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An Improved Iron-Catalyzed Epoxidation of Aromatic and Aliphatic Olefins with Hydrogen Peroxide as Oxidant

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A convenient and practical method for the iron-catalyzed epoxidation of aromatic and aliphatic olefins is described. The iron catalyst system is generated in situ from iron trichloride hexahydrate, pyridine-2,6-dicarboxylic acid (H_2pydic), and benzylamines. By variation of the benzylamine ligand, a variety of aliphatic and aromatic olefins were oxidized in high yield (up to 96 %) and good-to-excellent selectivity in the presence of hydrogen peroxide as the terminal oxidant.

Introduction

The epoxidation of olefins is an important synthetic method in organic chemistry as well as for the chemical industry. With respect to generality, it still remains challenging to discover catalytic epoxidations that allow efficient and selective reactions for both aromatic and aliphatic olefins.[1,2] In general, state-of-the-art epoxidations should run under environmentally benign reaction conditions with inexpensive catalysts by using sustainable terminal oxidants and simple operation protocols.[3] Traditionally, stoichiometric oxidants such as organic peracids have been applied in epoxidation reactions.[4] More recently, hydrogen peroxide has become one of the terminal oxidants of choice, because it produces only water as a byproduct and is advantageous regarding costs, safety, and storage.[5] With regard to catalysts, the use of Fe- or Mn-based complexes is attractive due to their price and low toxicity.[6,7] On the basis of ruthenium-catalyzed epoxidation of olefins with hydrogen peroxide,[8] we found that $FeCl_3 \cdot 6H_2O$ in combination with pyridine-2,6-dicarboxylic acid and pyrrolidine shows high reactivity and selectivity towards the epoxidation of mono- and disubstituted aromatic olefins.[9] Unfortunately, aliphatic olefins and highly substituted aromatic olefins were less reactive and selective under the conditions of our previous system. Hence, we are interested in improved Fe-catalyzed epoxidations, which can be applied to all classes of olefins.

Herein, we report the development of a general method for the epoxidation of a broad scope of olefins with hydrogen peroxide.

Results and Discussion

The key to the success of the Fe-catalyzed epoxidation is the use of pyridine-2,6-dicarboxylic acid (H_2pydic) as ligand. By studying the effect of the organic coligand on the epoxidation of cyclooctene as a model substrate, we observed a strong influence on the reactivity.

In Table 1 a small selection of the tested amines is shown. To our delight, the yield of cyclooctene oxide is improved from 4% (without ligand) up to 89% in the presence of *N*-(diphenylmethyl)methylamine (Table 1, entries 1 and 7). Notably, also our standard base pyrrolidine gave a significantly lower yield (16%) and selectivity with respect to epoxidation (Table 1, entry 2). Interestingly, in comparison to previous investigations the epoxidation of *trans*-stilbene with these amines did not display apparent differences in reactivity.[10] This can be attributed to the high reactivity of *trans*-stilbene. Hence, differences in the amine coligands did not show a significant influence on the reactivity. De novo analysis of the structural motif indicates that benzylamine is the important element in order to achieve high conversion. Strong coordinative 2-picolylamine gave inferior results as compared to benzylamine (Table 1, entries 5 and 8).[6a,6b,6d,6e] Slow dosing of hydrogen peroxide to the system increased the yield but is not the crucial factor. In fact, the addition of hydrogen peroxide can be performed within seconds, and cyclooctene oxide is obtained in 75% yield at 88% conversion. Further investigations on the concentration of the ligands showed 10 to 15 mol-% of the amine to be optimum. For better comparison and general applicability, the H_2O_2 addition time (1 h) and the amine concentration (12 mol-%) were maintained for all experiments. Replacement of H_2pydic with picolinic acid or quinaldic acid or the use of other iron sources resulted in a total loss of reactivity. Apparently, the H_2pydic component is essential in this system.[11]

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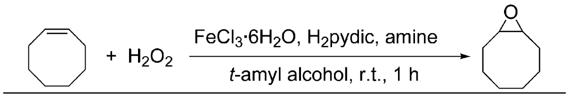
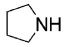
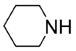
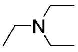
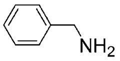
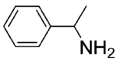
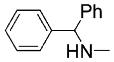
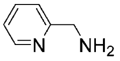
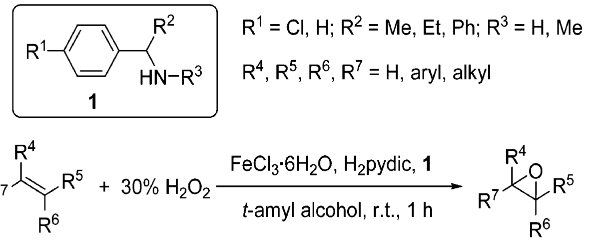
Table 1. Effect of the amine coligand on the epoxidation of cyclooctene.[a]



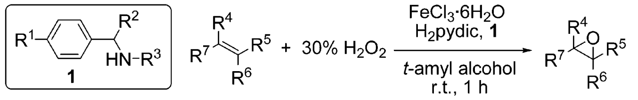
Entry	Amine	Conversion[b] [%]	Yield[b] [%]	Selectivity[c] [%]
1	–	7	4	57
2		23	16	70
3		33	21	64
4		44	32	73
5		56	43	77
6		65	51	78
7		100 (88)[d]	89 (75)	89 (85)
8		28	16	58

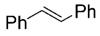
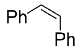
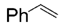
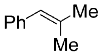
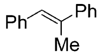
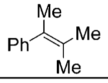
[a] Reaction conditions: In a test tube, $FeCl_3·6H_2O$ (0.025 mmol), H_2pydic (0.025 mmol), *tert*-amyl alcohol (9 mL), amine (0.060 mmol), cyclooctene (0.50 mmol), and dodecane (GC internal standard, 100 µL) were added in sequence at r.t. in air. To this mixture was added a solution of 30% hydrogen peroxide (114 µL, 1.0 mmol) in *tert*-amyl alcohol (886 µL) over a period of 1 h at r.t. by syringe pump. [b] Conversion and yield were determined by GC analysis. [c] Selectivity refers to the chemoselectivity of epoxide from olefin. [d] Addition of hydrogen peroxide within some seconds.



Scheme 1. Epoxidation of olefins with benzylamine derivatives **1**.

Table 2. Epoxidation of aromatic olefins with benzylamine derivative **1**.[a]



Entry	Substrate	R1	R2	R3	Conversion[b] [%]	Yield[b] [%]	Selectivity[c] [%]
1		Cl	Me	H	100	84	84
2		Cl	Me	H	48	24	50
3		Cl	Me	H	100	91	91
4		H	Ph	H	68	37	54
5		H	Ph	Me	95	68	72
6		H	Ph	Me	0	0	–

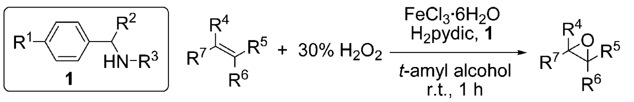
[a] Reaction conditions: In a test tube, $FeCl_3·6H_2O$ (0.025 mmol), H_2pydic (0.025 mmol), *tert*-amyl alcohol (9 mL), amine (0.060 mmol), olefin (0.50 mmol), and dodecane (GC internal standard, 100 µL) were added in sequence at r.t. in air. To this mixture was added a solution of 30% hydrogen peroxide (114 µL, 1.0 mmol) in *tert*-amyl alcohol (886 µL) over a period of 1 h at r.t. by syringe pump. [b] Conversion and yield were determined by GC analysis. [c] Selectivity refers to the chemoselectivity of epoxide from olefin.

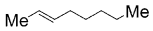
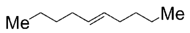
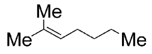
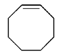
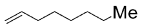
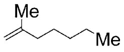
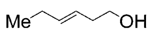
As shown in Table 1, it appears that benzylamine is a preferred structural element for the epoxidation of cyclooctene (Table 1, entries 5 to 7). For this reason we tested a selection of various commercially available benzylamines for the epoxidation of different classes of aromatic and aliphatic olefins (Scheme 1). Table 2 shows the epoxidation results for different substituted aromatic olefins. By applying the novel protocol, we could maintain the high reactivity and selectivity toward *trans*-stilbene and styrene as compared to our previous pyrrolidine system (Table 2, entries 1 and 3). Even though active catalysts for aliphatic olefins often lead to subsequent over oxidation reactions of the much-more reactive aromatic olefins, the benzylamine/H_2pydic/$FeCl_3$ system gives a general activity and good selectivity with respect to epoxidation in both of these classes of olefins.

Epoxidation of *cis*-stilbene proceeded in 24% yield in comparison to 8% yield with the pyrrolidine-based system.[10] In addition, we could also increase the yields for trisubstituted aromatic olefins such as *trans*-β-methylstilbene (Table 2, entry 5; from 21 to 68% yield, respectively) and 2-methyl-1-phenyl-1-propene (Table 2, entry 4; from 16 to 37% yield, respectively) in comparison to our previous system. However, the tetrasubstituted olefin 2-methyl-3-phenyl-2-butene gave no corresponding epoxide (Table 2, entry 6).

Aliphatic olefins work particularly well with the new catalyst system (Table 3). Internal olefins like *trans*-2-octene (Table 3, entry 1) and *trans*-5-decene (Table 3, entry 2) were oxidized in high yield and selectivity. Trisubstituted 2-methyl-2-heptene (Table 3, entry 3) and cyclic olefins (Table 3, entries 4 and 5) gave the corresponding epoxides in good yield. Terminal olefins are intrinsically poorly reactive substrates and catalytic methods for their epoxidation are limited.[6,7,12] Our system afforded 32% yield of 1-octene oxide, whereas 2-methyl-2-heptene was oxidized in 58% yield (Table 3, entries 6 and 7). Moreover, the iron catalyst system showed good chemoselectivity towards olefins in the presence of hydroxy and carboxyl groups (Table 3, entries 8 and 9).

Table 3. Fe-catalyzed epoxidation of aliphatic olefins with benzylamine derivative **1**.[a]



Entry	Substrate	R^1	R^2	R^3	Conversion[b] [%]	Yield[b] [%]	Selectivity[c] [%]
1		Cl	Me	H	100	87	87
2		H	Et	H	96	96	99
3		H	Et	H	100	58	58
4		H	Et	H	77	48	62
5		H	Ph	Me	100	89	89
6		Cl	Me	H	45	32	71
7		H	Ph	Me	67	58	87
8		Cl	Me	H	84	80	85
9	Elaidic acid	H	Et	H	82	80	98

[a] Reaction conditions: In a tube, $FeCl_3·6H_2O$ (0.025 mmol), H_2pydic (0.025 mmol), *tert*-amyl alcohol (9 mL), amine (0.060 mmol), olefin (0.50 mmol), and dodecane (GC internal standard, 100 μL) were added in sequence at r.t. in air. To this mixture was added a solution of 30% hydrogen peroxide (114 μL, 1.0 mmol) in *tert*-amyl alcohol (886 μL) over a period of 1 h at r.t. by syringe pump. [b] Conversion and yield were determined by GC analysis. [c] Selectivity refers to the chemoselectivity of epoxide from olefin.

Acetic acid is a well-known additive for the epoxidation of olefins with hydrogen peroxide by in situ formation of peracetic acid.[13] In contrast, addition of certain amounts of acetic acid to our catalyst system inhibited the conversion of 1-octene. Furthermore, to exclude the possibility of in situ formation of the alkyl hydroperoxide from *tert*-amyl alcohol, we used *tert*-BuOOH (70% aqueous) as an oxidant instead of hydrogen peroxide. Again no reactivity was observed for the epoxidation of cyclooctene. This indicates that *tert*-amyl hydroperoxide is not likely to be involved in the reaction and hydrogen peroxide is the only terminal oxidant in our system.

Conclusions

In conclusion, we developed an improved iron-catalyzed epoxidation, which can be performed under mild conditions with hydrogen peroxide as the terminal oxidant. The simple and practical catalyst system consists of iron trichloride hexahydrate, pyridine-2,6-dicarboxylic acid, and a benzylamine derivative. It was demonstrated that benzylamine is a preferred structural element for the coligand in this general epoxidation of aromatic and aliphatic olefins. The system showed good-to-excellent reactivity to mono-, di-, and trisubstituted aromatic olefins, as well as to internal di- and trisubstituted and functionalized aliphatic olefins. Noteworthy is that inactive aliphatic olefins can be oxidized in up to 96% yield. Currently, further efforts are underway to improve the protocol for tetrasubstituted aromatic and monosubstituted terminal aliphatic olefins and to investigate the mechanistic aspects of this reaction.

Experimental Section

General Remarks: All reagents were used as purchased from commercial suppliers (Aldrich, Fluka, Merck, etc.) without further purification. 2-Methyl-3-phenyl-but-2-ene (Table 2, entry 6) was synthesized according to literature procedures.[14] "30%" aqueous H_2O_2 from Merck was used as received. The peroxide content varied from 30% to 40% as determined by titration. GC analyses were performed with a Hewlett Packard HP 6890 model spectrometer. GC calibrations for alkenes and epoxides were carried out with authentic samples and dodecane as an internal standard.

General Procedure for the Epoxidation of Olefins: In a test tube, $FeCl_3·6H_2O$ (0.025 mmol), H_2pydic (0.025 mmol), *tert*-amyl alcohol (9 mL), amine (0.060 mmol), olefin (0.50 mmol) and dodecane (GC internal standard, 100 μL) were added in sequence at r.t. in air. To this mixture was added a solution of 30% hydrogen peroxide (aqueous, 114 μL, 1.0 mmol) in *tert*-amyl alcohol (886 μL) over a period of 1 h at room temperature by syringe pump. Conversion and yield were determined by GC analysis without further manipulations.

Acknowledgments

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