COMMUNICATION

ChemComm
www.rsc.org/chemcomm

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

Céline Pérollier and Alexander B. Sorokin*
Institut de Recherches sur la Catalyse, CNRS, 2, avenue A. Einstein, 69626 Villeurbanne Cedex, France.
E-mail: sorokin@catalyse.univ-lyon1.fr; Fax: +(33) 4 72 44 53 99; Tel: +(33) 4 72 44 53 37

Received (in Cambridge, UK) 30th April 2002, Accepted 6th June 2002
First published as an Advance Article on the web 19th June 2002

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 synthesis[2] 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 an 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-CH_2 group of alkyne (87.3 kcal mol^{-1} for pent-2-yne[4]) 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 tetrasulfophthalocyanine covalently supported onto silica (FePcS-SiO_2, **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 H_2O_2 was shown to be quite inert *vis-à-vis* double bonds.[8] These properties coupled with availability, chemical stability and easy grafting of metallophthalocyanines 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-SiO_2(**1**) and $FePcCl_{16}$-SiO_2(**2**) were prepared as previously described[7] 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 μmol 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-

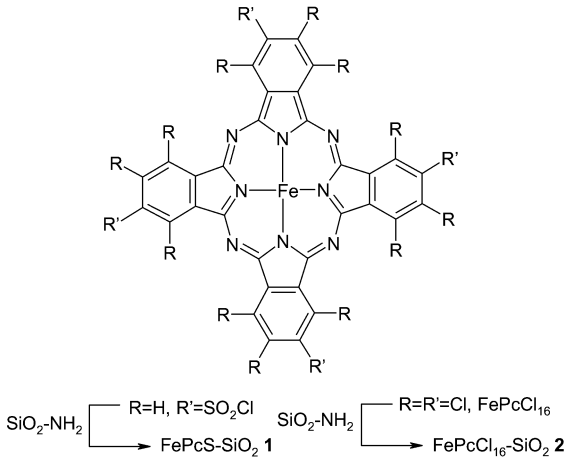
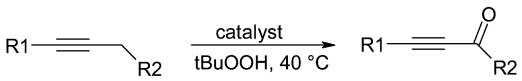


Fig. 1 Catalysts based on metallophthalocyanines.



Scheme 1 Catalytic oxidation of alkynes.

Table 1 Oxidation of alkynes by TBHP catalyzed by supported metallophthalocyanines[a]

Run	Substrate	Product	Conversion (%)[b]	Selectivity (%)[b]
1	$C_3H_7C{\equiv}CC_3H_7$	$C_3H_7C{\equiv}CC(O)C_2H_5$	80	89
2	$PhC{\equiv}CC_2H_5$	$PhC{\equiv}CC(O)CH_3$	75	83
3	$HC{\equiv}CC_6H_{13}$	$HC{\equiv}CC(O)C_5H_{11}$	38	38
4	$HC{\equiv}CC(OH)C_5H_{11}$	$HC{\equiv}CC(O)C_5H_{11}$	84	100
5[c]	$C_3H_7C{\equiv}CC_3H_7$	$C_3H_7C{\equiv}CC(O)C_2H_5$	81	85
6	$CH_3C{\equiv}CC_5H_{11}$	$CH_3C{\equiv}CC(O)C_4H_9$	64	47
7[d]	$C_3H_7C{\equiv}CC_3H_7$	$C_3H_7C{\equiv}CC(O)C_2H_5$	79	88
8[d]	$PhC{\equiv}CC_2H_5$	$PhC{\equiv}CC(O)CH_3$	86	93

[a] The reaction was carried out at 40 ·C for 24 h. [b] Conversions and selectivities were deter·ined by GC using 1-chloronaphthalene as an internal standard. [c] Under argon. [d] With $FePcCl_{16}$-SiO_2 **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/

DOI: 10.1039/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-SiO_2 and TBHP (Table 1).

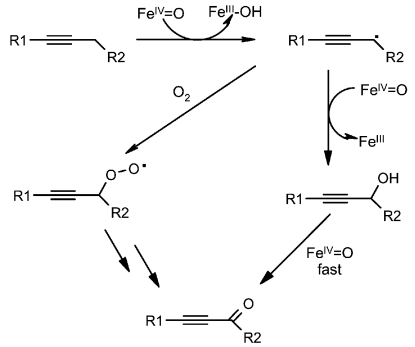
1-phenylbut-1-yne was also converted into 4-phenylbut-3-yn-2-one with high selectivity (run 2). When the reaction was carried out without catalyst, only 21% and 15% non-selective conversions were observed for oct-4-yne and 1-phenylbut-1-yne, respectively. Terminal oct-1-yne and oct-2-yne were less reactive 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 Et_2O 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 $^{18}O_2$.

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 O_2 was not involved in the oxidation. The source of product oxygen has been examined by a ^{18}O-labelling study to determine whether the oxygen transfer occurs from FePcS-based active species or from O_2. 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 ^{18}O 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% ^{18}O 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 $^{18}O_2$ and 72.4% of Ar, the ^{18}O-content of labelled ketone was found to be 61.7 ± 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 $^{18}O_2$ and 59.8% of Ar also produced ketone with 85.1 ± 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 $^{18}O_2$ 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 $^{18}O_2$ 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 O_2 to give an intermediate peroxo 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.

This work was supported by Fonds National de la Science. CP is indebted to the French Ministry of Education, Research and Technology for a post-doctoral fellowship.

Notes and references

‡ Typical procedure for the oxidation of alkynes (catalyst–alkyne–oxidant 1 : 50 : 200): to a solution of alkyne (400 μmol) in *t*-BuOH (4 mL) was added FePcS-SiO_2 (8 μmol), 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 × 77.3 μL). 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]

1 (*a*) C. F. Thompson, T. F. Jamison and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2001, **123**, 9974; (*b*) A. V. Kel'in and V. Gevorgyan, *J. Org. Chem.*, 2002, **67**, 95; (*c*) J. E. Baldwin, G. J. Pritchard and R. E. Rathmell, *J. Chem. Soc., Perkin Trans. 1*, 2001, 2906; (*d*) G. Cabarrocas, S. Rafel, M. Ventura and J. M. Villalgordo, *Synlett*, 2000, 595; (*e*) R. M. Adlington, J. E. Baldwin, G. J. Pritchard and K. C. Spencer, *Tetrahedron Lett.*, 2000, **41**, 575.

2 (*a*) H. D. Verkruijsse, Y. A. Heus-Kloos and L. Brandsma, *J. Organomet. Chem.*, 1988, 289; (*b*) C. Chowdhury and N. Kundu, *Tetrahedron*, 1999, **55**, 7011; (*c*) A. R. Katritzky and H. Lang, *J. Org. Chem.*, 1995, **60**, 7612 and references therein.

3 J. Muzard and O. Piva, *Tetrahedron Lett.*, 1988, **29**, 2321; J. E. Shaw and J. J. Sherry, *Tetrahedron Lett.*, 1971, **12**, 4379.

4 S. Sakaguchi, T. Takase, T. Iwahama and Y. Ishii, *Chem. Commun.*, 1998, 2037.

5 Li. Pei, W. M. Fong, L. C. F. Chao, S. Fung and I. D. Williams, *J. Org. Chem.*, 2001, **66**, 4087.

6 C. Pergrale and A. B. Sorokin, *C. R. Acad. Sci. Paris*, 2000, **3**, 803.

7 A. B. Sorokin and A. Tuel, *New J. Chem.*, 1999, **23**, 473; A. B. Sorokin and A. Tuel, *Catal. Today*, 2000, **57**, 45.

8 B. Meunier and A.B. Sorokin, *Acc. Chem. Res.*, 1997, **30**, 470.