxed for 12 h. After being cooled to room temperature, the solvent was removed under reduced pressure and the obtained residue was dissolved in ethyl acetate. The organic layer was washed with water (3 times), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give propargylated MeOPEG$_{5000}$ **4**; yield: 19.5 g (97%); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.98$ (s, 1H, CH), 3.42 (s, 3H, OMe).

Synthesis of azido iron(II) porphyrin: Into a stirred solution of azidoporphyrin (1 mmol, 0.853 g) in dry DMF (25 mL) was added iron(II) acetate (1.2 mmol, 0.2 g) at room temperature. The resulting solution was heated at 85 °C for 8 h under a nitrogen atmosphere. After completion, the solvent was evaporated under reduced pressure and the resulting residue was dissolved in ethyl acetate, washed with brine solution, dried and the solvent was evaporated under reduced pressure to yield azido iron(II) porphyrin; yield: 92%; MS: $m/z =$ 863 (M^+-N_2); IR: $\nu =$ 2933, 2870, 2220, 1981, 1638, 1492, 1231, 901 cm^{-1}; anal. calcd. for $C_{56}H_{51}FeN_7$: C 76.61, H 5.86, N, 11.17; found: C 72.95, H 5.70, N 10.38.

*Immobilization of azido iron(II) porphyrin **2** to PEG by the click reaction*: A solution of azidoiron(II) porphyrin (1.2 mmol, 1.0 g), CuI (5 mol%), triethylamine (1 mL) and propargylated MeOPEG$_{5000}$ **4** (1 mmol, 5.0 g) in dry CH_2Cl_2 (30 mL) was vigorously stirred under reflux for 12 h under a nitrogen atmosphere. After completion, the reaction mixture was concentrated under reduced pressure and the residue obtained was treated with diethyl ether. The precipitated black solid was isolated by filtration, washed thoroughly with 2-propanol, diethyl ether and dried under vacuum to afford PEG-immobilized Fe(II) porphyrin **5**; yield: 5.5 g (96%); UV-vis (CH_3CN): $\lambda_{max} = 355$, 310, 240 nm. The loading of the iron porphyrin compound **2** was found to be 0.15 mmol g^{-1} based on the nitrogen content (1.47% N) being determined by elemental analysis.[10] IR: $\nu = 2883$, 1622, 1540, 1466 cm^{-1}.

General Experimental Procedure for the Olefination of Aldehydes

Into a 10-mL Schlenk tube placed in a preheated oil bath at 80 °C were added aldehyde (1 mmol), ethyl diazoacetate (1.2 mmol), triphenylphosphine (1.2 mmol) and catalyst **5** (1 mol%) in toluene (2 mL) under a nitrogen atmosphere. The homogeneous mixture was stirred for the period indicated in Table 1. After completion of the reaction, the resulting mixture was cooled to room temperature and concentrated under reduced pressure. The residue was treated with diethyl ether, the precipitated PEG-supported iron porphyrin **5** was recovered by filtration and washed with Et_2O. The filtrate was concentrated under reduced pressure and purified by column chromatography using hexane/ethyl acetate (15:1) to give the pure olefin.

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