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Asymmetric Epoxidation of Terminal Alkenes with Hydrogen Peroxide Catalyzed by Pentafluorophenyl Pt^{II} Complexes

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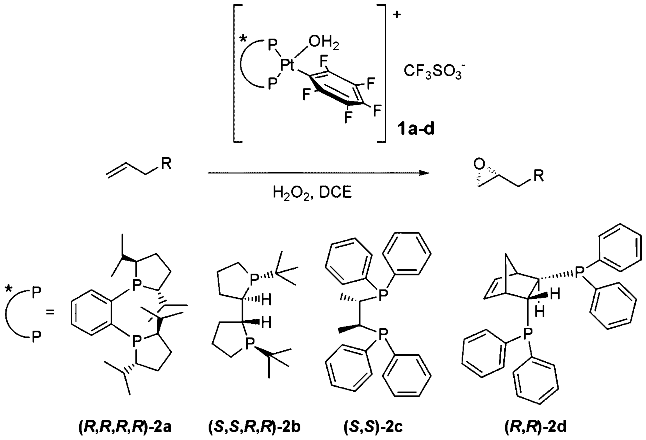
Homogeneous catalytic asymmetric epoxidation (AE) is a well-studied process that has been thoroughly investigated over the years and whose state of the art has been recently reviewed.[1] The discovery of the Ti^{IV}-diethyl tartrate (DET) catalytic system developed by Sharpless[2] for the stereoselective epoxidation of allylic alcohols has been a major landmark in AE. The substrate scope of the reaction was further extended by Jacobsen[3] and Katsuki[4] with Mn^{III}−Salen complexes to the asymmetric epoxidation of unfunctionalized di- and trisubstituted alkenes. More recently electron-poor C═C double bonds such as those in enones have been asymmetrically epoxidized under nucleophilic oxidation conditions.[5,1b] While the AE of styrene derivatives can be performed with several metal catalysts ranging from chiral iron and manganese porphyrins[6] to Ru^{III},[7] to organic catalysts,[8] simple terminal unfunctionalized alkenes are still challenging substrates for direct AE[9] because of their intrinsically low reactivity toward electrophilic oxidation, along with the difficulty to control the prochiral faces of the simply monosubstituted double bond.

The need of a different approach as far as the metal catalyst is concerned (capable of widening the substrate scope), is witnessed also by two recent examples, both employing Ti^{IV} catalysts,[10,11] and successfully tested only toward 1-octene with moderate yields and ee up to 82%. Similar substrate limitation in terminal alkene epoxidation is shown also by cytochrome P450, monooxygenases, and chloroperoxidases,[12] so that the only viable way to industrial production of enantioenriched terminal epoxides is hydrolytic kinetic resolution of racemates catalyzed by Co^{III}−Salen complexes.[13]

Thus far, all catalysts reported in the literature have aimed at oxidant activation with little or no interaction between the metal center and the alkene. Requirements for a successful AE of terminal alkenes seem to be: (i) a new catalyst design activating the substrate instead of the oxidant, hence, changing the role between electrophile and nucleophile in the system, (ii) a wide substrate scope, and (iii) a clean oxidant. In this respect hydrogen peroxide is gaining increasing attention[14] due to its many advantages, such as a relatively low cost, safe handling, high atom-economy, and waste-avoidance with water being the only byproduct.[15]

Recently, we have reported the synthesis, the catalytic activity, and the selectivity of Pt^{II} complexes in the epoxidation of terminal alkenes with one equivalent of hydrogen peroxide under mild conditions.[16] Herein we report the remarkable results observed in the AE of terminal alkenes with hydrogen peroxide catalyzed by a chiral version of the above-mentioned complexes with general formula $[(P{-}P)Pt(C_6F_5)(H_2O)]OTf$ **1** (P−P = chiral diphosphine ligands) (Scheme 1).[17] To the best of our knowledge this is the most versatile, active, and enantioselective system thus far developed for the AE of terminal, unfunctionalized alkenes.[18]

Scheme 1. Asymmetric Epoxidation of Terminal Alkenes with Hydrogen Peroxide Catalyzed by Pt^{II} Chiral Complexes **1a**−**d**



In Table 1 are reported the results for the AE of 4-methyl-1-pentene with catalysts **1a**−**d** characterized by a range of sterical and electronic properties but all forming a five-membered ring with the metal center. This property generates the most active catalysts as observed in the achiral version of the reaction.[16] Chiral alkyl diphosphines **2a** and **2b** lead to poorly active catalysts with moderate enantioselectivity (entries 1, 2), while bis-aryl diphosphines ligands **2c** and **2d** lead to active and enantioselective catalysts (entries 3−6) demonstrating that tuning the electronic and sterical properties of the catalyst is a key issue.

With catalyst **1c** we explored the substrate scope of the reaction, as reported in Table 2. Styrene was not epoxidized, while propene proved to be a suitable substrate, high yields being observed when performing the reaction at −10 to −25 °C (entries 1, 2). In all reactions reported in this work, epoxide was the only oxidation product. The length of the alkyl chain had a mild effect on selectivity with increase from propene to pentene and hexene (entries 1, 3, and 7), followed by a decrease for longer alkenes (entries 9 and 10). Analogously, increase in ee was observed for branched terminal alkenes when the substitution is closer to the double bond (entries 5 and 6). These data suggest the existence of a strong steric effect in the enantioselective epoxidation, as should be expected by considering that the active site of the complex is surrounded by aromatic rings. Allylbenzene derivatives proved to be suitable substrates, the electron density of the aromatic ring causing a marked negative effect on the activity but a positive effect on the enantioselectivity. A maximum 87% ee was observed for safrole (entry 16).

To further explore the potentials of catalyst **1c** with hydrogen peroxide as oxidant, we investigated the AE of substrates containing both a terminal and an internal double bond. The results reported in Table 3 are impressive: for all three dienes investigated, the epoxidation occurred exclusively at the terminal double bond with

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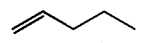
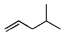
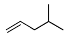
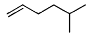
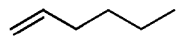
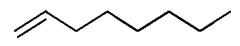
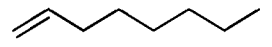
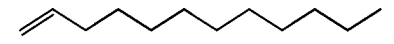
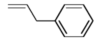
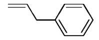
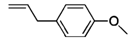
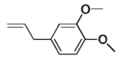
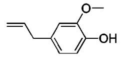
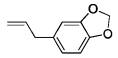
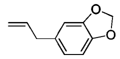
Table 1. Catalytic Asymmetric Epoxidation[a] of 4-Methyl-1-pentene with Hydrogen Peroxide Mediated by Chiral Pt^{II} Catalysts **1a−d**

entry	catalyst	*T* (°C)	time (h)	yield[b] (%)	ee[c] (%)	abs. config.[d]
1	**(*R*,*R*, *R*,*R*)-1a**	−10	48	5	49	(*S*)
2	**(*S*,*S*,*R*,*R*)-1b**	−10	48	4	36	(*S*)
3	**(*S*,*S*)-1c**	20	4	56	58	(*R*)
4	**(*S*,*S*)-1c**	−10	48	60	75	(*R*)
5	**(*R*,*R*)-1d**	20	6	58	59	(*S*)
6	**(*R*,*R*)-1d**	−10	48	71	72	(*S*)

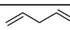
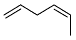
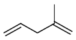
[a] Experimental conditions: Substrate 0.83 mmol, H_2O_2 0.83 mmol cat. 0.016 mmol (2%), solvent 1 mL dichloromethane (DCM). [b] Yield determined by GC analysis. [c] ee determined by CSP-GC on a β-cyclodex column. [d] Absolute configuration assigned from the GC elution order in β-cyclodex column.

Table 2. Catalytic Asymmetric Epoxidation[h] of Terminal Olefins with Hydrogen Peroxide Mediated by Pt^{II} Chiral Catalyst **1c**

Entry	Substrate	T (°C)	Time (h)	Yield[a] (%)	ee[b] (%)	Abs. Config.[c]
1		-10	24	98[d]	58	(*R*)-(+)
2		-25	24	78[d]	64	(*R*)-(+)
3		-10	24	99	74	(*R*)
4		-10[e]	48	57	72	(*R*)
5		-10[f]	48	63	78	(*R*)
6		-10	20	77	68	(*R*)
7		-10	20	48	83	(*R*)
8		20	5	76	64	(*R*)
9		-10	48	88	79	(*R*)
10		-10	48	81	71	(*R*)
11		20	24	75	66	(*R*)-(-)
12		-10	48	79	75	(*R*)-(-)
13		-10	48	45	76	(*R*)-(-)
14		-10	48	45	82	(*R*)-(-)
15		-10	48	27	84	(*R*)
16		-10	24	64	87	(*R*)
17		-10[g]	24	70	83	(*S*)

[a] Yield determined by GC analysis. [b] ee determined as reported in supplementary information. [c] Absolute configuration assigned as reported in Supporting Information. [d] Yield determined by ^1H NMR integration. [e] Solvent dichloroethane. [f] Solvent chloroform. [g] Catalyst **1d** was employed. [h] Experimental conditions as in Table 1.

Table 3. Catalytic Asymmetric Epoxidation[f] of Dienes with Hydrogen Peroxide mediated by **1c**

Entry	Substrate	T (°C)	Time (h)	Yield[a] (%)	Terminal epoxide/ Internal Epoxide[b]	ee[c] (%)	Abs. Config.[d]
1		-10	48	93	100/0	63	(*R*)
2		-10	48	96	100/0	86	(*R*)
3		-10	48	66	100/0[e]	98	(*R*)

[a] Yield determined by GC analysis. [b] Determined by ^1H NMR integration. [c] ee determined as reported in Supporting Information. [d] Absolute configuration assigned as reported in Supporting Information. [e] Monosubstituted/disubstituted epoxide. [f] Experimental conditions as in Table 1.

complete regioselectivity and ee up to 98%. To the best of our knowledge, any other metal catalyst reported in the literature would lead to the electrophilic asymmetric epoxidation of the more electron-rich double bond.[1]

In conclusion, new Pt^{II} chiral catalysts were developed for AE of terminal alkenes with environmentally friendly hydrogen peroxide as oxidant, resulting in the production of the corresponding terminal epoxides with moderate to good yields, ee up to 98%, and complete regioselectivity in the case of dienes. The key role on this behavior is played by the choice of Pt^{II} as the metal center and $-C_6F_5$ as ligand, imparting the proper electronic properties to the metal, while at the same time, increasing the rigidity and steric hindrance of the complexes.[19] This property explains the strong steric effect observed with different substrates. Investigation on the mechanism of the epoxidation reaction as well as in depth analysis of selectivity issues are currently underway.

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Supporting Information Available: Full experimental procedures and characterization data for complexes **1a**, **1b**, and **1d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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