

Preparation of α,β -acetylenic ketones by catalytic heterogeneous oxidation of alkynes†

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Covalent grafting of iron phthalocyanines onto silica affords active catalysts for selective oxidation of alkynes and propargylic alcohols to α,β -acetylenic ketones, highly valuable precursors in the preparation of fine chemicals.

The quest for efficient clean catalytic methods remains an important challenge for the preparation of fine and speciality chemicals. This is especially true for oxidation reactions where traditional stoichiometric oxidants are usually applied.

For example, α,β -acetylenic ketones are very useful building blocks for enantioselective total synthesis and for the preparation of heterocyclic compounds, nucleosides, non-proteinogenic amino-acids, pheromones and drugs.¹ Conjugated ynones are usually prepared by acylation of metal acetylenides and multistep synthesis² and only a few methods have been reported using direct α -oxidation of alkynes. Chromium complexes have been used to oxidize alkynes in moderate yields and a large excess of *tert*-butyl hydroperoxide (TBHP) was used.³ Ishii *et al.* reported a homogeneous catalytic method for oxidation of alkynes using *N*-hydroxyphthalimide combined with a transition metal under aerobic conditions.⁴ Recently Pei *et al.* reported the efficient homogeneous oxidation of alkynes to α,β -acetylenic ketones by TBHP in the presence of 4 mol % metallic salt.⁵ A mechanism of this oxidation is thought to be via an energetically favorable hydrogen atom abstraction from the α -CH₂ group of alkyne (87.3 kcal mol⁻¹ for pent-2-yne⁴) followed by the reaction with dioxygen or oxygen-centered radicals to form α,β -acetylenic ketones.^{4,5}

The catalysts immobilised on solid supports are especially attractive because they allow easy separation from the reaction mixture and possible recycling. We have recently showed that iron tetrasulphophthalocyanine covalently supported onto silica (FePcS-SiO₂, **1**) was an efficient catalyst in the oxidation of aromatic compounds (Fig. 1).^{6,7} These reactions operate via 1e⁻ oxidation steps. Additionally, FePcS in combination with H₂O₂ was shown to be quite inert *vis-à-vis* double bonds.⁸ These properties coupled with availability, chemical stability and easy grafting of metalophthalocyanines onto silica support make them good potential heterogeneous catalysts for the oxidation of alkynes to α,β -acetylenic ketones.

Indeed, homogeneous oxidation of oct-4-yne in the presence of FePcS having tetrabutylammonium cations to provide a solubility in organic solvents resulted in 60% conversion with near 100% selectivity for oct-4-yn-3-one formation. This promising result prompted us to anchor phthalocyanine complexes onto amino-modified silica. Here we report the first heterogeneous catalytic oxidation of alkynes to ynones under mild conditions (Scheme 1).

The heterogeneous catalysts FePcS-SiO₂(**1**) and FePcCl₁₆-SiO₂(**2**) were prepared as previously described⁷ and characterized by elemental analysis, surface area determination and

the diffuse reflectance UV-vis spectroscopy that evidenced the effective complex grafting. The complex loading was determined by metal analysis using an inductively coupled plasma-mass spectrometry method to be 30–40 μ mol g⁻¹.

The model substrate, oct-4-yne, was oxidized by TBHP into oct-4-yn-3-one with 80% conversion and 89% selectivity in the presence of 2 mol % of **1** (run 1, Table 1). Only trace amounts of oct-4-yn-3-ol (5%) and oct-4-yn-3,6-dione were found by GC-MS analysis. Remarkably, the oxidation of oct-4-yne was very selective, the second α -position being almost inactive. The main product, oct-4-yn-3-one, was completely stable under reaction conditions. On the contrary, propargylic alcohols which could be the initial products of the alkyne oxidation were rapidly converted into their corresponding ketones. Thus oct-

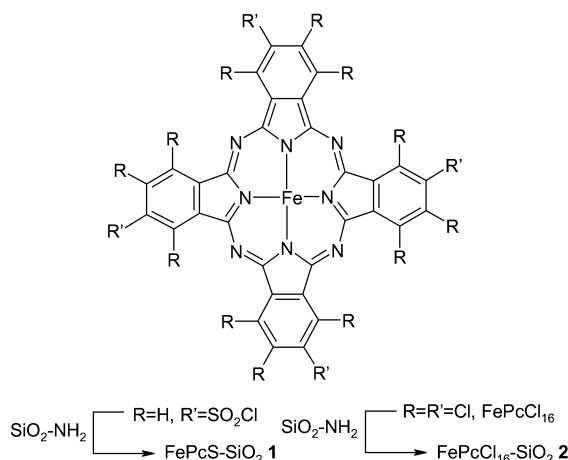
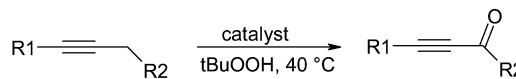


Fig. 1 Catalysts based on metalophthalocyanines.



Scheme 1 Catalytic oxidation of alkynes.

Table 1 Oxidation of alkynes by TBHP catalyzed by supported metalophthalocyanines^a

Run	Substrate	Product	Conversion (%) ^b	Selectivity (%) ^b
1	C ₃ H ₇ C≡CC ₃ H ₇	C ₃ H ₇ C≡CC(O)C ₂ H ₅	80	89
2	PhC≡CC ₂ H ₅	PhC≡CC(O)CH ₃	75	83
3	HC≡CC ₆ H ₁₃	HC≡CC(O)C ₅ H ₁₁	38	38
4	HC≡CC(OH)C ₅ H ₁₁	HC≡CC(O)C ₅ H ₁₁	84	100
5 ^c	C ₃ H ₇ C≡CC ₃ H ₇	C ₃ H ₇ C≡CC(O)C ₂ H ₅	81	85
6	CH ₃ C≡CC ₅ H ₁₁	CH ₃ C≡CC(O)C ₄ H ₉	64	47
7 ^d	C ₃ H ₇ C≡CC ₃ H ₇	C ₃ H ₇ C≡CC(O)C ₂ H ₅	79	88
8 ^d	PhC≡CC ₂ H ₅	PhC≡CC(O)CH ₃	86	93

^a The reaction was carried out at 40 °C for 24 h. ^b Conversions and selectivities were determined by GC using 1-chloronaphthalene as an internal standard. ^c Under argon. ^d With FePcCl₁₆-SiO₂ **2**.

† Electronic Supplementary information (ESI) available: details of the synthesis and characterisation of authentic ynones; kinetic curves of the oct-4-yne oxidation under air and under argon; mass spectra of oct-4-yn-3-one and 4-phenylbut-3-yn-2-one obtained in labelling studies; DR UV-vis spectra of catalyst **2** before and after 3 successive oxidations. See <http://www.rsc.org/suppdata/cc/b2/b204122g/>

1-yn-3-ol gave rapidly oct-1-yn-3-one with 84% conversion and 100% selectivity (run 4) while oct-1-yne showed only a 38% conversion (run 3) suggesting that the limiting step is the initial oxidation of alkyne into propargylic alcohol through an α -hydrogen atom abstraction. Other substrates were oxidized in the presence of FePcS-SiO₂ and TBHP (Table 1).

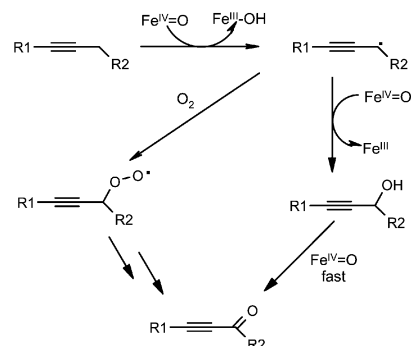
1-phenylbut-1-yne was also converted into 4-phenylbut-3-yn-2-one with high selectivity (run 2). When the reaction was carried out without catalyst, only 21% and 15% non-selective conversions were observed for oct-4-yne and 1-phenylbut-1-yne, respectively. Terminal oct-1-yne and oct-2-yne were less reactive and selective providing 38 and 64% conversions and 38 and 47% selectivities, respectively.

The perchlorinated catalyst **2** exhibited similar catalytic activity in the oxidation of oct-4-yne (run 7). Interestingly, **2** was superior to **1** in the oxidation of 1-phenylbut-1-yne providing 86% conversion along with 93% selectivity (run 8). When oct-4-yne and 1-phenylbut-1-yne were oxidized in the presence of 1 mol % of the catalysts **1** or **2** we obtained the same conversions and selectivities. Further decreasing of the catalyst **1** amount to 0.5 mol % resulted in decreasing of the selectivity of 15–20% while keeping the same conversion of oct-4-yne. It is noteworthy that the lower loading of catalyst **2** of 0.5 mol % provided the same high conversion and selectivity for the oxidation of 1-phenylbut-1-yne as for 2 mol % demonstrating a high efficiency of this catalyst.

The good results obtained with catalyst **2** have prompted us to study recyclability of the catalyst under the conditions of run 8. After completing the first run new portions of the substrate and oxidant were directly added to the reaction mixture. Three successive oxidations of 1-phenylbut-1-yne showed that the catalytic activity remained high, the conversions being 86, 84 and 73%, respectively. The selectivity of oxidation became slightly higher in successful oxidations: 93, 100 and 95%. The catalyst **2** recycled after 3 oxidations exhibited the same DR UV-vis spectrum as that of the initial supported catalyst indicating no degradation (see ESI†). A further set of experiments was carried out to examine the reusability of the phthalocyanine supported catalysts. After the first oxidation of 1-phenylbut-1-yne the catalyst **2** was isolated by filtration, washed with MeCN and Et₂O and dried. On reuse, 83% conversion and 95% selectivity of 1-phenylbut-1-yne oxidation were observed proving the high efficiency of the catalyst recovery.

The evidence for a mechanism involving an α -hydrogen atom abstraction as a limiting step was gained through a comparison of the kinetics of the reaction under air and under argon and through an isotope labelling study with ¹⁸O₂.

Under argon, the oxidation of oct-4-yne was as efficient as under air (run 5, Table 1) following the same kinetics (see ESI†). Apparently, this finding suggested that O₂ was not involved in the oxidation. The source of product oxygen has been examined by a ¹⁸O-labelling study to determine whether the oxygen transfer occurs from FePcS-based active species or from O₂. If a high-valent iron oxo species, which is generated by the O–O bond cleavage of the iron peroxo complex, is the only species involved, no ¹⁸O incorporated in α,β -acetylenic ketone formed would be detected. So we performed the oxidation of oct-4-yne with labelled molecular oxygen (98.5% ¹⁸O enrichment) in the presence of TBHP and **1**. The mass spectrum of unlabelled oct-4-yn-3-one exhibits a major ion at m/z = 95 corresponding to the adduct $[M - C_2H_5]^+$ along with weak M^+ at m/z = 124. Under an atmosphere containing 27.6% of ¹⁸O₂ and 72.4% of Ar, the ¹⁸O-content of labelled ketone was found to be $61.7 \pm 0.3\%$ as measured by the relative intensities of the molecular ions (m/z 124/126) and of the base peaks (m/z 95/97). The oxidation of 1-phenylbut-1-yne by TBHP in the presence of **2** under an atmosphere containing 40.2% of ¹⁸O₂ and 59.8% of Ar also produced ketone with $85.1 \pm 2.0\%$ labelled oxygen, as was measured from the relative intensities of the molecular peaks (m/z 144/146) and of the base peaks (m/z 129/131) resulting from the loss of methyl radical. In both cases the



Scheme 2 Proposed mechanism of the oxidation of alkynes by iron phthalocyanine-TBHP system under air.

incorporation of ¹⁸O₂ did not depend on the reaction time. The oxygen atom is thus incorporated into α,β -acetylenic ketone from both molecular oxygen and FePcS-based active species (Scheme 2). The proportion of the oxygen incorporated from these two sources seems to depend on the concentration of ¹⁸O₂ suggesting that the reaction rates of the two pathways are of the same order. In accord with this proposal, if the reaction is run under argon, the oxygen in the product derives from peroxide-FePcS active species. Since the kinetics of the reaction is practically the same under Ar as under air we can conclude that oxygen insertion is not the rate limiting step.

The above results lead us to propose the mechanism of this reaction (Scheme 2). At the first rate limiting step, iron phthalocyanine based active species abstract a hydrogen atom from the α -position. The radical formed reacts either with iron phthalocyanine active species to give propargylic alcohol or with O₂ to give an intermediate peroxy radical leading to acetylenic ketones in successive oxidation steps. Intermediate propargylic alcohol is rapidly converted to final product.†

In conclusion, we have demonstrated efficient and selective heterogeneous oxidation of alkynes to give valuable α,β -acetylenic ketones using phthalocyanine supported catalysts capable of re-use or continuous operation.

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Notes and references

† Typical procedure for the oxidation of alkynes (catalyst–alkyne–oxidant 1 : 50 : 200): to a solution of alkyne (400 μ mol) in *t*-BuOH (4 mL) was added FePcS-SiO₂ (8 μ mol), then six portions of a 3.45 M TBHP solution in 1,2-DCE or PhCl were added to the mixture at reaction times of 0, 1, 2, 3, 5, 7 h ($6 \times 77.3 \mu$ L). The reaction was carried out at 40 °C for 24 h and the progress of the reaction was monitored by using gas chromatography. The products were identified by NMR and GC-MS methods and quantified by GC using authentic samples prepared according published methods.⁵

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