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Synthetic Applications of Nonmetal Catalysts for Homogeneous Oxidations

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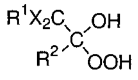
I. Introduction

The majority of bulk organic products contain oxygen functionalities. Many of these are produced in chemical and petrochemical industries by direct oxyfunctionalization of hydrocarbon feedstock. For this purpose, the homogeneous catalytic oxidation is widely applied in the manufacture of oxygenated hydrocarbon products. Epoxides, alcohols, and ketones, the direct oxidation products of hydrocarbons, may be transformed into a variety of valuable oxyfunctionalized derivatives, and therefore, they serve as important building blocks in organic synthesis.[1] Unquestionably, the selective and catalytic oxidation of organic substrates is an important process of timely interest.[2]

The usual oxidation catalyst contains a transition metal; the latter activates a suitable oxygen source for the oxyfunctionalization. Such a catalyst must withstand hostile oxidizing conditions, which may curtail the catalytic activity due to oxidative degradation of the metal complex. Alternatively, one may perceive the use of oxidatively resistant organic substances, which mediate catalytic homogeneous oxidations without the need of metal complexes. One of the major advantages of metal-free organic catalysts is their better environmental acceptance compared to transition-metal catalysts because most of the latter are toxic. Indeed, in recent years such nonmetal organic oxidants have become available and have been extensively employed in oxidations, most prominently the perhydrates **I**,[3] the dioxiranes **II**,[4−13] the oxaziridines **III**,[14−17] the oxaziridinium salts **IV**,[18,19] and oxoammonium salts **V**.[20,21] These oxidants are generated in situ under catalytic conditions from the corresponding organic catalysts by reaction with an appropriate oxygen source, most usually hydrogen peroxide and its derivatives. The specific organic catalysts are, respectively, the α-halocarbonyl compounds **1**, ketones **2**, imines **3**, iminium salts **4**, and nitroxyl radicals **5**. The present review covers the homogeneous catalytic oxidations by these catalysts **1**−**5** and emphasizes the synthetic applications rather than mechanistic detail of these nonmetal catalytic systems in oxidation chemistry. Stoichiometric oxidations by the oxidants **I**−**V** are only mentioned in the rosettes of the individual cases to provide an overview on the scope of these nonmetal oxidants.



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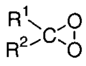

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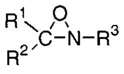

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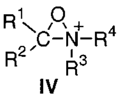

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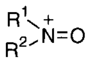

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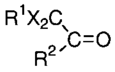

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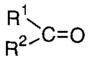

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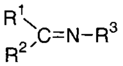

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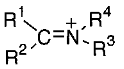

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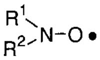

5

For the first time the pertinent literature is compiled on this rapidly developing facet of oxidation chemistry, which allows a detailed comparison of the

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[†] University of Würzburg.
[‡] Indian Petrochemicals Corporation Limited.

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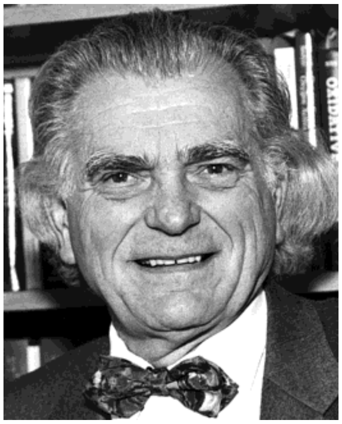
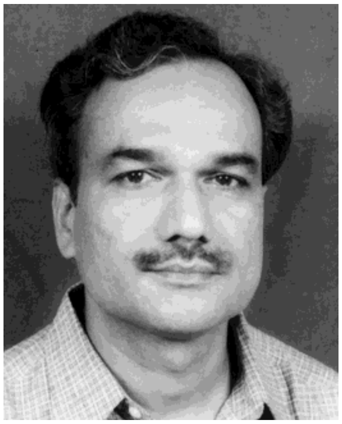


Waldemar Adam, born in 1937 in the Ukraine, was raised in Germany and received his education in the United States (Ph.D. degree 1961, MIT, with F. D. Greene). He started his academic career in 1961 at the University of Puerto Rico (Rio Piedras), where he was promoted to Full Professor in 1970. In 1980 he was appointed to the Chair of Organic Chemistry at the University of Würzburg. He has received numerous prizes and coauthored more than 860 scientific publications.

Chantu R. Saha-Möller was born in 1955 in Bangladesh and received his University education in Germany (Dr. rer. nat. degree 1986, University of Hamburg, with W. Walter). In 1986–1987 he worked as a postdoctoral associate with E. Block (SUNY Albany, NY). Subsequently, he joined Professor Adam's research group (University of Würzburg), and since 1994 he has been a permanent research associate. He is a coauthor of over 150 scientific publications.



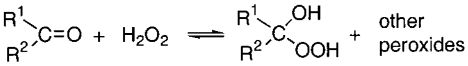
Pralhad A. Ganeshpure, born in 1954 in Maharashtra, India, received his Ph.D. degree in 1979 from the Nagpur University (India), under the guidance of Professor G. Bagavant. During 1979–1981 he worked as a postdoctoral fellow with Professor R. Stevenson at Brandeis University, Waltham, MA. From 1991 to 1993 he was a Guest Scientist and Alexander-von-Humboldt Fellow in Professor Adam's research group, University of Würzburg, Germany. Presently, he is Manager (Research and Development) at the Research Center of the Indian Petrochemicals Corporation Limited in Vadodara (India), which he joined in 1983. His main research interest is homogeneous catalytic oxidation reactions.

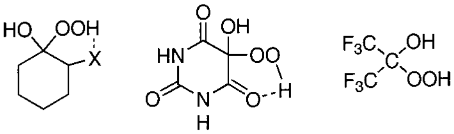
efficacy, utility, and benefits of such nonmetal catalysts among themselves and with appropriate metal-based catalysts. The review covers the literature through February 2001.

II. Perhydrate-Mediated, Ketone-Catalyzed Oxidations

Perhydrates **I**, also called α-hydroxy hydroperoxides, are mainly prepared by the addition of hydrogen peroxide to an aldehyde or a ketone, by the photooxygenation of nontertiary alcohols, and by the ozonolysis of alkenes in the presence of water or alcohols.[3] Of these, the addition of hydrogen peroxide to aldehydes and ketones is the more general and direct method for the generation of perhydrates (Scheme 1). Most of such perhydrates do not persist isolation and revert to the carbonyl precursor and hydrogen peroxide.[22] Exceptions are the isolable ketone perhydrates shown below.[3] Presumably, intramolecular hydrogen bonding is responsible for the persistence of these functionalized perhydrates. That the perhydrate of hexafluoroacetone (**Ia**) may be isolated as such is not overly surprising, when it is realized that the corresponding hydrate requires distillation from P_2O_5 to release the ketone.[3]

Scheme 1





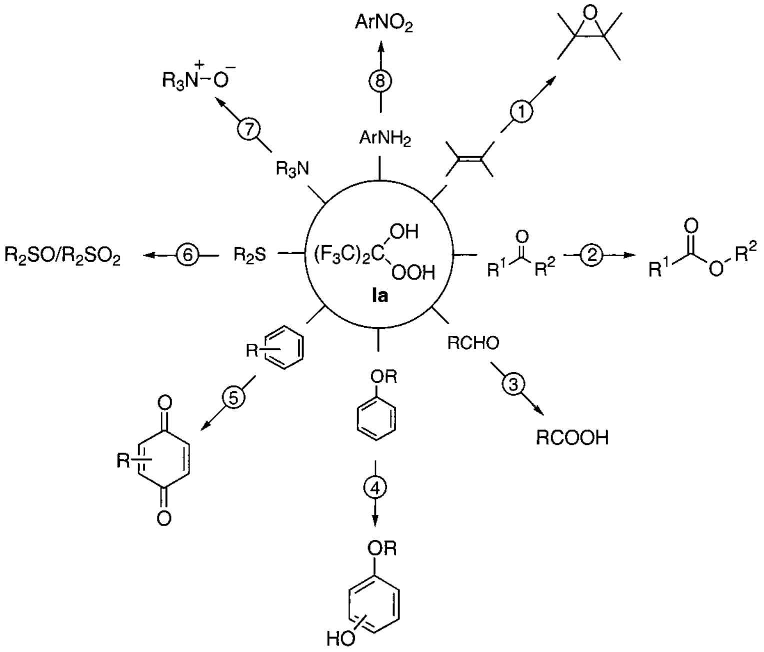
X = Cl, Br

Ia

Expectedly, the perhydrate **Ia** is a strongly electrophilic oxidant, which effectively oxyfuctionalizes a variety of organic compounds. Scheme 2 shows the scope of the oxidations performed by the perhydrate **Ia** in the form of a rosette, which includes catalytic as well as stoichiometric transformations. Although the focus in this review lies on *catalytic* activity, the *stoichiometric* cases have also been featured in the rosette to provide a complete overview of the oxidizing power of this most active perhydrate.

Perhydrate **Ia**, generated in situ, efficiently oxidizes unactivated olefins to epoxides (transformation 1 in Scheme 2).[3] Ketones are converted to esters[23] (transformation 2) and aldehydes to carboxylic acids[24] (transformation 3) by the Baeyer–Villiger reaction. Phenol, resorcinol, and anisole may be hydroxylated (transformation 4),[25,26] but under more strenuous conditions, phenol and alkyl-activated and polynuclear arenes may be oxidized completely to the respective quinones (transformation 5).[27] Perhydrate **Ia** also efficiently transfers oxygen to heteroatom substrates such as sulfides (transformation 6), which may be selectively and quantitatively oxidized to the corresponding sulfoxides or sulfones by employing

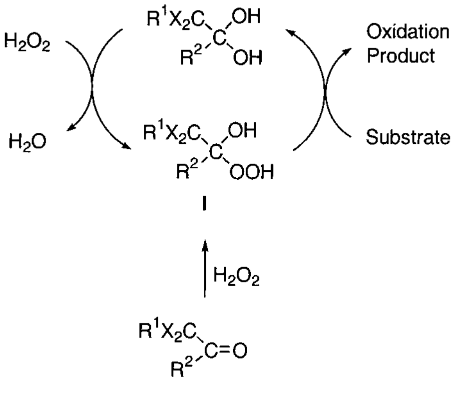
Scheme 2



either 1 or 2 equiv of H_2O_2 as the oxygen source.[28] Tertiary amines are oxidized to their *N*-oxides in nearly quantitative yields (transformation 7); this oxidation is performed selectively in the presence of CC double bonds.[28] The oxidation of primary aminobenzenes affords the respective nitroarenes (transformation 8).[23]

The catalytic cycle for perhydrate-mediated oxygen transfer is shown in Scheme 3. The process is initiated with the ketone hydrate and hydrogen peroxide by exchange of the hydroxy for the required hydroperoxy group to give the perhydrate oxidant under catalytic conditions. Subsequently, the perhydrate transfers an oxygen atom to the substrate to afford the desired oxidation product and the ketone hydrate is regenerated, which completes the catalytic cycle. The various catalytic oxidations by perhydrates shall now be considered in detail for the individual transformations.

Scheme 3



A. Epoxidations

1. Reactivity

Electron-deficient carbonyl compounds with α-halogen substituents efficiently catalyze the epoxidation of unactivated alkenes. Table 1 lists the aldehydes and ketones that have been used as catalysts for such epoxidation with hydrogen peroxide as the oxygen source. The pertinent literature is cited in the table and shall not be repeated in this text.

Trichloroacetaldehyde and its hydrate have been employed as catalysts (entries 1 and 2) as well as partially chlorinated acetone and chlorofluoroacetone (entries 3−5). Also, hexachloroacetone has been shown to catalyze the epoxidation of a variety of CC double bonds in steriodal compounds with high π-facial selectivity. Thus, the steroid (entry 6) with a 5,6 double bond gave the corresponding α epoxide in high yield. When two or three C═C bonds are present in the steroid molecule, the 5,10 double bond is regioselectively oxidized mainly to the α epoxide (entries 7−10).

Similarly, hexafluoroacetone catalyzes the epoxidation of acyclic, cyclic, and steroidal alkenes in a regio- and stereoselective manner (entries 12−18). More convenient is the direct use of hexafluoroacetone hydrate (commercially available as distillable liquid) rather than hexafluroacetone, which is a gas (bp −26 °C) at ambient temperature and must be laboriously liberated from its hydrate.[3]

Examples of the catalytic epoxidation by hexafluoroacetone hydrate are listed in entries 19−24. For allylic alcohols, only one example is cited (entry 20) as these are separately discussed in detail later in this section. The reaction exhibits regio- and stereoselectivity, as illustrated in the epoxidation of the steroidal dienes in entries 23 and 24. Although the weakly acidic hexafluoroacetone hydrate does not usually decompose epoxides, for acid-sensitive ones, it is advisable to buffer with sodium hydrogen phosphate. In this way, the acid-labile epoxide in entry 22 was prepared in high yield from the corresponding substrate.

Perfluoroheptadecan-9-one is an even more active catalyst than hexafluoroacetone, which catalyzes the

Table 1. Ketone-Catalyzed Epoxidation of Alkenes by Perhydrates with H_2O_2 as the Oxygen Source

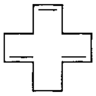
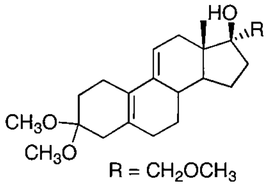
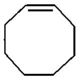
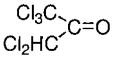
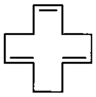
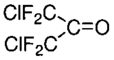
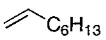
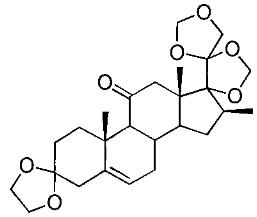
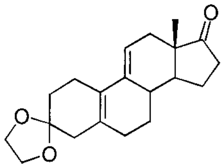
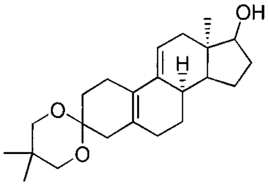
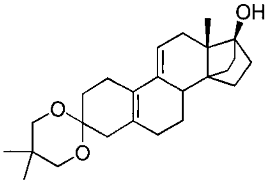
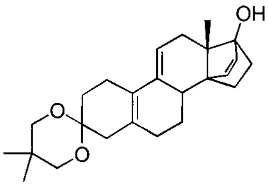
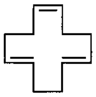
entry	catalyst (cat)	substrate (sub)	oxygen source (ox)	mole ratio cat:sub:ox	solvent	time (h)	temp (°C)	epoxide yield (%)	ref
1[a]	Cl_3CCHO		95% H_2O_2	1 : 5 : 5	-	8	60	95	29
2	$Cl_3CCH(OH)_2$	 R = CH_2OCH_3	30% H_2O_2	1 : 2.1 : 2.5	CH_2Cl_2	20	ca. 20	89[b]	30
3	$(Cl_2HC)_2C{=}O$		50% H_2O_2	1 : 5 : 10	$CHCl_3$	4	reflux	83	31
4[a]	 $(Cl_3C)(Cl_2HC)C{=}O$		95% H_2O_2	1 : 5 : 5	-	8	60	75	29
5	 $(ClF_2C)_2C{=}O$		50% H_2O_2	1 : 160 : 120	-	270	25	13	32
6	$(Cl_3C)_2C{=}O$		85% H_2O_2	1 : 4 : 6.5	CH_2Cl_2	96	20	80[c]	33
7	-"-		30% H_2O_2	1 : 2.4 : 6.7	CH_2Cl_2	72	ca. 20	76[b]	34
8	-"-		30% H_2O_2	1 : 11 : 17	CH_2Cl_2	12	ca. 20	47[b]	35
9	-"-		30% H_2O_2	1 : 2.6 : 4.3	CH_2Cl_2	81	ca. 20	81[d] (α/β 65:35)	36
10	-"-		30% H_2O_2	1 : 2.6 : 4.3	CH_2Cl_2	14	ca. 20	83[e]	36
11[a]	-"-		95% H_2O_2	1 : 5 : 5	-	8	60	86	29

Table 1 (Continued)

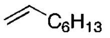
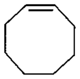
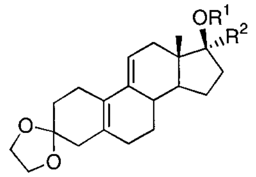
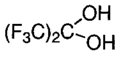
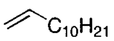
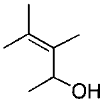
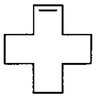
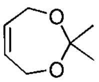
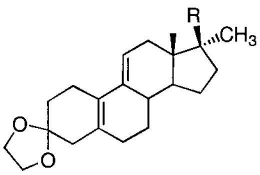
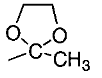
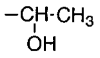
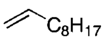
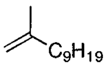
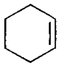
entry	catalyst (cat)	substrate (sub)	oxygen source (ox)	mole ratio cat:sub:ox	solvent	time (h)	temp (°C)	epoxide yield (%)	ref
12	$(F_3C)_2C{=}O$		50% H_2O_2	1 : 40 : 40	$(CF_3)_2CHOH$	8 min	60	25	32
13	-"-		100% H_2O_2	1 : 20 : 40	EtOAc	24	reflux	82	37
									
		R^1 R^2							
14	-"-	H H	30% H_2O_2	1 : 8 : 12	CH_2Cl_2	8-12	20	88^d (α/β 83:17)	38
15	-"-	COPh H	30% H_2O_2	1 : 6 : 12	CH_2Cl_2	8-12	20	94^d (α/β 77:23)	38
16	-"-	CH_2Ph H	30% H_2O_2	1 : 6 : 12	CH_2Cl_2	8-12	20	97^d (α/β 84:16)	38
17	-"-	CH_2OCH_3 H	30% H_2O_2	1 : 7 : 12	CH_2Cl_2	8-12	20	90^d (α/β 85:15)	38
18	-"-	$-CH_2CH_2O-$	30% H_2O_2	1 : 7 : 12	CH_2Cl_2	8-12	20	85^d (α/β 82:18)	38
19			90% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$	24	reflux	94	39
20	-"-		85% H_2O_2	1 : 20 : 40	CH_2Cl_2	5.5	reflux	95^f	40
21	-"-		90% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$	24	reflux	92	39
22	-"-		90% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$	24	reflux	83	39
									
23	-"-	R = 	85% H_2O_2	1 : 40 : 50	CH_2Cl_2	5	0-20	77^b	41
24	-"-	R =  $-CH(OH)-CH_3$	85% H_2O_2	1 : 40 : 50	CH_2Cl_2	5	0-20	$\sim 100^d$ (α/β 65:35)	41
25	$(C_8F_{17})_2C{=}O$		100% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$/ EtOAc (10:1)	18	reflux	72	37
26	-"-		100% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$/ EtOAc (10:1)	1.5	reflux	96	37
27	-"-		100% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$/ EtOAc (10:1)	2	reflux	92	37

Table 1 (Continued)

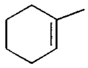
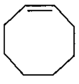
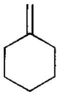
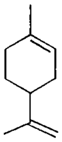
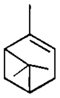
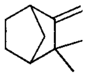
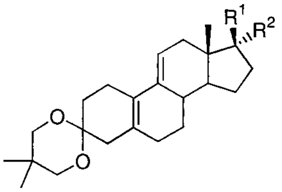
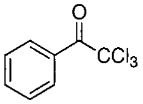
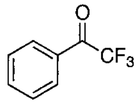
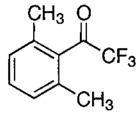
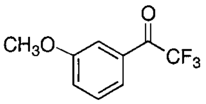
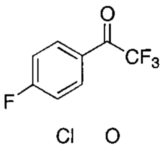
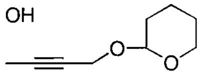
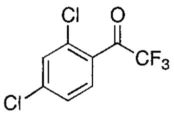
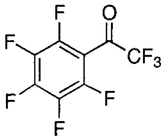
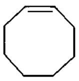
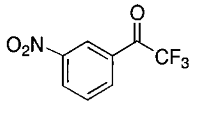
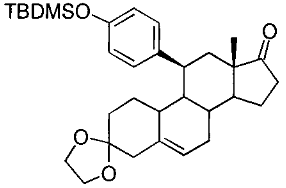
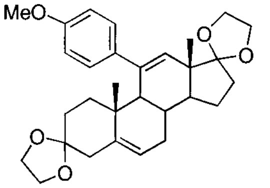
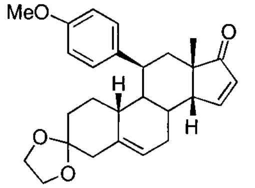
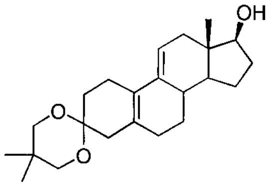
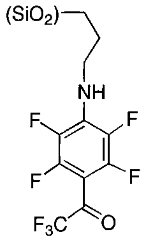
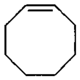
entry	catalyst (cat)	substrate (sub)	oxygen source (ox)	mole ratio cat:sub:ox	solvent	time (h)	temp (°C)	epoxide yield (%)	ref
28	-"-		100% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$/ EtOAc (10:1)	0.5	reflux	97	37
29	-"-		100% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$/ EtOAc (10:1)	2	reflux	100	37
30	-"-		100% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$/ EtOAc (10:1)	2	reflux	64	37
31	-"-		100% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$/ EtOAc (10:1)	0.5	reflux	72	37
32	-"-		100% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$/ EtOAc (10:1)	0.5	reflux	55	37
33	-"-		100% H_2O_2	1 : 20 : 40	$ClCH_2CH_2Cl$/ EtOAc (10:1)	1.5	reflux	49	37
									
34		R^1 = OH, R^2 = H	30% H_2O_2	1 : 1.8 : 15	CH_2Cl_2	17	40	71[b]	42
35		R^1 = OH, R^2 = H	30% H_2O_2	1 : 2.4 : 20	CH_2Cl_2	17	40	97[d] (α/β 89:11)	42
36		R^1, R^2 = O	30% H_2O_2	1 : 2.8 : 25	CH_2Cl_2	24	40	63[b]	42
37		R^1, R^2 = O	30% H_2O_2	1 : 2.3 : 18	CH_2Cl_2	16	40	78[b]	42
38		R^1 = OH R^2 = 	30% H_2O_2	1 : 1.6 : 20	CH_2Cl_2	18	40	72[b]	42
39		R^1, R^2 = O	30% H_2O_2	1 : 3.4 : 30	CH_2Cl_2	24	ca. 20	68[b]	42
40			100% H_2O_2	1 : 20 : 40	EtOAc	24	reflux	74	37

Table 1 (Continued)

entry	catalyst (cat)	substrate (sub)	oxygen source (ox)	mole ratio cat:sub:ox	solvent	time (h)	temp (°C)	epoxide yield (%)	ref
41			30% H_2O_2	1 : 2 : 8	CH_2Cl_2	120	25	82[c]	43
42	-"-		30% H_2O_2	1 : 2 : 8	CH_2Cl_2	6	ca. 20	94[c]	44
43	-"-		30% H_2O_2	1 : 2 : 9	CH_2Cl_2	60	25	53[c]	45
44	-"-		30% H_2O_2	1 : 2.5 : 9	CH_2Cl_2	3	ca. 20	84[d] (α/β 84:16)	42
45			60% H_2O_2	1 : 16 : 60	CH_3CN	24	80	78	46

[a] The configuration of the double bond in the substrate is not given. [b] 5α,10α-Epoxide. [c] 5α,6α-Epoxide. [d] 5(10)-Epoxide. [e] A mixture of 5α,10α- and 5*β*,10*β*-epoxides. [f] *Threo/erythro* 92:8.

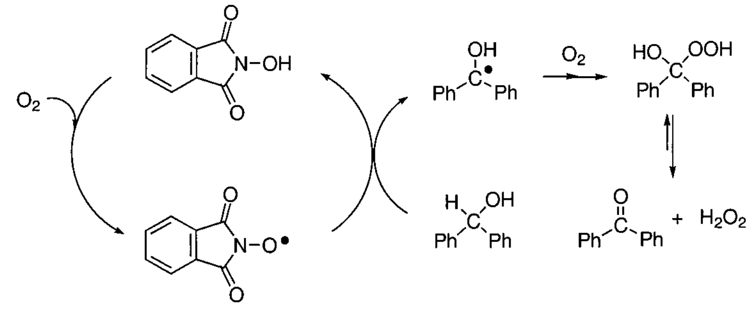
epoxidation of a variety of alkenes with anhydrous hydrogen peroxide in a dichloroethane–ethyl acetate mixture under reflux (entries 25–33). Terminal alkenes such as 1-decene (entry 25) react only slowly, but disubstituted (entries 26, 27, 29, 30, and 33) and trisubstituted (entries 28, 31, and 32) ones give the corresponding epoxides in high yields much faster (0.5–2 h). For limonene (entry 31), the trisubstituted endocyclic double bond is preferentially epoxidized, which reflects the regioselectivity of the electrophilic oxidants dimethyldioxirane and *m*-chloroperbenzoic acid.[47] The acid-sensitive epoxides α-pinene oxide (entry 32) and camphene oxide (entry 33) were obtained in moderate yields, but buffering with sodium hydrogen phosphate was required.

A special bonus is the fact that the ketone catalyst crystallizes out on cooling of the reaction mixture to 0 °C and may, thus, be recovered in up to 92% yield. Also, 60% aqueous hydrogen peroxide was employed with 2,2,2-trifluoroethanol as solvent, which gave moderate to high yields of the expected alkene epoxides; however, in this protocol the sodium hydrogen phosphate buffer is necessary in most of the cases to avoid decomposition of the epoxides.[37]

α,α,α-Trichloroacetophenone, α,α,α-trifluoroacetophenone, and its aryl-substituted derivatives have been used for the regio- and stereoselective epoxidation of olefinic double bonds of the steroids displayed in entries 34–44. 3-Nitro-α,α,α-trifluoroacetophenone (entries 41–44) was the most active catalyst for the selective catalytic epoxidation of such steroids. Expectedly, the enone double bond of the steroid in entry 43 was preserved, and exclusive epoxidation at the 5,6 position took place.

Recently, perfluoroacetophenone, immobilized on silica by a sol–gel method, has been used as the catalyst under heterogeneous conditions. The oxidation of *cis*-cyclooctene with this catalyst gave selectively the corresponding epoxide in high yield (entry 45); however, less nucleophilic alkenes such as 1-octene and 2-octene were converted poorly.[46] Although more reactive, the electron-rich alkenes such

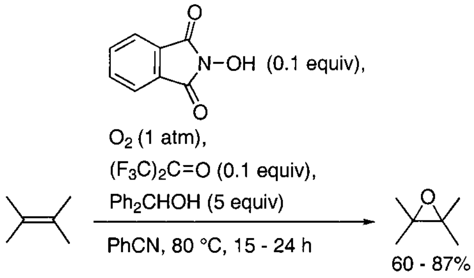
Scheme 4



as cyclohexene, 1-methylcyclohexene, and 2,3-dimethyl-2-butene showed a low selectivity for the epoxide due to the predominant formation of diols or pinacol-rearrangement products.

A clever way for the in-situ generation of hydrogen peroxide is shown in Scheme 4, in which molecular oxygen was allowed to react with benzhydrol in the presence of *N*-hydroxyphthalimide as the catalyst.[48] The in-situ-generated hydrogen peroxide converts alkenes to their respective epoxides, catalyzed by hexafluoroacetone. The reactions are performed with benzhydrol (5 equiv) in benzonitrile as solvent and require long reaction times (Scheme 5).

Scheme 5



The perhydrate epoxidations are usually performed in solvents such as dichloromethane, 1,2-dichloroethane, or ethyl acetate. Chlorinated hydrocarbons have been reported to stabilize the perhydrates.[49] 1,2-Dichloroethane and ethyl acetate are preferred because the exchange reaction between the ketone hydrate and hydrogen peroxide (Scheme 1) is faster under reflux conditions. Sometimes a mixture of these solvents is also used to facilitate solubility of a catalyst or a substrate. Also, the polar trifluoroethanol has been employed as solvent for such a purpose, but its high cost and environmental incompatibility limit its use in larger amounts. Nevertheless, trifluoroethanol activates hydrogen peroxide for oxygen transfer through hydrogen bonding,[50,51] and the epoxidation of electron-rich alkenes may be achieved in high yields.

2. Diastereoselectivity

To assess the diastereoselectivity of hexafluoroacetone perhydrate in catalytic epoxidations, a series of chiral allylic alcohols was utilized as a stereochemical probe (Scheme 6).[40,52,53] The observed diastereoselectivities are compared with those of the established oxidants *m*-CPBA and DMD (Table 2) to define the transition structure for the oxygen-transfer process.

Scheme 6

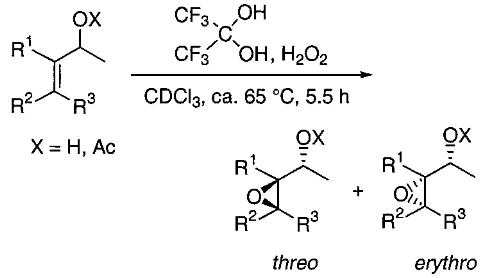
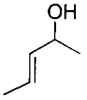
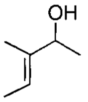
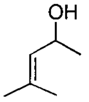
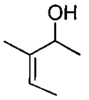


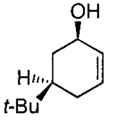
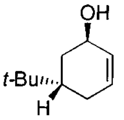
Table 2. Diastereoselectivities in the Catalytic Epoxidation of Chiral Allylic Alcohols by Hexafluoroacetone Perhydrate (HFAH/H_2O_2), *m*-Chloroperbenzoic Acid (*m*CPBA), and Dimethyldioxirane (DMD)

entry	substrate	convn	*threo: erythro* diastereoselectivity		
		(%)	HFAH/H_2O_2[a]	*m*CPBA[b]	DMD[c]
1		54	62:38	64:36	56:44
2		93	38:62	48:52	-
3		89	92:8	96:4	82:18
4		84	95:5	90:10	91:9

[a] Olefin (1 mmol), 85% H_2O_2 (2 mmol), HFAH (0.11 mmol), Na_2HPO_4 (2 mmol), $CDCl_3$ (5 mL), temp. 65 °C, 5.5 h, ref 40. [b] Ref 54. [c] Ref 55.

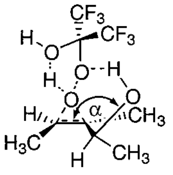
The chiral allylic alcohol without allylic strain (the double bond carries no α nor *β* substituents) shows expectedly a small *threo* selectivity (entry 1), while the substrate only with 1,2-allylic strain favors a slight *erythro* selectivity (entry 2). In contrast, a chiral allylic alcohol with 1,3-allylic strain showed a high *threo* preference (entry 3). When 1,2- and 1,3-allylic strain are in competition in one and the same molecule (entry 4), the epoxidation is still highly *threo*-selective, which clearly expresses the dominance of 1,3-allylic strain for *π*-facial control in the oxygen transfer. This *threo* stereoselectivity matches

Table 3. Diastereoselectivities in the Catalytic Epoxidation of Chiral Cyclohexenols by Hexafluoroacetone Perhydrate (HFAH/H_2O_2), *m*-Chloroperbenzoic Acid (*m*CPBA), and Dimethyldioxirane (DMD)

substrate	convn (%)	diastereoselectivity[a]		
		HFAH/H_2O_2[b]	*m*CPBA[c]	DMD[d]
 α ≈ 140°	49	94:6	96:4	82:18
 α ≈ 110°	47	70:30	84:16	58:42

[a] *cis:trans* ratios of the epoxides versus the hydroxy functionality. [b] Olefin (1 mmol), 85% H_2O_2 (2 mmol), HFAH (0.11 mmol), Na_2HPO_4 (2 mmol), $CDCl_3$ (5 mL), temp. 65 °C, 5.5 h, ref 40. [c] Ref 57. [d] Ref 55.

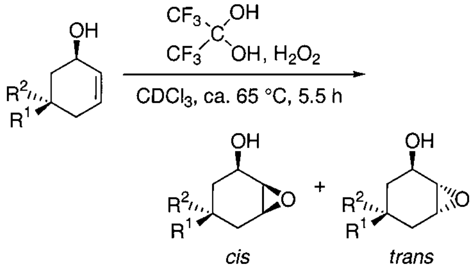
well with that reported for *m*-CPBA[54] and DMD.[55] Thus, the hydroxy-group directivity[56] for these three oxidants is similar, in which optimal hydrogen bonding between the oxygen-transfer agent and the allylic alcohol substrate operates for *threo* π-facial attack, as exhibited in the transition structure below.



TS for allylic alcohols

Also, chiral cyclic allylic alcohols were epoxidized in the same manner to assess the *syn:anti* selectivity as a function of the dihedral angle (α) between the allylic hydroxy group and the plane of the π system (Scheme 7). The comparative data in Table 3 show

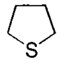
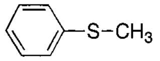
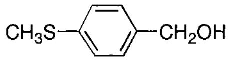
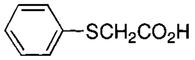
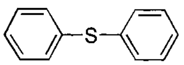
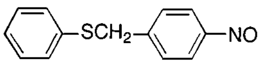
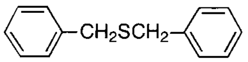
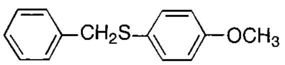
Scheme 7



	R^1	R^2
cis	*t*-Bu	H
trans	H	*t*-Bu

that a cis diastereoselectivity (relative to the hydroxy functionality) dominates in the epoxidation for the perhydrate, *m*-CPBA, and DMD.[40] Since for the *cis*/*trans*-diastereomeric pair of the *tert*-butyl-substituted cyclohexenol the perhydrate shows a more pronounced selectivity with the cis isomer, the larger dihedral angle (α = 140°) applies. This is in good agreement with the transition structure derived from the acyclic chiral allylic alcohols in Table 2.

Table 4. 1,1,1-Trifluoroacetone-Catalyzed Oxidation of Sulfides by H_2O_2 as the Oxygen Source[a]

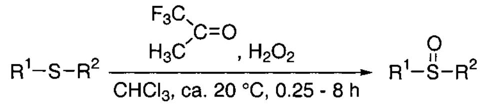
entry	sulfide	time (min)	sulfoxide yield (%)
1		15	98
2		90	94
3		90	92
4		150	80
5	*n*-C_4H_9–S–C_4H_9-*n*	15	98
6		480	96
7		300	95
8		90	98
9		120	93

[a] 35% aqueous H_2O_2 (1.12 equiv), 1,1,1-trifluoroacetone (0.11 equiv) in $CHCl_3$ at ca. 20 °C; complete consumption of the substrate, ref 58.

B. Heteroatom Oxidations

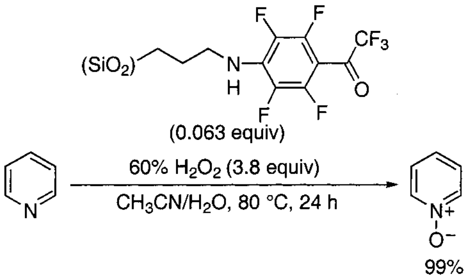
Although perhydrate **Ia** transfers an oxygen atom to sulfur in sulfides and to nitrogen in tertiary amines to give the corresponding oxides,[28] no catalytic examples appear to have been reported. Nevertheless, in principle it should be possible to use the ketones in the Table 1 as catalysts for these oxidations. 1,1,1-Trifluoroacetone catalyzes the oxidation of a variety of sulfides to their sulfoxides in high yields and selectivity (Scheme 8); the results are summarized in Table 4.[58] There is no overoxidation to the sulfones. Aliphatic sulfides react faster than those with aryl substituents. Recently, it has been demonstrated that the perhydrate derived from 2-bromocyclohexanone transfers its oxygen atom to sulfides to give the corresponding sulfoxides.[59]

Scheme 8



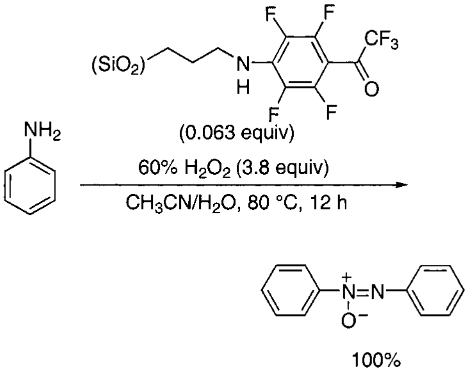
The silica-supported perfluoroacetophenone catalyzes the oxidation of pyridine to give *N*-oxide in nearly quantitative yield under heterogeneous conditions (Scheme 9).[46]

Scheme 9



2-Methylpyridine, 4-methylpyridine, quinoline, and 4-methylquinoline are also transformed to the corresponding *N*-oxides in high yields. Expectedly, electron-deficient 2,6-dichloropyridine is unreactive, while aniline is oxidized quantitatively to its diazene *N*-oxide (Scheme 10). Similarly, the corresponding diazene *N*-oxides have been obtained from 3-methylaniline, 2-ethylaniline, 3-trifluoromethylaniline, and 3-fluoroaniline,[46] while 4-hydroxyaniline and 3-nitroaniline afford the corresponding nitro derivatives quantitatively. However, 2-nitroaniline and 4-methoxy-2-nitroaniline do not react under these conditions.

Scheme 10



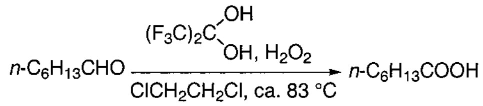
C. Arene Oxidations

Despite the fact that perhydrates oxidize arenes, which are activated by hydroxy and alkoxy groups, under stoichiometric conditions, catalytic examples are scarce.[3] We have developed a protocol for arene oxidations with hydrogen peroxide, catalyzed by hexafluoroacetone hydrate (Table 5).[27] Under these conditions, phenol is oxidized directly to benzoquinone (entry 1). The oxidation of durene gives duroquinone but in low yield (entry 2), while benzene does not react under these conditions. Naphthalene gave 1,4-naphthoquinone and 2-carboxycinnamic acid; the latter is probably formed by oxidative cleavage of the intermediary 1,2-naphthoquinone (entry 3). The oxidation of 1-methylnaphthalene afforded in good yields the industrially important 2-methyl-1,4-naphthoquinone (Vitamin K_3, an additive for animal feed), along with minor quantities of 6-methyl-1,4-naphthoquinone (entry 4). The primary oxidation products in the case of electron-rich arenes are more susceptible to further oxidation and, thus, lead exclusively to ring cleavage, as illustrated for 2-methoxynaphthalene (entry 5), which afforded in quite low yields 2-carboxycinnamic acid. Anthracene gave anthraquinone, but the major product was 9,9′-bianthryl-10,10′-dione (entry 6), while phenanthrene is oxidized to biphenyl-2,2′-dicarboxylic acid as the only product (entries 7).

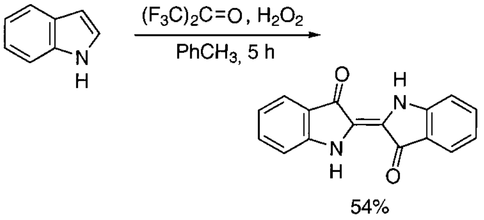
D. Miscellaneous Catalytic Oxidations

The oxidation of *n*-heptanol with hydrogen peroxide, catalyzed by hexafluoroacetone hydrate, gives heptanoic acid in 85% yield (Scheme 11).[24] The aldehyde oxidation with perhydrate **Ia** proceeds selectively in the presence of C=C bonds. The oxidation of indole by hydrogen peroxide in the presence of catalytic amounts of hexafluoroacetone leads to indigo in 54% yield (Scheme 12).[60]

Scheme 11



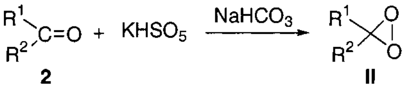
Scheme 12



III. Dioxirane-Mediated, Ketone-Catalyzed Oxidations

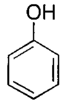
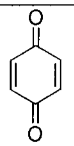
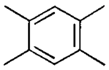
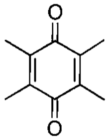
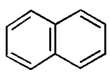
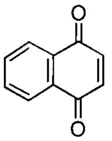
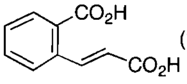
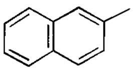
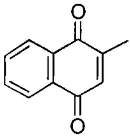
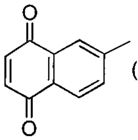
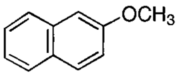
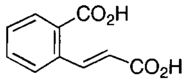
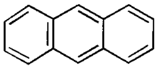
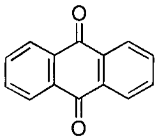
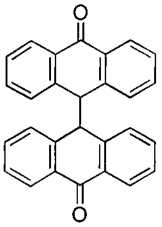
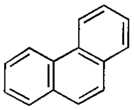
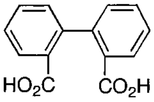
During the past decades, dioxiranes have risen from structural curiosities to very efficient and remarkably versatile oxidants.[4−13] These nonmetal peroxidic oxygen-transferring agents are readily prepared from suitable ketones and potassium monoperoxysulfate ($KHSO_5$), a low-cost industrial bulk chemical (trade names Oxone, Caroate, or Curox), under buffered conditions (Scheme 13). The oxidations may be performed either with in-situ-generated or with isolated (as solutions in the parent ketones) dioxiranes.[61−63] The latter procedure is properly suited for stoichiometric oxidations under strictly neutral conditions by which numerous acid- or base-sensitive or hydrolytically and thermally labile oxyfunctionalized products have been made available for the first time by this method.[64−70]

Scheme 13



The in-situ oxidation with dioxiranes is in principle a catalytic process, since the ketones are regenerated after oxygen transfer. Nevertheless, until recently, in most of the in-situ transformations with dioxiranes, the ketone mediators were used as solvent

Table 5. Oxidation of Arenes with H_2O_2 Catalyzed by Hexafluoroacetone Hydrate[a]

entry	substrate	convn (%)	products (% yield)[b]
1[c]		83	 (29)
2		58	 (19)
3		26	 (16)  (10)
4[d]		56	 (45)  (6)
5[e]		76	 (31)
6		90	 (22)  (47)
7		55	 (69)

[a] Substrate (20 mmol), H_2O_2 (70%, 100 mmol), hexafluoroacetone hydrate (4 mmol), 1,2-dichloroethane (5 mL), 70 °C, 4 h, ref 27. [b] On the basis of consumed substrate. [c] Reaction time 1 h. [d] At 45 °C and 3 h. [e] At 40 °C.

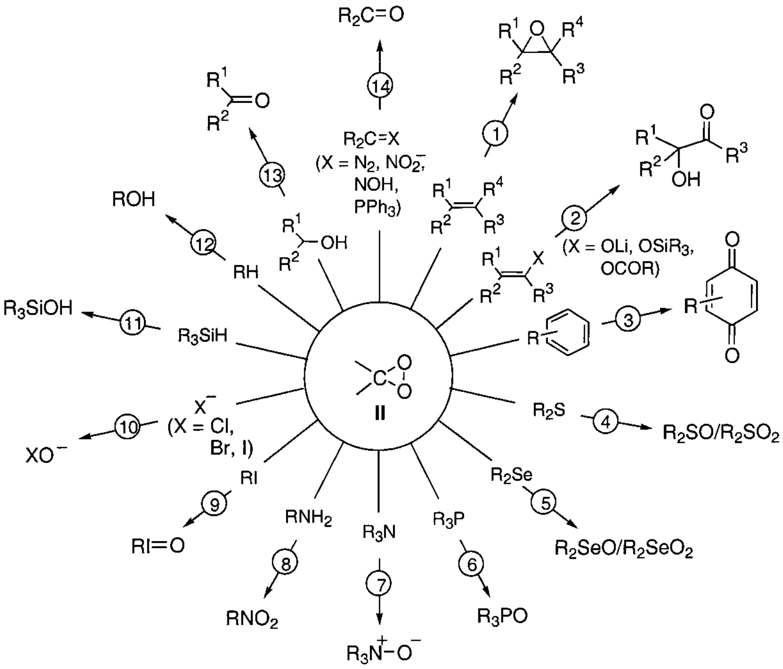
(for example, acetone and trifluoroacetone) or in stoichiometric and larger quantities. Fortunately, in the past few years, efficient in-situ methods have been developed for dioxirane-mediated oxidations, in particular epoxidations, by using catalytic amounts (<0.5 equiv) of ketones.[12,13] This review deals primarily with such catalytic dioxirane oxidations.

Although the main focus of this article lies on catalytic oxidations, an overview of the transformations performed by both isolated and in-situ-generated dioxiranes is displayed in the rosette of Scheme 14 to show the broad scope of these powerful oxidants. The pertinent literature for the transformations shown in Scheme 14 are cited in numerous reviews[4−13] on dioxirane chemistry, published during the past decade. These references are not repeated here, especially since in two very recent reviews[71,72] we compiled the dioxirane literature through March 2000.

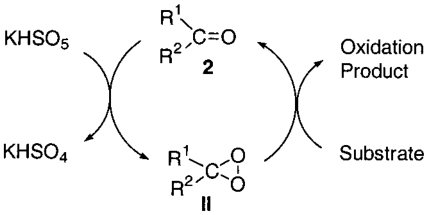
The oxyfunctionalizations in the rosette of Scheme 14 include the epoxidation of π systems (transformations 1 and 2), arene oxidation (transformation 3), heteroatom oxidations (transformations 4−8), halogen oxidations (transformations 9 and 10), oxygen-atom insertions into CH and SiH bonds (transformations 11 and 12), and oxidations of alcohols and C=X functionalities (X = N_2, NOH, NO_2^-, PPh_3) to carbonyl compounds (transformations 13 and 14).

During the past few years, catalytic oxyfunctionalizations, in particular asymmetric epoxidations, have been studied intensively with in-situ-generated dioxiranes. Recently, two reviews have been published on the dioxirane-mediated enantioselective epoxidation.[12,13] Presently, we summarize the major achievements in ketone-catalyzed racemic and enantioselective oxidations by in-situ-generated dioxiranes. The catalytic cycle for dioxirane-mediated oxidations is shown in Scheme 15.

Scheme 14



Scheme 15



A. Catalytic Epoxidations

1. Racemic Epoxidations

A variety of structurally diverse ketones catalyze the epoxidation of alkenes with $KHSO_5$ as the oxygen source. The achiral or racemic ketones, which have been successfully employed as catalysts for nonasymmetric epoxidations, are listed in Table 6. For a better comparison of the catalytic activities of the different ketones, the epoxidations of *trans*-stilbene and (*E*)-6-phenylmethoxy-2-hexene are shown as model substrates and the mole ratios of ketone:substrate: $KHSO_5$ as well as the yields of epoxides are given in the table. Furthermore, the pertinent literature has been cited for every entry and, therefore, shall not be repeated in the text.

Fluoro ketones readily catalyze the epoxidation of alkenes with $KHSO_5$ as the oxygen source (entries 1−7). Thus, the catalytic epoxidation of *trans*-stilbene by 1,1,1-trifluorododecan-2-one affords stereoselectively the *trans*-stilbene oxide in very high yield (entry 1). The immobilization of this fluoroketone through covalent attachment to silica gel (entry 2) increased remarkably its persistence under the conditions of the in-situ dioxirane generation, and fortunately, the catalytic activity remained unchanged compared to that of the free ketone (entries 1 and 2). The major advantage of the silica-bound trifluoromethyl ketone is the fact that this catalyst may be easily recovered after reaction by simple filtration and reused for several cycles without any significant loss of its catalytic activity.

Mono- and difluorinated cyclic ketones catalyze well the dioxirane-mediated epoxidation of alkenes (entries 3−7). The catalytic efficiency of the racemic α-monofluorinated 4-*tert*-butylcyclohexanones depends strongly on their relative configuration. Thus, *cis*-configurated ketone (entry 3) displays significantly higher (epoxide yields 100% vs 20%) catalytic activity than the trans diastereomer (entry 4). Also, the α,α′-difluorinated cyclohexanones (entries 6 and 7) possess different catalytic activities, which depends on the relative configuration of the fluorine substituents. Thus, the *cis*-configured ketone (entry 7) is superior (epoxide yields 100% vs 70%) in its catalytic action to the trans diastereomer (entry 6).

Not only do fluorine-activated cyclohexanones catalyze dioxirane epoxidations, but also six-membered-ring heterocyclic ketones show appreciable catalytic activity. For example, the catalytic dioxirane epoxidation of *trans*-stilbene with only 5 mol % of the sulfone ketone in entry 8 afforded the oxide in excellent yield. This ketone catalyst has also been successfully employed to epoxidize β-selectively Δ^5-unsaturated steroids (Scheme 16).[81]

Detailed studies have revealed that cyclic keto ammonium salts promote dioxirane epoxidations. Preparatively useful examples of this class of ketone catalysts are listed in entries 9−19. Modest to very good catalytic activity (epoxide yields 25−97%) was observed for 4-oxopiperidinium salts (entries 11−18) in the dioxirane-mediated epoxidation of alkenes. The chain length of the *N*-alkyl substituents (entries 11−13) and the counterions (entries 14−17) of these keto ammonium salts play a significant role in their catalytic action.

On the basis of the favorable experience that electron-withdrawing groups adjacent to the ketone functionality enhance the reactivity of the corre-

Table 6. Nonasymmetric Ketone-Catalyzed Epoxidations of Alkenes with $KHSO_5$ as the Oxygen Source[a]

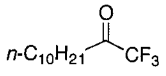
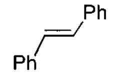
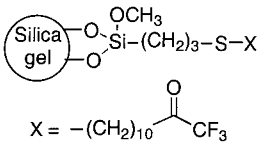
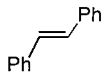
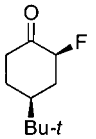
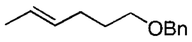
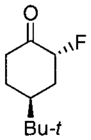
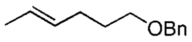
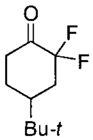
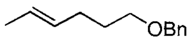
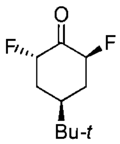
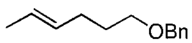
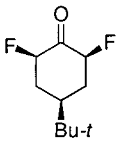
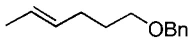
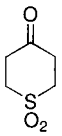
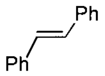
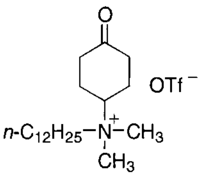
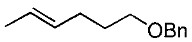
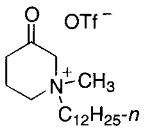
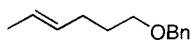
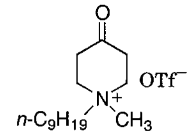
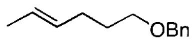
entry	catalyst (cat)	substrate (sub)	mole ratio (cat:sub:$KHSO_5$)	solvent	time (h)	temp (°C)	epoxide yield (%)	ref
1			1 : 2 : 4	CH_3CN/H_2O	5 min	ca. 20	93	73
2			1 : 2 : 4	CH_3CN/H_2O	5 min	ca. 20	94	73
3			1 : 10 : 40	CH_3CN/H_2O	24	0	100	74
4			1 : 10 : 40	CH_3CN/H_2O	24	0	20	74
5			1 : 10 : 40	CH_3CN/H_2O	24	0	45	74
6			1 : 10 : 40	CH_3CN/H_2O	24	0	70	74
7			1 : 10 : 40	CH_3CN/H_2O	10	0	100	74
8			1 : 20 : 30	CH_3CN/H_2O	5	ca. 20	95	75
9			1 : 10 : 100	CH_2Cl_2/H_2O	24	0	47	76
10			1 : 10 : 100	CH_2Cl_2/H_2O	24	0	22	76
11			1 : 10 : 100	CH_2Cl_2/H_2O	24	0	39	76

Table 6 (Continued)

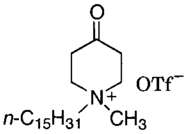
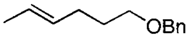
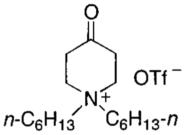
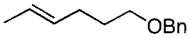
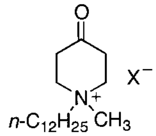
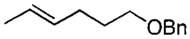
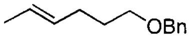
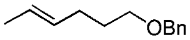
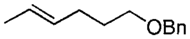
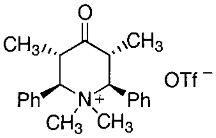
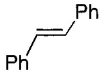
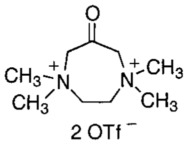
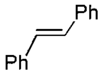
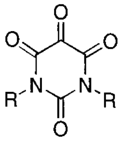
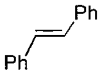
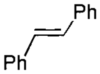
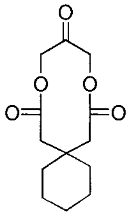
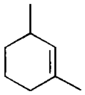
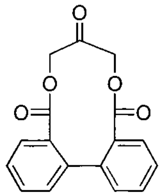
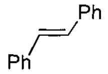
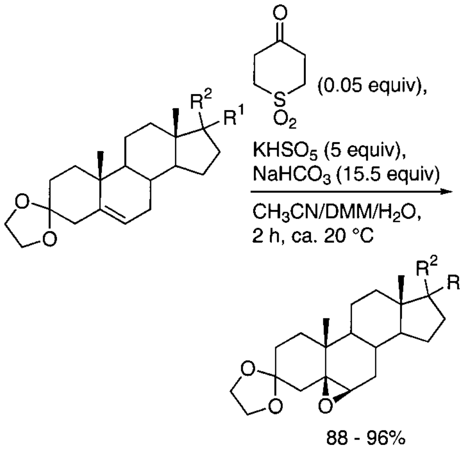
entry	catalyst (cat)	substrate (sub)	mole ratio (cat:sub:$KHSO_5$)	solvent	time (h)	temp (°C)	epoxide yield (%)	ref
12			1 : 10 : 100	CH_2Cl_2/H_2O	24	0	95	76
13			1 : 10 : 100	CH_2Cl_2/H_2O	24	0	25	76
								
14	$X = OTf^-$		1 : 10 : 100	CH_2Cl_2/H_2O	24	0	94	76
15	$X = BF_4^-$		1 : 10 : 100	CH_2Cl_2/H_2O	24	0	95	76
16	$X = NO_3^-$		1 : 10 : 100	CH_2Cl_2/H_2O	24	0	59	76
17	$X = ClO_4^-$		1 : 10 : 100	CH_2Cl_2/H_2O	24	0	31	76
18			1 : 5 : 7.5	CH_3CN/H_2O	1.5	ca. 20	97	75
19			1 : 10 : 100	CH_3CN/H_2O	22	0	33	77
								
20	$R = CH_3$		1 : 3.3 : 13	CH_3CN/H_2O	8	0	70	78
21	$R = CH_2Ph$		1 : 3.3 : 13	CH_3CN/H_2O	8	0	70	78
22			1 : 10 : 10	CH_3CN/H_2O	10 min	ca. 20	85	79

Table 6 (Continued)

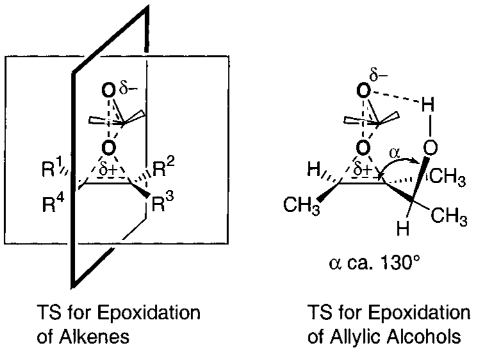
entry	catalyst (cat)	substrate (sub)	mole ratio (cat:sub:$KHSO_5$)	solvent	time (h)	temp (°C)	epoxide yield (%)	ref
23			1 : 100 : 400	CH_3CN/H_2O	12	ca. 20	98	80

[a] pH 7−8 was maintained by addition of $NaHCO_3$, K_2CO_3, or aqueous KOH; 10 mol % of n-$Bu_4N^+HSO_4^-$ (PTC) was added for CH_2Cl_2/H_2O media.

Scheme 16



Scheme 17



TS for Epoxidation of Alkenes

TS for Epoxidation of Allylic Alcohols

sponding dioxirane, it was recently demonstrated that N,N-dialkylalloxanes (entries 20 and 21) serve as effective catalysts for dioxirane-mediated epoxidations. Similarly, the diester-activated cyclic acetone derivatives in entries 22 and 23 catalyze the epoxidation of cyclic and acyclic alkenes by $KHSO_5$ as the oxygen source. The biphenyl derivative (entry 23) is so far one of the most efficient ketone catalysts for dioxirane-mediated epoxidations, since only 1 mol % of this ketone is required to oxidize *trans*-stilbene to the corresponding epoxide in 98% yield.

During the past decade, much experimental data has been acquired for the elucidation of the transition structure of the oxygen transfer in dioxirane epoxidations.[82−86] The reactivity of acyclic alkenes in the dimethyldioxirane (DMD) oxidation reveals that cis alkenes react significantly faster (by a factor of 10) than trans ones.[82] In view of this differentiated *cis/trans* reactivity and the complete stereochemical retention (cis and trans alkenes are converted stereoselectively to the corresponding cis and trans epoxides) observed in the DMD epoxidations,[83−86] a *spiro* transition structure (Scheme 17, left) was proposed[85,86] and corroborated by recent theoretical work.[87−93] The use of chiral allylic alcohols with allylic strain provided detailed information on the geometry of the transition structure for this oxygen-transfer process (Scheme 17, right).[94]

2. Asymmetric Epoxidations

Chiral ketone-catalyzed, asymmetric epoxidation with $KHSO_5$ as the oxygen source represents a useful method for the synthesis of optically active epoxides, which includes simple and functionalized alkenes. Such oxyfunctionalizations have been intensively studied in recent years;[13] we summarize in this section the major advances in this dioxirane chemistry.

The chiral ketones that have been applied in catalytic amounts (<0.5 equiv) to effect dioxirane-mediated asymmetric epoxidations are presented in Table 7. The pertinent literature is cited in the table and shall not be repeated here.

As early as 1984, the chiral ketones (S)-(+)-3-phenylbutan-2-one (entry 1) and (+)-isopinocamphone (entry 2) were used as catalysts in the asymmetric epoxidation of cyclic and acyclic (not shown in the table) alkenes. Unfortunately, these centrochiral ketones led to the corresponding epoxides in poor ee values. Very recently, the related chiral α-chloro- and α-fluoro-substituted cyclohexanone derivatives (entries 3−8) have been employed as catalysts to epoxidize electron-deficient p-methoxycinnamates with $KHSO_5$ as the oxygen donor, but again only low to moderate (up to 40% ee) enantioselectivities have been observed.

A number of oxyfunctionalized cyclohexanone derivatives, which are derived from quinic acid, catalyze dioxirane-mediated asymmetric epoxidations (enries 9−15). However, high enantioselectivities (up to 96% ee) were achieved only with β-substituted derivatives (entries 13−15). Thus, for the hydroxyisopropyl- and methoxyisopropyl-substituted cyclohexanone catalysts, *trans*-stilbene epoxide was obtained in 96% ee (entry 13, R = CMe_2OH, CMe_2OMe).

The major breakthrough in the catalytic, asymmetric epoxidation by dioxiranes was made with sugar-based ketones. The fructose-derived ketones

Table 7. Asymmetric Epoxidations Catalyzed by Chiral Ketones with $KHSO_5$ as the Oxygen Source[a]

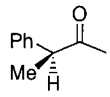
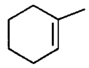
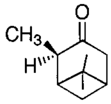
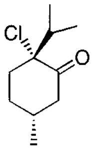
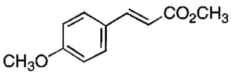
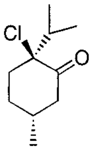
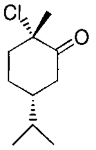
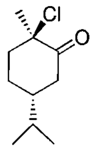
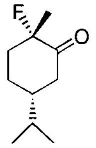
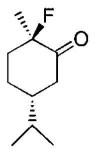
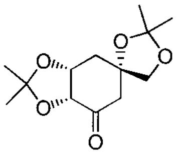
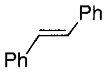
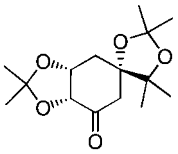
entry	catalyst (cat)	substrate (sub)	mole ratio (cat:sub:$KHSO_5$)	solvent	time (h)	temp (°C)	epoxide yield (%)	ee (%)	confg	ref
1			1 : 2 : 4.8	CH_2Cl_2/H_2O	8-24	5	92	12	(+)-(1*S*, 2*R*)	95
2			1 : 5 : 12	CH_2Cl_2/H_2O	8-24	5	85	10	(+)-(1*S*, 2*R*)	95
3			1 : 3.3 : 10	Dioxane/H_2O	6	ca. 20	24	2	(-)	96
4			1 : 3.3 : 10	Dioxane/H_2O	6	ca. 20	14	2	(-)	96
5			1 : 3.3 : 10	Dioxane/H_2O	6	ca. 20	73	22	(-)	96
6			1 : 3.3 : 10	Dioxane/H_2O	6	ca. 20	20	5	(-)	96
7			1 : 3.3 : 10	Dioxane/H_2O	6	ca. 20	99	40	(-)	96
8			1 : 3.3 : 10	Dioxane/H_2O	6	ca. 20	43	6	(+)	96
9			1 : 2 : 4.1	CH_3CN/ DMM/H_2O	8	0	33	66	(*R*,*R*)	97
10			1 : 2 : 4.1	CH_3CN/ DMM/H_2O	8	0	16	72	(*R*,*R*)	97

Table 7 (Continued)

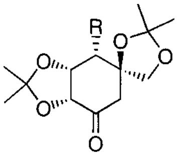
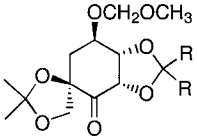
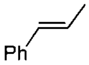
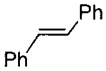
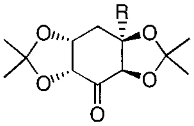
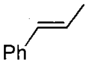
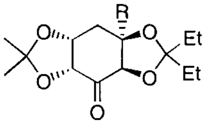
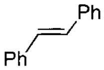
entry	catalyst (cat)	substrate (sub)	mole ratio (cat:sub:$KHSO_5$)	solvent	time (h)	temp (°C)	epoxide yield (%)	ee (%)	confg	ref
11										
	R = H		1 : 3.3 : 7	$CH_3CN/DMM/H_2O$	8	0	10	88	(*R*,*R*)	97
	R = OCH_2OCH_3		1 : 3.3 : 7	$CH_3CN/DMM/H_2O$	8	0	11	89	(*R*,*R*)	97
12										
	R = CH_3		1 : 3.3 : 7	$CH_3CN/DMM/H_2O$	8	-10	67	77	(*S*,*S*)	97
	R, R = $-(CH_2)_5-$		1 : 3.3 : 7	$CH_3CN/DMM/H_2O$	8	0	15	82	(*S*,*S*)	97
13										
	R = H		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	11	93	*R*	98 99
	R = CH_2OTBS		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	77	90	*R*	98 99
	R = CH_2OAc		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	95	90	*R*	98 99
	R = CH_2OCOPh		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	91	90	*R*	98 99
	R = CH_2F		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	71	89	*R*	98 99
	R = CMe_2OH		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	91	96	*R*	98 99
	R = CMe_2OMe		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	94	96	*R*	98 99
	R = CO_2Me		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	66	95	*R*	98 99
	R = CPh_2OH		1 : 20 : 28	DME/H_2O	1	-15	7	50	*R*	98 99
14										
	R = CH_2OAc		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	77	92	*R*	98 99
	R = CMe_2OH		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	57	95	*R*	98 99
	R = CO_2Me		1 : 10 : 14	$DME/DMM/H_2O$	6	-10	65	94	*R*	98 99

Table 7 (Continued)

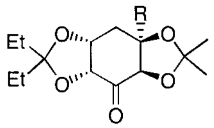
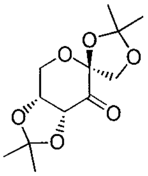
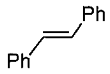
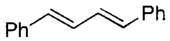
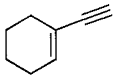
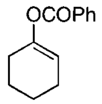
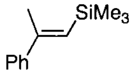
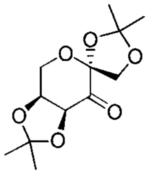
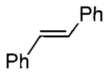
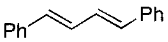
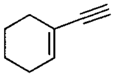
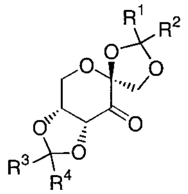
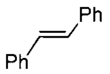
entry	catalyst (cat)	substrate (sub)	mole ratio (cat:sub:$KHSO_5$)	solvent	time (h)	temp (°C)	epoxide yield (%)	ee (%)	confg	ref
15										
	R = CH_2OAc		1 : 10 : 14	DME/DMM/ H_2O	6	-10	75	92	*R*	98 99
	R = CMe_2OH		1 : 10 : 14	DME/DMM/ H_2O	6	-10	57	94	*R*	98 99
	R = CO_2Me		1 : 10 : 14	DME/DMM/ H_2O	6	-10	58	93	*R*	98 99
16			1 : 3.3 : 4.6	CH_3CN/ DMM/H_2O	1.5	0	78	99	(+)-(*R*,*R*)	100
			1 : 4 : 4.5	CH_3CN/ DMM/H_2O	1.5	0	77[b]	97		101
			1 : 3.3 : 4.6	CH_3CN/ DMM/H_2O	3	-10	78	93	(*R*,*R*)	102 103
			1 : 3.3 : 4.6	CH_3CN/ DMM/H_2O	1.5	-5	82	93		104
			1 : 1.5 : 2	CH_3CN/ DMM/H_2O	3	0	74	94	(*R*,*R*)	105
17			1 : 3.3 : 4.6	CH_3CN/ DMM/H_2O	1.5	0	81	98	(-)-(*S*,*S*)	100
			1 : 5 : 5.6	CH_3CN/ DMM/H_2O	1.5	0	65[b]	97		101
			1 : 3.3 : 4.6	CH_3CN/ DMM/H_2O	3	-10	75	94	(*S*,*S*)	102, 103
18										
	R^1, R^2 — R^3, R^4									
	Et, Et — Et, Et		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	16	96	(*R*,*R*)	106
	$-(CH_2)_4-$ — $-(CH_2)_4-$		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	59	99	(*R*,*R*)	106
	$-(CH_2)_5-$ — $-(CH_2)_5-$		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	41	98	(*R*,*R*)	106
	$-(CH_2)_6-$ — $-(CH_2)_6-$		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	30	98	(*R*,*R*)	106
	Me, Me — Et, Et		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	38	94	(*R*,*R*)	106
	Me, Me — Bn, Bn		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	7	93	(*R*,*R*)	106

Table 7 (Continued)

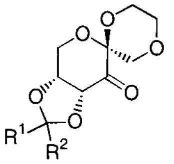
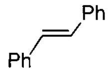
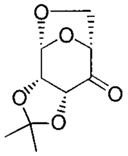
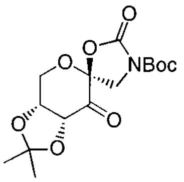
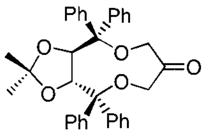
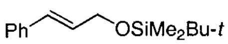
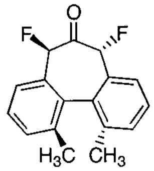
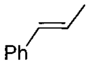
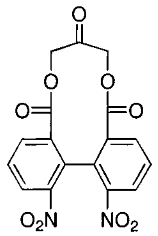
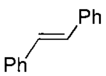
entry	catalyst (cat)	substrate (sub)	mole ratio (cat:sub:$KHSO_5$)	solvent	time (h)	temp (°C)	epoxide yield (%)	ee (%)	confg	ref
18	Me, Me −$(CH_2)_4$−		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	52	98	(*R,R*)	106
	Me, Me −$(CH_2)_5$−		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	59	92	(*R,R*)	106
	Me, Me Et, H		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	38	96	(*R,R*)	106
	Me, Me *i*-Pr, H		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	39	95	(*R,R*)	106
	Et, Et Me, Me		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	36	98	(*R,R*)	106
	−$(CH_2)_4$− Me, Me		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	66	98	(*R,R*)	106
	−$(CH_2)_5$− Me, Me		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	59	98	(*R,R*)	106
19										
	$R^1 = R^2 = Me$		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	34	90	(*R,R*)	106
	$R^1 = R^2 = Et$		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	25	85	(*R,R*)	106
	$R^1 R^2 = -(CH_2)_4-$		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	34	91	(*R,R*)	106
	$R^1 R^2 = -(CH_2)_5-$		1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	35	78	(*R,R*)	106
20			1 : 3.3 : 4.6	CH_3CN/H_2O	1.5	0	27	74	(*R,R*)	106
21			1 : 3.3 : 6	DME/DMM/ H_2O	3.5	0	65	94	(+)-(*R,R*)	107
22			1 : 2 : 2.8	CH_3CN/H_2O	5	ca. 20	80	79	(+)-(*R,R*)	108
23			1 : 10 : 40	CH_3CN/H_2O	10	0	80	88		12
24			1 : 10 : 50	CH_3CN/H_2O	35 min	ca. 20	94	50	(-)-(*S,S*)	109

Table 7 (Continued)

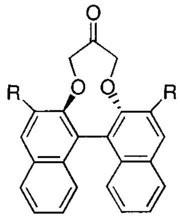
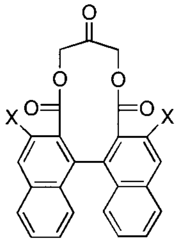
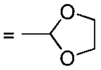
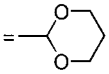
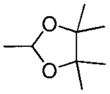
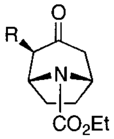
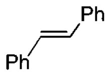
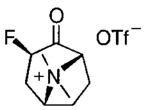
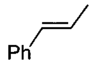
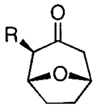
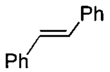
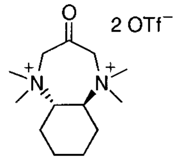
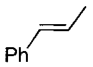
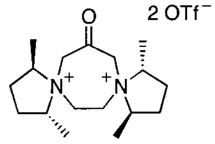
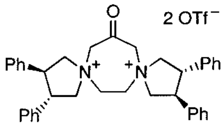
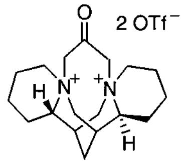
entry	catalyst (cat)	substrate (sub)	mole ratio (cat:sub:$KHSO_5$)	solvent	time (h)	temp (°C)	epoxide yield (%)	ee (%)	confg	ref
25										
	R = H		1 : 3.3 : 16.7	CH_3CN/H_2O	4	ca. 20	72	20	(*R,R*)	110
	R = Br		1 : 3.3 : 16.7	CH_3CN/H_2O	4	ca. 20	58	24	(*R,R*)	110
	R = Ph		1 : 3.3 : 16.7	CH_3CN/H_2O	4	ca. 20	90	2	(*R,R*)	110
26										
	X = H		1 : 10 : 50	CH_3CN/H_2O	1	ca. 20	91	47	(-)-(*S,S*)	109
	X = CH_3		1 : 10 : 50	CH_3CN/H_2O	1	ca. 20	93	56	(+)-(*R,R*)	109
	X = CH_2OCH_3		1 : 10 : 50	CH_3CN/H_2O	1.8	ca. 20	92	66	(-)-(*S,S*)	109
	X = 		1 : 10 : 100	DME/H_2O	20	0	90	77	(-)-(*S,S*)	109
	X = 		1 : 10 : 100	DME/H_2O	20	0	93	84	(-)-(*S,S*)	109
	X = 		1 : 10 : 100	DME/H_2O	20	0	91	75	(-)-(*S,S*)	109
	X = Ph		1 : 10 : 50	CH_3CN/H_2O	24	ca. 20	50	55	(-)-(*S,S*)	109
	X = Cl		1 : 10 : 50	CH_3CN/H_2O	2	ca. 20	95	76	(-)-(*S,S*)	109
	X = Br		1 : 10 : 50	CH_3CN/H_2O	3	ca. 20	92	75	(-)-(*S,S*)	109
	X = I		1 : 10 : 50	CH_3CN/H_2O	22	ca. 20	90	32	(-)-(*S,S*)	109
27										
	R = F		1 : 10 : 100	CH_3CN/H_2O	3	ca. 20	88	76	(*R,R*)	111
	R = OAc		1 : 5 : 50	CH_3CN/H_2O	3	ca. 20	100	66^c	(*R,R*)	112
28			1 : 10 : 50	CH_3CN/H_2O	24	0	85	35	(*R,R*)	74
29										
	R = F		1 : 5 : 50	CH_3CN/H_2O	1	ca. 20	100	63^c	-	112
	R = OAc		1 : 5 : 50	CH_3CN/H_2O	24	ca. 20	85	74^c	-	112

Table 7 (Continued)

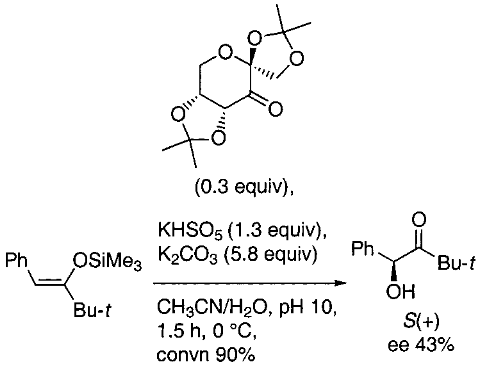
entry	catalyst (cat)	substrate (sub)	mole ratio (cat:sub:$KHSO_5$)	solvent	time (h)	temp (°C)	epoxide yield (%)	ee (%)	confg	ref
30			1 : 10 : 100	CH_3CN/H_2O	6	0	100	9		12
31			1 : 10 : 100	CH_3CN/H_2O	6	0	100	<10		12
32			1 : 10 : 100	CH_3CN/H_2O	3	0	100	<10		12
33			1 : 10 : 100	CH_3CN/H_2O	2	0	54	40		12

[a] $NaHCO_3$ or K_2CO_3 and dilute solution of Na_2EDTA were added. [b] 3–4% of diepoxide was also formed. [c] Ketone ee 76–80%; corrected for enantiomerically pure ketones; the epoxides would have up to 95% ee values (ref 112).

(entries 16–21) are so far the most efficient catalysts for the dioxirane-mediated asymmetric epoxidation of olefins. These chiral ketones efficiently catalyze the enantioselective epoxidation of unfunctionalized as well as functionalized alkenes, conjugated dienes, and even enynes by $KHSO_5$ as the oxygen source. For example, with the so-called Shi ketone (entry 16), *trans*-stilbene oxide was obtained in nearly enantiomerically pure form and in 78% yield (entry 16).

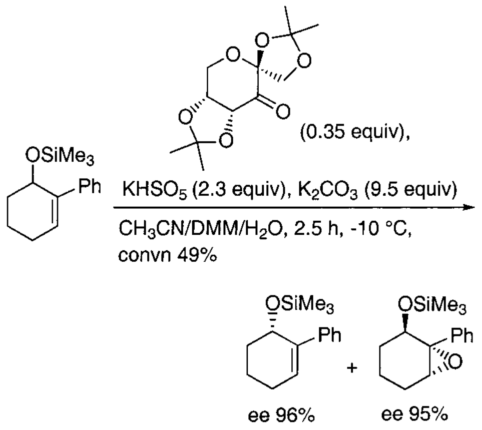
Extensive efforts have been made to improve the catalytic activity and selectivity of this ketone through substituent modification in the protecting groups of the alcohol functionalities (entries 18–21); however, the parent ketone is still the most effective and convenient catalyst for asymmetric oxidation and, consequently, the most frequently used. Thus, this fructose-drived ketone has been employed as the catalyst for the synthesis of optically active α-hydroxy ketones through the dioxirane-mediated epoxidation of silyl enol ethers (Scheme 18).[104,113]

Scheme 18



A noteworthy synthetic applications of this chiral ketone catalyst is the kinetic resolution of oxyfunctionalized olefins through enantioselective epoxidation (see Scheme 19).[114]

Scheme 19

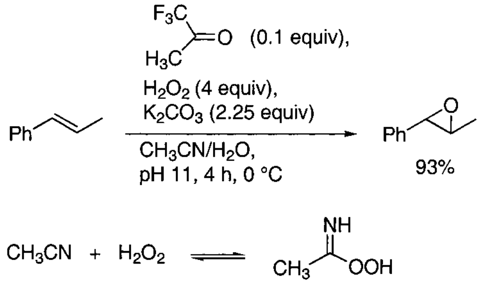


Several C_2-symmetric ketones have been employed for catalytic asymmetric epoxidations (entries 22–26). The TADDOL-derived ketone (entry 22) was introduced as chiral catalyst for the dioxirane-mediated enantioselective epoxidation of trans olefins. As expected, the electron-deficient α,α′-difluoro ketone (entry 23) possesses excellent catalytic activity (only 0.1 equiv of the catalyst is required) and good enantioselectivity (88% ee) for *trans*-β-methylstyrene. Also, the binaphthalene-derived ketone with bulky substituents at the 2,2′ positions (entry 26, fifth row) diplays good enantioselectivity (84% ee) for *trans*-stilbene.

Some heteroatom-containing bicyclic ketones (entries 27−29) have been used as catalysts for dioxirane-mediated asymmetric epoxidations. These chiral ketones afford enantioselectivities up to 76% ee with trans alkenes. Surprisingly, the optically active oxo bisammonium salts (entries 30−32) display poor enantioselectivity (ca. 10% ee), although they exhibit pronounced catalytic activity (quantitative epoxide formation with only 0.1 equiv of ketone) for *trans*-*β*-methylstyrene. With the sparteine-derived diammonium ketone (entry 33), a higher enantioselectivity (40% ee) was obtained, but the reactivity of this ketone is lower (epoxide yield 54%).

Potassium monoperoxysulfate ($KHSO_5$) has been used as the oxygen source nearly exclusively for the generation of dioxiranes from ketones. Recently, efforts have been expended to replace $KHSO_5$ by other oxygen sources, in particular hydrogen peroxide.[115,116] Indeed, good yields (55−90%) and high enantioselectivities (up to 95% ee) have been obtained for the asymmetric epoxidation of alkenes with hydrogen peroxide as the oxygen source and fructose-derived ketone as the catalyst.[115] By using the very reactive trifluoroacetone as the ketone catalyst and H_2O_2 as the oxygen donor, *trans*-*β*-methylstyrene was oxidized to the corresponding epoxide in 93% yield (Scheme 20).[116]

Scheme 20



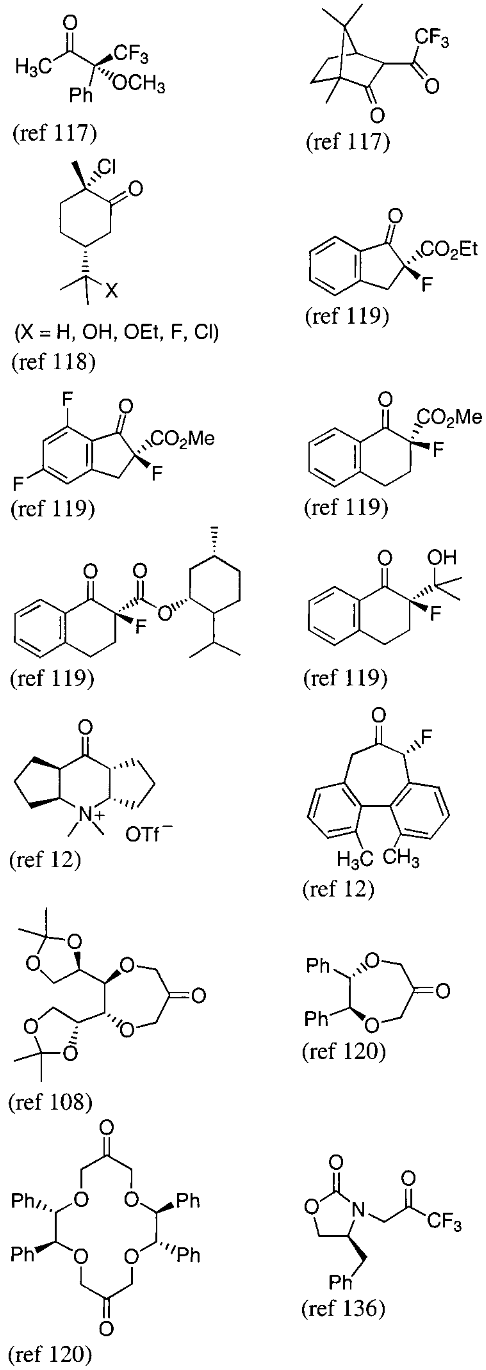
Control experiments have revealed that acetonitrile is crucial for this novel oxidation system, and it has been proposed that the peroxyimidic acid, produced from CH_3CN and H_2O_2 (Scheme 20), is the ultimate oxygen donor that reacts with the ketone to generate the oxidant.[116] However, very recently it has been reported[115b] that dioxirane is involved in the asymmetric epoxidation of olefins by the fructose-derived ketone as the catalyst and H_2O_2 as the oxygen source in acetonitrile.

B. In-Situ Stoichiometric Oxidations

As stated already in the Introduction, the emphasis of the present review lies on catalytic oxidations by nonmetal organic oxidants. Accordingly, in section A we elaborated on only those epoxidations by in-situ-generated dioxiranes, for which the ketone catalysts are used in substoichiometric amounts (<0.5 equiv).

To provide a complete overview, we present here the remaining ketones that have been employed for the in-situ generation of dioxiranes with stoichiometric and larger amounts of the ketone catalyst. Chart 1 lists the chiral ketones that have been used for asymmetric dioxirane epoxidations, while the achiral or racemic ketones are compiled in Chart 2; for convenience, the appropriate literature is cited directly in the charts. A discussion of the individual cases is dispensed with, since the oxidations have not been conducted under catalytic conditions and, thus, are not pertinent to this review.

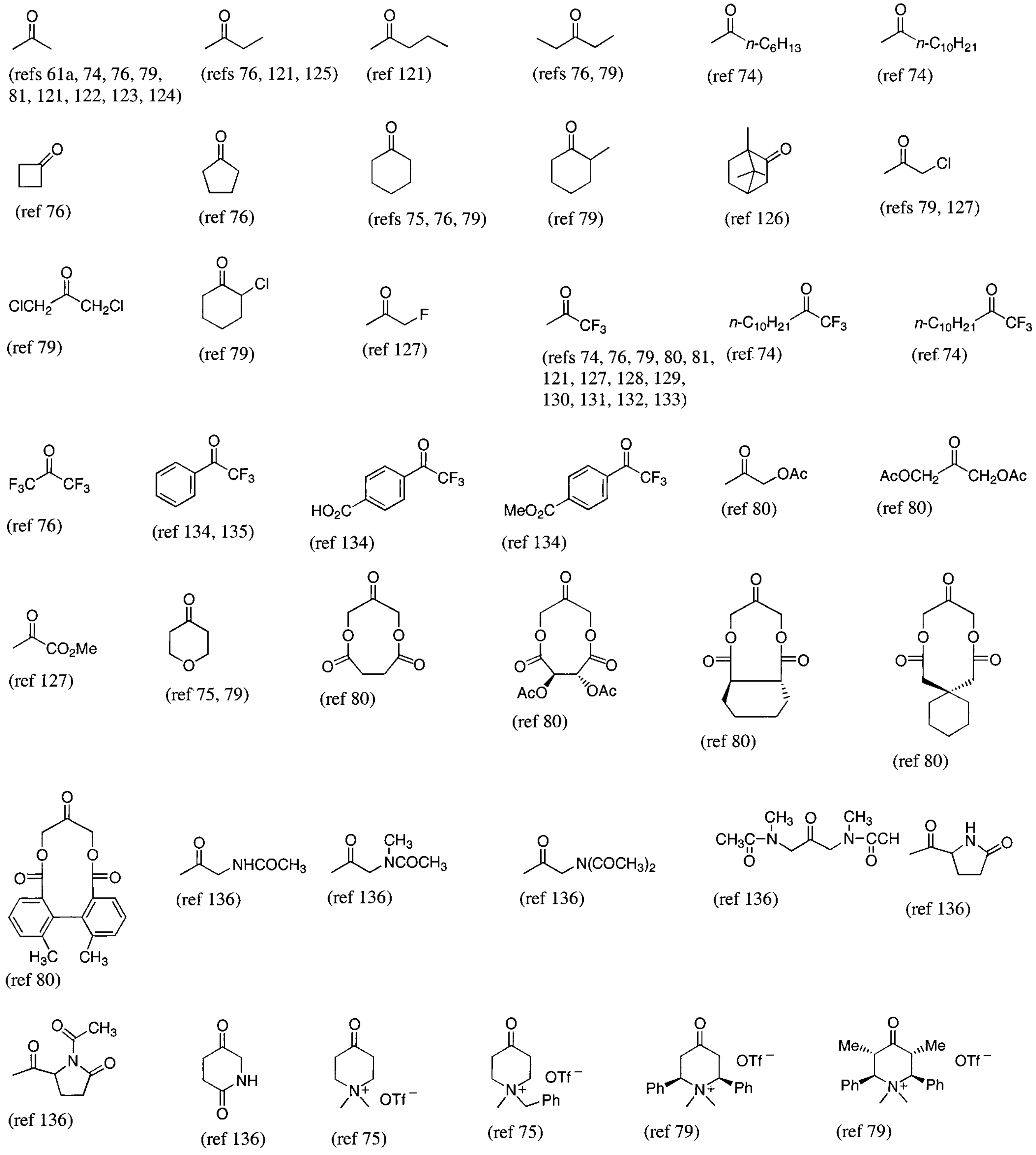
Chart 1. Ketones Used under in-situ Conditions (Stoichiometric or Larger Amounts) for Asymmetric Epoxidations



C. Miscellaneous Catalytic Oxidations

Epoxidations have so far been the most extensively studied transformations by in-situ-generated dioxiranes under catalytic conditions. Examples of other catalytic oxidations are scarce. Nevertheless, it has been reported[80] that the diester-activated cyclic ace-

Chart 2. Ketones Used under in-situ Conditions (Stoichiometric or Larger Amounts) for the Oxidations with $KHSO_5$

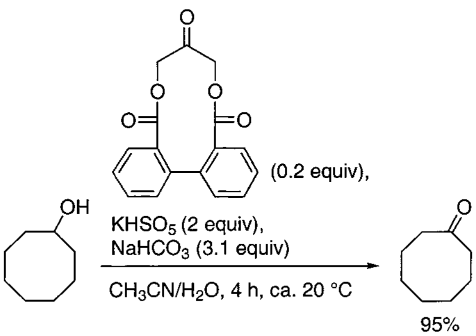


tone derivative in Scheme 21 catalyzes the CH oxidation of cyclooctanol with $KHSO_5$ as the oxygen source to afford cyclooctanone in excellent yield. Furthermore, the fructose-derived Shi's ketone has been employed as the catalyst for the enantioselective oxidation of *vic* diols to the corresponding optically active α-hydroxy ketones.[137] An illustrative example of this enantioselective CH oxidation is shown in Scheme 22.

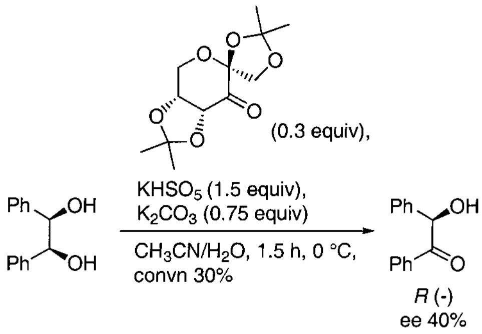
IV. Oxaziridine-Mediated, Imine-Catalyzed Oxidations

Oxaziridines **III** are nitrogen analogues of dioxiranes **II**, but they are generally less reactive than the latter. These nonmetal oxidants are most conveniently prepared by the oxidation of imines **3** with peroxy compounds such as peracids, monoperoxysulfate, and hydrogen peroxide.[138−140]

Scheme 21



Scheme 22



The reactivity of oxaziridines originates from their activating three-membered ring and the relatively weak N−O bond (ca. 53 kcal/mol). Although NH-, NR-, and NAr-substituted oxaziridines transfer their oxygen atom to phosphines to give phosphine oxides, they are sluggish for the epoxidation of alkenes and even for sulfoxidation.[14,138−140] An electron-withdrawing group such as a sulfonyl functionality on the nitrogen atom enhances significantly the oxygen-transfer reactivity.[14] Important oxygen-transfer reactions of the oxaziridines are shown in Scheme 23 in the form of a rosette to highlight the oxidation scope of these nonmetal reagents.

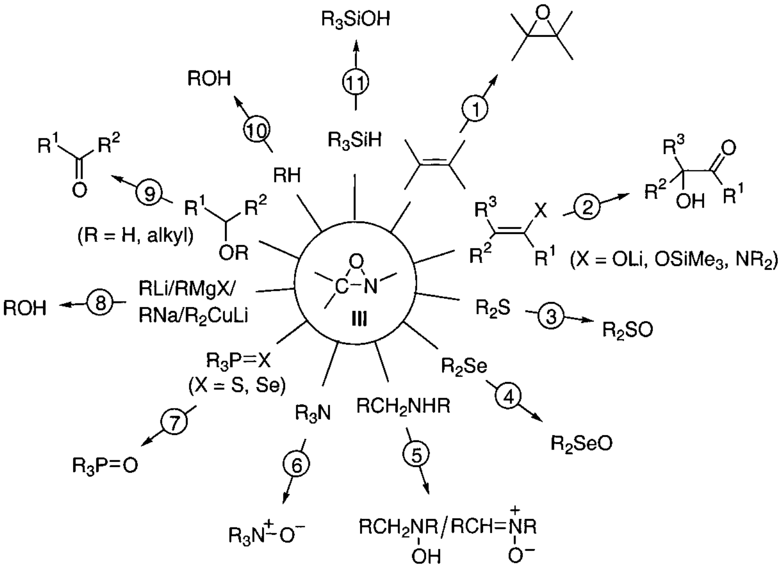
N-Sulfonyloxaziridines are relatively weak oxidants and react slowly with alkenes to give epoxides.[14] In contrast, perfluorinated oxaziridines[17] may be as powerful oxidants as dioxiranes and convert even unactivated alkenes to their epoxides (transformation 1 in Scheme 23).[141] Similarly, *N*-phosphinoyl oxaziridines also oxyfunctionalize alkenes to the corresponding epoxides.[142] The electron-rich enolates of ketones and amides, as well as silyl enol ethers, are readily converted to α-hydroxy compounds (transformation 2). Presumably the corresponding epoxides figure as intermediates, which rearrange in situ to the hydroxylated carbonyl product.[14,15] Theoretical work predicts a concerted mechanism in which the electrophilic oxygen atom of the oxaziridine is transferred to the nucleophilic π bond along a S_N2-type coordinate through either a planar or spiro transition structure.[143]

Among the heteroatom substrates, sulfides and selenides are efficiently oxidized to their oxides by oxaziridines (transformations 3 and 4).[14] While secondary amines are transformed into *N*-hydroxylamines and/or nitrones, tertiary amines give *N*-oxides (transformations 5 and 6).[14,144] Perfluorinated oxaziridines oxidize thiophosphoryl and selenophosphoryl groups to the phosphene oxides (transformation 7).[145] Lone-pair oxidations by *N*-sulfonyloxaziridines have also been extended to carbanions, namely, the organometallic substrates shown in transformation 8, which afford the corresponding alcohols.[14]

Also, σ-bond oxidations may be realized with oxaziridines. Thus, secondary alcohols and their alkyl ethers are converted to ketones by perfluorinated oxaziridines (transformation 9).[146] Even the CH bonds of unactivated alkanes are oxidized to alcohols (transformation 10) by the powerful perfluorinated oxaziridines.[17,147] Expectedly, the more reactive silanes are efficiently converted to their silanols under neutral conditions (transformation 11).[17]

Intensive work has been invested on the preparation and oxygen-transfer reactions of oxaziridines, particularly *N*-sulfonyl derivatives. Several reviews[14−16,148,149] describe the efficacy and scope of such nonmetal oxidants. Also, the synthesis of polyfluorinated oxaziridines and their usefulness for the

Scheme 23

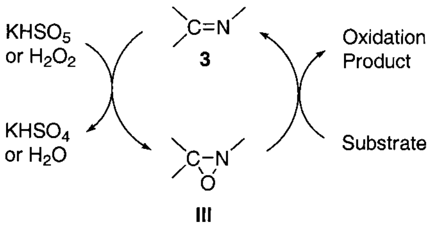


oxyfunctionalization of organic substrates has been reviewed.[17]

Most of the oxidation reactions with these reagents have been performed stoichiometrically with isolated oxaziridines. In several instances, imines have been identified or isolated in high yields at the end of the oxidation,[17] which implicates their catalytic propensity. Nevertheless, catalytic oxidations with oxaziridines are scarce and essentially limited to sulfoxidation.

This section deals only with catalytic oxidations by oxaziridines **III**, generated in situ from the imine catalyst **3** and an appropriate oxygen source; the catalytic cycle is displayed in Scheme 24. The imine catalyst **3** reacts with the oxygen source, usually $KHSO_5$ or H_2O_2, to afford the oxaziridine **III** as the catalytic oxidant. The electrophilic oxygen atom of the oxaziridine is transferred to the electron-rich substrate to give the oxygenated product with the release of the imine; thereby, the catalytic cycle has been completed.

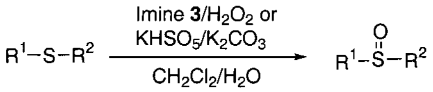
Scheme 24



A. Racemic Sulfide Oxidations

Imines **3** efficiently and selectively catalyze the oxidation of sulfides to the corresponding sulfoxides (Scheme 25). Examples of such sulfoxidations, catalyzed by imines and H_2O_2 or $KHSO_5$ as the oxygen source, are listed in Table 8.

Scheme 25



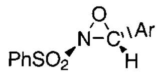
$$R^1{-}S{-}R^2 \xrightarrow[CH_2Cl_2/H_2O]{\text{Imine } \mathbf{3}/H_2O_2 \text{ or } KHSO_5/K_2CO_3} R^1{-}\overset{O}{\overset{\|}{S}}{-}R^2$$

Several imines have been screened[150] to assess their potential as sulfoxidation catalysts with H_2O_2 as the oxygen source. The simple imine *N*-benzylideneaniline gave poor yields of sulfoxides due to hydrolysis to its amine and carbonyl partner. The use of acetone oxime, cyclohexanone oxime derivatives, and *N*-cyclohexylidenebenzenesulfonamide gave moderate yields of sulfoxides. Of these, the cyclohexanone oxime (**3a**) showed the higher activity and was used under catalytic conditions (entry 1). The cyclic sulfonylimine **3b** derived from saccharin, namely, 3-*tert*-butylbenzisothiazole-1,1-dioxide, gave much higher yields of sulfoxide under catalytic conditions, but long reaction times were necessary (entry 2).

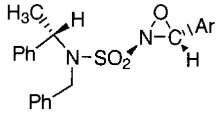
The *N*-(4-nitrobenzylidene)benzenesulfonamide (**3c**) was used as a catalyst for the oxidation of a variety of sulfides with $KHSO_5$ as the oxygen source (entries 3−14).[151] The sulfoxides were obtained generally in high yields and selectivity. Overoxidation to the sulfones took place only in traces (>5%) for a few cases. Expectedly, the oxidation of the more nucleophilic sulfides was faster, as manifested by the series n-Bu_2S > $PhSCH_2Ph$ > Ph_2S (entries 3, 7, and 8). The sulfoxidation is chemoselective and tolerates functionalities such as CC double bonds (entry 10) and the carbonyl group (entry 14). Computational work on the sulfoxidation concludes that the oxygen transfer takes place concertedly.[152]

B. Asymmetric Sulfide Oxidations

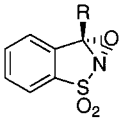
A valuable extension of the oxaziridine oxidation has been the use of optically active *N*-sulfonyloxaziridines for the asymmetric oxyfunctionalization of a variety of electron-rich substrates. These include the enolates of ketones, esters, lactones, and amides, silyl enol ethers, sulfides, selenides, and even alkenes.[14−16,148,149] High yields and good enantioselectivities were obtained in most of these oxidations; however, these oxyfunctionalizations have been performed stoichiometrically and are, therefore, not pertinent for the present review. Nonetheless, a few of the more important optically active *N*-sulfonyloxaziridines that have been used in the stoichiometric oxidations are shown below, for which the references are given in parentheses for each structure. The camphorsulfonylimine (**3d**) and its derivatives **3e**−**h** have been used as catalysts for the asymmetric sulfoxidation with hydrogen peroxide in the presence of the base K_2CO_3 or DBU (Table 9, entries 1−22).[159,160] The base accelerates the formation of the oxaziridine from the imine and H_2O_2 and also suppresses the direct racemic oxidation of the substrate by H_2O_2. The reactions were performed with one equivalent of the imine **3**, which could be recovered nearly quantitatively at the end of the reaction; thus, these reactions qualify as catalytic sulfoxidations.



(ref 153)

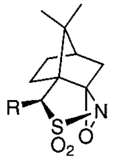


(ref 154)



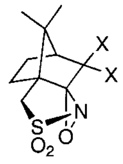
R = alkyl, aryl

(ref 155)



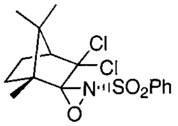
R = H, CH_2Ph

(ref 156)



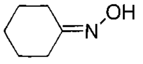
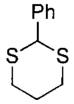
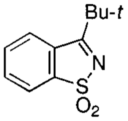
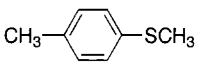
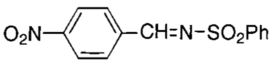
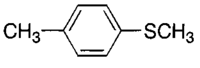
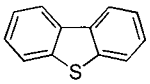
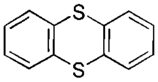
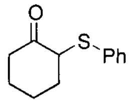
X = H, F, Cl, Br, OCH_3

(ref 157)



(ref 158)

Table 8. Imine-Catalyzed Oxidation of Sulfides[a]

entry	catalyst (cat)	substrate (sub)	oxygen source (ox)	mole ratio cat : sub : ox	time (h)	yield (%)	
						R_2SO	R_2SO_2
1[b]	 **3a**		30% H_2O_2	1 : 10 : 40	36	34	-
2[c]	 **3b**		30% H_2O_2	1 : 10 : 40	192	84	-
3	 **3c**	$(n\text{-Bu})_2S$	$KHSO_5$	1 : 5 : 7.5	0.5	95	-
4	-"-	$(sec\text{-Bu})_2S$	$KHSO_5$	1 : 5 : 7.5	0.5	95	-
5	-"-	$(t\text{-Bu})_2S$	$KHSO_5$	1 : 5 : 7.5	0.5	95	-
6	-"-	$PhSCH_3$	$KHSO_5$	1 : 5 : 7.5	0.5	95	4
7	-"-	$PhSCH_2Ph$	$KHSO_5$	1 : 5 : 15	4	96	-
8	-"-	PhSPh	$KHSO_5$	1 : 5 : 7.5	24	92	3
9	-"-		$KHSO_5$	1 : 5 : 7.5	0.5	91	5
10	-"-	$PhSCH{=}CH_2$	$KHSO_5$	1 : 5 : 7.5	24	90	4
11	-"-	$PhSCH_2CH_2Cl$	$KHSO_5$	1 : 5 : 7.5	0.5	92	-
12	-"-		$KHSO_5$	1 : 5 : 22.5	0.5	89	-
13	-"-		$KHSO_5$	1 : 5 : 7.5	18	90	-
14	-"-		$KHSO_5$	1 : 5 : 22.5	2	90	-

[a] In CH_2Cl_2/H_2O with K_2CO_3 as base at 25 °C; ref 150 for entries 1−2 and ref 151 for entries 3−14. [b] Performed at −20 °C. [c] DBU was used as a base.

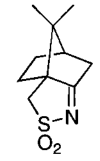
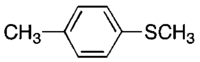
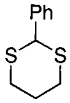
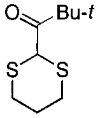
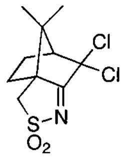
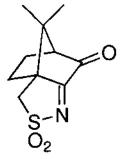
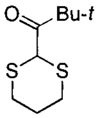
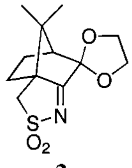
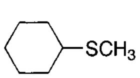
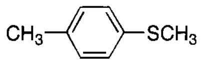
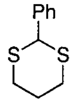
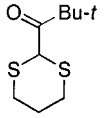
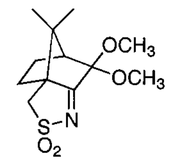
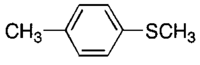
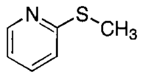
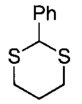
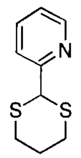
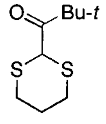
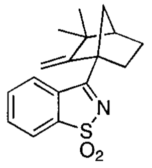
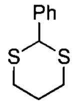
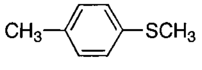
The camphorsulfonylimine **3d** gave the sulfoxides in high yields but only in moderate ee values of 20−49% (entries 1−5). Similarly, the 3,3-dichlorocamphorsulfonylimine (**3e**) and 3-oxocamphorsulfonylimine (**3f**) showed also low (20−25% ee) enantioselectivities (entries 6−8). The preformed oxaziridines derived from these imines gave good ee values of 50−80% for the sulfoxidation under stoichiometric conditions.[16]

The acetal derivatives **3g** and **3h** exhibited high catalytic activity, and in some cases excellent enantioselectivity was achieved (entries 9−22). The imine **3h** gave the best results for 2-phenyl-1,3-dithiane, for which the corresponding sulfoxide was obtained quantitatively and with 98% ee (entry 20).

Recently, the 3-substituted 1,2-benzisothiazole-1,1-dioxide **3i** was employed as a catalyst for the asymmetric sulfoxidation by H_2O_2 (entry 23) and also by potassium percarbonate (entries 24 and 25) as oxygen sources.[161] Although the sulfoxides were obtained in high yields, the enantioselectivities were low (14−34% ee).

The sulfides in the entries 15−17, 20, and 22 of Table 9 were also oxidized with the preformed oxaziridine derived from the imine **3h**.[162] Similar yields, ee values, and the same sense of asymmetric induction was observed as in the catalytic oxidation with the imine **3h** and H_2O_2. This implies the intermediacy of oxaziridine in this reaction. In contrast, opposite configurations of the *tert*-butyl methyl sulfoxide were observed in the catalytic oxidation with imine **3d** and H_2O_2 (entry 1) versus the stoichiometric oxidation by the preformed oxaziridine

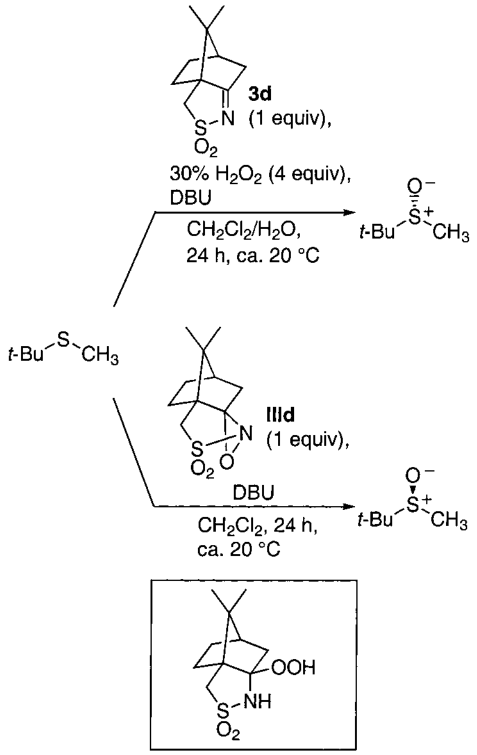
Table 9. Imine-Catalyzed Asymmetric Oxidation of Sulfides by H_2O_2 [a]

entry	catalyst (cat)	substrate (sub)	sulfoxide yield (%)	ee (%)	confg
1	 **3d**	*t*-BuSCH$_3$	83	42	*R*
2	-"-	PhCH$_2$SCH$_3$	100	35	*R*
3	-"-		100	20	*R*
4	-"-		100	44	*S*
5	-"-		66	49	*R*
6	 **3e**	PhCH$_2$SCH$_3$	100	25	-
7	 **3f**	PhCH$_2$SCH$_3$	34	23	-
8	-"-		23	20	-
9	 **3g**		100	68	(+)
10	-"-	*t*-BuSCH$_3$	100	82	*S*
11	-"-	PhCH$_2$SCH$_3$	100	46	*S*
12	-"-		100	37	*R*
13	-"-		100	94	*S*
14	-"-		74	68	*S*
15	 **3h**	*t*-BuSCH$_3$	100	86	*S*
16	-"-	PhCH$_2$SCH$_3$	100	63	*S*
17	-"-		96	60	*S*
18	-"-		75	38	*R*
19	-"-	PhSCH$_2$SPh	65	48	*S*
20	-"-		100	98	*S*
21	-"-		69	98	*S*
22	-"-		46	78	*S*
23[b]	 **3i**		100	34	*S*
24[c]	-"-	PhSCH$_3$	95	14	*R*
25[d]	-"-		100	14	*R*

[a] Imine (1 equiv), aqueous H_2O_2 (4 equiv), cat:sub:ox mol ratio 1:1:4, DBU (4 equiv), CH_2Cl_2, −20 °C, 24 h; ref 160 for entries 1−22 and ref 161 for entries 23−25. [b] Performed at −15 °C for 14 h. [c] Imine (0.2 equiv) and potassium percarbonate were used as the oxygen source at ca. 20 °C for 24 h. [d] Imine (0.1 equiv) and potassium percarbonate were used as the oxygen source at ca. 20 °C for 48 h.

IIId (Scheme 26).[159,162] Therefore, in this asymmetric sulfoxidation, the intermediary α-hydroperoxy amine has been proposed as oxidant, analogous to the Payne oxidation.[163]

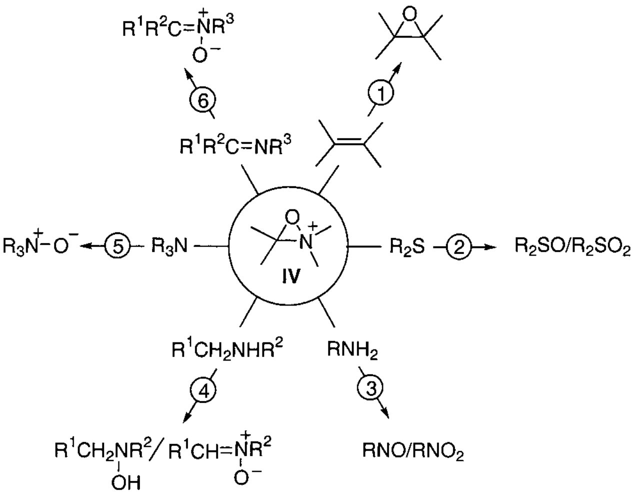
Scheme 26



V. Oxaziridinium-Ion-Mediated, Iminium-Ion-Catalyzed Oxidations

Oxaziridinium salts **IV** are conveniently prepared from the corresponding iminium salts **4** by oxidation with peracids or monoperoxysulfate.[164,165] Their oxidizing power derives from the strongly electrophilic oxygen atom, which may be transferred to a variety of substrates, as demonstrated in the rosette of Scheme 27. The display includes catalytic as well as stoichiometric oxidations to show the scope of the oxygen-transfer ability of this reagent. Thus, alkenes are efficiently oxidized to epoxides by oxaziridinium salts **IV** (transformation 1 in Scheme 27).[166,167]

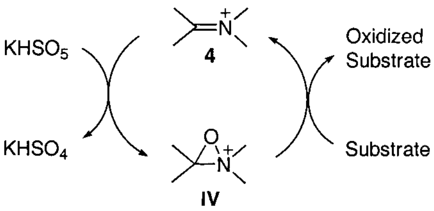
Scheme 27



Expectedly, the heteroatom oxidation is facile, as illustrated in the conversion of sulfides to sulfoxides or sulfones by the use of either one or two equivalents of the appropriate oxygen source (transformation 2).[165] The oxidation of amines by oxaziridinium salts is more complex.[168] Primary amines are converted to nitroso (or its dimer) and nitro products (transformation 3); which of these prevails depends on the amount of the oxaziridinium salt used. For example, the aromatic amine *p*-methylaniline affords exclusively the nitroarene with two equivalents of the oxidant. In contrast, the oxidation of secondary amines leads to nitrones and hydroxylamines (transformation 4), while tertiary amines give selectively the *N*-oxides in high yield (transformation 5). Finally, oxaziridinium salts **IV** convert imines to the respective nitrones (transformation 6). Thus, most of the current work has concentrated on alkene and heteroatom oxyfunctionalizations, while neither the CH oxidation in alkanes or even in alcohols nor the SiH oxidation in silanes appears to have been reported.

The present review on nonmetal oxidants deals with catalytic reactions; the relevant catalytic cycle for the oxaziridinium salts **IV** is shown in Scheme 28. The iminium ion **4** reacts with monoperoxysulfate to give the oxaziridinium ion **IV**, which serves as the actual oxidant. On transfer of the electrophilically activated oxygen atom to the substrate, the oxidation product results and the iminium catalyst is regenerated; thereby the catalytic cycle is completed.

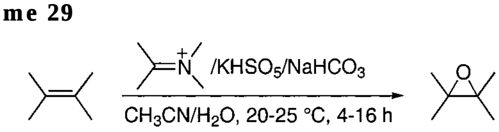
Scheme 28



A. Racemic Epoxidations

Iminium salts **4** efficiently catalyze the epoxidation of CC double bonds with buffered $KHSO_5$ as the oxygen source (Scheme 29). The reactions are performed under homogeneous conditions in an acetonitrile–water mixture at room temperature. Examples of such catalytic epoxidations by iminium catalysts are shown in Table 10.

Scheme 29

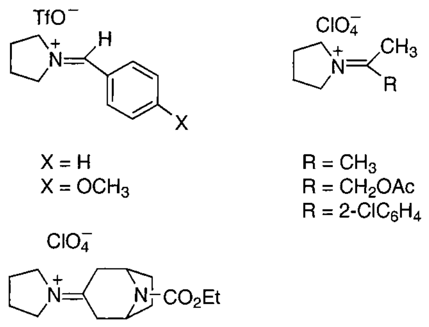


The use of dihydroisoquinolinium salt **4a** as the catalyst afforded the epoxide of (*E*)-2-undecen-1-ol quantitatively (entry 1).[169] With the set of ketiminium salts **4b**–**d**, their catalytic efficiency was examined for the epoxidation of *trans*-stilbene.[170] The derivatives **4b** and **4c** showed low activity (entries 2 and 3), presumably due to their hydrolysis to the corresponding amines and ketones. The salt **4d** displayed a much higher catalytic activity with stilbene (entry 9); consequently, this catalyst was used for the oxidation of a variety of olefinic substrates, which afforded the respective epoxides in most cases in good yields (entries 4–13).

Diastereomeric pairs of cis and trans alkenes gave the corresponding epoxides stereoselectively (entries 4, 5, 7, 8, 10, and 11), which implicates a concerted oxygen-transfer mechanism. The silyl enol ether derived from propiophenone gave α-hydroxypropiophenone in good yield (entry 13). In this overall α hydroxylation of carbonyl derivatives, presumably the intermediary epoxide rearranged under the reaction conditions.

The iminium salts **4e–h**, derived from pyrrolidine and aryl aldehydes, were evaluated for their potential as epoxidation catalysts with *trans*-stilbene as model substrate (entries 14–17). The derivatives **4e** and **4h** with *ortho* electron-withdrawing groups (chloro and trifluoromethyl substituents) showed better catalytic activity (entries 14 and 17). For the epoxidation of other alkenes (entries 18–23), the iminium salt **4h** was the best catalyst. Whereas these electron-rich alkenes afforded the respective epoxides in high yields, the electron-poor ethyl cinnamate did not react. Expectedly, the diastereomeric *cis*- and *trans*-stilbenes gave the corresponding epoxides stereoselectively (entries 17 and 18). The low *cis*–*trans* diastereoselectivity for limonene (entry 22), especially 2-cyclohexenol (entry 23), constitutes a definite disadvantage of this catalytic, nonmetal oxidant for preparative applications.

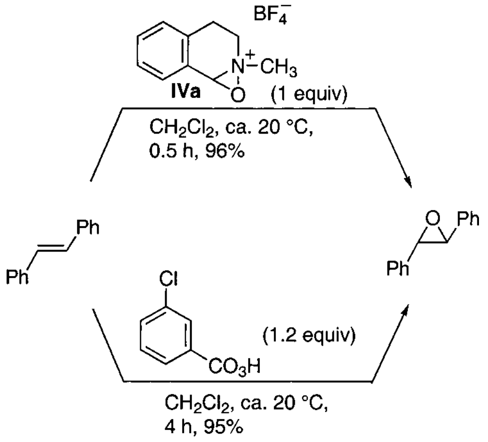
The exocyclic iminium salts shown below were also evaluated for their potential as epoxidation catalyst, but stoichiometric amounts of the salt were employed with *trans*-stilbene.[171] The iminium ion with the electron-releasing *p*-methoxy substituent was inactive, but the others gave also only poor yields of the stilbene epoxide, which curtails their use as oxidation catalysts. Hydrolysis is presumably responsible that these iminium salts do not persist under the reaction conditions.



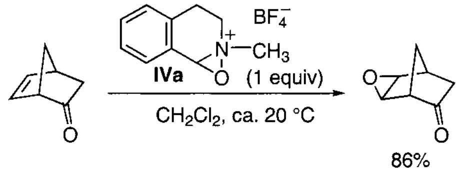
The oxygen-transfer reactivitiy of the oxaziridinium salt **IVa** has been compared with that of *m*-CPBA.[167] Under otherwise identical conditions, the oxaziridinium ion **IVa** epoxidizes *trans*-stilbene faster than *m*-CPBA (Scheme 30). Although the oxaziridinium salt **IVa** epoxidizes unactivated alkenes such as 1-nonene in high yield, it does not react with electron-deficient alkenes such as isophorone, cholestenone, methyl maleate, and methyl fumarate.

In regard to selectivity, the oxaziridinium salt **IVa** converts norbornenone chemo- and stereoselectively to the epoxy ketone without affecting the keto group (Scheme 31).[167]

Scheme 30

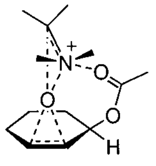


Scheme 31



Such a chemoselectivity is observed in DMD oxidations;[167] however, *m*-CPBA gives, besides the epoxy ketone, a mixture of lactones through the Baeyer–Villiger reaction.[172]

The hydroxy-group-directed epoxidation is well-known for peracids and DMD, in which the diastereoselectivity is controlled by allylic strain and hydrogen bonding.[55,56,173] This is not observed for the oxaziridinium salt **IVa**, as manifested by the low *cis/trans* ratio for the cyclohex-2-en-1-ol oxide (Table 11).[167] Evidently, the positively charged nitrogen atom in the oxaziridinium ion **IVa** does not favor hydrogen bonding between the strongly electrophilic oxygen atom and the allylic hydroxyl group. However, the acetyl derivative displays a high cis diastereoselectivity, much better than *m*-CPBA and DMD. This high cis diastereoselectivity for the iminium salt **4a** is astounding and implicates an attractive association between the positively charged nitrogen atom and the acetyl carbonyl group, as shown in the transition structure below. From computational work it was



concluded that a concerted spiro transition structure accounts best for the oxygen transfer to the CC double bond.[174]

B. Asymmetric Epoxidations

In view of the chiral nature of appropriately substituted oxazirdinium salts, their potential as asymmetric epoxidants under catalytic conditions has recently been intensively pursued. The available results are summarized in Table 12 and the pertinent references therein, which will not be repeated in the

Table 10. Iminium-Salt-Catalyzed Epoxidation of Alkenes by $KHSO_5$ as the Oxygen Source[a]

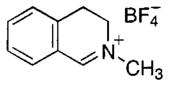
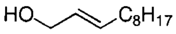
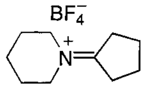
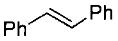
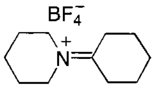
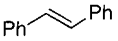
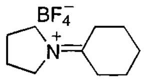
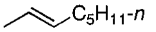
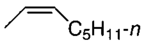
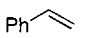
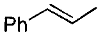
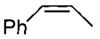
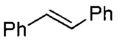
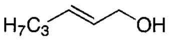
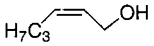
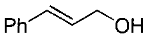
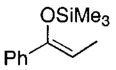
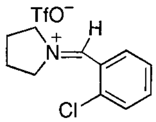
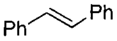
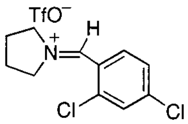
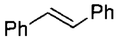
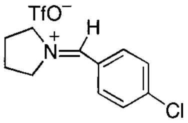
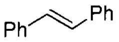
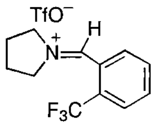
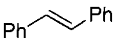
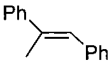
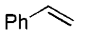
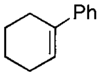
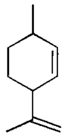
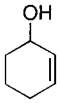
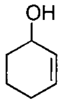
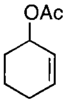
entry	catalyst **4** (cat)	substrate (sub)	mole ratio cat:sub:$KHSO_5$	time (h)	temp (°C)	epoxide[b] yield (%)	ref
1	 **4a**		-[c]	-	-	97	169
2	 **4b**		1:10:10	16	25	25	170
3	 **4c**		1:10:10	16	25	19	170
4	 **4d**		1:10:10	16	25	48	170
5	-"-		1:10:10	16	25	78	170
6	-"-		1:10:10	16	25	37	170
7	-"-		1:10:10	16	25	81	170
8	-"-		1:10:10	16	25	80	170
9	-"-		1:10:10	16	25	88	170
10	-"-		1:10:10	16	25	24	170
11	-"-		1:10:10	16	25	59	170
12	-"-		1:10:10	16	25	63	170
13	-"-		1:10:10	16	25	75[d]	170
14	 **4e**		1:10:20	4	ca. 20	82	171
15	 **4f**		1:10:20	4	ca. 20	28	171
16	 **4g**		1:10:20	4	ca. 20	24	171
17	 **4h**		1:10:20	4	ca. 20	89	171

Table 10 (Continued)

entry	catalyst **4** (cat)	substrate (sub)	mole ratio cat:sub:$KHSO_5$	time (h)	temp (°C)	epoxide[b] yield (%)	ref
18	-"-		1:10:20	4	ca. 20	50	171
19	-"-		1:10:20	4	ca. 20	92	171
20	-"-		1:10:20	4	ca. 20	38	171
21	-"-		1:10:20	4	ca. 20	93	171
22	-"-		1:10:20	4	ca. 20	72[e] (70:30)	171
23	-"-		1:10:20	4	ca. 20	100 (53:47)	171

[a] Performed in CH_3CN/H_2O. [b] The *cis/trans* ratio is given in parentheses. [c] Details not available. [d] The product is α-hydroxypropiophenone. [e] Only the cyclohexene epoxide is formed.

Table 11. Comparison of the Diastereoselectivities (*cis/trans*) in the Epoxidation of Cyclohex-1-en-2-ol and its Acetate by Oxaziridinium Salt IVa, *m*-CPBA and DMD[a]

substrate	yield[b] (%)	diastereoselectivity (*cis/trans*) oxaziridinium salt **IVa**	*m*-CPBA	DMD
	85	60 : 40	92 : 8	75 : 25
	92	95 : 5	50 : 50	35 : 65

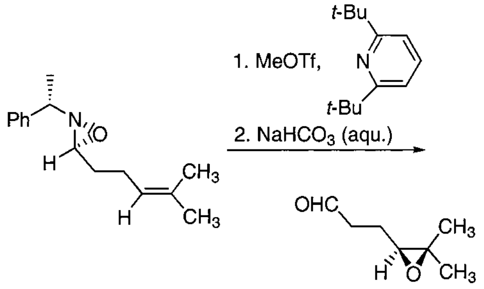
[a] Substrate (1 mmol), oxidant (1 equiv); in CH_2Cl_2 except for DMD in CH_2Cl_2/CH_3COCH_3. [b] In the oxidation with the oxaziridinium salt.

text. The enantiomerically pure 3,4-disubstituted 3,4-dihydroisoquinolinium salt **4i** was used as the catalyst for the epoxidation of the prochiral alkenes in entries 1 and 2; although the yields of the epoxides were high, the enantioselectivities were low. For the set of 3,4-dihydroisoquinolinium salts **4j**–**p** (entries 3–9), in which the stereogenic center is in the ammonium functionality, the efficacy of asymmetric epoxidation was tested with of 1-phenylcyclohexene as model alkene substrate. Good yields of the corresponding epoxide were obtained with these chiral catalysts, but again the enantioselectivities were low (8–32% ee). With the optically active iminium salt **4q** (entries 10–16), a variety of di- and trisubstituted alkenes were examined, but the asymmetric induction was also low (≤ 20% ee); the best ee value (40%) was found for 1-phenylcyclohexene.

The optically active binaphthyl-based iminium ion **4r** was used as the catalyst for the asymmetric epoxidation of various alkenes (entries 17–21). Except for 1-phenylcyclohexene (entry 21), for which a relatively high ee value of 71% was achieved (the best to date for iminium salt catalysts), the enantioselectivities were generally only low to moderate (8–45% ee).

Nonetheless, a very high (94% ee) enantioselectivity was observed in the intramolecular epoxidation of the CC double bond of the optically active oxaziridine in Scheme 32.[178]

Scheme 32



Presumably, under these oxygen-transfer conditions the corresponding oxaziridinium ion is the oxidant. Evidently, the previously mentioned spiro transition structure applies in this oxyfunctionalization.

C. Sulfide Oxidations

The oxidation of sulfides with the 3,4-dihydroisoquinoline-derived iminium salt **4a** as the catalyst and

Table 12. Asymmetric Epoxidation of Prochiral Alkenes with Monoperoxysulfate, Catalyzed by Optically Active Iminium Salts 4[a]

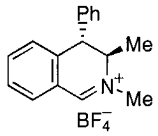
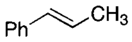
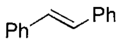
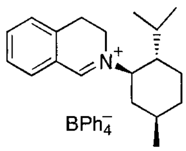
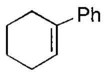
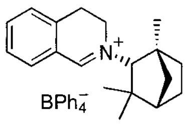
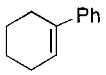
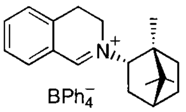
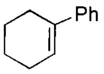
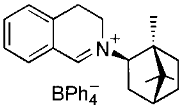
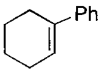
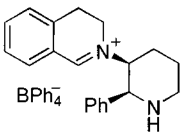
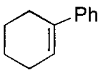
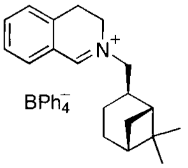
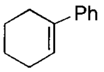
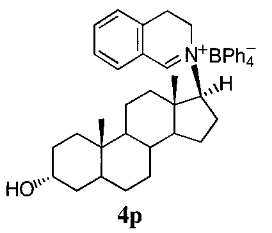
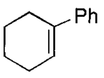
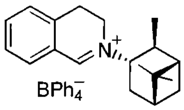
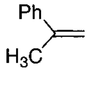
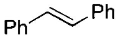
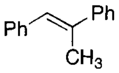
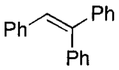
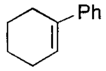
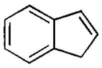
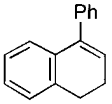
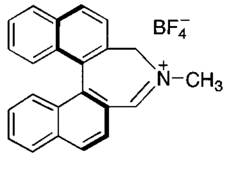
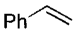
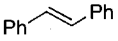
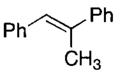
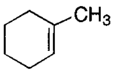
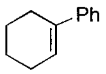
entry	catalyst **4** (cat)	substrate (sub)	mole ratio cat:sub:$KHSO_5$	time (h)	temp (°C)	epoxide yield (%)	ee (%)	config	ref
1	 **4i**		1:20:40	12	ca. 20	70	22	(*R*,*R*)	18, 175
2	-"-		1:20:40	12	ca. 20	80	35	(*R*,*R*)	18, 175
3	 **4j**		1:200:400	1	0	63	19	(+)-(*R*,*R*)	19, 176
4	 **4k**		1:200:400	1	0	45	32	(+)-(*R*,*R*)	19, 176
5	 **4l**		1:200:400	1	0	60	18	(+)-(*R*,*R*)	19, 176
6	 **4m**		1:200:400	1	0	58	8	(+)-(*R*,*R*)	19, 176
7	 **4n**		1:100:200	1	0	39	25	(-)-(*S*,*S*)	19, 176
8	 **4o**		1:200:400	1	0	66	12	(-)-(*S*,*S*)	19, 176
9	 **4p**		1:200:400	1	0	47	14	(-)-(*S*,*S*)	19, 176

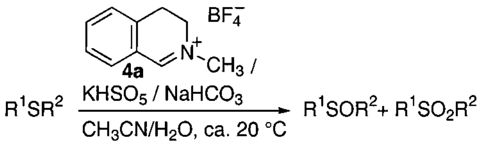
Table 12 (Continued)

entry	catalyst 4 (cat)	substrate (sub)	mole ratio cat:sub:$KHSO_5$	time (h)	temp (°C)	epoxide yield (%)	ee (%)	config	ref
10	 **4q**		1:20:40	0.75	0	68	8	(+)-(*R*,*R*)	19, 176
11	-"-		1:10:20	0.75	0	75	10	(+)-(*R*,*R*)	19, 176
12	-"-		1:20:40	0.75	0	72	15	(+)-(*R*,*R*)	19, 176
13	-"-		1:20:40	0.75	0	43	5	(+)-(*S*)	19, 176
14	-"-		1:20:40	0.75	0	68	40	(+)-(*R*,*R*)	19, 176
15	-"-		1:20:40	0.75	0	34	3	(+)-(1*S*,2*R*)	19, 176
16	-"-		1:20:40	0.75	0	73	20	(-)	19, 176
17	 **4r**		1:20:20	12	ca. 20	66	8		177
18	-"-		1:20:20	3	ca. 20	71	31	(*R*,*R*)	177
19	-"-		1:20:20	2	ca. 20	60	45	(*R*,*R*)	177
20	-"-		1:20:20	1	ca. 20	80	39	(1*S*,2*R*)	177
21	-"-		1:20:20	2	ca. 20	80	71	(*R*,*R*)	177

[a] Performed in CH_3CN/H_2O with 4 equiv of $NaHCO_3/Na_2CO_3$.

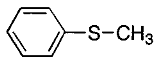
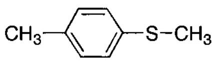
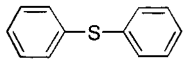
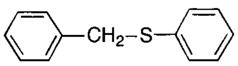
the buffered $KHSO_5$ as the oxygen source is shown in Scheme 33, and the results are given in Table 13.[165] While a high chemoselectivity was observed for sulfoxides with 1.1 equiv of $KHSO_5$, the sulfones were exclusively obtained with an excess (2.2 equiv) of this oxidant.

Scheme 33



The oxaziridine derived from 3,4-dihydroisoquinoline oxidizes sulfides to their sulfoxides[179] in the presence of trifluoroacetic acid. The oxygen transfer involves probably an oxaziridinium intermediate,

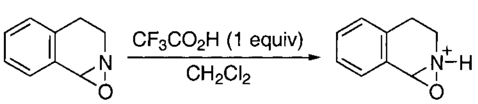
Table 13. Oxidation of Sulfides by Monoperoxysulfate, Catalyzed with the Iminium Salt 4a[a]

sulfide	mole ratio cat:sub:$KHSO_5$	time (min)	yields(%)	
			R_2SO	R_2SO_2
	1:10:11 1:10:22	10 90	90 traces	traces 85
	1:10:11 1:10:22	5 120	60 -	20 95
	1:10:11 1:10:22	45 180	90 -	traces 82
	1:10:11 1:10:22	5 30	92 -	- 80
$n\text{-}C_8H_{17}\text{-}S\text{-}CH_3$	1:10:11 1:10:22	10 30	60 -	20 65

[a] Performed in CH_3CN/H_2O at ca. 20 °C, ref 165.

formed by protonation of the oxaziridine with trifluoroacetic acid (Scheme 34).

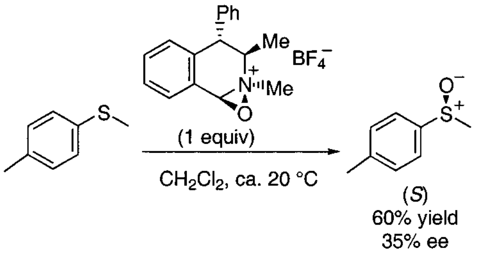
Scheme 34



Similar in-situ generations of oxaziridinium oxidants from the corresponding oxaziridines and methyl trifluorosulfonate were reported in intramolecular epoxidation reactions.[178,180]

Recently, the asymmetric sulfoxidation by the optically active oxaziridinium salt in Scheme 35 was

Scheme 35

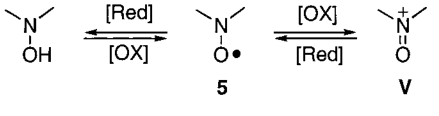


reported,[175,181] which gave the sulfoxide in a low (35% ee) enantioselectivity under stoichiometric conditions. To date, no catalytic enantioselective sulfoxidations by oxaziridinium salts have been reported.

VI. Oxoammonium-Ion-Mediated, Nitroxyl-Radical-Catalyzed Oxidations

Stable nitroxyl radials **5** may be obtained from secondary amines with no α hydrogen. Such nitroxyl radicals give on oxidation the oxoammonium ion and on reduction hydroxylamines (Scheme 36).[20]

Scheme 36



Nitroxyl radicals are weak oxidants, and by themselves they are limited to the oxidation of ascorbic acid and phenylhydrazine.[182,183] In these redox reactions, the nitroxyl radical **5** is converted to the corresponding hydroxylamine. In contrast, when the oxoammonium ion **V** is generated by oxidation of the nitroxyl radical **5**, a much stronger oxidant results, which is capable of oxidizing a large variety of substrates.

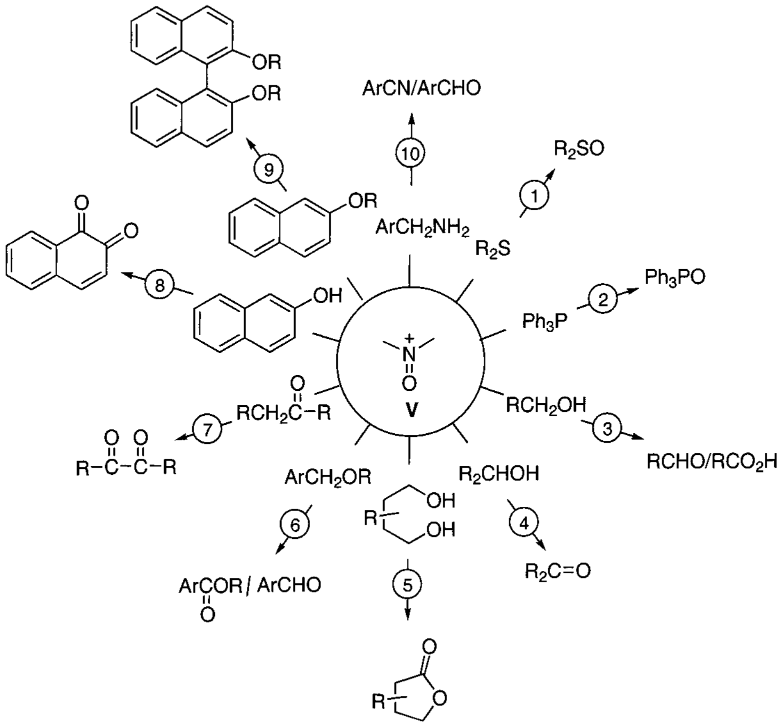
The important oxidative transformations effected by the oxoammonium ion **V** are shown in the form of a rosette in Scheme 37. These involve stoichiometric as well as catalytic conditions to illustrate the capabilities of this oxidant. Thus, the oxoammonium ion oxidizes sulfides selectively to their sulfoxides (tranformation 1 in Scheme 37),[184] and triphenylphosphine is converted to triphenylphosphine oxide in high yield (transformation 2).[185] The most thoroughly studied process is the efficient and selective oxidation of alcohols to carbonyl products (transformations 3−5). Primary alcohols are oxidized readily to either aldehydes or carboxylic acids (transformation 3),[21] while secondary alcohols react relatively slowly to give ketones (transformation 4) which depends on the reaction conditions. The oxidation of 1,4-butanediol affords selectively γ-butyrolactone in high yields (transformation 5).[186] Also, benzylic ethers undergo oxidation to the corresponding aldehydes or esters as the major products; the product selectivity may be controlled by the reaction conditions (transformation 6).[187,188] Even ketones with α hydrogens are oxidized to the respective α-dicarbonyl compounds, presumably through the intermediary enol (transformation 7).[185] Analogously, 2-naphthol affords 1,2-naphthoquinone in high yield (transformation 8).[185] In contrast, under electrochemical conditions (TEMPO-modified graphite electrode), 2-naphthol and its methyl ether afforded by oxidative coupling the corresponding binaphthyl derivatives nearly quantitatively (transformation 9).[189] Finally, the nitroxyl-radical-catalyzed electrochemical oxidation of primary amines gives aldehydes or ketones in high yields in the presence of water; however, nitriles are the major product under anhydrous conditions (transformation 10).[190]

The catalytic cycle for the oxidation with nitroxyl radical is shown in Scheme 38. The nitroxyl radical **5** is oxidized to the oxoammonium ion **V**; the latter serves as the catalytic oxidant. During the formation of the oxidation product, the oxoammonium ion **V** is reduced to the corresponding hydroxylamine, successive oxidation of the latter with a suitable oxidant [Ox] regenerates the oxoammonium ion **V** by way of the nitroxyl radical **5**, and thereby the catalytic cycle is completed.

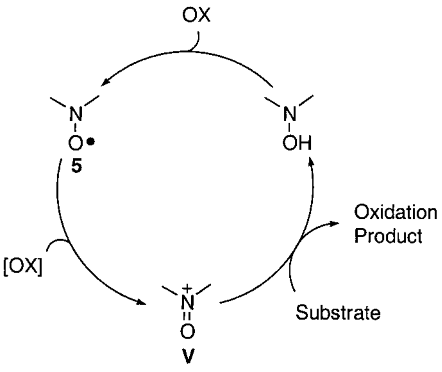
Under highly acidic (pH < 2) conditions, the nitroxyl radical **5** disproportionates rapidly to the oxoammonium ion **V** and its hydroxylamine (Scheme 39). Above pH 3, the reverse reaction occurs between the oxoammonium ion and hydroxylamine to give two nitroxyl radicals.[21] Thus, these reversible transformations participate in the catalytic cycle of Scheme 38, and their direction depends on the pH conditions.

In this section, only *catalytic* oxidations by the nitroxyl radical **5** are covered, in combination with a suitable oxidant to convert the nitroxyl radical to the

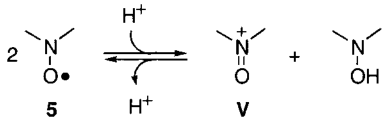
Scheme 37



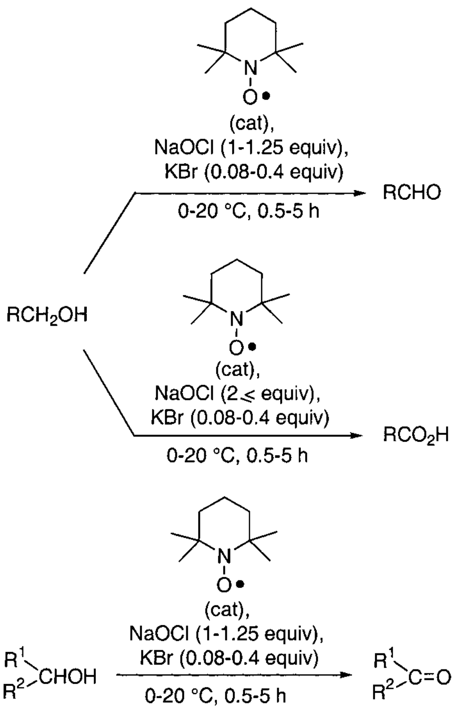
Scheme 38



Scheme 39



Scheme 40



oxoammonium ion **V**. Three review articles[20,21,191] have summarized the progress on the nitroxyl-radical oxidations since 1965, when the first example was reported.[192] The latest review presents the literature through 1995,[21] such that the present coverage features the recent work since 1995. Oxidations by nitroxyl radicals under electrochemical conditions have also been reviewed very recently,[193] and therefore, these are not dealt with here.

A. Alcohol Oxidations with Sodium Hypochlorite

Although the nitroxyl-radical system may oxidize a number of functionalities, the majority of the work is concerned with the oxidation of alcohols to the corresponding carbonyl products (transformations 3–5 in Scheme 37). We demonstrate that the nitroxyl radical **5** is a selective, efficient, and convenient catalyst for the oxidation of a variety of alcohols. Often only 1 mol % or even less of the nitroxyl radical is required as the catalyst, which is definitely competitive with the established metal-based oxidations.

The inexpensive and readily available sodium hypochlorite is commonly used as primary oxidant. The reactions are performed at room temperature or below and completed within a few hours. Primary alcohols are oxidized to the respective aldehydes with one equivalent or a slight excess of sodium hypochlorite. Carboxylic acids are obtained from the primary

Table 14. TEMPO-Catalyzed Oxidation of Alcohols by NaOCl[a]

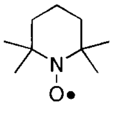
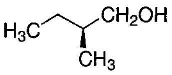
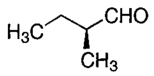
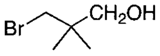
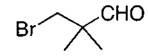
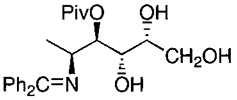
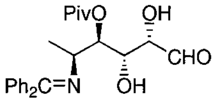
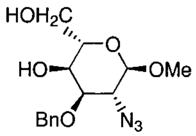
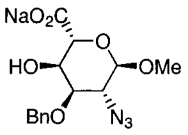
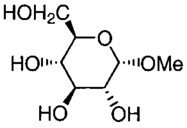
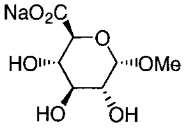
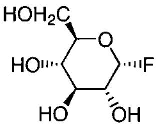
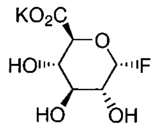
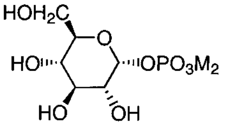
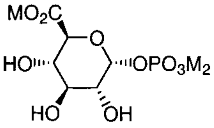
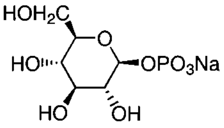
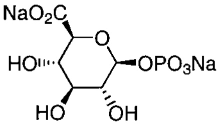
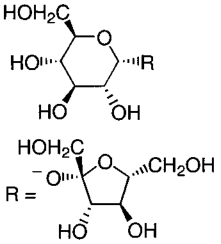
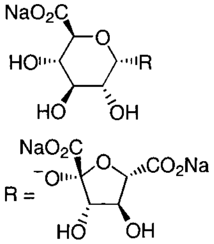
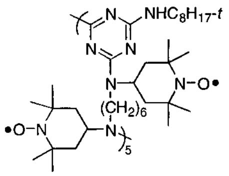
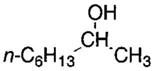
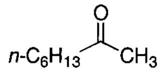
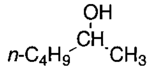
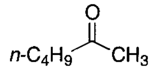
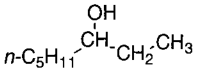
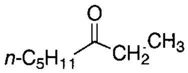
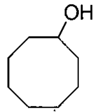
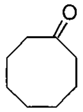
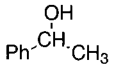
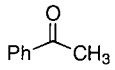
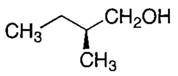
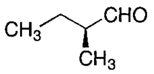
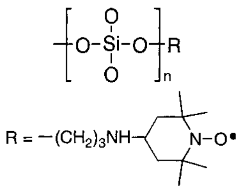
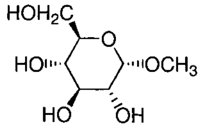
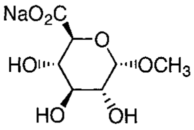
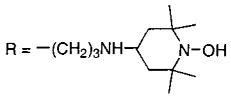
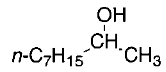
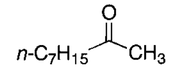
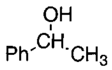
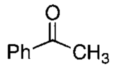
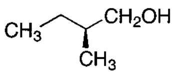
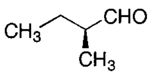
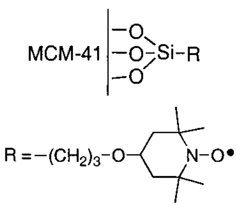
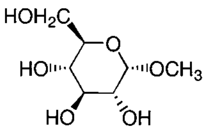
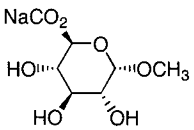
entry	catalyst (cat)	substrate (sub)	mole ratio cat:sub:NaOCl	solvent	temp (°C)	time (h)	product	yield (%)	ref
1	 **5a**		1:100:110	CH_2Cl_2/H_2O	10-15	0.25		92	196
2	-"-		1:20:21	CH_2Cl_2/H_2O	0	0.33		85	197
3	-"-		1:100:150	CH_2Cl_2/H_2O	-5	0.25		96	198
4	-"-		1:6.5:35	H_2O	ca. 20	2		62	200
5[b]	-"-		1:150:330	H_2O	5	0.25		87	201
6	-"-		1:40:90	H_2O	0	2		65	202
7	-"-	 (M = K, Na)	1:20:40	H_2O	0	1.5		85	202
8	-"-		1:35:65	H_2O	0	2		80	202
9[b]	-"-		1:50:330	H_2O	5	3		80	201 203
10		$n\text{-}C_7H_{15}CH_2OH$	1:100:125	MTBE/H_2O	0	0.75	$n\text{-}C_7H_{15}CHO$	75	204
11	-"-	$n\text{-}C_5H_{11}CH_2OH$	1:100:125	MTBE/H_2O	0	0.75	$n\text{-}C_5H_{11}CHO$	85	204
12	-"-	 $n\text{-}C_6H_{13}CH(OH)CH_3$	1:100:125	H_2O	0	0.75	 $n\text{-}C_6H_{13}C(O)CH_3$	98	204
13	-"-	 $n\text{-}C_4H_9CH(OH)CH_3$	1:100:125	H_2O	0	0.75	 $n\text{-}C_4H_9C(O)CH_3$	98	204

Table 14 (Continued)

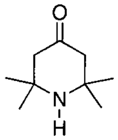
entry	catalyst (cat)	substrate (sub)	mole ratio cat:sub:NaOCl	solvent	temp (°C)	time (h)	product	yield (%)	ref
14	-"-	 $n\text{-}C_5H_{11}\overset{OH}{CH}CH_2CH_3$	1:100:125	H_2O	0	0.75		70	204
15	-"-		1:100:125	H_2O	0	0.75		99	204
16	-"-	$PhCH_2OH$	1:100:125	H_2O	0	0.5	PhCHO	99	204
17	-"-	 $Ph\overset{OH}{CH}CH_3$	1:100:125	H_2O	0	0.5		99	204
18	-"-		1:100:125	H_2O	0	0.75		89	204
19			1:20:44	H_2O	ca. 20	4		95	205
20	(silica) • R 	$n\text{-}C_6H_{13}CH_2OH$	1:100:125	CH_2Cl_2/H_2O	0	0.5	$n\text{-}C_6H_{13}CHO$	90	206
21	-"-	$n\text{-}C_7H_{15}CH_2OH$	1:100:125	CH_2Cl_2/H_2O	0	0.5	$n\text{-}C_7H_{15}CHO$	88	206
22	-"-	$n\text{-}C_8H_{17}CH_2OH$	1:100:125	CH_2Cl_2/H_2O	0	0.5	$n\text{-}C_8H_{17}CHO$	90	206
23	-"-	$n\text{-}C_{11}H_{23}CH_2OH$	1:100:125	CH_2Cl_2/H_2O	0	0.5	$n\text{-}C_{11}H_{23}CHO$	81	206
24	-"-	 $n\text{-}C_7H_{15}\overset{OH}{CH}CH_3$	1:100:125	CH_2Cl_2/H_2O	0	0.5		65	206
25	-"-	$PhCH_2OH$	1:100:125	CH_2Cl_2/H_2O	0	0.5	PhCHO	92	206
26	-"-	 $Ph\overset{OH}{CH}CH_3$	1:100:125	CH_2Cl_2/H_2O	0	0.5		91	206
27	-"-		1:100:125	CH_2Cl_2/H_2O	0	0.5		60	206
28			1:23:47	H_2O	0	[c]		[c]	207

[a] KBr/NaBr (0.08−0.4 equiv) was used except in entries 6−8 and 10−18. [b] Ultrasound applied. [c] Not reported.

alcohols with two equivalents or more of the hypochlorite; of course, secondary alcohols result in ketones (Scheme 40).[21] Since primary alcohols are oxidized substantially faster than secondary ones, a high selectivity for the former may be obtained. Generally, mild alkaline conditions, e.g. $NaHCO_3$ buffer, increase the reactivity and selectivity for primary alcohols.[21]

In nitroxyl-radical-mediated oxidations, catalytic amounts of the bromide ion (usually as KBr or NaBr) are often added, which increases the rate of the oxidation.[186] The bromide ion reacts with hypochlorite to generate hypobromite in situ, which is a stronger oxidant.

Among the various nitroxyl-radical catalysts, 2,2,6,6-tetramethylpiperidin-1-oxyl (**5a**), commonly called TEMPO, is most frequently used, since it is commercially available. The 4-keto-substituted TEMPO is readily accessible from the respective keto derivative, which is prepared from acetone and ammonia.[194] Therefore, TEMPO, in combination with sodium hypochlorite, has become the choice for the oxidation



of alcohols (Table 14).[195] For convenience, the pertinent references are again cited directly in the table and, thus, are not repeated in the text.

The oxidation of primary alcohols affords the corresponding aldehydes in high yields (entries 1−3). (*S*)-2-Methylbutan-1-ol is selectively oxidized to (*S*)-2-methylbutanal without reaction at the chirality center (entry 1). The reaction is highly chemoselective, since the secondary alcohol and imino functionalities are not affected (entry 3). Unquestionably, this catalytic method is superior to the stoichiometric PCC oxidation,[199] which generates toxic chromium waste.

The TEMPO-catalyzed procedure is particularly convenient for the oxidation of primary hydroxy groups in carbohydrates. Thus, a variety of carbohydrates were selectively oxidized to their carboxylate derivatives in high yields (entries 4−9). The oxidation of sucrose gave sucrose tricarboxylate in good yields, when an excess of sodium hypochlorite was employed (entry 9).

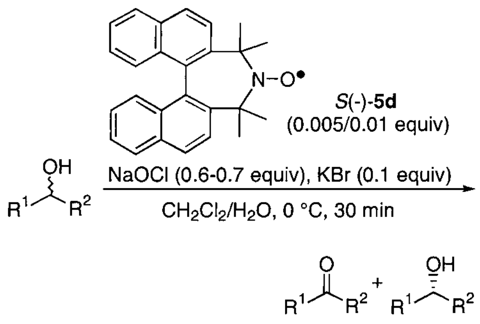
Immobilization of TEMPO on a polymer or inorganic support affords heterogeneous catalysts, which have the advantage of facile separation from the reaction mixture. The polymer-immobilized TEMPO (entry 10) from the commercially available polymer stabilizer Chimassorb 944 efficiently and selectively oxidizes primary and secondary alcohols to their carbonyl compounds with aqueous NaOCl (entries 10−18). The reactions are complete within 45 min and obviate the need of bromides as cocatalyst and organic solvent. Methyl *tert*-butyl ether (MTBE) was added as a cosolvent in the oxidation of 1-octanol and 1-hexanol (entries 10 and 11). The catalyst is insoluble in MTBE, which prevented overoxidation to carboxylic acids.

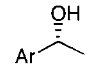
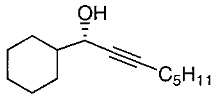
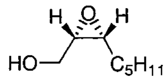
Recently, TEMPO was immobilized on a silica matrix by the sol−gel method and used as a heterogeneous catalyst for the selective oxidation (95% yield) of methyl α-D-glucopyranoside to the uronate (entry 19). The silica-supported TEMPO catalyst (see entry 20), in which the TEMPO precursor is attached to the aminopropyl-functionalized silica, selectively oxidizes primary and secondary alcohols to the respective aldehydes and ketones in good yields (entries 20−27). TEMPO, supported on the mesoporous MCM-41 zeolite, was shown to catalyze the hypochlorite oxidation of α-methyl glucoside selectively to 1-*O*-methyl glucuronate (entry 28).

The TEMPO catalyst has been employed in the oxidation of primary alcohol functionality by sodium hypochlorite in the presence of bromide ion to carboxylic acids in several oligo- and polysaccharides (not shown in Table 14). Such oxidations modify the properties of these polysaccharides and improve solubility in water to suit various commercial applications. Thus, β-cyclodextrin was oxidized to a mixture of mono- and dicarboxy-β-cyclodextrin sodium salts.[208] The selective oxidation of several naturally occurring polysaccharides was conducted to afford their carboxy derivatives, e.g., wheat starch, potato amylose, potato amylopectin, chitin, chitosan, pullulan, alternan, regular comb dextran, cellulose (AVICEL), α-cellulose, and carboxymethyl cellulose.[209] The procedure has also been applied to the oxidation of pseudo-amorphous celluloses,[210] starch,[211] chitins,[212] and other polysaccharides of natural origin.[213]

The optically active binaphthyl-based nitroxyl radical *S*-(−)-**5d** was used as the catalyst for the kinetic resolution of racemic secondary alcohols (Scheme 41).[214] The in-situ-generated chiral oxoammonium ion **Vd** showed excellent (98% ee) enantioselectivity for the oxidation of one enantiomer.

Scheme 41



recovered alcohol	% ee	convn (%)
	57-98[a]	56-87
	41	66
	19	58

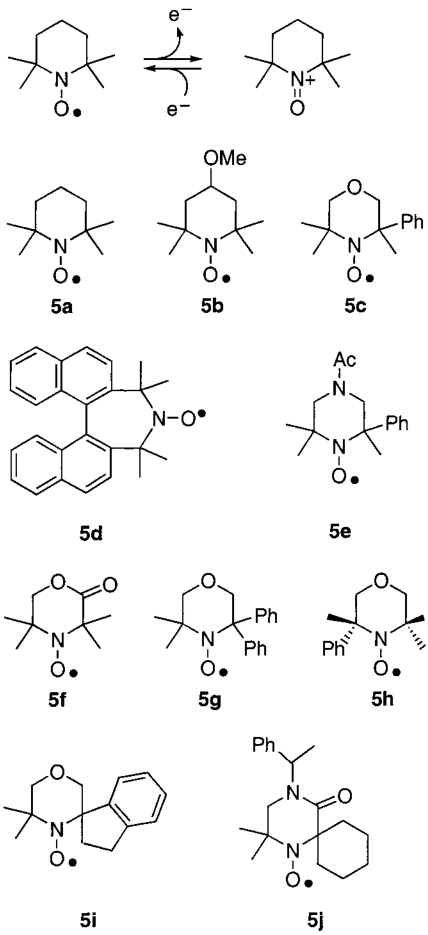
[a]Six examples

The persistent nitroxyl radicals **5a**−**j** (Scheme 42) were also prepared and their catalytic activity compared in the oxidation of secondary alcohols to ketones by NaOCl.[215] The nitroxyl radicals **5a**−**d** showed high catalytic activity, while **5e** performed relatively poorly (40% yield), and the more elaborate derivatives **5f**−**j** were practically inactive (<10% yield). The redox potentials of these nitroxyl radicals were determined by cyclic voltammetry and shown to correlate with their catalyst activity. It was found that the active catalysts **5a**−**d** possess oxidation potentials between 638 and 807 mV, whereas the inactive ones **5e**−**j** are above 852 mV. A computational method was developed to predict the redox potential of nitroxyl radicals, and a good correlation was found between the calculated and measured values.[215]

B. Alcohol Oxidations with Various Oxidants

Although sodium hypochlorite is commonly used as the primary oxidant in the TEMPO-catalyzed

Scheme 42



oxidations, other oxidants have also been successfully employed. The oxidations of alcohols with the TEMPO (**5a**) catalyst and various oxidants are given in Table 15. *m*-CPBA oxidizes secondary alcohols to the corresponding ketones in high yields, even in the presence of only 1 mol % of the TEMPO catalyst and 1 mol % of *n*-Bu_4NBr (entries 1–4). The latter serves as a source for the bromide-ion cocatalyst. Alternatively, the TEMPO precursor 2,2,6,6-tetramethylpiperidinium hydrobromide may be used directly as the catalyst in place of TEMPO and *n*-Bu_4NBr (entry 5). The oxidation of *cis*-1,2-cyclohexanedimethanol gave the γ-lactone and not the dialdehyde (entry 6).

Also, $KHSO_5$ was employed as primary oxidant in the presence of *n*-Bu_4NBr in nonaqueous media (entries 7–15). Benzylic alcohols gave high yields of their carbonyl derivatives (entries 10–12, 14, 15), except the electron-rich 4-methoxybenzyl alcohol (entry 13); however, aliphatic alcohols were oxidized in lower yields (entries 7–9). *tert*-Butyldimethylsilyl-protected 4-hydroxybenzyl alcohol gave a good yield of the corresponding aldehyde without affecting the silyl-ether linkage (entry 14).

tert-Butyl hypochlorite was used as a primary oxidant in the TEMPO-catalyzed oxidation of β-D-glucosides to give the respective β-D-glucuronides in aqueous solutions (entries 16–19). This procedure facilitates isolation of the products, because the NaOCl oxidant produces salts and such contamination encumbers purification of the rather water-soluble products.

Two equivalents of sodium chlorite in the presence of catalytic amounts both of TEMPO and sodium hypochlorite provided an effective procedure for the oxidation of primary alcohols directly to carboxylic acids in excellent yields (entries 20–31). The $NaClO_2$ efficiently oxidizes in situ the initially formed aldehydes to the respective carboxylic acid; it itself is converted to NaOCl. Thus, the $NaClO_2$ serves as a source of hypochlorite; however, addition of 2 mol % of hypochlorite right from the start eliminates the induction period.

Benzylic alcohols and 2-arylethanols afforded the corresponding acids in nearly quatitative yields (entries 20–26). The reaction tolerates acetylenic-, cyclopropyl-, and cbz-protected amino groups (entries 27, 28, and 31). Racemization or epimerization did not occur in the oxidation of alcohols with chirality centers (entries 29–31).

In general, this procedure gives better yields of carboxylic acids from primary alcohols than the TEMPO–NaOCl method.[195a] The $NaClO_2$ procedure was applied in the final step of the synthesis of the endothelin-receptor antagonist without racemization or damage of the electron-rich aromatic ring (entry 32).

Use of *N*-chlorosuccinimide as primary oxidant in the TEMPO-catalyzed oxidation of alcohols gives carbonyl compounds selectively without overoxidation to the respective carboxylic acids (entries 33–47). Primary aliphatic, benzylic, and allylic alcohols produce the corresponding aldehydes in high yields; however, secondary alcohols react more slowly (entries 34, 39, and 42). Thus, the primary hydroxy functionality may be selectively oxidized in the presence of secondary ones (entries 37, 46, and 47).

Also, the hypervalent iodine compound, (diacetoxyiodo)benzene, served as the primary oxidant (entries 48–68). Primary alcohols were selectively oxidized in the presence of secondary hydroxy, epoxy, sulfide, and selenide functionalities (entries 56–58, 64, and 65). No racemization occurred at the chirality center in the oxidation of the epoxides in entries 56 and 57.

The combination of peroxydisulfate and alumina-supported silver was employed with good success as a primary oxidant in the TEMPO-catalyzed oxidation of methyl α-D-glucopyranoside (entry 69). The multicomponent MTO/HBr/TEMPO/H_2O_2 catalytic system oxidizes benzyl alcohols to their aldehydes in high yields (entries 70 and 71). Here the H_2O_2 converts MTO first to its diperoxo complex CH_3ReO_5, the latter oxidizes Br^- to OBr^- catalytically, and the hypobromite then performs the usual TEMPO-catalyzed oxidation of the alcohol substrate.

Molecular oxygen, the oxygen source of choice, has been used directly in combination with the $RuCl_2(PPh_3)_3$ complex to generate in situ the required oxidant for the TEMPO-catalyzed oxidations. In this manner a variety of alcohols were selectively transformed to their carbonyl compounds (entry 72–84). Molecular oxygen was also used in conjunction with the copper complex derived from $CuBr/Me_2S$ and perfluoroalkylated bipyridine (entries 85–97). Aliphatic, benzylic, and allylic primary and secondary

Table 15. TEMPO-Catalyzed Oxidation of Alcohols by Various Oxidants

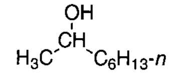
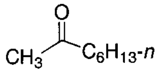
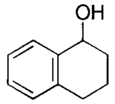
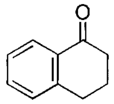
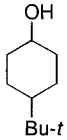
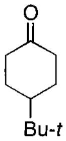
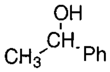
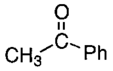
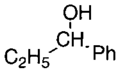
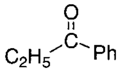
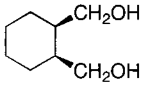
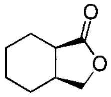
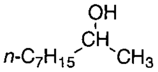
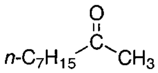
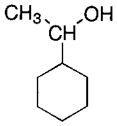
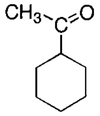
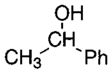
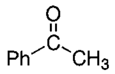
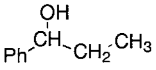
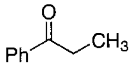
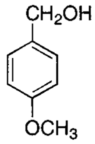
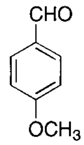
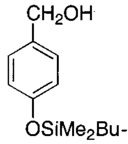
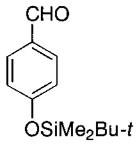
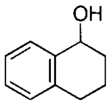
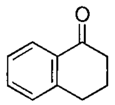
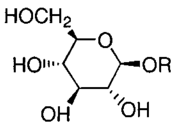
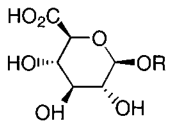
entry	oxidant (ox)	substrate (sub)	mole ratio cat:sub:ox	solvent	temp (°C)	time (h)	product	yield (%)	ref
1	*m*-CPBA[a]	 $H_3C\text{-}CH(OH)\text{-}C_6H_{13}\text{-}n$	1:100:120	CH_2Cl_2	0-23	0.67	 $CH_3\text{-}C(=O)\text{-}C_6H_{13}\text{-}n$	92	216
2	-"-		1:100:120	CH_2Cl_2	0-23	0.67		97	216
3	-"-		1:100:120	CH_2Cl_2	0-23	0.67		94	216
4	-"-	 $CH_3\text{-}CH(OH)\text{-}Ph$	1:100:120	CH_2Cl_2	0-23	0.67	 $CH_3\text{-}C(=O)\text{-}Ph$	91	216
5[b]	-"-	 $C_2H_5\text{-}CH(OH)\text{-}Ph$	1:100:120	CH_2Cl_2	0-23	0.67	 $C_2H_5\text{-}C(=O)\text{-}Ph$	98	216
6	-"-		1:100:240	CH_2Cl_2	0-23	0.67		89	216
7	$KHSO_5$[c]	$n\text{-}C_8H_{17}CH_2OH$	1:100:120	CH_2Cl_2	ca. 20	12	$n\text{-}C_8H_{17}CHO$	67	217
8	-"-	 $n\text{-}C_7H_{15}\text{-}CH(OH)\text{-}CH_3$	1:100:120	toluene	ca. 20	12	 $n\text{-}C_7H_{15}\text{-}C(=O)\text{-}CH_3$	56	217
9	-"-		1:100:220	toluene	ca. 20	12		71	217
10	-"-	$PhCH_2OH$	1:100:220	CH_2Cl_2	ca. 20	12	$PhCHO$	90	217
11	-"-	 $CH_3\text{-}CH(OH)\text{-}Ph$	1:100:220	toluene	ca. 20	12	 $Ph\text{-}C(=O)\text{-}CH_3$	91	217
12	-"-	 $Ph\text{-}CH(OH)\text{-}CH_2\text{-}CH_3$	1:100:220	toluene	ca. 20	12		93	217
13	-"-		1:100:220	CH_2Cl_2	ca. 20	12		37	217
14	-"-		1:100:220	CH_2Cl_2	ca. 20	12		81	217
15	-"-		1:100:220	toluene	ca. 20	12		96	217
16	*t*-BuOCl	 R = CH_3	1:60:120	H_2O	ca. 20	0.5	 R = CH_3	34	218
17	-"-	R = Ph	1:60:120	H_2O	ca. 20	0.5	R = Ph	78	218

Table 15 (Continued)

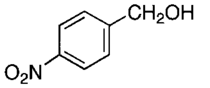
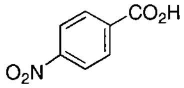
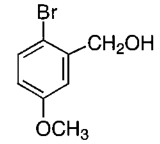
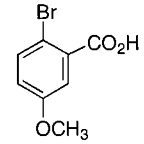
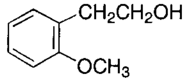
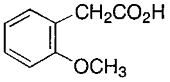
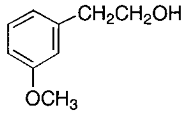
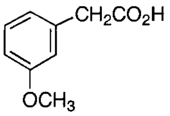
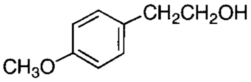
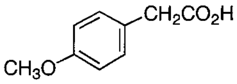
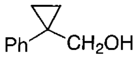
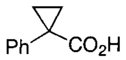
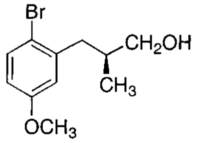
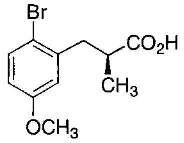
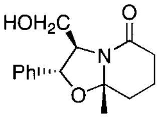
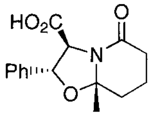
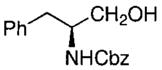
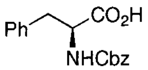
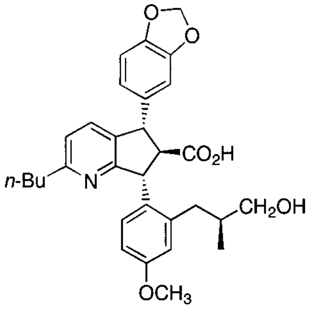
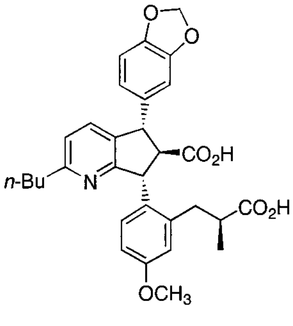
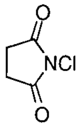
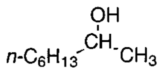
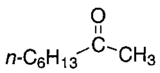
entry	oxidant (ox)	substrate (sub)	mole ratio cat:sub:ox	solvent	temp (°C)	time (h)	product	yield (%)	ref
18	t-BuOCl	R = 2-FC_6H_4	1:60:120	H_2O	ca. 20	0.5	R = 2-FC_6H_4	97	218
19	-"-	R = 4-$NO_2C_6H_4$	1:60:120	H_2O	ca. 20	0.5	R = 4-$NO_2C_6H_4$	64	218
20	$NaClO_2$[d]	$PhCH_2OH$	1:14:28	CH_3CN/H_2O	35	2-5	$PhCO_2H$	98	219
21	-"-		1:14:28	CH_3CN/H_2O	35	2-5		100	219
22	-"-		1:14:28	CH_3CN/H_2O	35	2-5		96	219
23	-"-	$PhCH_2CH_2OH$	1:14:28	CH_3CN/H_2O	35	2-5	$PhCH_2CO_2H$	100	219
24	-"-		1:14:28	CH_3CN/H_2O	35	2-5		99	219
25	-"-		1:14:28	CH_3CN/H_2O	35	2-5		96	219
26	-"-		1:14:28	CH_3CN/H_2O	35	2-5		100	219
27	-"-	Ph—≡—CH_2OH	1:14:28	CH_3CN/H_2O	35	2-5	Ph—≡—CO_2H	90	219
28	-"-		1:14:28	CH_3CN/H_2O	35	2-5		95	219
29	-"-		1:14:28	CH_3CN/H_2O	35	2-5		92	219
30	-"-		1:14:28	CH_3CN/H_2O	35	2-5		95	219
31	-"-		1:14:28	CH_3CN/H_2O	35	2-5		85	219
32	$NaClO_2$[e]		1:10:20	CH_3CN/H_2O	35	4		90	220
33[f]		n-$C_7H_{15}CH_2OH$	1:10:13	CH_2Cl_2/H_2O	ca. 20	3.5	n-$C_7H_{15}CHO$	100	221
34	-"-	 $n\text{-}C_6H_{13}CH(OH)CH_3$	1:10:12	CH_2Cl_2/H_2O	ca. 20	6	 $n\text{-}C_6H_{13}C(=O)CH_3$	26	221

Table 15 (Continued)

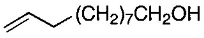
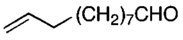
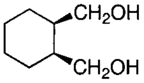
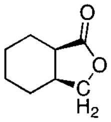
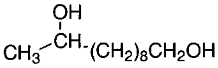
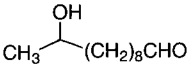
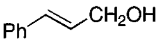
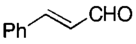
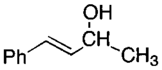
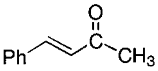
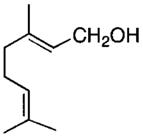
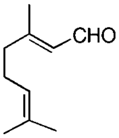
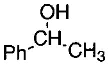
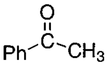
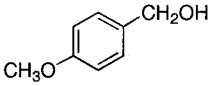
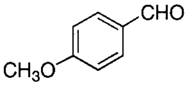
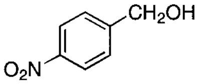
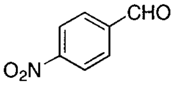
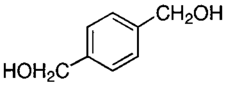
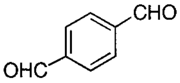
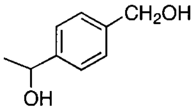
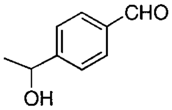
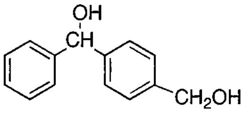
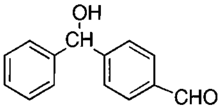
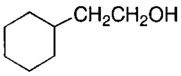
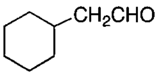
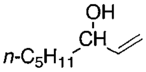
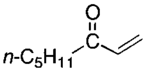
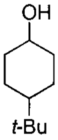
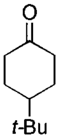
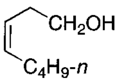
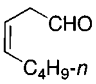
entry	oxidant (ox)	substrate (sub)	mole ratio cat:sub:ox	solvent	temp (°C)	time (h)	product	yield (%)	ref
35	-"-		1:10:20	CH_2Cl_2/H_2O	ca. 20	24		92	221
36	-"-		1:10:30	CH_2Cl_2/H_2O	ca. 20	2		94	221
37	-"-		1:10:15	CH_2Cl_2/H_2O	ca. 20	2.15		82	221
38	-"-		1:10:16	CH_2Cl_2/H_2O	ca. 20	2		83	221
39	-"-		1:10:22	CH_2Cl_2/H_2O	ca. 20	24		55	221
40	-"-		1:10:18	CH_2Cl_2/H_2O	ca. 20	3		100	221
41	-"-	$PhCH_2OH$	1:10:12.5	CH_2Cl_2/H_2O	ca. 20	2	PhCHO	99	221
42	-"-		1:10:12	CH_2Cl_2/H_2O	ca. 20	3.5		68	221
43	-"-		1:10:13	CH_2Cl_2/H_2O	ca. 20	7		100	221
44	-"-		1:10:11	CH_2Cl_2/H_2O	ca. 20	0.5		100	221
45	-"-		1:10:26	CH_2Cl_2/H_2O	ca. 20	6		95	221
46	-"-		1:10:11	CH_2Cl_2/H_2O	ca. 20	2.15		65	221
47	-"-		1:10:11	CH_2Cl_2/H_2O	ca. 20	3		77	221
48	$PhI(OAc)_2$		1:10:11	CH_2Cl_2	ca. 20	2.5		80	222
49	-"-		1:10:11	CH_2Cl_2	ca. 20	2.5		95	222
50	-"-		1:10:11	CH_2Cl_2	ca. 20	7		90	222
51	-"-		1:10:11	CH_2Cl_2	ca. 20	2.5		95	222

Table 15 (Continued)

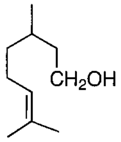
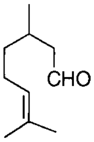
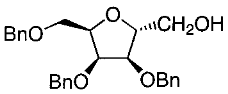
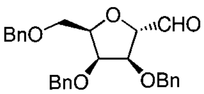
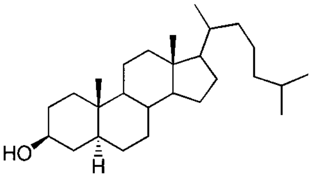
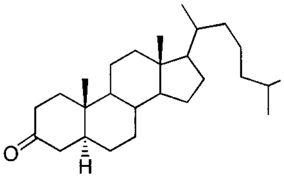
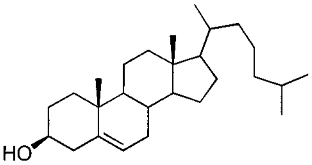
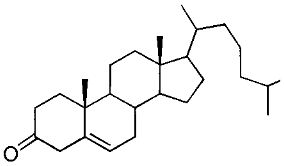
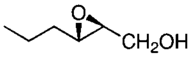
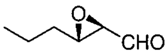
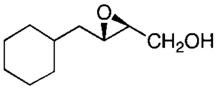
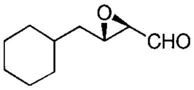
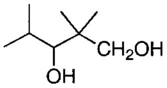
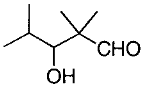
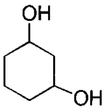
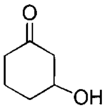
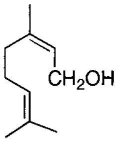
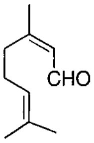
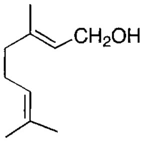
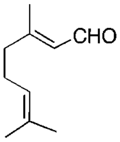
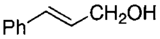
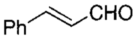
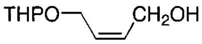
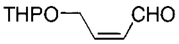
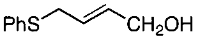
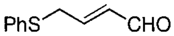
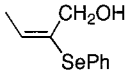
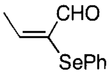
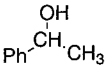
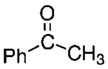
entry	oxidant (ox)	substrate (sub)	mole ratio cat:sub:ox	solvent	temp (°C)	time (h)	product	yield (%)	ref
52	-"-		1:10:11	CH_2Cl_2	ca. 20	0.5		90	222
53	-"-		1:10:11	CH_2Cl_2	ca. 20	15		75	222
54	-"-		1:10:11	CH_2Cl_2	ca. 20	5		80	222
55	-"-		1:10:11	CH_2Cl_2	ca. 20	5		80	222
56	-"-		1:10:11	CH_2Cl_2	ca. 20	1		70	222
57	-"-		1:10:11	CH_2Cl_2	ca. 20	2		75	222
58	-"-		1:10:11	CH_2Cl_2	ca. 20	2.5		70	222
59	-"-		1:10:11	CH_2Cl_2	ca. 20	8		90	222
60	-"-		1:10:11	CH_2Cl_2	ca. 20	1.5		95	222
61	-"-		1:10:11	CH_2Cl_2	ca. 20	0.1		95	222
62	-"-		1:10:11	CH_2Cl_2	ca. 20	1		95	222
63	-"-		1:10:11	CH_3CN/H_2O	ca. 20	0.2		95	222
64	-"-		1:10:11	CH_2Cl_2	ca. 20	1		70	222
65	-"-		1:10:11	CH_2Cl_2	ca. 20	15		55	222
66	-"-	$PhCH_2OH$	1:10:11	CH_2Cl_2	ca. 20	0.5	$PhCHO$	95	222
67	-"-	 $PhCH(OH)CH_3$	1:10:11	CH_2Cl_2	ca. 20	1.5	 $PhC(=O)CH_3$	95	222

Table 15 (Continued)

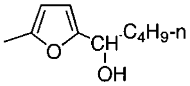
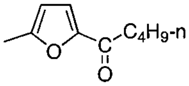
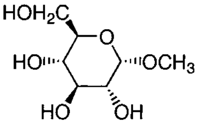
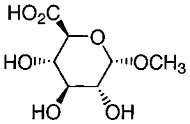
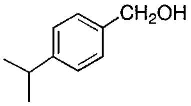
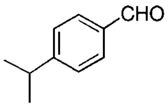
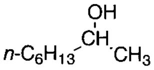
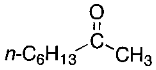
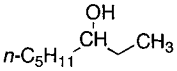
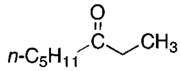
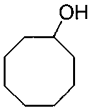
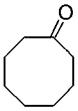
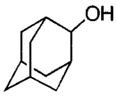
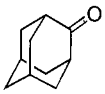
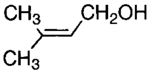
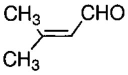
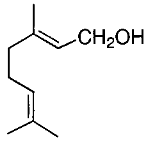
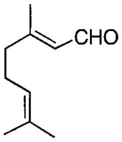
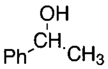
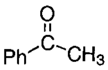
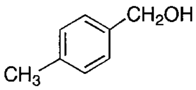
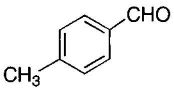
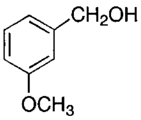
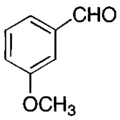
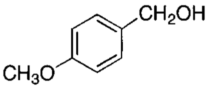
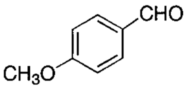
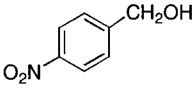
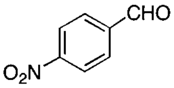
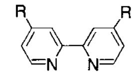
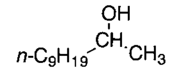
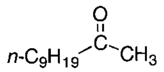
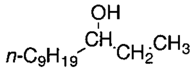
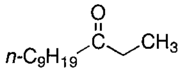
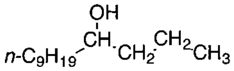
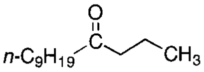
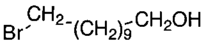
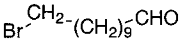
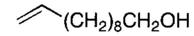
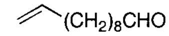
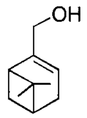
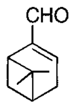
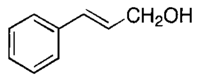
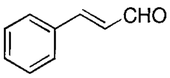
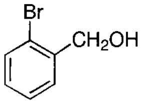
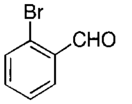
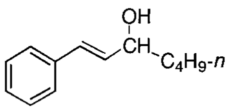
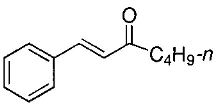
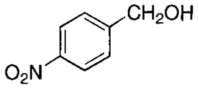
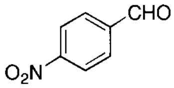
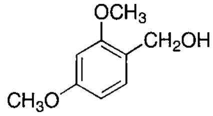
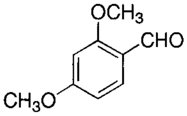
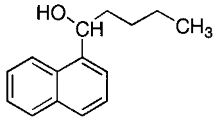
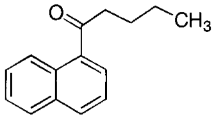
entry	oxidant (ox)	substrate (sub)	mole ratio cat:sub:ox	solvent	temp (°C)	time (h)	product	yield (%)	ref
68	-"-		1:10:11	CH_2Cl_2	ca. 20	3		95	222
69	$S_2O_8^{2-}$, $Ag\text{-}Al_2O_3$		1:50:100	H_2O	ca. 20	25		78	223
70	30% H_2O_2, CH_3ReO_3, Br^-	$PhCH_2OH$	1:33:165	$AcOH/H_2O$	ca. 20	2	$PhCHO$	81	224
71	-"-		1:33:165	$AcOH/H_2O$	ca. 20	2		90	224
72	O_2, $RuCl_2(PPh_3)_3$	$n\text{-}C_7H_{15}CH_2OH$	1:20:-	PhCl	100	7	$n\text{-}C_7H_{15}CHO$	85	225
73	-"-	 $n\text{-}C_6H_{13}CH(OH)CH_3$	1:22:-	PhCl	100	7	 $n\text{-}C_6H_{13}C(=O)CH_3$	95	225
74	-"-	 $n\text{-}C_5H_{11}CH(OH)CH_2CH_3$	1:22:-	PhCl	100	7	 $n\text{-}C_5H_{11}C(=O)CH_2CH_3$	85	225
75	-"-		1:22:-	PhCl	100	7		85	225
76	-"-		1:33:-	PhCl	100	7		92	225
77	-"-		1:22:-	PhCl	100	7		96	225
78	-"-		1:22:-	PhCl	100	7		91	225
79	-"-	$PhCH_2OH$	1:33:-	PhCl	100	5	$PhCHO$	100	225
80	-"-	 $PhCH(OH)CH_3$	1:33:-	PhCl	100	7	 $PhC(=O)CH_3$	91	225
81	-"-		1:33:-	PhCl	100	4		100	225
82	-"-		1:33:-	PhCl	100	4		100	225
83	-"-		1:33:-	PhCl	100	3		100	225
84	-"-		1:33:-	PhCl	100	7		68	225

Table 15 (Continued)

entry	oxidant (ox)	substrate (sub)	mole ratio cat:sub:ox	solvent	temp (°C)	time (h)	product	yield (%)	ref
85	O$_2$, CuBr·Me$_2$S,  R = −(CH$_2$)$_4$−C$_8$F$_{17}$	n-C$_9$H$_{19}$CH$_2$OH	1:30:-	C$_8$F$_{18}$/PhCl	90	7-13	n-C$_9$H$_{19}$CHO	73	226
86	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	8		71	226
87	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	12		69	226
88	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	17		31	226
89	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	7-13		81	226
90	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	7-13		78	226
91	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	7-13		76	226
92	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	2-7		79	226
93	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	2-7		96	226
94	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	2-7		84	226
95	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	4		93	226
96	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	2-7		93	226
97	-"-		1:30:-	C$_8$F$_{18}$/PhCl	90	2-7		91	226

[a] n-Bu$_4$NBr (0.01 equiv) was added. [b] 2,2,6,6-Tetramethylpiperidinium hydrobromide (0.01 equiv) was used instead of TEMPO and n-Bu$_4$NBr. [c] n-Bu$_4$NBr (0.04 equiv) was added. [d] NaOCl (0.02 equiv) was added. [e] NaOCl (0.036 equiv) was added. [f] n-Bu$_4$NCl (0.1 equiv) was added.

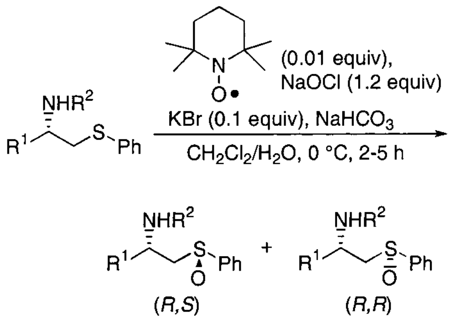
alcohols were oxidized to their aldehydes and ketones in high yields and good selectivities.

Recently, a polymer-bound bromite complex was employed as primary oxidant.[227] In the presence of catalytic amounts of TEMPO, primary alcohols were oxidized to aldehydes and secondary ones (not listed in Table 15) to ketones.

C. Miscellaneous Catalytic Oxidations

The TEMPO/KBr/NaOCl system selectively oxidizes sulfides to sulfoxides without overoxidation to sulfones. Thus, N-protected β-amino sulfides gave readily separable diastereomeric sulfoxides in high yields (Scheme 43).[228] (R,R)-Sulfoxides were obtained as the major diastereomer in ee values up to 88%. The TEMPO/KBr/NaOCl combination also performs efficiently and selectively the Baeyer−Villiger oxidation of α-hydroxy- and α-keto β-lactams to the respective mixed anhydrides in very high yields (Scheme 44).[229] The low reaction temperature (0 °C) and the near neutral pH ensured that no epimerization occurred. The procedure was also employed in

Scheme 43



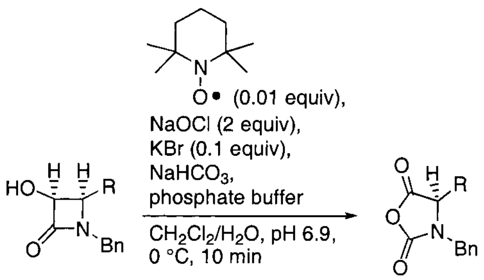
R^1	R^2	yield (%)	
		(*R*,*S*)	(*R*,*R*)
C_2H_5	CO_2Bu-*t*	35	55
C_2H_5	CO_2Ph	34	56
i-Pr	CO_2Bu-*t*	30	68
i-Pr	COPh	35	62
i-Pr	CO_2CH_3	20	75
i-Pr	$CO_2C_2H_5$	16	76
$PhCH_2$	CO_2Bu-*t*	18	80
$PhCH_2$	COPh	43	49
$PhCH_2$	CO_2CH_3	30	59
Ph	CO_2Bu-*t*	10	80
Ph	COPh	14	78
Ph	CO_2CH_3	5	85

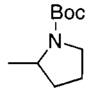
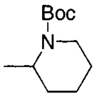
the oxidation of benzylic ethers to their esters in moderate to good yields (Scheme 45),[188] in which benzaldehydes and benzoic acids were formed as byproducts.

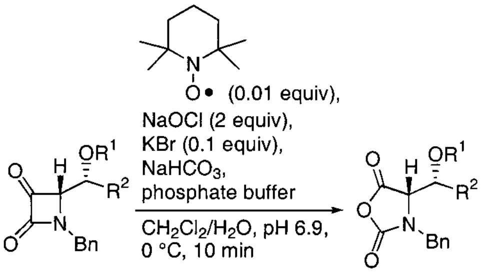
VII. Summary

Nonmetal oxidation catalysts have gained much attention in recent years. The reason for this surge in activity is 2-fold: On one hand, a number of such catalysts has become readily accessible; on the other hand, such catalysts are quite resistant toward self-oxidation and compatible under aerobic and aqueous reaction conditions. In this review, we have focused on five nonmetal catalytic systems which have attained prominence in the oxidation field in view of their efficacy and their potential for future development; stoichiometric cases have been mentioned to provide overview and scope. Such nonmetal oxidation catalysts include the α-halo carbonyl compounds **1**, ketones **2**, imines **3**, iminium salts **4**, and nitroxyl radicals **5**. In combination with a suitable oxygen source (H_2O_2, $KHSO_5$, NaOCl), these catalysts serve as precursors to the corresponding oxidants, namely, the perhydrates **I**, dioxiranes **II**, oxaziridines **III**, oxaziridinium ions **IV**, and finally oxoammonium ions **V**. A few of the salient features about these nonmetal, catalytic systems shall be reiterated in this summary.

Scheme 44



R	yield (%)
$-CH(NHBoc)CH_3$	96
$-CH(NHBoc)CHMe_2$	92
$-CH(NHBoc)CH_2Ph$	97
	98
	96

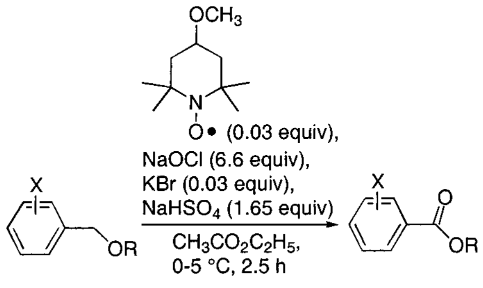


R^1	R^2	yield (%)
t-$BuMe_2Si$	Ph	96
t-$BuMe_2Si$	*i*-Pr	95

The first class entails the α-halo ketones, which catalyze the oxidation of a variety of organic substrates by hydrogen peroxide as the oxygen source. The perhydrates **I**, formed in situ by the addition of hydrogen peroxide to the α-halo ketones, are quite strong electrophilic oxidants and expectedly transfer an oxygen atom to diverse nucleophilic acceptors. Thus, α-halo ketones have been successfully employed for catalytic epoxidation, heteroatom (S, N) oxidation, and arene oxidation. Although high diastereoselectivities have been achieved by these nonmetal catalysts, no enantioselective epoxidation and sulfoxidation have so far been reported. Consequently, it is anticipated that catalytic oxidations by perhydrates hold promise for further development, especially, and should ways be found to transfer the oxygen atom enantioselectively.

The second class, namely, the dioxiranes, has been extensively used during the last two decades as a convenient oxidant in organic synthesis. These powerful and versatile oxidizing agents are readily available from the appropriate ketones by their treatment

Scheme 45



X	R	yield (%)
H	CH_3	75
2-CH_3	CH_3	50
4-CH_3	CH_3	71
4-OCH_3	CH_3	58
2-Cl	CH_3	68
4-Cl	CH_3	68
4-NO_2	CH_3	62
4-CH_3	C_2H_5	60
2-Cl	C_2H_5	37
4-Cl	C_2H_5	53
2-NO_2	C_2H_5	34
H	CH_2Ph	88

with potassium monoperoxysulfate. The oxidations may be performed either under stoichiometric or catalytic conditions; the latter mode of operation is featured in this review. In this case, a variety of structurally diverse ketones have been shown to catalyze the dioxirane-mediated epoxidation of alkenes by monoperoxysulfate as the oxygen source. By employing chiral ketones, highly enantioselective (up to 99% ee) epoxidations have been developed, of which the sugar-based ketones are so far the most effective. Reports on catalytic oxidations by dioxiranes other than epoxidations are scarce; nevertheless, fructose-derived ketones have been successfully employed as catalysts for the enantioselective CH oxidation in *vic* diols to afford the corresponding optically active α-hydroxy ketones. To date, no catalytic asymmetric sulfoxidations by dioxiranes appear to have been documented in the literature, an area of catalytic dioxirane chemistry that merits attention.

A third class is the imines; their reaction with hydrogen peroxide or monoperoxysulfate affords oxaziridines. These relatively weak electrophilic oxidants only manage to oxidize electron-rich substrates such as enolates, silyl enol ethers, sulfides, selenides, and amines; however, the epoxidation of alkenes has been achieved with activated oxaziridines produced from perfluorinated imines. Most of the oxidations by in-situ-generated oxaziridines have been performed stoichiometrically, with the exception of sulfoxidations. When chiral imines are used as catalysts, optically active sulfoxides are obtained in good ee values, a catalytic asymmetric oxidation by oxaziridines that merits further exploration.

The fourth class is made up by the iminium ions, which with monoperoxysulfate lead to the corresponding oxaziridinium ions, structurally similar to the above oxaziridine oxidants except they possess a much more strongly electrophilic oxygen atom due to the positively charged ammonium functionality. Thus, oxaziridinium ions effectively execute besides sulfoxidation and amine oxidation the epoxidation of alkenes under catalytic conditions. As expected, chiral iminium salts catalyze asymmetric epoxidations; however, only moderate enantioselecitivities have been obtained so far. Although asymmetric sulfoxidation has been achieved by using stoichiometric amounts of isolated optically active oxaziridinium salts, iminium-ion-catalyzed asymmetric sulfoxidations have not been reported to date, which offers attractive opportunities for further work.

The fifth and final class of nonmetal catalysts concerns the stable nitroxyl-radical derivatives such as TEMPO, which react with the common oxidizing agents (sodium hypochlorite, monoperoxysulfate, peracids) to generate oxoammonium ions. The latter are strong oxidants that chemoselectively and efficiently perform the CH oxidation in alcohols to produce carbonyl compounds rather than engage in the transfer of their oxygen atom to the substrate. Consequently, oxoammonium ions behave quite distinctly compared to the previous four classes of oxidants in that their catalytic activity entails formally a dehydrogenation, one of the few effective nonmetal-based catalytic transformations of alcohols to carbonyl products. Since less than 1 mol % of nitroxyl radical is required to catalyze the alcohol oxidation by the inexpensive sodium hypochlorite as primary oxidant under mild reaction conditions, this catalytic process holds much promise for future practical applications.

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