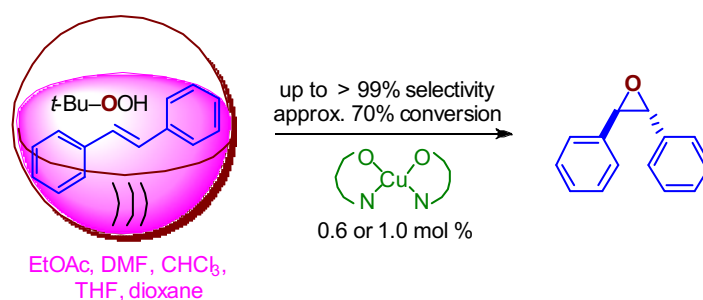# Evaluation of some 5-pyrazolone-based copper(II) complexes as catalysts for the oxidation of *trans*-stilbene

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The catalytic properties of the azo- and bisazo-5-pyrazolone-based three copper(II) complexes have been studied. Heating under reflux with or without ultrasonic irradiation was applied for the different equivalent amounts of three copper(II) catalysts (0.6 and 1.0 mol %) in ethyl acetate. It has been shown that all pyrazolone-based copper(II) complexes are active for catalytic oxidation of *trans*-stilbene in the presence of *tert*-butyl hydroperoxide as the oxidant, providing high selectivity and good conversion values. Heating was applied to the different solvents: chloroform, tetrahydrofuran, *N,N*-dimethylformamide, and dioxane. All catalysts can be safely used near to the boiling point of the oxidant without decomposition and the efficacy of ethyl acetate under conventional heating and heating–ultrasonic conditions has been determined. Heating–ultrasonic conditions and 1.0 mol % of catalysts gave higher conversion than conventional heating and 0.6 mol % of catalysts. A mechanism is proposed for the catalytic oxidation of *trans*-stilbene with *tert*-butyl hydroperoxide.

Keywords: copper(II) complexes, 5-pyrazolone, *trans*-stilbene oxide, catalytic oxidation, epoxidation, sonochemistry.
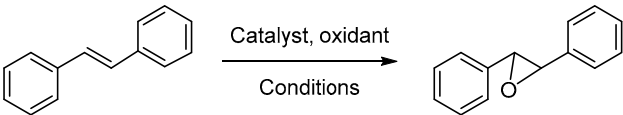
Transition metal complexes are versatile molecules and can serve as catalysts of oxidation, as well as reduction, of organic substrates.[1,2] They are stable in the presence of air and moisture, can be easily separated from reaction products, and have a potential for recycling.[3] The potential catalytic abilities of copper have received increasing interest in recent years: a very interesting study showed that copper nanoparticles catalyze the epoxidation of propylene in the presence of visible light as an efficient catalytic system.[4]

Epoxides are not common in nature and are being increasingly used in both synthetic organic chemistry and chemical technology because of their versatility as intermediates.[5,6] They are also being used in the synthesis of fine chemicals, such as pharmaceuticals, food additives, or flavors and fragrances,[7] as well as for the synthesis of various polymers.[8] Enantiopure stilbene oxides (*R,R* and *S,S*) are useful starting materials for the synthesis of chiral ligands, building blocks, etc.[9] Sharpless who has made many contributions to the epoxidation chemistry[10] published the first practical method for asymmetric epoxidation in 1980.[11] After this, he developed a simple two-step

procedure for the synthesis of enantiopure stilbene oxide by starting from a *R,R*-diol.[9]

Several researchers have reported the catalytic epoxidation of *trans*-stilbene mainly using complexes of oxovanadium(IV),[12] manganese(III),[13] and molybdenum(VI).[14] The results indicated moderate conversion and low selectivity against by-products, such as benzaldehyde, benzil, *cis*-stilbene, and *cis*-stilbene oxide. There are some examples of epoxidation of *trans*-stilbene in the presence of copper(II)-based catalysts in the literature (Table 1). In these works, the researchers have used copper(II) complexes,[15–18] including a polymer-anchored catalyst[19] or nanowires,[20] and obtained good conversion values with low to moderate selectivities. Epoxidation chemistry is well explored in the literature, yet epoxidation reactions *via* pyrazolone-based metal complexes as catalysts are rare and not well documented, and the optimum reaction conditions are still not established.

The use of ultrasound in synthetic organic chemistry in solution provides a wide range of applications from multiphasic to ionic reactions. A physical phenomenon,

Table 1. Oxidation of *trans*-stilbene catalyzed by a variety of copper(II) catalysts

Catalyst	*trans*-Stilbene/Catalyst	Oxidant	Reaction conditions	Conversion, %*	Selectivity for *trans*-stilbene oxide, %*	TOF**
[Cu$_4$(O)(L^{II})$_2$(OAc)$_4$]***	10 mmol/0.05 mmol	TBHP (20 mmol)	MeCN, 50°C, 24 h	82.0	88.0[15]	68.3
[Cu$_2$(L^2)(N$_3$)Cl$_2$]***	10 mmol/0.05 mmol	TBHP (20 mmol)	MeCN, 50°C, 24 h	81.0	85.0[16]	11.2
[Cu$_2$L(N$_3$)$_3$]***	0.5 g/0.1 g	TBHP (1 equiv)	MeCN, 60°C, 24 h	92.0	83.0[17]	5.3
Cu(MeCN)$_4$PF$_6$	Molar ratio 20/1	MCPBA (2 equiv)	CH$_2$Cl$_2$, –40°C, 10 h	70.0[4*]	Not reported[18]	–
A polymer-anchored Cu(II) catalyst	5 mmol/1.05×10^{-2} mmol	TBHP (10 mmol)	H$_2$O, 60°C, 8 h	67.0	6.0[19]	39.8
CuO@Ag nanowires	0.25 mmol/0.5 mg	In air	Xylene, 100°C, 24 h	> 99.0	84.0[20]	–

* Determined by GC-MS; conversion of the substrate into all products.
** Turnover frequency expressed as moles of substrate converted per mole of metal complex per hour.
*** L^{II} = 4-methyl-2,6-bis(5-hydroxypentyliminomethyl)phenol; L^2 = 4-methyl-2,6-bis(3-morpholinoethyliminomethyl)phenol; L = 4-methyl-2,6-bis(phenyl-methyliminomethyl)phenol.
[4*] Isolated yield of *trans*-stilbene oxide.

"acoustic cavitation" plays an important role in the activation of reactions. Using a standard laboratory ultrasonic bath, mainly a physical rate acceleration effect was mediated.[21]

Pyrazole and its derivative pyrazolone are important heterocyclic compounds.[22] Azo- and bisazopyrazol-5-one complexes, which contain nitrogen- or oxygen-chelating atoms, are challenging for catalysis because of their various steric and/or electronic effects. Our recent research has been focused on the synthesis of new azo-, bisazopyrazolones and their metal complexes.[23–26] This research is a continuation of these works and the objective is to show the catalytic effects of copper(II) complexes derived from bidentate azo- and bisazopyrazol-5-one ligands in the presence of *tert*-butyl hydroperoxide (TBHP) under conventional heating and heating combined with ultrasonic irradiation.

In this work, the catalytic activity of the azo- and bisazopyrazol-5-one-based copper(II) complexes **1**–**3** (Fig. 1) in the epoxidation of *trans*-stilbene using TBHP as the oxidant was evaluated. All complexes were prepared according to the literature.[23]

All the reactions were carried out after assigning the best equivalent amount of TBHP (2 equiv per 1 mol substrate) and reaction time (7 h) determined experimentally. To get a comparison between all used solvents (considering their boiling points) and to keep the oxidant in the reaction medium (boiling point of TBHP is 89°C), an optimum temperature of 75°C was chosen.

All experiments were evaluated and compared with the blank experiment (run under the same conditions, but containing no catalyst). The reaction mixtures were agitated with magnetic stirrer under heating with or without
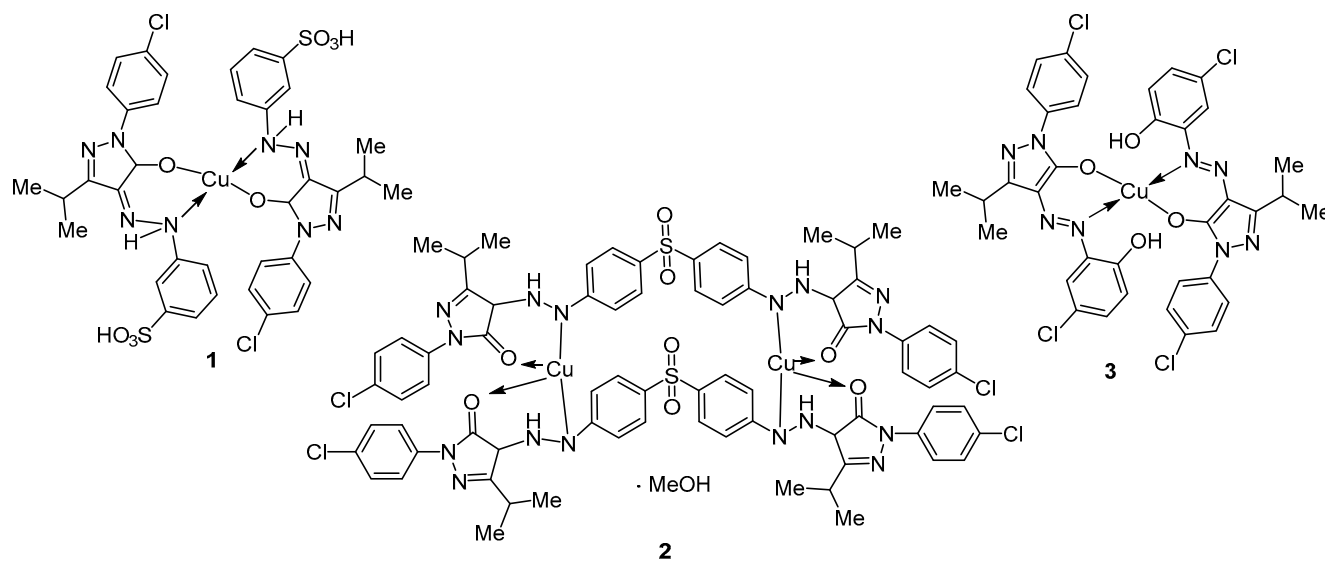
Figure 1. 5-Pyrazolone-based copper(II) complexes **1**–**3**.

Scheme 1
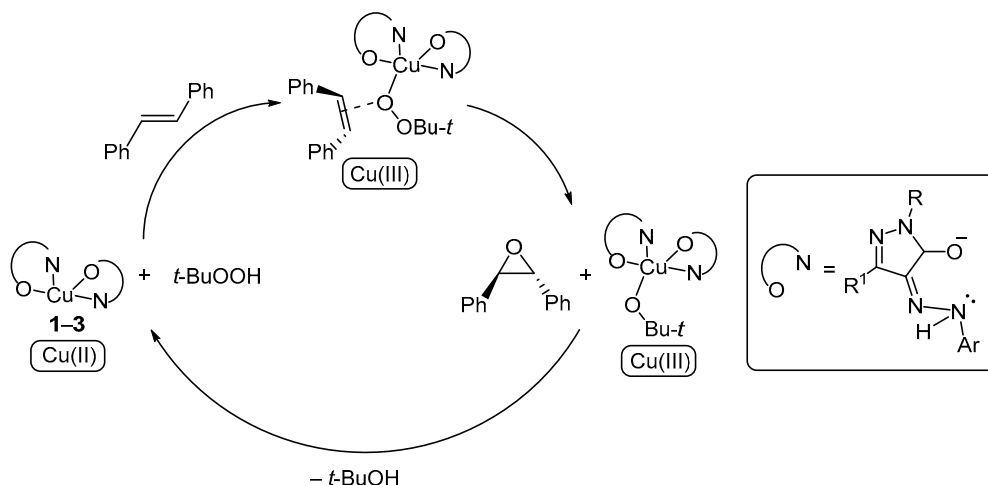
ultrasonic treatment. The course of the reaction was followed by electron spectroscopy as *trans*-stilbene (294 nm)[27] and *trans*-stilbene oxide (210 and 228 nm)[28] show characteristic peaks in the UV region. The liquid layer was analyzed by a GC-MS spectrometer. A relative evaluation was done using peak areas of total ion chromatograms, and the peaks belonging to the components of the liquid layer were identified by the comparison with known standards.

Different solvents, in which all three catalysts are soluble under heating, including dioxane, tetrahydrofuran, ethyl acetate, chloroform, and *N,N*-dimethylformamide (normalized empirical parameters of solvent polarity (E_T^N) 0.164, 0.207, 0.228, 0.259, 0.386, respectively)[29] were evaluated for their effect on the reaction. After 7 h, cooling of the reaction flask to room temperature, the catalyst was precipitated with decreasing volume of solvent and, then recovered by filtration. Interestingly, in ethyl acetate, high selectivity for *trans*-stilbene was observed, while working with the other solvents, very low conversion and selectivity were observed under these conditions. This could be because ethyl acetate may have the optimum polarity value for the reaction and additionally may supply the stability of copper(III) intermediate *via* releasing the unpaired electrons of the carbonyl oxygen to the metal on the basis of the proposed mechanism (Scheme 1). After determining the efficacy of this solvent, in order to evaluate the effect of catalyst concentration on the oxidation of the substrate, tests continued with only ethyl acetate at different equivalent ratios with catalysts **1**–**3** (0.6 and 1.0 mol %) while keeping a fixed amount of *trans*-stilbene (0.22 mmol) and TBHP (0.44 mmol). The equivalent ratio of TBHP was determined after carrying out an experiment with 2 and 3 equiv of TBHP *vs* the substrate and the conversion of *trans*-stilbene to *trans*-stilbene oxide was not changed significantly (from 42.0 to 37.5%, respectively). It was observed that with a higher catalyst load conversion of the substrate increased slightly both under conventional heating and heating–ultrasonic conditions. Working under ultrasonic conditions causes an increase of the *trans*-stilbene conversion by approximately 10%. Obtained results are presented in Table 2.

The best conversion values were obtained with catalyst **3**, and lower, but similar conversion results were obtained with catalysts **1** and **2** (Table 2). A possible explanation of this could be that the electron-donating hydroxy group in catalyst **3** affects the reaction *via* facilitating formation of a copper(III) intermediate by interaction between the metal and the oxygen atom of TBHP, according to the proposed mechanism (Scheme 1).

In order to test the optimized reaction conditions, they were applied to the epoxidation of two aromatic substituted alkenes: *cis*-stilbene and styrene. The obtained results are presented in Tables 3 and 4. In the work with *cis*-stilbene, the major product was *trans*-stilbene oxide with 21.1% conversion and 85.3% selectivity with the very low conversion to *cis*-stilbene oxide and *trans*-stilbene of 3.5 and 0.1%, respectively. This could be due to the fast conversion of *cis*-stilbene to the *trans*-isomer with higher thermal stability to form *trans*-stilbene oxide under these conditions. For the reaction of styrene, very good selectivity (>99.0%) and conversion values (91.3%) were achieved.

Epoxidation of olefins is a diastereospecific process using typical peroxide reagents as the source of an oxygen atom. However, for the epoxidation of *trans*-stilbene under conventional heating and heating–ultrasonic conditions with catalyst **1** (0.6 mol %), *cis*-stilbene and *cis*-stilbene oxide formation, and for the epoxidation of *cis*-stilbene under the optimized reaction conditions, *trans*-stilbene and *trans*-stilbene oxide formations were observed. There are several possible reasons for this moderate stereospecificity in the literature.[18,30]

On the basis of the product distribution in this catalytic experiment, relevant literature data,[31,32] and UV-Vis spectra (Fig. 2) a mechanism for the oxidative process can be proposed (Scheme 1). The copper(II) complexes **1**–**3** form (*tert*-butylperoxy)copper(III) compounds by binding the oxygen of TBHP. After the cleavage of *trans*-stilbene oxide, copper(III) intermediate forms the initial copper(II) compound by leaving the *tert*-butoxy group.

UV-Vis spectroscopy is a suitable technique to explain the mechanism of some catalytic reactions. With this

Table 2. Oxidation of *trans*-stilbene in EtOAc with TBHP and catalysts **1–3**
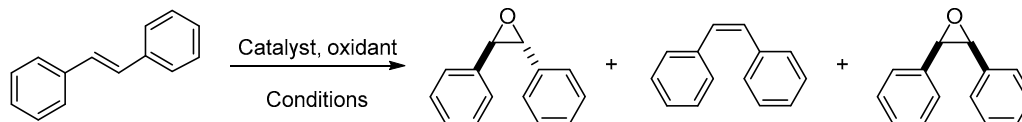
Conditions*/catalyst	Catalyst, mol %	Conversion, %**	Selectivity, %			
			trans-stilbene oxide	*cis*-stilbene	*cis*-stilbene oxide	TOF
HR/	–	9.1	>99.0	–	–	–
UR/	–	10.3	77.5	18.0	4.5	–
HR/**1**	0.6	42.0	74.5	11.8	13.6	10.0
UR/**1**	0.6	50.9	87.5	2.0	10.5	12.1
HR/**2**	0.6	42.1	>99.0	–	–	10.0
UR/**2**	0.6	50.4	>99.0	–	–	12.0
HR/**3**	0.6	59.2	>99.0	–	–	14.1
UR/**3**	0.6	68.3	>99.0	–	–	16.3
HR/**1**	1.0	55.6	>99.0	–	–	7.9
UR/**1**	1.0	60.7	>99.0	–	–	8.7
HR/**2**	1.0	43.5	>99.0	–	–	6.2
UR/**2**	1.0	59.7	>99.0	–	–	8.5
HR/**3**	1.0	60.1	>99.0	–	–	8.6
UR/**3**	1.0	69.3	>99.0	–	–	9.9

* HR and UR stand for reactions at conventional heating and heating–ultrasonic conditions, respectively.
** Determined by GC-MS. Conversion to target product (*trans*-stilbene oxide).

Table 3. Oxidation of *cis*-stilbene under the reaction conditions optimized for *trans*-stilbene*
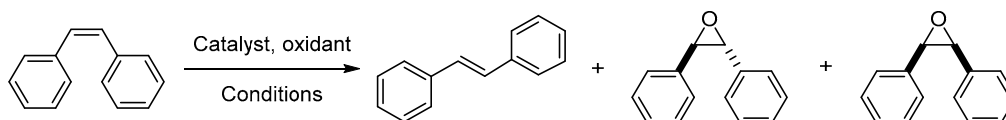
Catalyst **3**, mol %	Conversion, %**	Selectivity, %			
		trans-stilbene	*trans*-stilbene oxide	*cis*-stilbene oxide	TOF
–	6.2	–	–	> 99.0	–
1.0	3.5	0.4	85.3***	14.2	0.5

* *cis*-Stilbene (0.22 mmol), 70% TBHP (0.44 mmol), ethyl acetate (4 ml), temperature 75°C, ultrasound, time 7 h.
** Conversion to target product (*cis*-stilbene oxide).
*** Conversion to *trans*-stilbene oxide is 21.1%.

technique electron transfers between orbitals or bands of molecules can be investigated. The detection of the changes in these transition bands provides important information on the reaction mechanism.[33] In order to follow the interaction between copper(II) complexes and TBHP which are precursors of copper(III) intermediate according to the proposed mechanism (Scheme 1), the ethyl acetate solution of catalyst **3** (0.4 mM) was treated with TBHP under heating–ultrasonic reaction conditions.

Table 4. Oxidation of styrene at the optimum reaction conditions*

Catalyst **3**, mol %	Conversion, %**	Selectivity, styrene oxide, %	TOF
–	62.6	> 99.0	–
1.0	91.3	> 99.0	13.0

* Styrene (0.22 mmol), 70% TBHP (0.44 mmol), ethyl acetate (4 ml), temperature 75°C, ultrasound, time 7 h.
** Conversion to target product (styrene oxide).
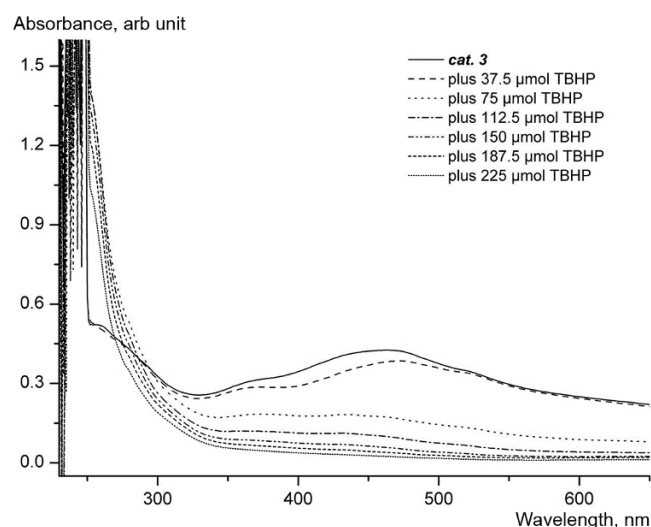
Figure 2. UV-Vis spectra of catalyst **3** and the reactivity of catalyst **3** with TBHP.

The course of the reaction was monitored by UV-Vis spectroscopy (Fig. 2). Ethyl acetate solution of TBHP (1.2 ml, 187.5 mM) was added in portions (0.2 ml, 37.5 µmol) and a spectrum of a sample (0.2 ml) of the reaction mixture was recorded after every addition and waiting for 15 min. The first addition was resulted in a bathochromic shift for the n–π* and ligand-to-metal (L–M) transition bands (to 373 and 474 nm, respectively) with coordinating oxygen, and after the subsequent additions all the transitions (π–π*, L–M, and n–π*; at 262, 367, and 464 nm, respectively in ethyl acetate) slowly became weaker and disappeared as expected. These results are in accord with previous reports[34,35] and the formation of the peroxo copper(III) intermediate species in the suggested mechanism.

In summary, it was found that three different azo- and bisazopyrazol-5-one-based copper(II) catalysts are all active in the catalytic oxidation of *trans*-stilbene. All catalysts are soluble in ethyl acetate under heating, but easy recovery of the catalyst is available from the reaction mixture. The catalysts can be used without further decomposition at 75°C. The catalysts are all active under heating with and without simultaneous ultrasonic treatment, but ultrasonic irradiation gives rise to higher yields of *trans*-stilbene oxide. These results, once more, show the importance of sonochemistry in organic synthesis, especially for catalytic reactions. The catalytic potential in ethyl acetate of these complexes is high in terms of selectivity and conversion compared with the other solvents used: chloroform, tetrahydrofuran, *N,N*-dimethylformamide, and dioxane. The catalytic oxidation of *trans*-stilbene is found to range between 42.0–69.3% conversion, where the major oxidation product is *trans*-stilbene oxide. Two of the catalysts are water soluble, therefore, work to extend their applicability toward catalytic oxidations under green conditions is in progress.

Experimental

Electronic spectra in the 200–400 nm range (200–800 nm for the mechanism determination work) were obtained on a Shimadzu UV 1800 spectrophotometer. Gas chromato-mass spectrometry (GC-MS) analysis was performed on a Shimadzu QP2010 instrument operating in the split mode (ratio 10:1) using Restek/Rtx®-5 30 m × 0.25 mm column and chromatographic grade helium as the carrier gas. In GC calculations, all peaks amounting to at least 0.5% of the total products were taken into account. All reactions were carried out in a two-necked glass flask fitted with a water condenser. The ultrasonic reactions were performed in a Bandelin-Sonorex Super RK 100(H) ultrasonic cleaner with a frequency of 35 kHz and a total power of 320 W. The reaction flask was located in the water bath of the equipment. All reagents and solvents were supplied from Sigma-Aldrich or Merck in the highest purity grade available and used without further purification. 70% TBHP in water was used as the oxidant.

Blank experiment of *trans*-stilbene oxidation. *trans*-Stilbene (40 mg, 0.22 mmol) and TBHP (56.4 mg, 0.44 mmol) were dissolved in ethyl acetate (4 ml), and the reaction mixture was heated to 75°C for 7 h with stirring in an oil bath or ultrasonic bath. For the analysis, the reaction mixture sample (0.1 ml) was diluted to 1 ml and 0.05 ml was taken in a GC-MS sequential injection flask and completed to a volume of 2 ml with ethyl acetate or acetonitrile.

Catalytic experiment of *trans*-stilbene oxidation. The appropriate catalyst **1**–**3** (1.32 µmol (0.6 mol %) or 2.2 µmol (1 mol %)) was added to a solution of *trans*-stilbene (40 mg, 0.22 mmol) and TBHP (56.4 mg, 0.44 mmol) in ethyl acetate (4 ml). The reaction mixture was heated to 75°C for 7 h with stirring in an oil bath or ultrasonic bath. The reaction mixture of ethyl acetate was left cooling to room temperature. The catalyst precipitated upon the evaporation of the solvent and filtered off. The solid was rinsed with an appropriate cold solvent (2×3 ml). For the analysis, the sample of the liquid layer (0.1 ml) was diluted to 1 ml and 0.05 ml was taken in a GC-MS sequential injection flask and completed to a volume of 2 ml with ethyl acetate or acetonitrile.

Catalytic experiment of *trans*-stilbene oxidation with different solvents (chloroform, tetrahydrofuran, *N,N*-dimethylformamide, and dioxane). Catalyst **3** (1.1 mg, 1.32 µmol, 0.6 mol %) was added to a solution of *trans*-stilbene (40 mg, 0.22 mmol) and TBHP (56.4 mg, 0.44 mmol) in solvent (4 ml), and the reaction mixture was heated to 75°C for 7 h with stirring in an oil bath. For the analysis, the reaction mixture sample (0.1 ml) was diluted to 1 ml and 0.05 ml was taken in a GC-MS sequential injection flask and completed to a volume of 2 ml with ethyl acetate or acetonitrile.

Catalytic oxidation of *cis*-stilbene and styrene. Catalyst **3** (1.84 mg, 2.2 µmol, 1.0 mol %) was added to a solution of *cis*-stilbene (40 mg, 0.22 mmol) or styrene (22.88 mg, 0.22 mmol) and TBHP (56.4 mg, 0.44 mmol) in ethyl acetate (4 ml). The reaction mixture was heated to 75°C for 7 h in an ultrasonic bath. The reaction mixture was filtered and, for the analysis, 0.1 ml of the filtrate was diluted to 1 ml and 0.05 ml was taken in a GC-MS sequential injection flask and completed to a volume of 2 ml with ethyl acetate or acetonitrile.

Supplementary information file, containing GC chromatograms and mass spectra of the reaction mixture in experiments and UV-Vis spectra according to the reaction time determination, is available at the journal website at http://link.springer.com/journal/10593.

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