5 available *in four steps* from commercially available materials represents a most direct synthetic intermediate for their synthesis.

Acknowledgment. We thank the National Institutes of Health for support of this work.

Registry No. 1 (R = CH_3), 40815-75-6; **3a**, 90554-78-2; **3b**, 90554-75-9; **4a**, 95999-44-3; **4b**, 95999-45-4; **5**, 95999-46-5; **8a**, 95999-47-6; **8b**, 95999-48-7; **9**, 95999-49-8; ClCOCH=CHCH=$CHCH_3$, 90554-82-8; $ClCOCH{=}CHCH_3$, 10487-71-5; acetoxybutadiene, 1515-76-0; butadiene, 106-99-0.

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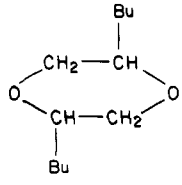
Ferric Chloride Induced Activation of Hydrogen Peroxide for the Epoxidation of Alkenes and Monoxygenation of Organic Substrates in Acetonitrile

Summary: In dry acetonitrile anhydrous $Fe^{III}Cl_3$ activates H_2O_2 for the efficient epoxidation of alkenes and the monoxygenation of alkanes, alcohols, ethers, aldehydes, thioethers, and sulfoxides.

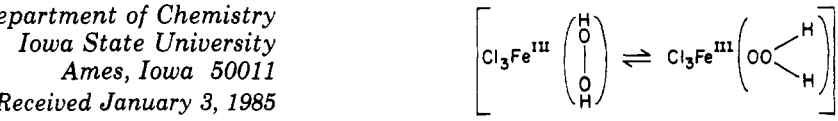
Sir: The recent observation[1] that iron(II) in ligand-free acetonitrile activates hydrogen peroxide to act as a monoxygenase and dehydrogenase (but *not* as an initiator of radical reactions via Fenton chemistry)[2] has prompted the consideration of other iron salts. Here we report that anhydrous ferric chloride ($Fe^{III}Cl_3$) in dry acetonitrile (MeCN) activates hydrogen peroxide to epoxidize alkenes and to monoxygenate or dehydrogenate other organic substrates.

Table IA summarizes the conversion efficiencies and product distributions for a series of alkene substrates subjected to the $Fe^{III}Cl_3$–H_2O_2/MeCN system. The extent of the $Fe^{III}Cl_3$-induced monoxygenations is enhanced by higher reaction temperatures and increased concentrations of the reactants (substrate, $Fe^{III}Cl_3$, and H_2O_2). For 1-hexene (representative of all of the alkenes) a substantial fraction of the product is the dimer of 1-hexene oxide, a disubstituted dioxane.[3]



With other organic substrates (RH) $Fe^{III}Cl_3$ activates H_2O_2 for their monoxygenation; the reaction efficiencies and product distributions are summarized in Table IB.[4] In the case of alcohols, ethers, and cyclohexane a substantial fraction of the product is the alkyl chloride, and with aldehydes [PhCH(O)] the acid chloride represents one-half of the product. In the absence of substrate the $Fe^{III}Cl_3$/MeCN system catalyzes the rapid disproportionation of H_2O_2 to O_2 and H_2O. Within the time constraints for the experiments (<20 min) there is no net reaction between H_2O_2 and the substrates or solvent in the absence of the $Fe^{III}Cl_3$ catalyst.

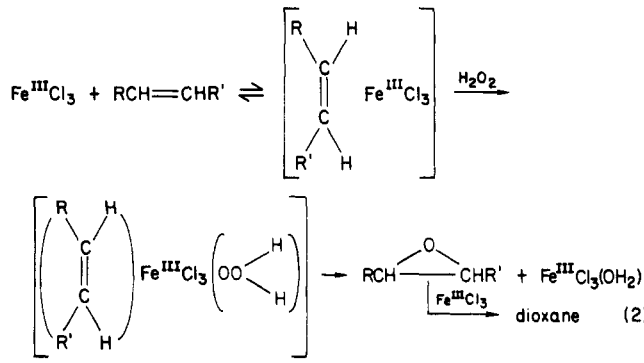
The activation of H_2O_2 by $Fe^{III}Cl_3$, which is an exceptionally strong Lewis acid and electrophilic center,[5] probably involves the initial formation of at least two reactive forms of an $Fe^{III}Cl_3$(HOOH) acid–base adduct that are in dynamic equilibrium (eq 1). We propose that this adduct



(1)

stimulates the disproportionation of H_2O_2 via concerted transfer of the two hydrogen atoms from a second H_2O_2. This dehydrogenation of H_2O_2 is a competitive process with the $Fe^{III}Cl_3$–substrate–H_2O_2 reactions. The controlled introduction of dilute H_2O_2 into the $Fe^{III}Cl_3$–substrate solution limits the concentration of H_2O_2 and ensures that the substrate–H_2O_2 reaction can be competitive with the second-order disproportionation process. The substrate reaction efficiencies in Table I appear to be proportional to the relative rates of reaction for the $Fe^{III}Cl_3$–H_2O_2 adduct with substrates and H_2O_2. The mode of activation of H_2O_2 by $Fe^{III}Cl_3$ is likely to be analogous to that by $Fe^{II}(MeCN)_4^{2+}$;[1] both are strong electrophiles in ligand-free dry MeCN and induce H_2O_2 to monoxygenate organic substrates.

The epoxidation of alkenes (Table IA) appears to involve an O-atom transfer from the end-on configuration of the $Fe^{III}Cl_3$(HOOH) adduct. The electrophilicity of $Fe^{III}Cl_3$ should promote the initial activation of the alkene bond prior to the binding of H_2O_2 (eq 2). The resulting epoxides



(2)

are rapidly dimerized to dioxanes. A control experiment has demonstrated that the complete conversion of an alkene to its epoxide is precluded; the more complete the conversion the higher the fraction of dioxane in the product mixture. With the cyclohexadienes and the stilbenes (PhCH=CHPh), the $Fe^{III}Cl_3$–H_2O_2/MeCN system promotes their dehydrogenation via a parallel catalytic process (Table IA), which may be equivalent to that for H_2O_2.

The present electrophilic activation of H_2O_2 by $Fe^{III}Cl_3$ for the epoxidation of olefins is much more facile and efficient than that by base in aqueous or methanolic sol-

(1) Sugimoto, H.; Sawyer, D. T. *J. Am. Chem. Soc.* **1984**, *106*, 4283.
(2) Walling, C. *Acc. Chem. Res.* **1976**, *9*, 175.
(3) Independent experiments confirm that $Fe^{III}Cl_3$ in dry MeCN catalyzes the rapid dimerization of epoxides to dioxanes.
(4) For all of the experiments summarized in Table I, the $Fe^{III}Cl_3$ catalyst remains completely in the Fe(III) state and there is no evidence for radical processes or for attack of the solvent. In dry MeCN the reduction potential for the $Fe^{III}Cl_3/Fe^{II}Cl_3^-$ couple is +0.46 V vs. NHE, and for the $Fe^{III}Cl_4^-/(Fe^{II}Cl_3^- + Cl^-)$ couple is +0.34 V.
(5) Donor solvents and ligands neutralize the acidity of $Fe^{III}Cl_3$. The addition of Cl^- to the $Fe^{III}Cl_3$–RH–H_2O_2/MeCN reaction system promotes formation of $Fe^{III}Cl_4^-$, which does not activate H_2O_2 for its disproportionation or for the monoxygenation of substrates and does not catalyze the dimerization of epoxides.

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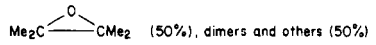
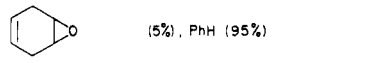
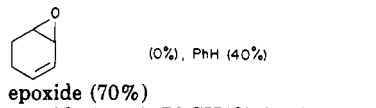
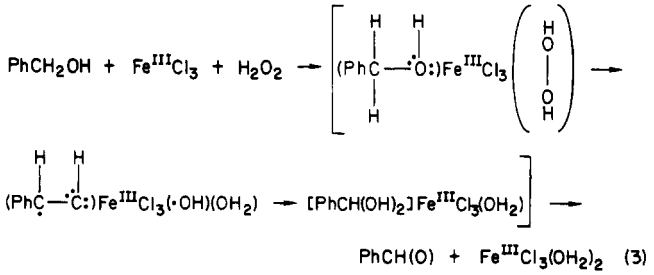
Table I. Products and Conversion Efficiencies for the Ferric Chloride ($Fe^{III}Cl_3$) Induced Oxygenation/Dehydrogenation of Olefins and Organic Substrates (RH) by H_2O_2 in Acetonitrile

substrate (RH)	reactn convn[a,b] efficiency, %	products[c]
	A. Olefins (−5 °C, 10-min reaction times)	
blank (H_2O_2)	100	O_2, H_2O
1-hexene	10	epoxide (1-hexene oxide) (71%), dimer (dioxane) (10%), others (19%)
1-hexene (+5 °C)[d]	23	epoxide (55%), dimer (15%), others (30%)
1-hexene (+25 °C)[e]	55	epoxide (0%), dimer (75%), others (25%)
1-hexene (+5 °C, $2H_2O_2$)[d,f]	45	epoxide (35%), dimer (25%)
1-octene	60	epoxide (53%), dimer (10%)
cyclohexene	25	epoxide (45%), dimer (30%)
cyclohexene (−20 °C)[g]	50	epoxide (36%), dimer (5%)
cyclohexene ($Fe^{III}Cl_4^-$)[h]	11	epoxide (60%), dimer (2%)
$Me_2C{=}CMe_2$	40	 (50%), dimers and others (50%)
1,4-cyclohexadiene	60	 (5%), PhH (95%)
1,3-cyclohexadiene	45	 (0%), PhH (40%)
$PhOCH_2CH{=}CH_2$ (20 min)[i]	10	epoxide (70%)
$PhCH{=}CH_2$ (20 min)[i]	15	epoxide (80%), PhCH(O) (5%)
PhCH=CHMe	8	epoxide (81%), PhCH(O) (8%)
cis-PhCH=CHPh	49	cis epoxide (40%), trans epoxide (17%), PhCH(O) (14%), PhC≡CPh (29%)
cis-PhCH=CHPh ($Fe^{III}Cl_4^-$)[h]	36	cis epoxide (48%), trans epoxide (16%), PhCH(O) (17%), PhC≡CPh (10%)
trans-PhCH=CHPh	42	epoxide (17%), PhCH(O) (37%), PhC≡CPh (7%)
trans-PhCH=CHPh ($Fe^{III}Cl_4^-$)[h]	40	PhCH(O) (44%), PhC≡CPh (26%)
	B. Other Substrates (+5 °C, 20-min reaction times)	
cyclohexanol	52	cyclohexanone (88%)
$PhCH_2OH$	63	PhCH(O) (51%), $PhCH_2Cl$ (21%), PhC(O)OH (14%), PhC(O)Cl (14%)
$PhCH_2OCMe_3$	56	PhCH(O) (72%), $PhCH_2Cl$ (11%), PhC(O)OH (3%), PhC(O)Cl (14%)
PhCH(O)	75	PhC(O)OH (55%), PhC(O)Cl (45%)[j]
$PhCH_2Ph$	10	PhC(O)Ph (85%)
$PhCH_3$ (25 °C)[e]	2	$PhCH_2OH$, PhCH(O), PhC(O)Cl, PhC(O)OH, cresols
PhH	trace	PhOH
cyclohexane	22	cyclohexyl chloride (45%), cyclohexanol (40%), cyclohexanone (15%)
Ph_2S	58	Ph_2SO (100%)
Ph_2SO	60	Ph_2SO_2 (100%)
Ph_3P	80	Ph_3PO (100%)
PhC≡CPh (40 min)[k]	30	PhC(O)C(O)Ph (70%), [PhCH(O), PhC(O)Cl, PhC(O)OH] (30%)

[a] RH and $Fe^{III}Cl_3$ (1.0 mmol of each) combined in 10–20 mL of dry MeCN, followed by the slow addition of 1 mmol of H_2O_2 [1 M H_2O_2 (98%) in MeCN]. [b] Percentage of substrate converted to products. [c] After the indicated reaction time, the product solution was quenched with water, extracted with diethyl ether, and analyzed by capillary gas chromatography and GC-MS. [d] Reaction at +5 °C. [e] Reaction at +25 °C. [f] 2 mmol of H_2O_2 added. [g] Reaction at −20 °C. [h] An equivalent (1 mmol) of $(Me_4N)Cl$ present; $Fe^{III}Cl_3 + Cl^- \rightleftharpoons Fe^{III}Cl_4^-$. [i] 20-min reaction time. [j] Hydrolysis of PhC(O)Cl to PhC(O)OH was less than 2% for reaction and analysis conditions. [k] 40-min reaction time.

vents (50–80% yields after reaction times of 3–40 h).[6-8]

The results of Table IB indicate that the $Fe^{III}Cl_3$(HO-OH) adduct monoxygenates selected alkanes, alcohols, and aldehydes. A mechanism that is consistent with this involves the homolytic scission of the HO–OH bond in the side-on configuration, induced by the bound substrate, and the subsequent abstraction by one HO· of an H-atom from the α-carbon and addition of the second HO· to the resulting carbon radical (eq 3). An analogous process ap-



$$PhCH(O) + Fe^{III}Cl_3(OH_2)_2 \quad (3)$$

pears to occur for the oxygenation of benzaldehyde to benzoic acid by the side-on $Fe^{III}Cl_3$(HOOH) adduct, but 50% of the product is the acid chloride.

This result indicates that the activated side-on complex has some hypochlorous acid (HOCl) character and can add a chlorine atom to the carbon radical that results from the H-atom abstraction by the ·OH group. This also occurs with alkanes, alcohols, and ethers (Table IB). Such chemistry is similar to the activation of chloride ion and H_2O_2 to HOCl by myeloperoxidase (a heme protein).[9,10]

Phosphines, dialkyl sulfides, and sulfoxides appear to be monoxygenated by the end-on configuration of the $Fe^{III}Cl_3$(HOOH) adduct in a manner that is analogous to that for the epoxidation of alkenes (see eq 2).

Acknowledgment. This work was supported by the National Science Foundation under Grant No. CHE-8212299. We are grateful to Dr. Richard Kondrat for assistance with the mass spectral analyses (the departmental VG-ZAB mass spectrometer facility was funded in part by the National Science Foundation).

Registry No. $CH_2{=}CH(CH_2)_3CH_3$, 592-41-6; $CH_2{=}CH(CH_2)_5CH_3$, 111-66-0; $(CH_3)_2C{=}C(CH_3)_2$, 563-79-1; $PhOCH_2CH{=}CH_2$, 1746-13-0; $PhCH{=}CH_2$, 100-42-5; $PhCH{=}CHCH_3$, 637-50-3;

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cis-PhCH=CHPh, 645-49-8; *trans*-PhCH=CHPh, 103-30-0; CH_2=$CH(CH_2)_5CH_3$ (epoxide), 2984-50-1; CH_2=$CH(CH_2)_5CH_3$ (oxide dimer), 95999-50-1; $(CH_3)_2\overline{COC}(CH_3)_2$, 5076-20-0; C_6H_6, 71-43-2; PhCHO, 100-52-7; PhCH=$CHCH_3$ (epoxide), 4436-22-0; PhCH=CHPh (*cis*-epoxide), 1689-71-0; PhCH=CHPh (*trans*-epoxide), 1439-07-2; PhC≡CPh, 501-65-5; $PhOCH_2\overline{CHOCH_2}$, 122-60-1; $Ph\overline{CHOCH_2}$, 96-09-3; $PhCH_2OC(CH_3)_3$, 3459-80-1; $PhCH_2Ph$, 101-81-5; $PhCH_3$, 108-88-3; Ph_2S, 139-66-2; Ph_2SO, 945-51-7; Ph_3P, 603-35-0; $PhCH_2OH$, 100-51-6; $PhCH_2Cl$, 100-44-7; $PhCO_2H$, 65-85-0; PhCOCl, 98-88-4; PhCOPh, 119-61-9; PhOH, 108-95-2; Ph_2SO_2, 127-63-9; Ph_3PO, 791-28-6; PhCOCOPh, 134-81-6; $\overline{CH_2OCH(CH_2)_3CH_3}$, 1436-34-6; cyclohexene, 110-83-8; 1,4-cyclohexadiene, 628-41-1; 1,3-cyclohexadiene, 592-57-4; cyclohexene epoxide, 286-20-4; (cyclohexene oxide)$_2$, 25500-50-9; 4,5-epoxy-1-cyclohexene, 6253-27-6; 3,4-epoxy-1-cyclohexene, 6705-51-7; cyclohexane, 110-82-7; cyclohexanol, 108-93-0; cyclohexyl chloride, 542-18-7; cyclohexanone, 108-94-1; 1-hexene oxide dimer, 96128-93-7.

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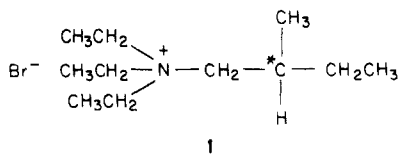
Chiral Phase-Transfer Catalysis. Enantioselective Alkylation of Racemic Alcohols with a Nonfunctionalized Optically Active Phase-Transfer Catalyst

Summary: Racemic *sec*-phenethyl alcohol and 1-phenyl-1-propanol can be alkylated to produce optically active methyl ethers in a phase-transfer-catalyzed reaction with dimethyl sulfate when the optically active quaternary ammonium salt **1** is used as the phase-transfer agent.

Sir: Recent literature reports have demonstrated the viability of conducting asymmetric syntheses using the principle of chiral phase-transfer catalysis.[1] Virtually all of the work reported in this area has dealt with the use of highly functionalized quaternary ammonium salts derived from cinchonidine, ephidrine, quinine, and most commonly cinchonine.[2] An elegant ion pairing scheme based on crystal structure data and molecular modeling studies has been invoked to explain functional group interactions in intimate ion pairs and the efficiency of this chiarl phase-transfer agents.[3] We report the first example of asymmetric induction in the phase-transfer-catalyzed alkylation of racemic alcohols employing the simple, nonfunctionalized, chiral quaternary ammonium salt **1**.



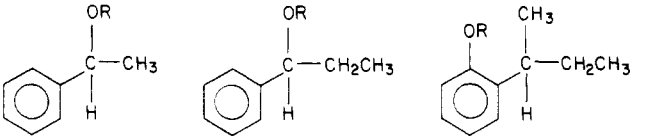
1

Table I. Methylation of *sec*-Phenethyl Alcohol in the Presence of 1[a]

solvent	methyl ether product **5** $[\alpha]^{25}_D$, deg	ee, %	yield, %	uncatalyzed yield[b] of **5**, %
pentane	+18.4	48	84	0.0
toluene	+15.8	39	88	0.5
dichloromethane	+3.2	8	87	5.0

[a] 1.0 mol % catalyst on the basis of starting alcohol was used. [b] Yield of methyl ether after 1 h at 25 °C.

Alkylation of triethylamine with (*S*)-(+)-1-bromo-2-methylbutane, $[\alpha]^{25}_D$ +3.80° (acetonitrile), in refluxing acetonitrile for 24 h followed by evaporation to dryness and washing with ethyl acetate afforded a 91% yield of the optically active quaternary ammonium salt **1** $[\alpha]^{25}_D$ +3.15° (acetonitrile), as colorless needles, mp 97–98 °C.[4] The methylation of 1.0 equiv (4.88 g) of racemic **2** with 0.5



2, R = H
5, R = Me

3, R = H
6, R = Me

4, R = H
7, R = Me

equiv (2.52 g) of dimethyl sulfate in a two-phase system (50% aqueous NaOH, 10.0 g/pentane, 40.0 g) with 0.1 g (1.0 mol %) of **1** as a phase-transfer catalyst was performed at 25 °C for 1 h. Neutralization of the reaction mixture with 8 mL of 50% NH_4OH followed by aqueous extraction, drying (Na_2SO_4), and evaporation produced an 84% yield of the crude methyl ether as an oil contaminated with a trace of acetophenone.[5] Purification by column chromatography (CH_2Cl_2/silica gel) afforded (*R*)-(+)-1-phenyl-1-methoxyethane (**5**) in 48% ee in 75% overall yield.[6] Attempts to verify the enantiomeric excesses by ^1H NMR with chiral shift reagents were unsuccessful as the enantiomers of **5** were not resolved. However, the unreacted alcohol recovered from the aqueous phase by acidification afforded (*S*)-(−)-*sec*-phenethyl alcohol in 40% ee. These results were most surprising in view of the absence of functional groups in the chiral phase-transfer catalyst **1**. In control reactions, only unreacted starting material was recovered in the absence of a phase-transfer catalyst while the product obtained from a methylation reaction employing tetrabutylammonium bromide as a catalyst exhibited no optical activity. Similarly, the methylation of racemic 1-phenyl-1-propanol (**3**) in the presence of **1** afforded, after isolation and purification, a 73% yield of 1-phenyl-1-methoxypropane (**6**), $[\alpha]^{25}_D$ +13.6° (acetonitrile). In contrast the methylation of racemic 2-*sec*-butylphenol (**4**) in the presence of the chiral phase-transfer catalyst yielded only the racemic methyl ether **7**. We first thought that this result might suggest that the chiral center located three bonds away from the reaction site had reduced the ability of the catalyst to differentiate

(1) (a) Saigo, K.; Koda, H.; Nohira, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3119. (b) Julia, S.; Ginabreda, A. *Tetrahedron Lett.* **1979**, 2171. (c) Colonna, S.; Fornasier, R.; Pfeiffer, U. *J. Chem. Soc., Perkin Trans. 1* **1978**, 8. (d) Colonna, S.; Fornasier, R. *J. Chem. Soc., Perkin Trans. 1* **1978**, 371. (e) Julia, S.; Ginebreda, A.; Guixer, J. *J. Chem. Soc., Chem. Commun.* **1978**, 742. (f) Balcells, J.; Colonna, S.; Fornasier, R. *Synthesis* **1976**, 266.

(2) (a) Wynberg, H.; Helder, R.; Hummelen, J.; Laane, R.; Wiering, J. *Tetrahedron Lett.* **1976**, 1831. (b) Wynberg, H.; Hummelen, J. *Tetrahedron Lett.* **1978**, 1089. (c) Julia, S.; Ginebreda, A.; Guixer, J.; Tomas, A. *Tetrahedron Lett.* **1980**, 21, 3709.

(3) Dolling, U.; Davis, P.; Grabowski, E. *J. Am. Chem. So.* **1984**, *106*, 446.

(4) ^1H NMR ($CDCl_3$): δ 1.25 (18 H, m), 3.25 (2 H, d), 3.55 (6 H, q); ^{13}C NMR (ppm) 8.70, 11.07, 19.75, 29.09, 29.70, 46.13, 54.04, 64.12; high resolution atom bombardment ionization mass spectra, M (*m/e*) calcd, 172.2065, obsd 172.2044, quaternary ammonium ion.

(5) Optically pure (*R*)-(+)-1-phenyl-1-methoxyethane, $[\alpha]^{25}_D$ +38.3° (acetonitrile), was synthesized from optically pure (*R*)-(+)-*sec*-phenethyl alcohol, $[\alpha]^{25}_D$ +39.5° (acetonitrile), via phase-transfer-catalyzed methylation with dimethyl sulfate.

(6) The isolated product was identified by comparison with an authentic sample and gave satisfactory spectral analyses. Enantiomeric excesses were measured by optical rotation and comparison with an authentic sample.

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