

Selective copper-catalyzed allylic oxidations using a 1/1 ratio of cycloalkene and *tert*-butylperbenzoate

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Abstract

With $\text{Cu}(\text{MeCN})_4\text{BF}_4$ as catalyst and benzotrifluoride as solvent, the allylic oxidation of cyclohexene by *tert*-butyl perbenzoate was performed at room temperature in 75% yield without requiring an excess of the olefin. The benzyloxylation of other cycloalkenes in using such a substrate/perester ratio required additives such as DBU, DBN or DMAP, and often an increase of the reaction temperature. © 2002 Elsevier Science B.V. All rights reserved.

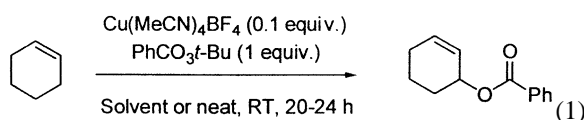
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1. Introduction

The copper-catalyzed allylic oxidation of olefins with peresters has been the subject of numerous synthetic and mechanistic investigations [1–10]. This process, which is popularly known as the Kharasch–Sosnovsky reaction, allows the direct functionalization of olefins in exploiting the special nature of the allylic C–H bond. The allylic esters thus obtained can be converted into allylic alcohols by hydrolysis or reduction methods. The whole transformation is very important from a synthetic organic chemist's viewpoint; furthermore, we [11–13] and others [14–16]¹ have proposed enantioselective versions of this process. An important limiting factor of the Cu-methods reported in the literature is the high olefin/perester ratio which is required to obtain good selectivities. The excess of olefins prevents sec-

ondary reactions [7] and could accelerate the reaction rate. Since the use of an excess of substrate could be a problem in the case of expensive or synthesized olefins, the development of procedures using a 1/1 olefin/perester ratio remains challenging.

In this paper, we report experimental conditions which allow the Cu-catalyzed benzyloxylation of cyclohexene in good yield without using an excess of the olefin (Eq. (1)). The allylic oxidation of other cycloalkenes is also presented:



2. Experimental

2.1. Materials and apparatus

All reactions and distillations were carried out under an argon atmosphere. Alkenes, acetonitrile,

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¹ For reviews, see Refs. [17,18].

dichloromethane and benzotrifluoride (BTF, α,α,α -trifluorotoluene) were distilled over CaH_2 prior to use. Acetone was distilled over K_2CO_3 . $\text{Cu}(\text{MeCN})_4\text{BF}_4$ (**1**) was freshly prepared prior to use from Cu_2O and HBF_4 according to the procedure reported by Kubas [19]. Other reagents were used as-received.

2.2. General oxidation procedure

A Schlenk flask was charged with a freshly prepared sample of **1** (62 mg, 0.2 mmol), solvent (5 ml) and additive (0 or 0.2 mmol). The alkene (2 mmol) was added, followed by dropwise addition of *tert*-butylperbenzoate (**2**) (0.38 ml, 2 mmol). The reaction mixture was stirred at the appropriate temperature until disappearance of perbenzoate (TLC analysis, SiO_2 , petroleum ether/EtOAc = 95/5, R_f = 0.4). The mixture was diluted with saturated NaHCO_3 aqueous solution (50 ml), stirred for 10 min, extracted with Et_2O (3×20 ml) and dried over MgSO_4 . Products were purified by column chromatography (SiO_2 , petroleum ether/EtOAc = 95/5) and characterized by NMR spectroscopy.

3. Results and discussion

As a model reaction, 1 eq. of cyclohexene was reacted at room temperature for 20 h with a stoichiometric quantity of **2** and a catalytic amount of **1**. A cationic salt was chosen as catalyst since the absence of a strongly coordinating anion creates coordination sites on the Cu atom that are more accessible to the substrates entering the catalytic cycle. Using acetonitrile or acetone as solvent,² 2-cyclohexenyl-1-benzoate was isolated in 12–14% yields (Table 1, entries 1 and 2). Thus, we decided to examine this reaction in less coordinating solvents. In dichloromethane, the yield was increased to 64% (entry 3); the use of BTF, a solvent which has already improved the efficiency of other oxidations [20–25], yielded 75% of the ester (entry 4). With these two latter solvents, the conversion of the oxidizing agent was complete and only traces of side products were detected from TLC analysis. It

² Recent studies of the Cu-catalyzed allylic oxidation of alkenes by **2** were generally performed in acetonitrile or acetone [9,14,16–18].

is interesting to note that this 75% yield obtained in using a 1/1 ratio of cyclohexene and **2** at room temperature for 20 h is close to the 80% yield recently reported by Sekar et al. [9] from a 0.1/0.12/10/1 mixture of $\text{Cu}(\text{OTf})_2/1,8\text{-diazabicyclo}[5.4.0]\text{undec-7-ene}$ (DBU)/cyclohexene/**2** stirred at room temperature for 32 h in acetone.

These results show that cyclohexene could be easily oxidized in good yield without requiring an excess of the starting material if the right solvent is used. Acetonitrile and acetone are ligating to the metal and act probably as a shield around the copper center. The lower coordinating ability of CH_2Cl_2 and BTF leads probably to a more “naked” metal with thus, a better reactivity. These observations urge us to carry out the oxidation in the absence of solvent but the yield was reduced to 53% (entry 5).


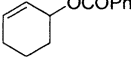

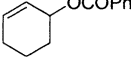

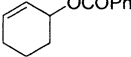

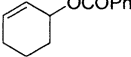

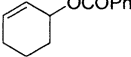

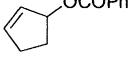

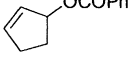

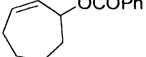

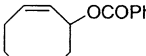

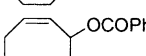
The reaction in BTF was homogeneous at the beginning but a blue precipitate³ was produced in the course of the oxidation and its amount increased with time. The mass spectrum of this solid showed three fragments attributed to $[\text{PhCO}_2\text{Cu}]^+$ (185, 100%), $[\text{PhCO}_2\text{Cu}]_2^+$ (369, 56%), $[\text{PhCO}_2\text{Cu}]_3^+$ (553, 11%). The presence in this precipitate of the counter-anion BF_4^- was revealed by a wide band in IR spectroscopy (1073 cm^{-1}) [26]. From these data, the structure of the blue complex is tentatively attributed to the cationic copper trimer $(\text{PhCO}_2\text{Cu})_3(\text{BF}_4)_3$ (**3**).⁴ Interestingly, we have observed that the use of **3** in BTF, acetonitrile, acetone or dichloromethane did not catalyze the allylic oxidation of cyclohexene by **2**.

The generally accepted mechanism for such oxidations involves homolysis of the perester oxygen–oxygen bond by copper(I) leading to copper(II) benzoate **A** and the *tert*-butoxy radical (Scheme 1, step a). Abstraction of an allylic hydrogen atom by this radical affords *tert*-butanol and an allylic radical (step b) which reacts with **A** to give copper(III) intermediate **B** (step c). The final step would be a pericyclic reaction of **B** providing the allylic ester and regenerating the copper(I) catalyst (step d) [6].

³ A blue precipitate was also observed when the reaction was carried out in the absence of solvent (run 5).

⁴ We did not succeed to obtain suitable crystals of **3** for X-rays. The crystal structure of a neutral trinuclear copper(II)carboxylate has been recently documented [27].

Table 1
Copper-catalyzed oxidation of olefins by stoichiometric amounts of *tert*-butylperbenzoate^a

Entry	Substrate	Solvent	Additive ^b	<i>t</i> (°)	Time	Product	Yield (%) ^c
1		MeCN	No	RT	20 h		12
2		Acetone	No	RT	20 h		14
3		CH ₂ Cl ₂	No	RT	20 h		64
4		BTF	No	RT	20 h		75
5		Neat	No	RT	24 h		53
6		CH ₂ Cl ₂	DBU	RT	6 days		64
7		BTF	DBU	RT	6 days		63
8		CH ₂ Cl ₂	DBN	40	7 days		32
9		CH ₂ Cl ₂	DMAP	40	7 days		23
10		CH ₂ Cl ₂	DMAP	40	5 days		53

^a For the experimental conditions, see the Section 2.2.

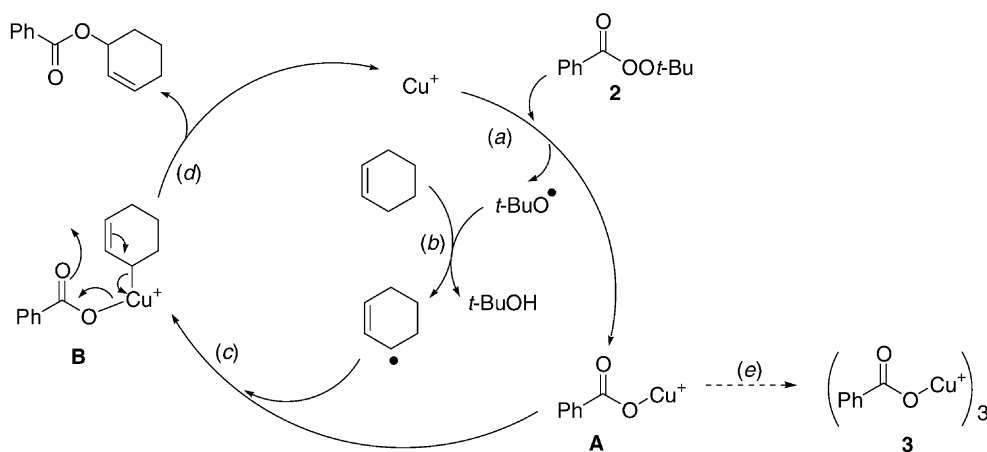
^b DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene; DBN: 1,5-diazabicyclo[4.3.0]non-7-ene; DMAP: 4-dimethylaminopyridine.

^c Isolated yield.

We propose that supramolecular associations of **A** afford **3** (step e). The formation under our conditions of such a stable complex which is not able to induce catalysis could explain why the reactions reported in the literature have been mainly developed in using excesses of alkene. Higher amounts of alkene should facilitate step b and consequently, the reaction of the allylic radical with **A** (step c). Thus, the formation of

B would be more efficient than self-associations of copper intermediates which result in the quenching of the copper.

The **1**-catalyzed oxidation of a 1/1 mixture of cyclopentene and **2** in BTF afforded only traces of the expected allylic ester after a few hours; prolonging the reaction time gave secondary reactions and decomposition of the oxidizing agent. Similar results



Scheme 1.

were obtained when the reaction was performed in dichloromethane or acetone. The allylic oxidation procedure reported by Sekar et al. [9] suggested us to carry out the reaction in the presence of an additive such as DBU. In fact, the addition of 0.1 eq. of DBU allowed a clean reaction to occur in trifluorotoluene or dichloromethane; the reaction proceeded slowly giving 2-cyclopentenyl-1-benzoate in 63–64% yield (entries 6 and 7). Sekar et al. [9] have stated that the presence of DBU increased the rate of their oxidation process. We suggest that this additive could coordinate to Cu-intermediates, this precluding the self-association of **A** and/or promoting some steps of the catalytic cycle.⁵

Even under these modified conditions, less than 10% of conversion was observed with cycloheptene. Nevertheless, exchange of DBU for 1,5-diazabicyclo[4.3.0]non-7-ene (DBN) improved slightly the conversion and increasing the reaction temperature to 45 °C produced 2-cycloheptenyl-1-benzoate in 32% yield (entry 8).

Cyclooctene and 1,5-cyclooctadiene behave differently than above alkenes. When their oxidation was attempted in BTF or dichloromethane in the presence of **1** and in the absence of any additive, no reaction occurred. Addition of DBU or DBN allowed the oxidations to start but produced only traces of expected products after 3 days, side reactions being also observed. Changing from DBU and DBN to 4-dimethylaminopyridine (DMAP) gave less impurities.⁶ Consequently, both reactions were thus carried out at 45 °C in dichloromethane providing the corresponding allylic esters in 23 and 53% yield, respectively (entries 9 and 10); we did not isolated compounds corresponding to dioxidation of cyclooctadiene.

4. Conclusions

In using a weakly coordinating solvent and a catalytic amount of a cationic copper(I) complex, the

allylic oxidation of cyclohexene by a stoichiometric amount of *tert*-butylperbenzoate has been efficiently carried out. Under such conditions, cyclopentene and cycloheptene gave mainly decomposition reactions while no reaction was observed from cyclooctene and 1,5-cyclooctadiene. Nitrogen additives such as DBU, DBN or DMAP can play a role as stabilizing or activating agents in these cases, and have allowed the reactions to be performed in modest to fair yields without using excesses of the alkene.

Acknowledgements

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⁵ We have, however, observed that the oxidation of cyclohexene in CH₂Cl₂ became more sluggish in the presence of DBU.

⁶ Modifications of reactivity by structural variations of the amine catalyst have been documented for Baylis–Hillman reactions [28,29].

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