Direct Selective Oxidative Functionalization of C–H Bonds with H_2O_2: Mn-Aminopyridine Complexes Challenge the Dominance of Non-Heme Fe Catalysts

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Abstract: Non-heme iron(II) complexes are widespread synthetic enzyme models, capable of conducting selective C–H oxidation with H_2O_2 in the presence of carboxylic acid additives. In the last years, structurally similar manganese(II) complexes have been shown to catalyze C–H oxidation with similarly high selectivity, and with much higher efficiency. In this mini-review, recent catalytic and mechanistic data on the selective C–H oxygenations with H_2O_2 in the presence of manganese complexes are overviewed. A distinctive feature of catalyst systems of the type Mn complex/H_2O_2/carboxylic is the existence of two alternative reaction pathways (as found for the oxidation of cumenes), one leading to the formation of alcohol, and the other to ester. The mechanisms of formation of the alcohol and the ester are briefly discussed.

1. Introduction

Given increasing demand for efficient and scalable methods of fine organic syntheses (mostly the syntheses of natural products, pharmaceuticals, biologically active molecules), the design of rigorous synthetic approaches, ensuring precise control of the carbon skeleton and oxidation state, continues to be one of the foremost challenges of synthetic chemistry. In the last years, selective catalytic oxidations of unactivated C–H bonds have attracted great attention: this approach, if implemented on preparative scale, could provide easy and efficient methodologies for the directed introduction of oxygen atom into complex organic molecules at late stages of multistep syntheses, on the basis of novel synthetic strategies [1–11]. Selective C–H oxidation reactions may lead to formation of new C–C and C–X (e.g., C–O, C–N, C–S, C–halogen, etc. [10]) bonds; in this paper, we will solely focus on the *oxygenation* processes, converting alkane groups into C–OH or C=O functionalities.

Metal-mediated *C–H activation* (including C–H bond cleavage and formation of C-metal σ-bonds) has been known for decades; one could mention in this context the works of Shilov [1,8,12], Periana [1,8,13], and others [1,8], dating back to the 1960s–1980s. Typically, C–H activation reactions require that the substrate should first coordinate to the catalytic complex of transition metal (Pt, Rh, Ir, etc.), which is relatively easy if the substrate has π electrons. In contrast to unsaturated substrates, alkanes have only σ electrons and thus are poor nucleophiles, coordinating only weakly to metals [8], which complicates the C–H activation step. On the other hand, to obtain a functionalized molecule, the activation step should be combined with subsequent functionalization step, which may represent some obstacles [8]. That is why in the last years, *direct* C–H oxofunctionalization, which does

not imply the intermediate formation of a metal-carbon bond, has attracted close attention as a promising strategy for the selective oxidative modification of challenging substrates like alkanes. An additional advantage of the direct C–H oxidations is that most of them rely on catalysts based on complexes of cheap and abundant first-row transition metals (Fe, Cu, Mn, V, etc.).

Nowadays, the design of homogeneous catalysts for the direct C–H oxygenation largely follows the biomimetic approach, which implies modeling the catalytic functions of natural metalloenzymes (like cytochrome P450 or methane monooxygenase) with synthetic low-molecular weight complexes. It is not surprising that the major part of reported examples of catalytic C–H oxidations deal with catalysts based on complexes of Fe—the latter is the most widespread metal in natural metalloenzymes [14–27]. Most often, H_2O_2 is used as the "green" oxidant.

Today, non-heme (essentially nonporphyrinic) Fe complexes dominate the area, due to the versatility of the ligand structures, and the rich possibilities of their structural modifications. First examples of non-heme-Fe-catalyzed oxidations appeared in early 1990s [24,28]; however, the breakthrough was achieved after 2007, when White with co-workers contributed a series of milestone works, presenting the bipyrrolidine-derived non-heme iron catalyst **1** (Figure 1) and its structural analogs, ensuring reasonably high level of predictability in the selective oxidation of $C(sp^3)$-H groups [29–34]. In competitive contribution, Costas and co-workers showed that the introduction of additional steric crowd at the pyridine moieties, as well as manipulating with the symmetry of the chiral ligand can divert the oxidation selectivity from 3° $C(sp^3)$-H bonds to stronger 2° $C(sp^3)$-H bonds, which is critical for the selective oxygenation of complex molecules such as natural products [35–38]. The mechanism of non-heme iron catalyzed oxidations has been extensively studied experimentally [39]; it has now been accepted that the C–H oxidation proceeds via the classical rebound mechanism [40] (Figure 1), with participation of the elusive oxoperferryl species [41–49].
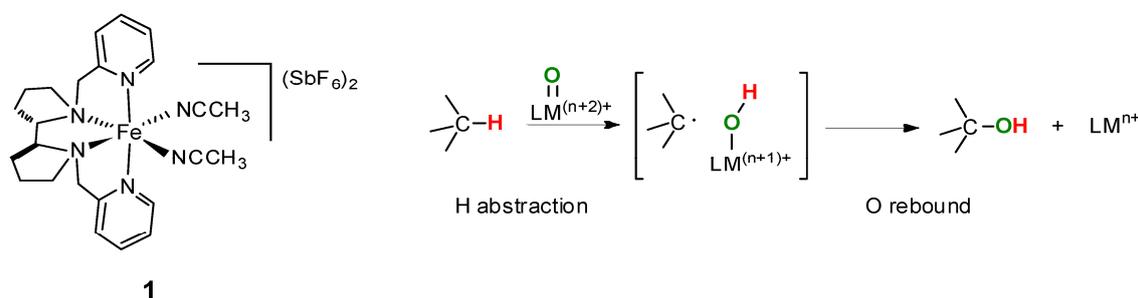

Figure 1. The structure of White's catalyst **1** (**left**) and the rebound-mechanism (**right**).

In contrast to non-heme Fe complexes, the catalytic activity (as well as the mechanism of catalytic action) of structurally related Mn complexes have so far been much less studied. Nevertheless, the Mn based catalyst systems for C–H oxidation, reported so far, demonstrate good practical promise; the Mn-catalyzed C–H oxidation mechanism seems to be mostly similar to that for the Fe-mediated direct C–H oxidation. In this contribution, we will briefly summarize the related synthetic and mechanistic data published to date, and discuss a new mechanistic feature, previously unobserved for Fe-catalyzed C–H oxidations, which seems to be characteristic of Mn-mediated C–H oxidations.

2. C–H Oxidations with H_2O_2 in the Presence of Mn Porphyrins

In 1986, Mansuy with co-workers reported the catalytic oxidation of alkanes with H_2O_2 in the presence of Mn porphyrin complex **2** (Figure 2) [50]. Upon slow addition of H_2O_2 (5 equiv.) to the acetonitrile:dichloromethane solution of cyclohexane, catalyst **2** (2.5 mol %), and imidazole as additive (60 mol %), led to the formation of cyclohexanol and cyclohexanone (Table 1, entry 1) [50]. The 3:1 cyclohexanol:cyclohexanone ratio, the high (11.5) 3°:2° adamantane oxidation selectivity, the absence of effect of dioxygen on the oxidation outcome, and selective (non-statistical) oxygenation of heptane were indicative of a metal-mediated rather than radical-driven oxidation mechanism [51]. The authors

hypothesized that the oxidation could be performed by the $Mn^V=O$ intermediate, the role of imidazole consisting in promoting the heterolytic cleavage of the O–O bond, to form the manganese-oxo species [52].
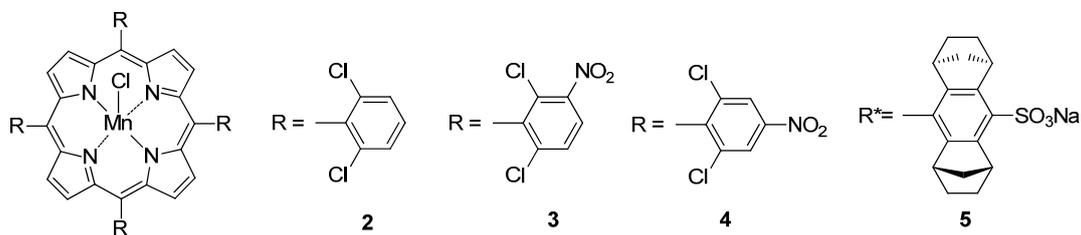

Figure 2. Structures of Mn porphyrins, studied in C–H oxidations.

Banfi with co-workers considered a series of Mn-porphyrin complexes **2–4** as alkane oxidation catalysts and found that the introduction of a nitro group (**3** and **4** vs. **2**) resulted in an increase of activity and stability of the catalysts, eventually resulting in higher yields of oxygenated products [53]. It was shown that other heterocyclic bases may be efficiently used as additives, in combination with benzoic acid (Table 1, entries 2, 3). The proposed mechanism assumed the key role of a "$Mn^V=O$" intermediate [53,54]. Complex **2** and its Br_8-analog also demonstrated the capability of catalyzing the oxidation of aromatic compounds (such as anisole, naphthalene, phenantrene) with H_2O_2, in the presence of imidazole as additive (Table 1, entries 4, 5) [55]. The yields were low, and the high selectivities were only achieved at high substrate/oxidant/Mn ratios (typically 700:10:1). The hydroxylation of anisole occurred preferentially at the *p*-position; furthermore, some *O*-demethylation was detected (Table 1, entry 5) [55]. Mansuy with co-workers found that ammonium acetate is a more efficient co-catalyst than imidazole [56], the use of CH_3COONH_4 led (under similar conditions) to higher alkane conversions (but lower alcohol/ketone ratios, Table 1, entries 6, 7).

Table 1. Examples of C–H oxidations catalyzed by porphyrinic Mn complexes.

No.	Cat.	Substrate	Additive	Products (yield [a])	Ref.
1	**2**	cyclohexane	imidazole	cyclohexanol (12), cyclohexanone (4)	[50]
2	**3**	cyclohexane	*p-t*Bu-pyridine/benzoic acid	cyclohexanol (233 [b]), cyclohexanone (47 [b])	[53]
3	**4**	cyclooctane	*p-t*Bu-pyridine/benzoic acid	cyclooctanol (565 [b]), cyclooctanone (235 [b])	[53]
4	**2**	naphthalene	imidazole	1-naphthol (3.5), 2-naphthol (0.4)	[55]
5	**2**	anisole	imidazole	*p*-OH-anisole (4.7), *o*-OH-anisole (0.35), phenol (0.2)	[55]
6	**2**	cyclohexane	imidazole	cyclohexanol (12.4), cyclohexanone (1.6)	[56]
7	**2**	cyclohexane	CH_3COONH_4	cyclohexanol (20), cyclohexanone (5.2)	[56]
8	**5**	*p*-Et-toluene	imidazole	*p*-acetyltoluene (2.8), 1-(*p*-tolyl)ethanol (37.2, 57% *ee*)	[57]

[a] Yield of oxygenated products is given in mol/mol Mn; [b] In the original publication, alkane conversion was reported.

More recently, Simonneaux with co-workers developed the first Mn-porphyrin catalyzed enantioselective benzylic hydroxylations with H_2O_2 in the presence of catalyst **5** (Figure 2) [57]. The reactions could be readily performed in aqueous methanolic solutions, due to the good solubility of complex **5**. Enantioselectivities ranging from 32% to 57% *ee* were reported (Table 1, entry 8), and the catalyst performed up to 40 turnovers. The occurrence of asymmetric induction is evidence of non-radical hydroxylation mechanism. The highest enantioselectivities were documented for those substrates that ensured the highest alcohol selectivities at the same time (e.g., for the oxidation of 4-ethyltoluene: 97% conversion, alcohol/ketone = 93:7, enantioselectivity 57%), which rules out the possibility for generation of *ee* at the kinetic resolution step. SO_3Na was the best substituent; its replacement with H, NMe_2, or NO_2 afforded less chemo- and enantioselective catalysts [58]. Conducting the reaction in a biphasic system (CH_2Cl_2/H_2O_2) deteriorated the oxidation outcome [58].

To date, the catalysts for C–H oxidation on the basis of Mn porphyrin complexes have been very rare (focusing on complex **2** or its modifications); the catalytic reactions have some characteristics of metal-mediated (non-radical) process (presumably driven by high-valent Mn=O species [21]). However, the mechanism of Mn-porphyrin-catalyzed C–H hydroxylations with H_2O_2 has not yet been reliably established.

3. C–H Oxidations with H_2O_2 in the Presence of Mn Complexes with Me$_3$tacn Derived Ligands

The selective C–H oxidations with H_2O_2 in the presence of non-porphyrinic Mn complexes have so far been extensively developed. The milestone in the area had been the communication of Shul'pin and Lindsay Smith [59,60] that dinuclear Mn(IV) complex **6** (Wieghardt's complex [LMn^{IV}(O)$_3$Mn^{IV}L](PF$_6$)$_2$, where L = 1,4,7-trimethyl-1,4,7-triazacyclononane, Me$_3$tacn [61], Figure 3) catalyzed the oxidation of alkanes (hexane, cyclohexane, cycloheptane) with H_2O_2. In acetonitrile, catalyst **6** was very efficient, performing up to 1350 turnovers (Table 2). Carboxylic acid was reported to be an essential catalytic additive, and acetic acid was the best in the series [60]. The addition of radical scavenger BrCCl$_3$ dramatically suppressed the yield of oxidized products. On the other hand, formation of sizable amounts of alkyl hydroperoxides was detected, and partial erosion of stereochemistry upon the oxidation of *cis*- and *trans*-1,2-dimethylcyclohexanes was documented, suggesting considerable impact of free radical driven oxidation pathways [62].
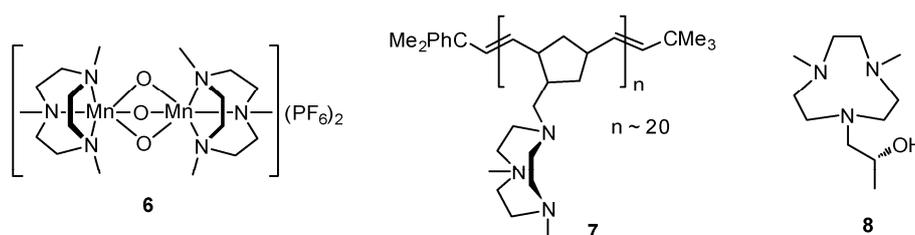

Figure 3. Structures of Mn complexes with Me$_3$tacn derived ligands.

Catalyst **6** appeared to be extremely efficient in the oxidation of light alkanes (methane, ethane: Table 2, entry 2), as well as higher normal and branched alkanes at room temperature (performing up to 3100 turnovers) [63,64].

A polymer-bound complex was prepared starting from Me$_3$tacn-derived ligand **7** (Figure 3) and Mn(OAc)$_2$, which also conducted alkane oxygenation with H_2O_2/AcOH, demonstrating a lower activity as compared to its homogeneous prototype [65]. The reactivity profile of the polymer-bound catalyst was somewhat different from that of the dinuclear catalyst **6**, in particular higher k_H/k_D (2.8 vs. 1.3; cyclohexane/cyclohexane-d$_{12}$) and different selectivity for the hydroxylation of isooctane were documented [65].

Shul'pin with co-workers studied systematically the role of additives. Without additives, Mn complex **6** did not react with H_2O_2 in acetonitrile. However, even small amounts of acetic acid promoted both the catalytic decomposition of hydrogen peroxide and the alkane oxidation. If tiny amount of base was added to the acetic acid, the catalase activity of the **6** substantially increased, while the oxygenase activity decreased [66,67].

An interesting result was documented for the oxidation of alkanes with H_2O_2 in biphasic systems (H$_2$O/alkane, without organic solvents) and in CH$_3$CN, in the presence of **6** as catalyst, and oxalic acid as additive [68]. The latter, used as co-catalytic additive, led to higher hydroxylation stereospecificities than acetic acid (*cis*-1,2-dimethylcyclohexane oxidation, 80% retention of configuration, *RC*, with oxalic acid vs. 48% *RC* with acetic acid). Alkylhydroperoxides were the primary reaction products; they decomposed in the course of the reaction to the corresponding ketones and alcohols [68]. Crucially, screening a series of different (including aromatic) carboxylic acid additives revealed pyrazine-2,3-dicarboxylic and trifluoroacetic acids as extremely efficient co-catalysts [69,70].

Kim and co-workers studied the reactivity of the catalyst system **6**/H_2O_2 (with the Mn catalyst prepared in situ) towards cyclohexane in aqueous acetone in the presence of several carboxylic acids and their sodium salts [71]. In all cases, cyclohexanone was the major reaction product. Interestingly, in the presence of sodium oxalate, the oxidation of hexane demonstrated a high selectivity for hexanones (Table 2, entry 3), and the oxidation of *cis*- and *trans*-1,2-dimethylcyclohexanes was highly stereoretentive (>99% *RC*), which, in combination with the relatively high k_H/k_D for cylcohexane oxidation (2.7), may be considered as evidence against radical type oxidation mechanism [71].

Srinivas and co-workers examined the benzylic oxidations in the presence of a Mn complex prepared in situ from Me_3tacn and $MnSO_4$ [72]. Ethylbenzene oxidations with H_2O_2 proceeded with good acetophenone selectivities, while the addition of carboxylate buffers increased the yield of 1-phenylethanol (Table 2, entry 4). High ketone selectivities were reported for benzylic oxidations, catalyzed by **6**, in the presence of trichloroacetic acid [73].

A set of Me_3tacn derivatives, including optically pure structures of the type **8** (Figure 3), were prepared and tested as ligands in Mn-catalyzed oxidation of isopropyl alcohol and several alkanes with H_2O_2, either with oxalate or with ascorbic acid as co-catalysts [74].

Overall, C–H oxidations with H_2O_2 in the presence of Mn complexes, ligated by Me_3tacn derivatives, has been rather extensively studied. To date, there are no decisive data on the common oxidation mechanism, which, owing to the involvement of atmospheric dioxygen, appears to be very complex. The provisional mechanistic picture can be found in [62,66]. In [65,66], one can also find a useful synopsis of early Mn-Me_3tacn type catalyst systems, capable of conducting various oxidative transformations, using H_2O_2 as oxidant.

4. C–H Oxidations with H_2O_2 in the Presence of Mn Complexes with N,O Donor Ligands

Fernandes and co-workers reported the water-soluble manganese(II) complex with ligand **9** (Figure 4), of the type [(**9**)Mn(η_1-NO_3)(η_2-NO_3)], which catalyzed the oxidation of cyclohexane with H_2O_2 (at 50 °C) in CH_3CN or in *t*BuOH [75]. Moderate efficiencies were reported (up to 62 turnovers), with cyclohexyl hydroperoxide as the major product [75]. The cyclohexanol/cyclohexanone ratios were in the range 1.3-1.4, indicating a sizeable contribution of a radical oxidation pathway.

Figure 4. Structures of Mn complexes with N,O-donor ligands.

Ogawa and co-workers contributed Mn complex **10** (Figure 4) with a macrocyclic ligand, which catalyzed the oxidation of C–H groups in different hydrocarbons (cyclohexane, cyclooctane, ethylbenzene, benzene), performing up to 9 catalytic cycles without any co-catalytic additives [76]. For the oxidations of cyclohexane and cyclooctane, alcohol/ketone ratios of 19 and 8.2 were documented, without reported formation of cycloalkyl hydroperoxides [76].

In 1997, Mn-Salen type complexes **11** and **12** were mentioned to catalyze the oxidation of ethylbenzene (preferentially to acetophenone) with H_2O_2; it is questionable, however, whether this oxidation can be considered "catalytic" since the reported turnover numbers (TNs) were less than unity [77]. Much later, complex **13** was shown to catalyze benzylic oxidations with unexpectedly high

efficiency (up to several thousand TN) in acetonitrile at room temperature, without any co-catalysts, affording ketones with high selectivity (Table 2, entry 5) [78]. The reaction required a high excess of H_2O_2 (10–20 mol per mol of substrate). Apparently, pronounced decomposition of (added in one portion) hydrogen peroxide occurred. A series of structurally related salen and salan (tetrahydrosalen) complexes were studied as catalysts in the oxidation of diphenylmethane [79]. The ligand structure has been shown to have crucial effect on the oxidation selectivity (the benzophenone:diphenylmethanol ratio varying from 100:0 to 15:85).

Table 2. Examples of C–H oxidations catalyzed by Mn complexes with Me$_3$tacn derived and with *N,O*-donor ligands.

No.	Cat.	Substrate	Additive	Products (yield [a])	Ref.
1	**6**	hexane	AcOH	hexanones (775), hexanols (575)	[59]
2	**6**	ethane (20 bar)	AcOH	EtOOH (260), EtOH (120), MeCHO (20)	[64]
3	**6**	hexane	Na oxalate	2-hexanol (4.5), 3-hexanol (4.5), 2-hexanone (29), 3-hexanone (29)	[71]
4	**6**	ethylbenzene	oxalate buffer	1-phenylethanol (48.5), acetophenone (102)	[72]
6	**13**	ethylbenzene	none	1-phenylethanol (7), acetophenone (683)	[78]

[a] Yield of oxygenated products is given in mol/mol Mn.

5. C–H Oxidations with H_2O_2 in the Presence of Mn Complexes with Aminopyridine Ligands

The current renascence of the Mn catalyzed selective C–H oxidations with H_2O_2 is associated with the appearance of Mn aminopyridine complexes. Initially, Costas and co-workers reported that complexes [(Me$_2$Py-tacn)Mn(CF$_3$SO$_3$)$_2$] (**14**) and [((*S,S*)-bpmcn)Mn(CF$_3$SO$_3$)$_2$] (**15**) (Figure 5) demonstrated moderate oxidation reactivity towards *cis*-1,2-dimethylcyclohexane (with 1% and 8% yields, respectively) [80]. We also have to mention the report by Golchoubian and Ghasemi, who examined the oxidation of diphenylmethane with a series of Mn complexes with N$_4$-donor ligands, including two aminopyridine, ligands (complexes **16**, **17**) [79]. With both complexes, alcohol was preferentially formed [79] (Table 3, entry 1).
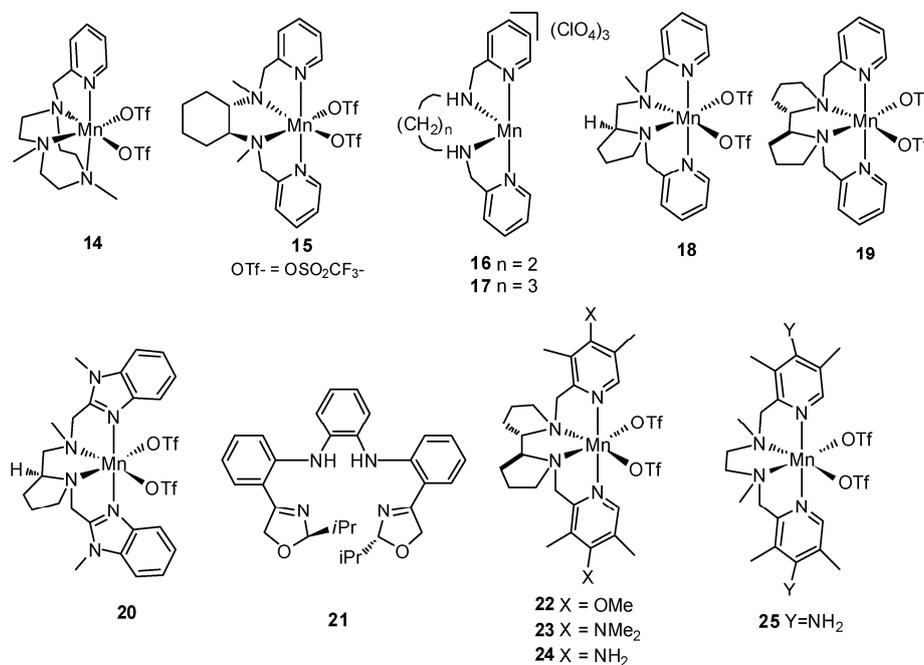
Figure 5. Structures of Mn complexes with aminopyridine ligands.

Bryliakov and co-workers documented excellent catalytic efficiencies in the oxidations of a variety of 2° and 3° alkane C–H groups with H_2O_2, catalyzed by complexes **15**, **18** and **19**

in the presence of acetic acid [81]. The Mn complexes performed up to 970 catalytic cycles. Cyclohexanol/cyclohexanone ratios of 4.9-5.1 and high 3°/2° selectivities of adamantane oxidation (40–49) pointed to a metal-mediated rather than a radical-driven oxidation mechanism. The high sensitivity of the oxygen-transferring species to electronic effects, and high selectivity and stereospecificity (>99% *RC*) in the oxidation of *cis*-1,2-dimethylcyclohexane also support the metal-mediated oxidation mechanism [81]. Under "practical" conditions, methylenic CH_2 groups preferentially converted to ketone functionalities (Table 4, entry 1) [81].

More recently, Sun with co-workers reported the catalyst system based on complex **20** (Figure 5) [82]. In the presence of acetic acid as additive, the latter efficiently (up to 154 TN) catalyzed the oxygenation of secondary benzylic and aliphatic C–H bonds, with preferential formation of ketones (Table 3, entry 2). The same catalyst has shown good catalytic efficiency in the oxidation of secondary alcohols, performing up to 4700 catalytic turnovers [83]. Another laboratory has reported the oxidation of alcohols with H_2O_2 in the presence of Mn complex, formed in situ from ligand **21** (Figure 5) and Mn(OTf)$_2$ [84], with substantially lower catalytic efficiencies. The authors screened a series of different carboxylic acid additives, of which adamantane carboxylic acid was chosen as ensuring the highest yield of ketone. Interestingly, the oxidation of substrates bearing both olefinic and primary or secondary alcoholic moieties, proceeded selectively towards the formation of *α*,*β*-unsaturated carbonyl compounds [84].

Bryliakov and co-workers synthesized complexes **22** and **23**, bearing electron-donating substituents, that exhibited superior efficiencies (as compared with catalysts **15**, **18**, **19**) in benzylic oxidations (Table 3, entries 6 and 7) [85]. Cumenes were oxidized preferentially into the corresponding alcohols, while ethylbenzene afforded mostly acetophenone.

Recently, a comparative study by Malik and co-workers revealed the most evident advantages of the catalyst systems based on the [((*S*,*S*)-pdp)Mn(OTf)$_2$] type complexes (**19**, **20**, **22**–**24**, Figure 4) [86]. Within the range of practically promising catalyst systems studied, the Mn-aminopyridine catalysts (1) are used in very small amount (0.1 mol %; structurally similar Fe complexes are typically used in up to 15 mol % loadings [29–34]); (2) require a small (1.3 equiv.) excess of the green oxidant—commercially available 30% aqueous H_2O_2; and (3) exhibit reasonably high yields in the oxidation of differently *p*-substituted cumenes, ensuring high cumyl alcohol selectivity [86].

So far, Mn catalyzed selective oxidative syntheses of complex organic molecules, such as natural products, or biologically active compounds, have been rarely reported. A few procedures are collected in Scheme 1. We expect the emergence of other practically relevant examples in the near future.
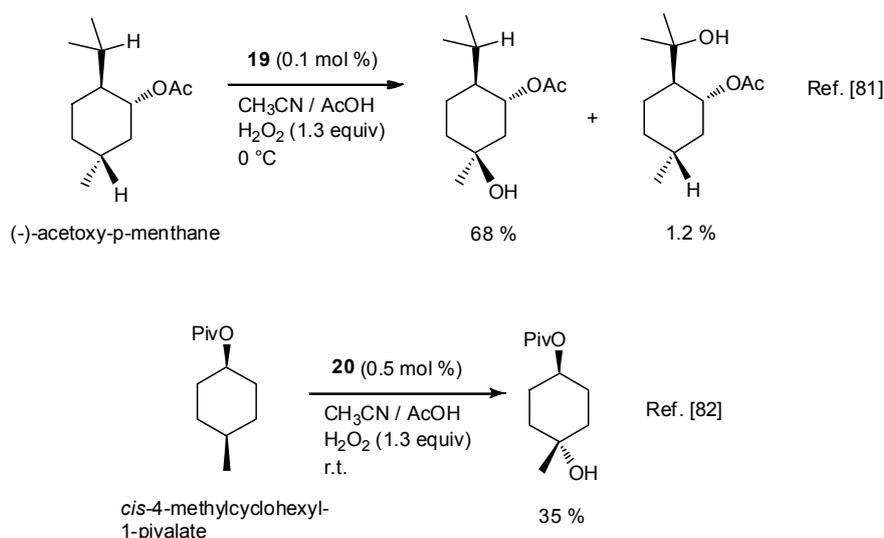
Scheme 1. *Cont.*
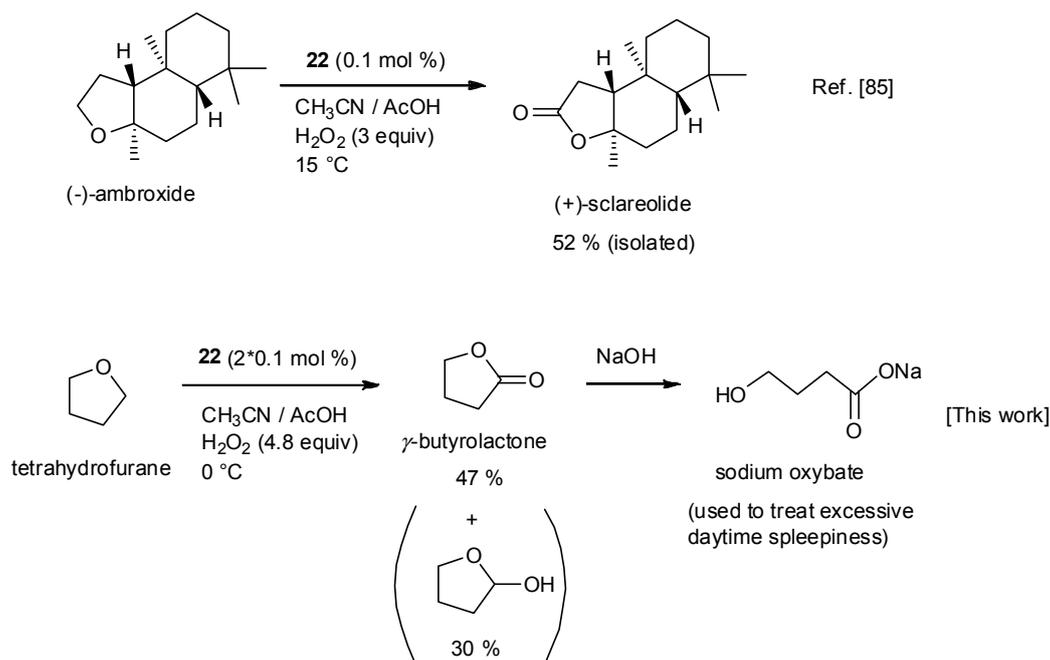
Scheme 1. Examples of selective C–H oxidations of practical synthetic relevance in the presence of aminopyridine Mn complexes.

## 6. Elucidation of the Mechanism of C–H Oxidations with H_2O_2 in the Presence of Mn Complexes

So far, experimental data on the mechanism(s) of C–H oxygenation with H_2O_2 in the presence of Mn complexes have been rather restricted in the literature. On the basis of indirect data, it has been generally assumed (see Section 2) that high-valent Mn-oxo complexes (presumably $[(L)Mn^V=O]$ or $[(L^{\bullet+})Mn^{IV}=O]$) are the most likely active species in the catalyst systems based on Mn porphyrins/H_2O_2/additive (for mechanistic considerations and precedents of porphyrinic Mn^VO complexes see [21,39,52,57] and references therein.

On the contrary, catalyst systems based on Mn-Me₃tacn type complexes exhibit various characteristics of radical-type mechanism (Section 3), which may be evidence of significant contribution of free-diffusing-radicals into the oxidation outcome.

To date, it is only the mechanism of catalytic C–H hydroxylation on Mn-aminopyridine catalysts that has been studied in more detail [85]; in particular, the analysis of kinetic isotope effect (k_H/k_D), isotopic labeling data, and linear free energy relationships has been reported. The crucial findings were the observation of (1) a primary k_H/k_D of 3.5–3.9 for the oxidation of cumene/α-^{2}H-cumene, indicating that the hydrogen atom lies on the reaction coordinate and participates in C–H bond breaking step; (2) linear Hammett correlation for the oxidation of a series of *p*-substituted cumenes, with the ρ^+ of -1.0, witnessing electrophilic active species, and electron-deficient transition state; (3) linear correlation between the C–H bond dissociation energies (BDEs) of the substrates and the logarithms of rates of their oxidations, reflecting a common oxidation mechanism; and (4) partial incorporation of ^{18}O from added ^{18}O-labeled water into the hydroxylated product, supporting the "water-assisted" [87,88] pathway for the formation of active, presumably oxomanganese(V), species [85]. In the presence of carboxylic acid additive, the mechanism of formation of the active species is diverted to the "carboxylic acid assisted" one (Scheme 2) [44,89–92]. The hydroxylation step has been concluded to proceed via the rebound mechanism (Scheme 3, top). This mechanistic landscape apparently dominates for the oxidation of unactivated C–H groups in aliphatic compounds.

Very recently, the mechanism of formation of the minor oxidation product—cumyl acetate has been studied in detail [93]. Counter to the earlier expectations [85], the possibility of esterification of the initially formed alcohol has been ruled out since separate experiments have shown that under the

oxidation conditions, cumyl alcohol does not react with acetic acid. Moreover, the isotopic labeling data witness that both oxygen atoms of the acetate stem exclusively from the acetic acid molecule, which does not conform to the common Fischer esterification mechanism [93].
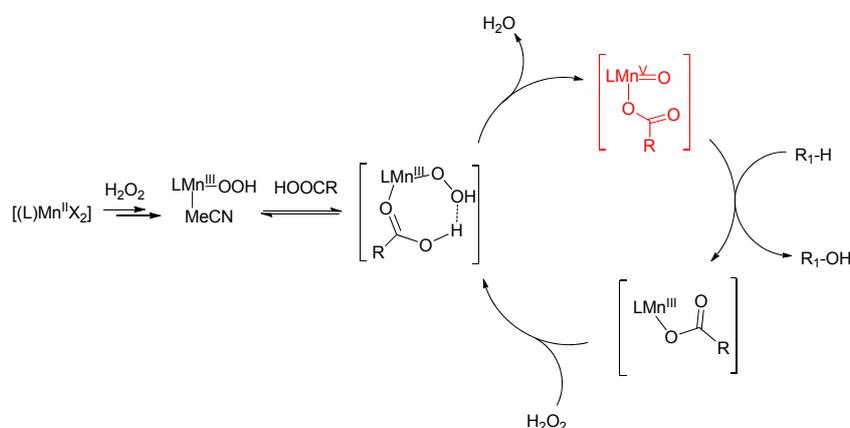
Scheme 2. Proposed catalytic cycle for the selective C–H oxidations with H_2O_2 in the presence of aminopyridine manganese complexes and carboxylic acid RCOOH.
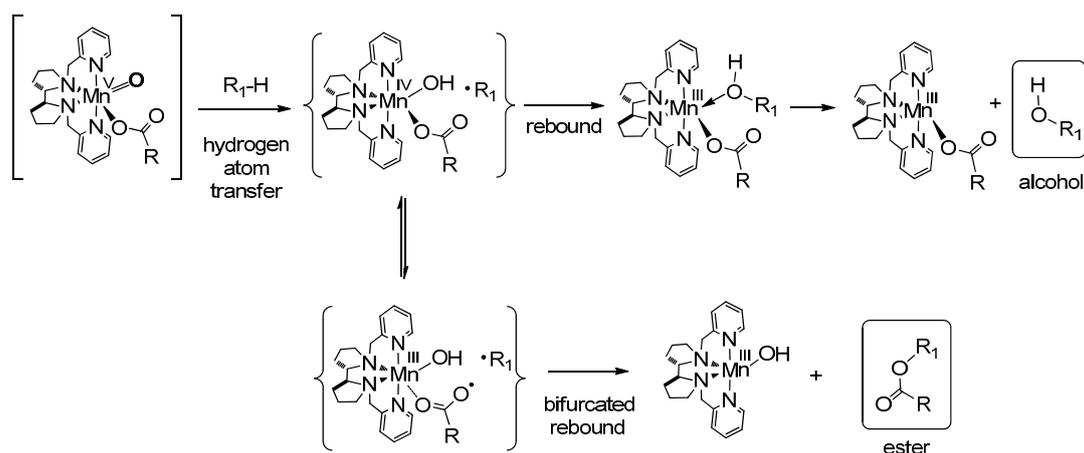
Scheme 3. The proposed mechanism of Mn catalyzed C–H hydroxylation.

It has been concluded that the only feasible possibility remaining is the direct formation of the ester after the H abstraction step, via transfer of the acetoxy radical to the intermediate carbon-centered organic radical. Based on the catalytic, isotopic labeling, and density functional theory (DFT) study, the authors have proposed the "bifurcated rebound mechanism" (Scheme 3, bottom) which explains the observed acetate formation [93]. One of the two alternative rebound pathways, conducted by the intermediate [(PDP)Mn^{IV}–OH(OC(O)R)] (Scheme 3) leads to the alcohol product, and the other, associated with the intermediate [(PDP)Mn^{III}–OH(OC(O•)R)]) affords the ester. The competitive •OC(O)R/•OH transfer has so far been unprecedented for bioinspired oxidations in the presence of non-heme Fe and related Mn complexes, for which effect the term "bifurcated rebound mechanism" has been proposed [93].

In the series of the Mn complexes studied, catalyst **24** (with the strongest electron-donor substituents) afforded the highest alcohol/acetate ratio (Table 3, entry 8 vs. entries 6, 7). The oxidations of cumene with H_2O_2 in the presence of a series of different aliphatic carboxylic acids were conducted (Table 4) [93]. The yield of the ester was lower (and the alcohol/ester ratio was higher) for carboxylic acids with tertiary *α*-carbon, as compared to those with primary or secondary *α*-carbon (cf. entries 4–8 vs. 1–3). The highest alcohol/ester ratio of 44.7 has been documented for the oxidation with

2-ethylbutyric acid (EBA, Table 4, entry 8). The lowest yield of ester for the acids with tertiary α-C may be due to additional stabilization of the [(PDP)Mn^{III}–OH(OC(O$^\bullet$)R)] intermediate, owing to the existence of tautomeric, α-C-centered radical species, attenuating its reactivity. The use of branched (with tertiary α-carbon atom) carboxylic acids can be recommended for practical hydroxylations, in order to improve the alcohol formation selectivity.

Table 3. Examples of C–H oxidations catalyzed by Mn aminopyridine complexes.

No.	Cat.	Substrate	Additive	Products (yield [a])	Ref.
1	**17**	diphenylmethane	none	benzophenone (250), diphenylmethanol (530)	[79]
2	**19**	cyclohexane	AcOH	cyclohexanol (28), cyclohexanone (842)	[81]
3	**20**	cyclohexane	AcOH	cyclohexanone (122)	[82]
4	**20**	1-Ph-ethanol	AcOH	acetophenone (4700)	[83]
5	**21**/Mn(OTf)$_2$	cyclohexanol	Ada-COOH	cyclohexanone (38)	[84]
6	**19**	cumene	AcOH	cumyl alcohol (209), cumyl acetate (139)	[93]
7	**23**	cumene	AcOH	cumyl alcohol (560), cumyl acetate (75), acetophenone (30)	[85]
8	**24**	cumene	AcOH	cumyl alcohol (492), cumyl acetate (61), acetophenone (110)	[93]

[a] Yield of oxygenated products is given in mol/mol Mn.

Table 4. Oxidation of cumene with H_2O_2 in the presence of complex **25** and various carboxylic acids [93].
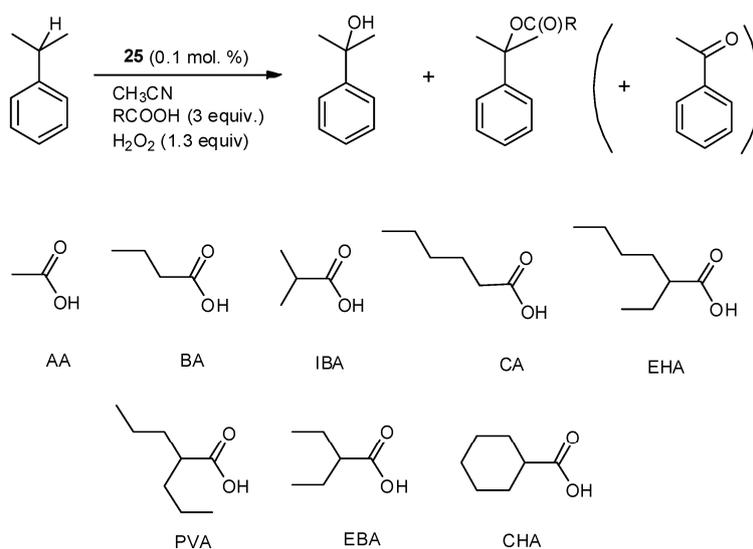
No	Additive	Conversion (%)	Yield of Alcohol/Acetate/Other [a] (%)	Alcohol/Ester Ratio
1	AA	82.9	62.9/12.1/7.9	5.2/1
2	BA	74.7	60.2/7.3/7.2	8.2/1
3	CA	56.5	46.6/4.3/5.6	10.8/1
4	CHA	34.3	30.3/2.0/2.0	15.4/1
5	IBA	61.8	51.7/3.2/6.9	16.2/1
6	EHA	29.8	26.1/1.6/2.1	16.3/1
7	PVA	38.6	34.5/0.9/3.2	36.7/1
8	EBA	39.2	35.4/0.8/3.0	44.7/1

[a] side product: acetophenone.

7. Experimental Conditions

Oxidation of tetrahydrofuran (THF) to γ-butyrolactone was performed as follows: a solution of freshly distilled THF (40.5 μL, 500 μmol) and of manganese complex **22** (0.5 μmol) in CH$_3$CN (0.40 mL) and AcOH (28.6 μL, 500 μmol) was thermostatted at 0 °C. 30% aqueous H$_2$O$_2$ (1200 μmol, dissolved in CH$_3$CN, total volume 200 μL) was delivered to this mixture with a syringe pump over 60 min at 0 °C. Then, the second portion of manganese complex **22** (0.5 μmol) was added, followed by the syringe

pump addition (over 60 min) of the second portion of H_2O_2 (1200 μmol, 200 μL of solution in CH_3CN). The mixture was stirred for additional 2 h at 0 °C. An internal standard (1,4-dioxane) was added and the mixture was subjected to gas chromatography–mass spectrometry (GC-MS) analysis.

8. Conclusions and Outlook

Synthetic complexes of Mn with polydentate ligands demonstrate the ability to act as biomimetic catalysts of direct C–H oxidation with H_2O_2, converting organic molecules into the oxygenated products (alcohols, ketones, and others). To date, the available library of catalytically active Mn complexes is rather wide, providing catalysts suited for C–H oxidations, ranging from the oxidation of benzylic C–H groups, through unactivated aliphatic C–H, to C–H groups of arenes. The oxidations typically proceed in a selective (and sometimes enantioselective [57,58]) fashion.

As a general trend, Mn based catalysts demonstrate higher (even much higher) oxidation efficiencies as compared to their Fe based structural analogs, with retention of similarly high selectivity. Moreover, in some cases Mn catalysts require a smaller excess of H_2O_2, down to only 1.3 equiv. relative to substrate.

The mechanisms of Mn-catalyzed C–H oxidations (generally taken, i.e., the mechanism of active species formation and the mechanisms of C–H activation and functionalization) have so far been rather underinvestigated. The data available to date give evidence for close similarities between the mechanistic landscapes of C–H oxidations in the presence of Fe- and Mn-aminopyridine complexes; providing indirect proof for the oxomanganese(V) active species. An important distinctive feature of Mn-aminopyridine based catalysts is the possibility of existence of two alternative reaction pathways, one leading to the formation of alcohol, and the other to the ester. The mechanism of the ester formation has been proposed, assuming competitive $^{\bullet}OC(O)R/^{\bullet}OH$ transfer to the alkyl radical formed at the H abstraction step. This mechanism, unprecedented for bioinspired oxidations in the presence of non-heme Fe and related Mn complexes, is proposed to be called "bifurcated rebound mechanism".

Mn based catalysts for selective C–H oxidations with H_2O_2 provide novel opportunities for direct (without coordination of the substrate to the catalyst or formation of metal-carbon bond) functionalization of C–H bonds. Although at the current, laboratory stage of their development, the oxidations with H_2O_2 have not yet been reported to generate technically useful amounts of required oxygenated materials [94], the authors believe that Mn based "green" C–H oxidation systems will go beyond the laboratory scale in the near future.

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References

1. Shilov, A.E.; Shul'pin, G.B. Activation of C–H bonds by metal complexes. *Chem. Rev.* **1997**, *97*, 2879–2932. [CrossRef] [PubMed]
2. Shilov, A.E.; Shteinman, A.A. Oxygen atom transfer into C–H bond in biological and model chemical systems. Mechanistic aspects. *Acc. Chem. Res.* **1999**, *32*, 763–771. [CrossRef]
3. Christmann, M. Selective Oxidation of Aliphatic C–H Bonds in the Synthesis of Complex Molecules. *Angew. Chem. Int. Ed.* **2008**, *47*, 2740–2742. [CrossRef] [PubMed]
4. Newhouse, T.; Baran, P.S. If C–H Bonds Could Talk: Selective C–H Bond Oxidation. *Angew. Chem. Int. Ed.* **2011**, *50*, 3362–3374. [CrossRef] [PubMed]
5. Che, C.M.; Kar-Yan Lo, V.; Zhou, C.Y.; Huang, J.S. Selective functionalisation of saturated C–H bonds with metalloporphyrin catalysts. *Chem. Soc. Rev.* **2011**, *40*, 1950–1975. [CrossRef] [PubMed]
6. McMurray, L.; O'Hara, F.; Gaunt, M.J. Recent developments in natural product synthesis using metal-catalysed C–H bond functionalisation. *Chem. Soc. Rev.* **2011**, *40*, 1885–1898. [CrossRef] [PubMed]

7. Yamaguchi, J.; Yamaguchi, A.D.; Itami, K. C–H Bond Functionalization: Emerging Synthetic Tools for Natural Products and Pharmaceuticals. *Angew. Chem. Int. Ed.* **2012**, *51*, 8960–9009. [CrossRef] [PubMed]

8. Gunnoe, T.B. *Alkane C–H Activation by Single-Site Metal Catalysis*; Pérez, P.J., Ed.; Springer: Dordrecht, Germany, 2012; pp. 1–15.

9. Roduner, E.; Kaim, W.; Sarkar, B.; Urlacher, V.B.; Pleiss, J.; Gläser, R.; Einicke, W.D.; Sprenger, G.A.; Beifuß, U.; Klemm, E.; Liebner, C.; Hieronymus, H.; Hsu, S.F.; Plietker, B.; Laschat, S. Selective Catalytic Oxidation of C–H Bond with Molecular Oxygen. *ChemCatChem* **2013**, *5*, 82–112. [CrossRef]

10. Qiu, Y.; Gao, S. Trends in applying C–H oxidation to the total synthesis of natural products. *Nat. Prod. Rep.* **2016**, *33*, 562–581. [CrossRef] [PubMed]

11. Shul'pin, G.B. New Trends in Oxidative Functionalization of Carbon-Hydrogen Bonds: A Review. *Catalysts* **2016**, *6*, 50. [CrossRef]

12. Gol'dshleger, N.F.; Tyabin, M.B.; Shilov, A.E.; Shteinman, A.A. Activation of Saturated Hydrocarbons. H/D Exchange in Solutions of Transition Metal Complexes. *Zh. Fiz. Khim.* **1969**, *43*, 2174–2175. (In Russian)

13. Periana, R.A.; Bergman, R.G. Oxidative Addition of Rhodium to Alkane C–H Bonds: Enhancement in Selectivity and Alkyl Group Functionalization. *Organometallics* **1984**, *3*, 508–510. [CrossRef]

14. Solomon, E.I.; Brunold, T.C.; Davis, M.I.; Kemsley, J.N.; Lee, S.K.; Lehnert, N.; Neese, F.; Skulan, A.J.; Yang, Y.S.; Zhou, J. Geometric and Electronic Structure/Function Correlations in Non-Heme Iron Enzymes. *Chem. Rev.* **2000**, *100*, 235–350. [CrossRef] [PubMed]

15. Costas, M.; Chen, K.; Que, L., Jr. Biomimetic nonheme iron catalysts for alkane hydroxylation. *Coord. Chem. Rev.* **2000**, *200*, 517–544. [CrossRef]

16. Costas, M.; Mehn, M.P.; Jensen, M.P.; Que, L., Jr. Dioxygen Activation at Mononuclear Nonheme Iron Active Sites: Enzymes, Models, and Intermediates. *Chem. Rev.* **2004**, *104*, 939–986. [CrossRef] [PubMed]

17. Tanase, S.; Bowman, E. *Advances in Inorganic Chemistry*; van Eldik, R., Reedijk, J., Eds.; Academic Press: Amsterdam, The Netherlands, 2006; pp. 29–75.

18. Battaini, G.; Granata, A.; Monzani, E.; Gullotti, M.; Casella, L. *Advances in Inorganic Chemistry*; van Eldik, R., Reedijk, J., Eds.; Academic Press: Amsterdam, The Netherlands, 2006; pp. 185–233.

19. Shteinman, A.A. Iron oxygenases: Structure, mechanism and modeling. *Russ. Chem. Rev.* **2008**, *77*, 945–966. [CrossRef]

20. Shul'pin, G.B. Hydrocarbon Oxygenations with Peroxides Catalyzed by Metal Compounds. *Mini-Rev. Org. Chem.* **2009**, *6*, 95–104. [CrossRef]

21. Costas, M. Selective C–H oxidation catalyzed by metalloporphyrins. *Coord. Chem. Rev.* **2011**, *255*, 2912–2932. [CrossRef]

22. Company, A.; Gómez, L.; Costas, M. *Iron Containing Enzymes: Versatile Catalysts of Hydroxylation Reactions in Nature*; de Visser, S.P., Kumar, D., Eds.; RCS Publishing: Cambridge, UK, 2011; pp. 148–208.

23. Talsi, E.P.; Bryliakov, K.P. Chemo- and stereoselective C–H oxidations and epoxidations/*cis*-dihydroxylations with H_2O_2, catalyzed by non-heme iron and manganese complexes. *Coord. Chem. Rev.* **2012**, *256*, 1418–1434. [CrossRef]

24. Bryliakov, K.P. *Environmentally Sustainable Catalytic Asymmetric Oxidations*; CRC Press: Boca Raton, FL, USA, 2014; pp. 109–119.

25. Canta, M.; Rodriguez, M.; Costas, M. Recent Advances in the Selective Oxidation of Alkyl C–H Bonds Catalyzed by Iron Coordination Complexes. *Top. Curr. Chem.* **2016**, *372*, 27–54. [PubMed]

26. Afanasiev, P.; Sorokin, A.B. *μ*-Nitrido Diiron Macrocyclic Platform: Particular Structure for Particular Catalysis. *Acc. Chem. Res.* **2016**, *49*, 583–593. [CrossRef] [PubMed]

27. Olivo, G.; Lanzalunga, O.; di Stefano, S. Non-Heme Imine-Based Iron Complexes as Catalysts for Oxidative Processes. *Adv. Synth. Catal.* **2016**, *358*, 843–863. [CrossRef]

28. Sheu, C.; Reichert, S.A.; Cofré, P.; Ross, B., Jr.; Sobkowiak, A.; Sawyer, D.T.; Kanofski, J.R. Iron-Induced Activation of Hydrogen Peroxide for the Direct Ketonization of Methylenic Carbon [c-C_6H_{12}→c-C_6H_{10}(O)] and the Dioxygenation of Acetylenes and Arylolefins. *J. Am. Chem. Soc.* **1990**, *112*, 1936–1942. [CrossRef]

29. Chen, M.S.; White, M.C. A Predictably Selective Aliphatic C–H Oxidation Reaction for Complex Molecule Synthesis. *Science* **2007**, *318*, 783–787. [CrossRef] [PubMed]

30. Chen, M.S.; White, M.C. Combined Effects on Selectivity in Fe-Catalyzed Methylene Oxidation. *Science* **2010**, *327*, 566–571. [CrossRef] [PubMed]

31. Bigi, M.A.; Reed, S.A.; White, M.C. Diverting non-haem iron catalysed aliphatic C–H hydroxylations towards desaturations. *Nat. Chem.* **2011**, *3*, 216–222. [CrossRef] [PubMed]

32. Bigi, M.A.; Reed, S.A.; White, M.C. Directed Metal (Oxo) Aliphatic C–H Hydroxylations: Overriding Substrate Bias. *J. Am. Chem. Soc.* **2012**, *134*, 9721–9726. [CrossRef] [PubMed]

33. Gormisky, P.; White, M.C. Catalyst-Controlled Aliphatic C–H Oxidations with a Predictive Model for Site-Selectivity. *J. Am. Chem. Soc.* **2013**, *135*, 14052–14055. [CrossRef] [PubMed]

34. Howell, J.M.; Feng, K.; Clark, J.R.; Trzepkowski, L.J.; White, M.C. Remote Oxidation of Aliphatic C-H Bonds in Nitrogen-Containing Molecules. *J. Am. Chem. Soc.* **2015**, *137*, 14590–14593. [CrossRef] [PubMed]

35. Prat, I.; Gomez, L.; Canta, M.; Ribas, X.; Costas, M. An Iron Catalyst for Oxidation of Alkyl CH Bonds Showing Enhanced Selectivity for Methylenic Sites. *Chem. Eur. J.* **2013**, *19*, 1908–1913. [CrossRef] [PubMed]

36. Gomez, L.; Canta, M.; Font, D.; Prat, I.; Ribas, X.; Costas, M. Regioselective Oxidation of Nonactivated Alkyl C–H Groups Using Highly Structured Non-Heme Iron Catalysts. *J. Org. Chem.* **2013**, *78*, 1421–1433. [CrossRef] [PubMed]

37. Canta, M.; Font, D.; Gomez, L.; Ribas, X.; Costas, M. The Iron(II) Complex [Fe(CF$_3$SO$_3$)$_2$(mcp)] as a Convenient, Readily Available Catalyst for the Selective Oxidation of Methylenic Sites in Alkanes. *Adv. Synth. Catal.* **2014**, *356*, 818–830. [CrossRef]

38. Font, D.; Canta, M.; Milan, M.; Cusso, O.; Ribas, X.; Gebbink, R.J.M.K.; Costas, M. Readily Accessible Bulky Iron Catalysts Exhibiting Site Selectivity in the Oxidation of Steroidal Substrates. *Angew. Chem. Int. Ed.* **2016**, *55*, 5776–5779. [CrossRef] [PubMed]

39. Bryliakov, K.P.; Talsi, E.P. Active sites and mechanisms of bioinspired oxidation with H$_2$O$_2$, catalyzed by non-heme Fe and related Mn complexes. *Coord. Chem. Rev.* **2014**, *276*, 73–96. [CrossRef]

40. Groves, J.T. High-valent iron in chemical and biological oxidations. *J. Inorg. Biochem.* **2006**, *100*, 434–447. [CrossRef] [PubMed]

41. Lyakin, O.Y.; Bryliakov, K.P.; Britovsek, G.J.P.; Talsi, E.P. EPR Spectroscopic Trapping of the Active Species of Nonheme Iron-Catalyzed Oxidation. *J. Am. Chem. Soc.* **2009**, *131*, 10798–10799. [CrossRef] [PubMed]

42. Lyakin, O.Y.; Bryliakov, K.P.; Talsi, E.P. EPR, ^{1}H and ^{2}H NMR, and Reactivity Studies of the Iron–Oxygen Intermediates in Bioinspired Catalyst Systems. *Inorg. Chem.* **2011**, *50*, 5526–5538. [CrossRef] [PubMed]

43. Prat, I.; Mathieson, J.S.; Güell, M.; Ribas, X.; Luis, J.M.; Cronin, L.; Costas, M. Observation of Fe(V)=O using variable-temperature mass spectrometry and its enzyme-like C–H and C=C oxidation reactions. *Nat. Chem.* **2011**, *3*, 788–793. [CrossRef] [PubMed]

44. Lyakin, O.Y.; Ottenbacher, R.V.; Bryliakov, K.P.; Talsi, E.P. Asymmetric Epoxidations with H$_2$O$_2$ on Fe and Mn Aminopyridine Catalysts: Probing the Nature of Active Species by Combined Electron Paramagnetic Resonance and Enantioselectivity Study. *ACS Catal.* **2012**, *2*, 1196–1202. [CrossRef]

45. Lyakin, O.Y.; Prat, I.; Bryliakov, K.P.; Costas, M.; Talsi, E.P. EPR detection of Fe(V)=O active species in nonheme iron-catalyzed oxidations. *Catal. Commun.* **2012**, *29*, 105–108. [CrossRef]

46. Oloo, W.N.; Meier, K.K.; Wang, Y.; Shaik, S.; Münck, E.; Que, L. Identification of a low-spin acylperoxoiron(III) intermediate in bio-inspired non-heme iron-catalysed oxidations. *Nat. Commun.* **2014**, *5*, 3046. [CrossRef] [PubMed]

47. Lyakin, O.Y.; Zima, A.M.; Samsonenko, D.G.; Bryliakov, K.P.; Talsi, E.P. EPR Spectroscopic Detection of the Elusive Fe^V=O Intermediates in Selective Catalytic Oxofunctionalizations of Hydrocarbons Mediated by Biomimetic Ferric Complexes. *ACS Catal.* **2015**, *5*, 2702–2707. [CrossRef]

48. Serrano-Plana, J.; Oloo, W.N.; Acosta-Rueda, L.; Meier, K.K.; Verdejo, B.; García-España, E.; Basallote, M.G.; Münck, E.; Que, L., Jr.; Company, A.; Costas, M. Trapping a Highly Reactive Nonheme Iron Intermediate That Oxygenates Strong C–H Bonds with Stereoretention. *J. Am. Chem. Soc.* **2015**, *137*, 15833–15842. [CrossRef] [PubMed]

49. Zima, A.M.; Lyakin, O.Y.; Ottenbacher, R.V.; Bryliakov, K.P.; Talsi, E.P. Dramatic Effect of Carboxylic Acid on the Electronic Structure of the Active Species in Fe(PDP)-Catalyzed Asymmetric Epoxidation. *ACS Catal.* **2016**, *6*, 5399–5404. [CrossRef]

50. Battioni, P.; Renaud, J.P.; Bartoli, J.F.; Mansuy, D. Hydroxylation of alkanes by hydrogen peroxide: And efficient system using manganese porphyrins and imidazole as catalysts. *J. Chem. Soc. Chem. Commun.* **1986**, 341–343. [CrossRef]

51. Talsi, E.P.; Ottenbacher, R.V.; Bryliakov, K.P. Bioinspired oxidations of aliphatic C–H groups with H$_2$O$_2$ in the presence of manganese complexes. *J. Organomet. Chem.* **2015**, *793*, 102–107. [CrossRef]

52. Battioni, P.; Renaud, J.P.; Bartoli, J.F.; Reina-Artiles, M.; Fort, M.; Mansuy, D. Monooxygenase-like Oxidation of Hydrocarbons by H_2O_2 Catalyzed by Manganese Porphyrins and Imidazole: Selection of the Best Catalytic System and Nature of the Active Oxygen Species. *J. Am. Chem. Soc.* **1988**, *110*, 8462–8470. [CrossRef]

53. Banfi, S.; Maiocchi, A.; Moggi, A.; Montanari, F.; Quici, S. Hydrogen peroxide oxygenation of alkanes catalysed by manganese(III)-tetraarylporphyrins: The remarkable co-catalytic effect of lipophilic carboxylic acids and heterocyclic bases. *J. Chem. Soc. Chem. Commun.* **1990**, *24*, 1794–1796. [CrossRef]

54. Banfi, S.; Legramandi, F.; Montanari, F.; Pozzi, G.; Quici, S. Biomimetic models of cytochrome P-450. A doubly tailed manganese(III)–tetraaryl porphyrin; an extremely efficient catalyst for hydrocarbon oxygenations promoted by 30% H_2O_2. *J. Chem. Soc. Chem. Commun.* **1991**, *18*, 1285–1287. [CrossRef]

55. Carrier, M.N.; Scheer, C.; Gouvine, P.; Bartoli, J.F.; Battioni, P.; Mansuy, D. Biomimetic hydroxylation of aromatic compounds: Hydrogen peroxide and manganese-polyhalogenated porphyrins as a particularly good system. *Tetrahedron Lett.* **1990**, *31*, 6645–6648. [CrossRef]

56. Thellend, A.; Battioni, P.; Mansuy, D. Ammonium acetate as a very simple and efficient cocatalyst for manganese porphyrin-catalysed oxygenation of hydrocarbons by hydrogen peroxide. *J. Chem. Soc. Chem. Commun.* **1994**, 1035–1036. [CrossRef]

57. Srour, H.; Le Maux, P.; Simonneaux, G. Enantioselective Manganese-Porphyrin-Catalyzed Epoxidation and C–H Hydroxylation with Hydrogen Peroxide in Water/Methanol Solutions. *Inorg. Chem.* **2012**, *51*, 5850–5856. [CrossRef] [PubMed]

58. Amiri, N.; Le Maux, P.; Srour, H.; Nasri, H.; Simonneaux, G. Nitration of Halterman porphyrin: A new route for fine tuning chiral iron and manganese porphyrins with application in epoxidation and hydroxylation reactions using hydrogen peroxide as oxidant. *Tetrahedron* **2014**, *70*, 8836–8842. [CrossRef]

59. Lindsay Smith, J.R.; Shul'pin, G.B. Efficient stereoselective oxygenation of alkanes by peroxyacetic acid or hydrogen peroxide and acetic acid catalysed by a manganese(IV) 1,4,7-trimethyl-1,4,7-triazacyclononane complex. *Tetrahedron Lett.* **1998**, *39*, 4909–4912. [CrossRef]

60. Shul'pin, G.B.; Lindsay Smith, J.R. Oxidation with the "H_2O_2-managanese(IV) complex-carboxylic acid" reagent. 1. Oxidation of saturated hydrocarbons with peroxy acids and hydrogen peroxide. *Russ. Chem. Bull.* **1998**, *47*, 2379–2386. [CrossRef]

61. Wieghardt, K.; Bossek, U.; Nuber, B.; Weiss, J.; Bonvoisin, J.; Corbella, M.; Vitols, S.E.; Girerd, J.J. Synthesis, Crystal Structures, Reactivity, and Magnetochemistry of a Series of Binuclear Complexes of Manganese(II), -(III), and -(IV) of Biological Relevance. The Crystal Structure of $[L'M^{IV}(\mu\text{-}O)_3M^{IV}L'](PF_6)_2 \cdot H_2O$ Containing an Unprecedented Short Mn$\cdots$Mn Distance of 2.296 Å. *J. Am. Chem. Soc.* **1998**, *110*, 7398–7411.

62. Shul'pin, G.B.; Nesterov, D.S.; Shul'pina, L.S.; Pombeiro, A.J.L. A hydroperoxo-rebound mechanism of alkane oxidation with hydrogen peroxide catalyzed by binuclear manganese(IV) complex in the presence of an acid with involvement of atmospheric dioxygen. *Inorg. Chim. Acta* **2016**. [CrossRef]

63. Shul'pin, G.B.; Süss-Fink, G.; Lindsay Smith, J.R. Oxidations by the system "hydrogen peroxide—manganese(IV) complex—acetic acid"—Part II. Hydroperoxidation and hydroxylation of alkanes in acetonitrile. *Tetrahedron* **1999**, *55*, 5345–5358. [CrossRef]

64. Shul'pin, G.B.; Süss-Fink, G.; Shul'pina, L.S. Oxidations by the system "hydrogen peroxide–manganese(IV) complex–carboxylic acid": Part 3. Oxygenation of ethane, higher alkanes, alcohols, olefins and sulfides. *J. Mol. Catal. A Chem.* **2001**, *170*, 17–34. [CrossRef]

65. Nizova, G.V.; Bolm, C.; Ceccarelli, S.; Pavan, C.; Shul'pin, G.B. Hydrocarbon Oxidations with Hydrogen Peroxide Catalyzed by a Soluble Polymer-Bound Manganese(IV) Complex with 1,4,7-Triazacyclononane. *Adv. Synth. Catal.* **2002**, *344*, 899–905. [CrossRef]

66. Shul'pin, G.B.; Nizova, G.V.; Kozlov, Y.N.; Pechenkina, I.G. Oxidations by the "hydrogen peroxide–manganese(IV) complex–carboxylic acid" system. Part 4. Efficient acid-base switching between catalase and oxygenase activities of a dinuclear manganese(IV) complex in the reaction with H_2O_2 and an alkane. *New J. Chem.* **2002**, *26*, 1238–1245. [CrossRef]

67. Shul'pin, G.B. Metal-catalysed hydrocarbon oxidations. *C. R. Chim.* **2003**, *6*, 163–178. [CrossRef]

68. Shul'pin, G.B.; Nizova, G.V.; Kozlov, Y.N.; Arutyunov, V.S.; dos Santos, A.C.M.; Ferreira, A.C.T.; Mandelli, D. Oxidations by the system "hydrogen peroxide–$[Mn_2L_2O_3][PF_6]_2$(L = 1,4,7-trimethyl-1,4,7-triazacyclononane)–oxalic acid". Part 6. Oxidation of methane and other alkanes and olefins in water. *J. Organomet. Chem.* **2005**, *690*, 4498–4504. [CrossRef]

69. Nizova, G.V.; Shul'pin, G.B. A unique rate-accelerating effect of certain amino acids in the H_2O_2 oxidation of alkanes catalyzed by a dinuclear manganese complex containing 1,4,7-trimethyl-1,4,7-triazacyclononane. *Tetrahedron* **2007**, *63*, 7997–8001. [CrossRef]

70. Shul'pin, G.B.; Matthes, M.G.; Romakh, V.B.; Barbosa, M.I.F.; Aoyagi, J.L.T.; Mandelli, D. Oxidations by the system 'hydrogen peroxide–$[Mn_2L_2O_3][PF_6]_2$(L=1,4,7-trimethyl-1,4,7-triazacyclononane)–carboxylic acid'. Part 10: Co-catalytic effect of different carboxylic acids in the oxidation of cyclohexane, cyclohexanol, and acetone. *Tetrahedron* **2008**, *64*, 2143–2152. [CrossRef]

71. Ryu, J.Y.; Kim, S.O.; Nam, W.; Heo, S.; Kim, J. Alkane Oxidation Catalyzed by Manganese-tmtacn Complexes with H_2O_2. *Bull. Korean Chem. Soc.* **2003**, *24*, 1835–1837. [CrossRef]

72. Bennur, T.H.; Sabne, S.; Desphande, S.S.; Srinivas, D.; Sivasanker, S. Benzylic oxidation with H_2O_2 catalyzed by Mn complexes of *N,N′,N′′*-trimethyl-1,4,7-triazacyclononane: Spectroscopic investigations of the active Mn species. *J. Mol. Catal. A Chem.* **2002**, *185*, 71–80. [CrossRef]

73. Saisaha, P.; Buettner, L.; van der Meer, M.; Hage, R.; Feringa, B.L.; Browne, W.R.; de Boer, J.W. Selective Catalytic Oxidation of Alcohols, Aldehydes, Alkanes and Alkenes Employing Manganese Catalysts and Hydrogen Peroxide. *Adv. Synth. Catal.* **2013**, *355*, 2591–2603. [CrossRef]

74. Romakh, V.B.; Therrien, B.; Süss-Fink, G.; Shul'pin, G.B. Dinuclear Manganese Complexes Containing Chiral 1,4,7-Triazacyclononane-Derived Ligands and Their Catalytic Potential for the Oxidation of Olefins, Alkanes, and Alcohols. *Inorg. Chem.* **2007**, *46*, 1315–1331. [CrossRef] [PubMed]

75. Lessa, J.A.; Horn, A.; Bull, É.S.; Rocha, M.R.; Benassi, M.; Catharino, R.R.; Eberlin, M.N.; Casellato, A.; Noble, C.J.; Hanson, G.R.; Schenk, G.; Giselle, C.; Silva, O.A.; Antunes, O.A.C.; Fernandes, C. Catalase vs. Peroxidase Activity of a Manganese(II) Compound: Identification of a Mn(III)–(μ-O)$_2$–Mn(IV) Reaction Intermediate by Electrospray Ionization Mass Spectrometry and Electron Paramagnetic Resonance Spectroscopy. *Inorg. Chem.* **2009**, *48*, 4569–4579. [CrossRef] [PubMed]

76. Nakayama, N.; Tsuchiya, S.; Ogawa, S. Hydrocarbon oxidation with hydrogen peroxide and pentafluoroiodosylbenzene catalyzed by unusually distorted macrocycle manganese complexes. *J. Mol Catal. A Chem.* **2007**, *277*, 61–71. [CrossRef]

77. Lee, N.H.; Lee, C.S.; Jung, D.S. Selective Oxidation of Benzylic Hydrocarbons to Carbonyl Compounds Catalyzed by Mn(III) Salen Complexes. *Tetrahedron Lett.* **1998**, *39*, 1385–1388. [CrossRef]

78. Mardani, H.P.; Golchoubian, H. Selective and efficient C–H oxidation of alkanes with hydrogen peroxide catalyzed by a manganese(III) Schiff base complex. *J. Mol. Catal. A. Chem.* **2006**, *259*, 197–200. [CrossRef]

79. Golchoubian, H.; Ghasemi, N. Diphenylmethane Oxidation Catalyzed by Mononuclear Mn(III) Complexes. *J. Chin. Chem. Soc.* **2011**, *58*, 470–473. [CrossRef]

80. Gómez, I.; Garcia-Bosch, A.; Company, J.; Benet-Buchholz, A.; Polo, X.; Sala, X.; Ribas, M.; Costas, M. Stereospecific C–H Oxidation with H_2O_2 Catalyzed by a Chemically Robust Site-Isolated Iron Catalyst. *Angew. Chem. Int. Ed.* **2009**, *48*, 5720–5723. [CrossRef] [PubMed]

81. Ottenbacher, R.V.; Samsonenko, D.G.; Talsi, E.P.; Bryliakov, K.P. Highly Efficient, Regioselective, and Stereospecific Oxidation of Aliphatic C–H Groups with H_2O_2, Catalyzed by Aminopyridine Manganese Complexes. *Org. Lett.* **2012**, *14*, 4310–4313. [CrossRef] [PubMed]

82. Shen, D.; Miao, C.; Wang, S.; Xia, C.; Sun, W. Efficient Benzylic and Aliphatic C–H Oxidation with Selectivity for Methylenic Sites Catalyzed by a Bioinspired Manganese Complex. *Org. Lett.* **2014**, *16*, 1108–1111. [CrossRef] [PubMed]

83. Shen, D.; Miao, C.; Xu, D.; Xia, C.; Sun, W. Highly Efficient Oxidation of Secondary Alcohols to Ketones Catalyzed by Manganese Complexes of N_4 Ligands with H_2O_2. *Org. Lett.* **2015**, *17*, 54–57. [CrossRef] [PubMed]

84. Dai, W.; Lv, Y.; Wang, L.; Shang, S.; Chen, B.; Li, G.; Gao, S. Highly efficient oxidation of alcohols ca4alyzed by a porphyrin-inspired manganese complex. *Chem. Commun.* **2015**, *51*, 11268–11271. [CrossRef] [PubMed]

85. Ottenbacher, R.V.; Talsi, E.P.; Bryliakov, K.P. Mechanism of Selective C–H Hydroxylation Mediated by Manganese Aminopyridine Enzyme Models. *ACS Catal.* **2015**, *5*, 39–44. [CrossRef]

86. Adams, A.M.; Du Bois, J.; Malik, H.A. Comparative Study of the Limitations and Challenges in AtomTransfer C–H Oxidations. *Org. Lett.* **2015**, *17*, 6066–6069. [CrossRef] [PubMed]

87. Costas, M.; Que, L., Jr. Ligand Topology Tuning of Iron-Catalyzed Hydrocarbon Oxidations. *Angew. Chem. Int. Ed.* **2002**, *41*, 2179–2181. [CrossRef]

88. Chen, K.; Costas, M.; Que, L., Jr. Spin state tuning of non-heme iron-catalyzed hydrocarbon oxidations: Participation of Fe^{III}–OOH and Fe^V=O intermediates. *J. Chem. Soc. Dalton Trans.* **2002**, 672–679. [CrossRef]

89. Que, L., Jr. The Road to Non-Heme Oxoferryls and Beyond. *Acc. Chem. Res.* **2007**, *40*, 493–500. [CrossRef] [PubMed]

90. Mas-Ballesté, R.; Que, L., Jr. Iron-Catalyzed Olefin Epoxidation in the Presence of Acetic Acid: Insights into the Nature of the Metal-Based Oxidant. *J. Am. Chem. Soc.* **2007**, *129*, 15964–15972. [CrossRef] [PubMed]

91. Mas-Ballesté, R.; Fujita, M.; Que, L., Jr. High-valent iron-mediated cis-hydroxyacetoxylation of olefins. *Dalton Trans.* **2008**, 1828–1830. [CrossRef] [PubMed]

92. Ottenbacher, R.V.; Samsonenko, D.G.; Talsi, E.P.; Bryliakov, K.P. Highly Enantioselective Bioinspired Epoxidation of Electron-Deficient Olefins with H_2O_2 on Aminopyridine Mn Catalysts. *ACS Catal.* **2014**, *4*, 1599–1606. [CrossRef]

93. Ottenbacher, R.V.; Shubin, A.A.; Shashkov, M.V.; Talsi, E.P.; Bryliakov, K.P. Evidence for "Bifurcated Rebound Mechanism" in Biomimetic C–H Hydroxylation Mediated by Manganese-Aminopyridine Complexes. **2016**, Submitted.

94. Hartwig, J.F.; Larsen, M.A. Undirected, Homogeneous C–H Bond Functionalization: Challenges and Opportunities. *ACS Cent. Sci.* **2016**, *2*, 281–292. [CrossRef] [PubMed]