Review

Catalytic Oxidations with *Meta*-Chloroperoxybenzoic Acid (*m*-CPBA) and Mono- and Polynuclear Complexes of Nickel: A Mechanistic Outlook

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Abstract: Selective catalytic functionalization of organic substrates using peroxides as terminal oxidants remains a challenge in modern chemistry. The high complexity of interactions between metal catalysts and organic peroxide compounds complicates the targeted construction of efficient catalytic systems. Among the members of the peroxide family, *m*-chloroperoxybenzoic acid (*m*-CPBA) exhibits quite complex behavior, where numerous reactive species could be formed upon reaction with a metal complex catalyst. Although *m*-CPBA finds plenty of applications in fine organic synthesis and catalysis, the factors that discriminate its decomposition routes under catalytic conditions are still poorly understood. The present review covers the advances in catalytic C–H oxidation and olefine epoxidation with *m*-CPBA catalyzed by mono- and polynuclear complexes of nickel, a cheap and abundant first-row transition metal. The reaction mechanisms are critically discussed, with special attention to the O–O bond splitting route. Selectivity parameters using recognized model hydrocarbon substrates are summarized and important factors that could improve further catalytic studies are outlined.

Keywords: *m*CPBA; nickel complexes; oxidative catalysis; free radicals; cyclohexane oxidation; stereoselectivity

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1. Introduction

Peroxides constitute a class of compounds of exhaustive importance in the current chemical industry as well as in laboratory practice and biological studies [1–4]. Being strong oxidants, peroxide compounds often show low selectivity and do not discriminate chemical groups of close reactivities, which represents a drawback for targeted synthesis. Catalytic activation is the best way to control the peroxide's power [5,6]. The natural enzymatic systems demonstrate an exciting example of such control, where the metal-containing active centers can hydroxylate organic substrates using peroxides as terminal oxidants [7,8]. While the simplest and most used peroxide compound, hydrogen peroxide, is a cheap and readily available oxidant [9], the organic peroxides (ROOH or ROOR') reveal advantages in terms of higher stability and selectivity—important features for fine organic synthesis. Moreover, organic peroxides can produce highly active and selective intermediates in combination with auxiliary reagents [10–12]. However, in contrast to H₂O₂, organic peroxides may generate a broader range of radical species [13]. Therefore, the role of the catalyst is not only to activate the O–O bond in a desired way, but also to efficiently suppress the minor reaction pathways leading to the formation of side attacking species (such as free radicals). Among all organic peroxides of practical significance, *m*-chloroperoxybenzoic acid (*m*-CPBA) shows some of the most complex behavior [13–15]. The oxidizing potential of *m*-CPBA is sufficient even for the hydroxylation of methane using P450 enzyme [16] or its model systems (iron porphyrin complexes) as catalysts [17]. Moreover, *m*-CPBA is commonly used for asymmetric catalytic epoxidations and other

processes dealing with the activation and functionalization of C–H bonds—one of the most challenging reactions in modern chemistry [18–20]. Typically, the role of a catalyst in a highly selective peroxide system is to form high-valence metal-oxo (HVMO) species, whose reactivity can be further controlled by the ligand's nature [18,21]. Although *m*-CPBA is a convenient and easy-to-handle terminal oxidant for such reactions, it is prone to the formation of a series of O- and C-centered radical species, all of which are capable of H abstraction (Scheme 1). Moreover, all these species show different degrees of reactivity and selectivity, in this way interfering with the main (non-free radical) reaction mechanism and complicating the establishment of the C–H attacking species. To date, the factors that favor the O–O bond homolysis of *m*-CPBA and trigger its free radical activity are still to be established.

Scheme 1. General representation of the intermediates formed upon reaction of *m*-CPBA with a metal center depending on the reaction mechanism. All depicted species, except for *m*-chlorobenzoic acid, ArC(O)OH , are capable of H abstraction. Charges are not shown.

Mono- and polynuclear compounds of nickel have attracted great attention as catalysts for C–H oxidation and epoxidation with peroxides, particularly *m*-CPBA [22]. However, the nature of C–H attacking species has become a matter of heated debate [23]. Complexes of nickel demonstrate high catalytic efficiency and, furthermore, Ni(III) HVMO intermediates are stable enough to be trapped with convenient methods such as ESI-MS and EPR spectroscopies [24–26]. On the other hand, there are signs of a significant contribution of free radical reactions, where HVMO nickel species could be formed simply as a by-product. Thus, while the initial reports suggested the metal-mediated reaction mechanism [27], the latest studies indicate free organic radicals as the main C–H attacking species in Ni/*m*-CPBA catalytic systems [23].

The set of bond-, regio- and stereoselectivity parameters of a catalytic system is an important indicator for the nature of C–H attacking species [6,28]. The typical model substrates used for bond selectivity studies are methylcyclohexane and adamantane. However, the difference between 3° and 2° reactivities itself (Scheme 2) does not carefully distinguish between the attacking species, which may fall within the same region of 3°:2° ratios. One of the most efficient tests for the presence of free radicals is the oxidation of tertiary C–H bonds, which allows epimerization of the stereoconfiguration [29–32]. The typical substrates are dimethylcyclohexanes or decahydronaphthalenes (Scheme 3) [30,33,34]. In the event that the reaction proceeds completely through the long-lived alkyl radicals (as expected for H abstraction by $\text{RO}\bullet$ or $\text{RC}\bullet$ species, Scheme 1), the *cis*- and *trans*-products will form in nearly equal quantities, independently of the starting stereoconfiguration of the substrate. Unfortunately, this simple test is often omitted in catalytic studies of *m*-CPBA, although it could give a direct answer regarding the existence of long-lived free radicals. In this review, we focus on the nickel mono- and polynuclear complexes as catalysts for C–H oxidation with *m*-CPBA, with special attention paid to selectivity studies and the nature of attacking species.

Scheme 2. Typical model substrates and their products used for determination of 3°:2°:1° and 3°:2° bond selectivity of the catalytic C–H oxidation.

Scheme 3. Hydroxylation of a tertiary C–H bond of *cis*-1,2-dimethylcyclohexane as a test system for the presence of long-lived alkyl radical intermediates (the latter results in a nearly 1:1 ratio of *cis*- and *trans*-products).

2. Discussion

The catalytic interaction of nickel complexes with *m*-CPBA was practically not studied before the report in 2006 of the pronounced catalytic activity of the $[\text{Ni}^{\text{II}}(\text{L}^1)(\text{OAc})(\text{H}_2\text{O})]\text{BPh}_4$ (**Ni1**) (L^1 = tris(2-pyridylmethyl)amine) compound in the oxidation of hydrocarbons (Figure 1) [35]. The polypyridyl ligand TPA and its derivatives are known to stabilize oxo and peroxo complexes of iron [36]. Although the respective nickel species are expected to be less stable, they could also be stabilized by the L^1 family. The complex **Ni1** catalyzes the oxidation of cyclohexane (Scheme 4), cyclooctane, adamantane and ethylbenzene to the respective alcohols and ketones, with a maximum TON of 676 (for cyclooctane), which corresponds to a 68% yield based on the oxidant. Cyclohexane oxidation revealed similar reactivity, with TON of 656, while ethylbenzene was the least reactive substrate, as evidenced by the respective TON of 256. Only trace amounts of ϵ -caprolactone by-product were detected in the oxidation of cyclohexane. Adamantane was oxidized with 3°:2° bond selectivity of 13:1. All reactions proceeded in the mixed $\text{CH}_3\text{CN}/\text{CH}_2\text{Cl}_2$ (3:1) media.

Complexes of cobalt, iron and manganese with the same L^1 ligand were tested and showed lower catalytic activity under similar conditions. The authors proposed the participation of NiO^+ species as reaction intermediates [35].

Figure 1. (Left) Schematic representation of the ligand L^1 . (Right) Molecular structure (CSD ref-code XESVEX) of the complex $[Ni^{II}(L^1)(OAc)(H_2O)]BPh_4$ (**Ni1**) [35]. The hydrogen atoms and the uncoordinated BPh_4 anion are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; C, grey.

Scheme 4. Oxidation of cyclohexane, a typical model reaction used for evaluation of the catalytic activities of the discussed complexes.

A series of coordination compounds of nickel with tris(2-pyridylmethyl)amino, bis(2-pyridylmethyl)amino and bis(2-pyridylethyl)amino ligands L^1 – L^3 (Figures 1 and 2, left) have been investigated with the aim of understanding the influence of the ligand on the catalytic activity [27]. The highest TON in the oxidation of cyclohexane (745 for sum of cyclohexanol and cyclohexanone) was exhibited by the complex $[Ni^{II}(L^{2a})(OAc)(MeOH)]BPh_4$ (**Ni2**) (L^{2a} = 6-[*N,N*-bis(2-pyridylmethyl)aminomethyl]-2,4-di-*tert*-butylphenol) (Figure 2, right), showing the alcohol/ketone ratio of 7.5. An important observation was the elevated yield of chlorobenzene, whose amounts reached 50% based on the other products. Since chlorobenzene originates from the rapid decarboxylation of the *m*-chlorobenzoate radical, homolytic splitting of the *m*-CPBA O–O bond was assumed as a principal route of formation of the radical nickel-oxo species $Ni^{II}-O\bullet$ (Scheme 5). The overall reaction mechanism proposed by the authors [27] foresees the involvement of two *m*-CPBA molecules per catalytic cycle and one product molecule. This limits the theoretical yield of products to 50% based on the oxidant. However, the experimentally documented yields reach 60–70%, in this way contradicting the proposed overall mechanism [27].

Figure 2. (Left) Schematic representation of the ligand families L^2 and L^3 . (Right) Molecular structure (CSD refcode LEYSUE) of the complex $[\text{Ni}^{\text{II}}(\text{L}^{2a})(\text{OAc})(\text{MeOH})]\text{BPh}_4$ (**Ni2**) [27]. The hydrogen atoms are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; C, grey.

Scheme 5. Fragment of the proposed catalytic mechanism showing formation of $\text{Ni}^{\text{II}}\text{-O}\bullet$ species and its reactivity towards hydroxylation of cyclohexane [27]. The charges are not shown.

Similar results in cyclohexane oxidation (Scheme 4) were obtained for a series of Ni(II) complexes with tetradentate tripodal N-donor ligands L^4 (Figure 3, left) [37]. The highest yields of products (73%) were observed for the catalyst $[\text{Ni}^{\text{II}}(\text{L}^{4a})(\text{H}_2\text{O})(\text{CH}_3\text{CN})](\text{ClO})_2$ (**Ni3**) ($L^{4a} = N,N$ -dimethyl- N',N' -bis(pyrid-2-ylmethyl)ethane-1,2-diamine). Oxidation of cumene catalyzed by **Ni3** afforded 2-phenyl-2-propanol in a 44% yield (TON = 438). For ethylbenzene, a TON of 443 was observed, which corresponds to a yield of 44%. In contrast to cumene, oxidation of ethylbenzene afforded a mixture of alcohol and ketone, with the respective ratio of 3.6. The $3^\circ:2^\circ$ bond selectivity in adamantane oxidation ranged from 12.5 to 17.3. The amounts of chlorobenzene by-products in the reactions with **Ni3** were nearly the same as those for the **Ni2** catalyst. Hence, the C–H bond attacking species was proposed to be $\text{Ni}^{\text{II}}\text{-O}\bullet$ (Scheme 5).

Figure 3. (Left) Schematic representation of the ligand family L^4 . (Right) Molecular structure (CSD refcode EXUCAC) of the complex $[\text{Ni}^{\text{II}}(L^{4a})(\text{H}_2\text{O})(\text{CH}_3\text{CN})](\text{ClO})_2$ (**Ni3**) [37]. The hydrogen atoms are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; C, grey.

A family of nickel compounds with pentadentate N-donor ligands of polypyridyl type (Figure 4, left) were investigated as catalysts for the mild oxidation of alkanes with *m*-CPBA [38]. All complexes of this series revealed similar properties and catalytic activities. The crystal structure of the representative example $[\text{Ni}^{\text{II}}(L^{5c})(\text{CH}_3\text{CN})](\text{BPh}_4)_2$ (**Ni4**) (L^{5c} = *N*-methyl-*N,N'*-bis(pyrid-2-ylmethyl)-*N'*-(6-methylpyrid-2-ylmethyl)ethylenediamine) is shown in Figure 4, right. The complex **Ni4** catalyzes the oxidation of cyclohexane to cyclohexanol, cyclohexanone and ϵ -caprolactone (53:1:7 ratio of products; Scheme 4), with an overall TON of 484 and yield of 48% (based on the oxidant). Substantial amounts of chlorobenzene were obtained (75–85% based on the oxidant). Oxidation of cumene resulted in 2-phenyl-2-propanol, with a TON of 418 (42% of yield). Similar results have been obtained for adamantane (TON = 527 and yield = 53%), showing 3°:2° bond selectivity of 11:1 for all catalysts of this type. Extensive DFT calculations revealed the high-spin $\text{Ni}^{\text{II}}\text{-O}\bullet$ species as the most likely high-valence intermediate, abstracting the H atom through the radical rebound mechanism, in a way similar to that depicted in Scheme 5. However, no further experimental efforts (e.g., UV or EPR spectroscopic measurements) to confirm the participation of the $\text{Ni}^{\text{II}}\text{-O}\bullet$ species were made. Moreover, rather low bond selectivity in adamantane oxidation suggests the possible involvement of other C–H attacking species.

Figure 4. (Left) Schematic representation of the ligand family L^5 . (Right) Molecular structure (CSD refcode MOGKIE) of the complex $[\text{Ni}^{\text{II}}(L^{5c})(\text{CH}_3\text{CN})](\text{BPh}_4)_2$ (**Ni4**) [38]. The hydrogen atoms and BPh_4 anions are omitted for clarity. Color scheme: Ni, light green; N, blue; C, grey.

Coordination compound $[\text{Ni}^{\text{II}}(L^6)(\text{OTf})](\text{OTf})$ (**Ni5**) (HOTf = trifluoromethanesulfonic acid) bearing a tetrapodal non-aromatic N_4 -donor ligand L^6 (tris[2-(*N*-tetramethylguanidyl)ethyl]amine) (Figure 5) was shown to favor the homolytic O–O cleavage of *m*-CPBA with the formation of a mixture of nickel(III) intermediates $[\text{Ni}^{\text{III}}(\text{O})(L^6)]^+$ (**Ni5-1**) and $[\text{Ni}^{\text{III}}(\text{OH})(L^6)]^{2+}$ (**Ni5-2**) [39]. The reaction of **Ni5** with one equivalent of *m*-CPBA at -30°C in CH_2Cl_2 afforded a deep blue solution of **Ni5-1**/**Ni5-2** with UV absorption maxima at 464, 520 and

794 nm. EPR spectra (measured at 10 K) of this solution revealed two signals of rhombic $S = 1/2$ species, attributed to geometrically different nickel(III) complexes **Ni5-1** and **Ni5-2**. The authors excluded the possibility of the heterolytic splitting of *m*-CPBA based on the GC–MS analysis of reaction mixtures, where chlorobenzene, but not *m*-chlorobenzoic acid (a product of O–O bond heterolysis), was detected. The signs of heterolytic splitting were observed only under the conditions of ESI–MS experiments, where peaks attributable to $\text{Ni}^{\text{IV}}=\text{O}$ species were detected (Scheme 6). The mixture of metastable complexes **Ni5-1**/**Ni5-2** hydroxylates (at $-30\text{ }^{\circ}\text{C}$) methylenic C–H bonds in xanthene, 9,10-dihydroanthracene (DHA) and 1,4-cyclohexadiene at high reaction rates were comparable for oxygen transfer to PPh_3 . Oxidation of 1-benzyl-1,4-dihydronicotinamide with **Ni5-1**/**Ni5-2** proceeds at least two orders faster. A large kinetic isotope effect of 3.9 was found for parallel oxidations of normal and d_4 -DHA [39]. It is noteworthy that the strength of the doublet EPR signals decays along with the reduction process (Figure 6), as expected for $\text{Ni}(\text{III}) \rightarrow \text{Ni}(\text{II})$ transformation (the divalent nickel complex **Ni5** is highly likely to be EPR-silent in the X-band due to the large zero-field splitting [40,41]).

Figure 5. (Left) Schematic representation of the ligand L^6 . (Right) Molecular structure (CSD refcode ZARNAJ) of the complex $[\text{Ni}^{\text{II}}(\text{L}^6)(\text{OTf})](\text{OTf})$ (**Ni5**) [39]. The hydrogen atoms and OTf anions are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; S, yellow; F, yellow–green; C, grey.

Scheme 6. Fragment of the proposed catalytic mechanism showing formation of **Ni5-1** and **Ni5-2** species [39]. The charges are not shown.

Figure 6. Decay of the doublet EPR signal assigned to the mixture of **Ni5-1** and **Ni5-2** species upon their reaction with PPh_3 . Adapted with permission from [39], Royal Society of Chemistry, 2012.

Further development in the field was achieved by employing scorpionate ligands (Figure 7, left) [42], which are known to stabilize nickel(II)-alkylperoxo species [43]. The model catalytic system comprised cyclohexane (Scheme 4) or methylcyclohexane (Scheme 2), *m*-CPBA and a nickel catalyst in $\text{C}_6\text{H}_5\text{CF}_3$ or CH_2Cl_2 . The maximum TONs did not exceed 42, for $[\text{Ni}_2(\text{L}^{7a})_2(\text{OH})_2]$ (**Ni6**) (Figure 7, right) [42]. The system displayed only a weak preference towards oxidation of the tertiary C–H bond of methylcyclohexane, as evidenced by the low 3°:2° bond selectivity of 5:1 (the catalyst-free test revealed 33:1 bond selectivity under the same conditions). Based on spectroscopic studies, the authors concluded that the mononuclear nickel(II)-acylperoxo species, formed after the reaction of **Ni6** with *m*-CPBA, are able to abstract H atoms from C–H bonds in a concerted mechanism (Scheme 7), although the possibility of O–O homolysis with the formation of $\text{Ni}^{\text{II}}\text{--O}\bullet$ and $\text{Ni}^{\text{III}}\text{=O}$ species was not excluded. No ^{18}O -labeled oxygen in cyclohexanol was detected when oxidizing cyclohexane in the presence of H_2^{18}O . The observation of labeled cyclohexanone, however, was mistakenly interpreted [42] as an indication of the presence of different formation pathways of cyclohexanol and cyclohexanone. Ketones are known to exchange oxygen with water [44–47]; this mechanism is the main source of ^{18}O -enriched cyclohexanones in the presence of H_2^{18}O .

Figure 7. (Left) Schematic representation of the ligand family L^7 . (Right) Molecular structure (CSD refcode UFABOS) of the complex $[\text{Ni}_2(\text{L}^{7a})_2(\text{OH})_2]$ (**Ni6**) [42]. The hydrogen atoms are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; B, brown–green; C, grey.

Scheme 7. Proposed reaction pathways for oxidation of the substrate RH with *m*-CPBA catalyzed by Ni6 [42].

The reaction of $[\text{Ni}^{\text{II}}(\text{L}^{\text{7e}})(m\text{-CBA})]$ (**Ni7**) (L^{7e} = scorpionate ligand L^{7} (Figure 7, left), where $\text{R}^1 = \text{CF}_3$, $\text{R}^2 = \text{H}$ and $\text{R}^3 = \text{CH}_3$; *m*-CBA = *m*-chlorobenzoic acid), with two equivalents of *m*-CPBA resulted in the successive conversion of **Ni7** to $[\text{Ni}^{\text{II}}(\text{L}^{\text{7e}})(m\text{-CPBA})]$ (**Ni7-1**), where *m*-CPBA coordinated bidentately with a nickel center (Figure 8) [48]. The compound **Ni7-1** is thermally stable, as evidenced by the decomposition rate constant of $1.6 \times 10^{-5} \text{ s}^{-1}$ at 70°C in benzene. This remarkable stability allows crystallization and the determination of the structure of **Ni7-1** through conventional single crystal X-ray diffraction. The similar complex $[\text{Ni}^{\text{II}}(\text{L}^{\text{7a}})(m\text{-CPBA})]$, bearing CH_3 groups instead of CF_3 ones, was unstable even at low temperatures (below -20°C). The complex **Ni7-1** is capable of the direct oxidation of various substrates in toluene medium. Thioanisole was oxidized to the respective sulfoxide with a 96% yield (Scheme 8) [48]. From the kinetic data, the authors concluded that this oxidation proceeds through the Michaelis–Menten-type mechanism, showing the fast, reversible formation of a substrate–oxidant adduct with subsequent oxidation and oxygen atom transfer. At the elevated temperature of 70°C in toluene or trifluorotoluene, **Ni7-1** epoxidizes cyclohexene and styrene (Scheme 9) with 66% and 95% yields, respectively (based on the oxidant, **Ni7-1**). Oxidation of substrates having secondary or tertiary sp^3 C–H bonds (1,4-cyclohexanediene, 1,10-dihydroanthracene, xanthene (Scheme 9), fluorene and methylcyclohexane) in benzene or toluene was suggested to proceed without cleavage of the O–O bond of **Ni7-1** (through the concerted mechanism) [48]. Further, the oxidation of methylcyclohexane (Scheme 2) was claimed to proceed with a preference towards the oxidation of secondary C–H bonds rather than a tertiary one. This observation was explained by the steric crowding of the tertiary C–H bond of methylcyclohexane. However, normalization of the obtained yields of products (taking into account the numbers of C–H bonds in the methylcyclohexane molecule) gives rather low $3^\circ:2^\circ:1^\circ$ bond selectivity of 8:2:1, where the tertiary C–H shows a significant preference over secondary and primary ones.

Figure 8. Molecular structures of the complexes $[\text{Ni}^{\text{II}}(\text{L}^{7\text{e}})(m\text{-CBA})]$ (**Ni7**) and $[\text{Ni}^{\text{II}}(\text{L}^{7\text{e}})(m\text{-CPBA})]$ (**Ni7-1**), where the coordinated *m*-CPBA is highlighted in purple [48]. CSD refcodes TIWMAP and TIWLUI for **Ni7** and **Ni7-1**, respectively. The hydrogen atoms are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; Cl, green; F, yellow-green; C, grey.

Scheme 8. Proposed reaction pathway for stoichiometric oxidation of thioanisole with **Ni7-1**. X = Br, CH₃, OCH₃.

Scheme 9. Stoichiometric oxidation of various substrates with **Ni7-1**. X = Br, H, CH₃, OCH₃.

Direct evidence of the participation of high-valence nickel-oxo species in Ni/*m*-CPBA catalytic systems was obtained based on the example of the complex $[\text{Ni}^{\text{II}}(\text{L}^8)]$ (**Ni8**) with the pincer-like tetradentate 2,6-pyridinecarboxamidate ligand H_2L^8 (Figure 9, left) [49]. The addition of three equivalents of *m*-CPBA to **Ni8** at -30°C leads to the formation of the **Ni8-*m*-CPBA** adduct and the subsequent appearance of $\text{Ni}^{\text{III}}\text{-O}\bullet$ species (**Ni8-1**) (Figure 9). No chlorobenzene or CO_2 were detected by GC-MS analysis, while *m*-chlorobenzoic acid was formed in quantitative amounts, indicating that the heterolytic pathway is dominant (in comparison with the compound **Ni5**, which exclusively favors homolytic splitting [39]). The structure of **Ni8-1** was established by DFT calculations, supported by extended X-ray absorption fine structure (EXAFS) and cryospray ionization mass spectrometry (CSI-MS) spectroscopies. The UV/Vis spectra of **Ni8-1** feature the characteristic absorption at 420 nm. The reaction of **Ni8-1** with alkenes at -30°C affords epoxides with yields of more than 50% based on the amount of **Ni8**. Cyclohexane, ethylbenzene or toluene were oxidized by **Ni8-1** to the respective aldehydes and ketones with a 21–47% yield (based on **Ni8**), under the same conditions. Control tests confirmed that the background activity of *m*-CPBA under the conditions of the experiment was negligible. Furthermore, the reaction rates exhibited

by **Ni8-1** in the oxidation of methylenic sp^3 C–H bonds were found to be considerably faster (more than 200 times) than those of **Ni5-1**/**Ni5-2** under the same conditions and ca. three orders faster than that of **Ni7-1**.

Figure 9. (Left) Schematic representation of the ligand H_2L^8 . (Right) Molecular structure of the complex $[Ni^{II}(L^8)]$ (**Ni8**) (CSD refcode ZEFQOT) and DFT optimized structure of the HVMO derivative $Ni^{III}-O\bullet$ (**Ni8-1**) [49]. Hydrogen atoms are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; C, grey.

Oxidation of adamantane under other catalytic conditions (150 equivalents of substrate and *m*-CPBA relative to **Ni8**) proceeded with bond selectivity $3^\circ:2^\circ = 18:1$, being very close to that observed for **Ni1** and **Ni3** catalysts. However, the retention of the stereoconfiguration of *cis*-1,2-dimethylcyclohexane (Scheme 3) was only at the 84% level, indicating the possible escape of an alkyl radical with the subsequent epimerization of a stereoconfiguration.

The coordination compound $[Ni^{II}(L^9)Cl]$ (**Ni9**) shown in Figure 10 is based on the ligand HL^9 (2-[bis(pyridin-2-ylmethyl)amino]-*N*-(quinolin-8-yl)acetamide) [50]. Complex **Ni9** catalyzes the epoxidation of alkenes, with the maximum yield of products up to 72% (based on the oxidant) and TON of 7 observed for the oxidation of cycloheptene, while *trans*-2-octene was the least reactive substrate, showing a yield of 36% (a 10-fold excess of substrate was used). Inversion of the stereoconfiguration was observed in the oxidation of *cis*-stilbene, which afforded the *trans*-product in a 24% yield, while the *cis*-product was obtained in a 2% yield only (Scheme 10). The authors explained this effect by the participation of a long-lived radical intermediate in the oxidation route. *cis*-2-Octene and *cis*-hexene revealed a lower degree of inversion, while *trans*-stilbene was converted exclusively to *trans*-oxide (along with benzaldehyde and 2-phenylacetophenone by-products). Small amounts (1–5%) of chlorobenzene were obtained in all tests, suggesting at least the partial involvement of the homolytic *m*-CPBA cleavage pathway. Epoxidation of cyclohexene in the presence of $H_2^{18}O$ in a CH_3CN/CH_2Cl_2 medium resulted in 7% of ^{18}O -labeled epoxide. When the same reaction was conducted in $CH_3CN/CH_2Cl_2/CH_3OH$ medium (10% of CH_3OH), the incorporation level was increased to 15%. This fact was interpreted by the authors as evidence of the participation of Ni(III)-oxo and Ni(IV)-oxo species in the reaction, where the contribution of tetravalent ones, resulted from *m*-CPBA O–O bond heterolysis, increases for a protic solvent. Further evidence of Ni(III) species participation was obtained from EPR spectra of a frozen solution of **Ni9** with six equivalents of *m*-CPBA, mixed at 0 °C (Figure 11), which showed a signal typical for Ni(III). Heating the mixture to room temperature led to the disappearance of the EPR signal, as expected for the Ni(III) → Ni(II) reaction (Figure 11).

Figure 10. (Left) Schematic representation of the ligand L^9 . (Right) Molecular structure (CSD refcode HATDUE) of the complex $[Ni^{II}(L^9)Cl]$ (**Ni9**) [50]. The hydrogen atoms are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; Cl, green; C, grey.

Scheme 10. (Top) Oxidation of *cis*-stilbene with *m*-CPBA, catalyzed by the complex **Ni9**, affording the *trans*-epoxide as the main product. (Bottom) Proposed *cis*/*trans* isomerization mechanism [50].

Figure 11. (Left) The EPR spectrum of the Ni(III) species formed upon treatment of the complex **Ni9** with *m*-CPBA (recorded at 113 K). (Right) Decay of the spectrum when heated to room temperature. Adapted with permission from [50], Wiley, 2017.

The catalytic activity of the azide-containing complex $[Ni(H_3L^{10})(N_3)_2]_2$ (**Ni10**) bearing the polydentate N,O-donor ligand ($H_3L^{10} = N$ -(2-pyridylmethyl)- N' -(2-hydroxyethyl)-ethylenediamine) (Figure 12) was studied using 2.8-fold excess of *m*-CPBA over the substrate (in contrast to **Ni9**:*m*-CPBA = 1:1 ratio discussed above) [51]. Under these conditions, quantitative conversions of alkene substrates were achieved, with average selectivity towards epoxides of ca. 70%. The catalytic system **Ni10**/*m*-CPBA was quite efficient towards the epoxidation of vinylcyclohexane (87% conversion in CH_3CN/CH_2Cl_2 media) as well as

terminal olefines (89–100% conversion) (Scheme 11), known to be less reactive due to their electron-deficient nature. Moreover, the catalytic system **Ni10**/*m*-CPBA revealed distinct selectivity towards the *trans*-epoxides. Both *cis*- and *trans*-stilbene oxidation resulted in *trans*-epoxide with 65% yield, showing less than 10% of *cis*-epoxide. Such behavior is similar to that observed for the catalyst **Ni9** (Scheme 10). The blank test in the absence of a catalyst revealed a 10% yield of products, while NiCl_2 or $\text{Ni}(\text{NO}_3)_2$ did not catalyze the reaction at all. The appearance of 5% of ^{18}O -labeled epoxide from H_2^{18}O in the course of cyclohexene oxidation was considered by the authors as evidence for high-valence nickel-oxo species, as the latter may exchange oxygen with water. Mixing the complex **Ni10** with six equivalents of *m*-CPBA at -40°C in $\text{CH}_3\text{CN}/\text{CH}_2\text{Cl}_2$ afforded a red solution with broad absorption at 500 nm, presumably constituting a high-valence nickel intermediate, **Ni10-1**. The EPR spectrum of **Ni10-1** revealed a rhombic signal, typical for nickel(III) species (Figure 13). The authors proposed $\text{Ni}(\text{IV})=\text{O}$ species as those responsible for the olefin epoxidations, while $\text{Ni}(\text{III})=\text{O}$ ones were presumed to promote less selective allylic C–H oxidation [51].

Figure 12. (Left) Schematic representation of the ligand H_3L^{10} . (Right) Molecular structure (CSD refcode HARSUR) of the complex $[\text{Ni}^{\text{II}}(\text{H}_3\text{L}^{10})(\text{N}_3)_2]_2$ (**Ni10**) [51]. The hydrogen atoms are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; C, grey.

Scheme 11. Epoxidation of vinylcyclohexane and terminal olefins ($n = 2, 4\text{--}12, 14$) with *m*-CPBA, catalyzed by **Ni10** [51].

Figure 13. The EPR spectrum of the $\text{Ni}(\text{III})$ species formed upon treatment of the complex **Ni10** with *m*-CPBA, recorded at 100 K. Reproduced with permission from [51], Wiley, 2017.

The catalytic system **Ni10**/PPAA (where PPAA = phenylperacetic acid) was used to evaluate the contribution of homolytic O–O bond splitting to the overall reaction mechanism by monitoring the toluene formation, which appears from the decarboxylation of the $\text{PhCH}_2\text{C}(\text{O})\text{O}\bullet$ radical. From the observed yields of toluene (50%), the contribution of PPAA homolysis can be considered rather high. This observation raises the question of whether the attacking species are nickel HVMO species or oxyl radicals $\text{PhCH}_2\text{C}(\text{O})\text{O}\bullet$ or $\text{ArC}(\text{O})\text{O}\bullet$ (for PPAA and *m*-CPBA catalytic systems, respectively) because the O-centered carboxyl radicals, as well as their decarboxylation products, $\text{PhCH}_2\bullet$ and $\text{Ar}\bullet$ ones, respectively, are capable of H atom abstraction from C–H bonds as well as the epoxidation of olefins.

A similar investigation of epoxidation catalytic activity was performed for the substituted porphyrin complex $[\text{Ni}^{\text{II}}(\text{L}^{11})]$ (**Ni11**) (where H_2L^{11} = 5,10,15,20-tetrakis[2,6-di(*n*-butoxy)phenyl]porphyrin) [52]. In contrast to the catalyst **Ni10**, oxidation of *cis*-2-octene catalyzed by **Ni11** resulted in *cis*-epoxide as the main product, while the stereoconfiguration of *cis*-stilbene was epimerized, showing nearly equal amounts of *cis*- and *trans*-epoxides. The catalyst **Ni11** showed a lower contribution of homolytic O–O splitting, as evidenced by the tests using PPAA oxidant (where the percentage of homolytic splitting was estimated from the sum of the amounts of benzaldehyde, benzyl alcohol and toluene). The highest percentage of the homolytic mechanism in the epoxidation of cyclohexene (27%) was observed for the protic media ($\text{CH}_3\text{CN}/\text{H}_2\text{O}$) and polar aprotic media (CH_3CN), while the less polar aprotic solvents (CH_2Cl_2 or toluene) resulted in the homolysis contribution ranging from 4 to 24%. The participation of Ni(II)–OOC(O)R, Ni(III) and Ni(IV) oxo intermediates was proposed, depending on the nature of the solvent. The incorporation of ^{18}O into the cyclohexene oxide from H_2^{18}O was at the 5% level, suggesting the participation of HVMO species as key oxidation intermediates. However, since the enrichment level is low, the results of such ^{18}O -labeling studies should be treated cautiously. For example, oxidation of *trans*-decahydronaphthalene with *m*-CPBA, catalyzed by phthalocyanine complexes $[\text{M}^{\text{II}}(\text{pc})]$ ($\text{M} = \text{Fe}, \text{Ni}$ and Co) in the presence of H_2^{18}O and a nitric acid promoter, afforded nearly equal ^{18}O incorporation levels of 3% into the alcohols [53]. Since the stabilities and lifetimes of iron, nickel and cobalt HVMO species drastically decrease in this order [54,55] (the so-called “oxo wall” [55]), it is unlikely that the rates of oxygen exchange would increase at the same magnitude, leading to the same ^{18}O -enrichment in all cases. Hence, the most plausible explanation is the existence of some other mechanism of the ^{18}O -incorporation (apart from the direct exchange between the product and water, which is usually excluded), while the ^{18}O tests in the above studies could not serve as clear evidence for the presence of HVMO intermediates.

A series of mononuclear complexes with oxazoline-containing tertiary amine ligand L^{12} (Figure 14, left), differing by coordinated anions $[\text{Ni}^{\text{II}}(\text{L}^{12})\text{X}](\text{BPh}_4)$ ($\text{X} = \text{Cl}, \text{OAc}, \text{NO}_3, m\text{-CBA}$), was synthesized and tested towards catalytic alkane oxidation with *m*-CPBA [56]. The most active complex of this series, $[\text{Ni}^{\text{II}}(\text{L}^{12})\text{Cl}](\text{BPh}_4)$ (**Ni12**) (Figure 14, right), catalyzed the oxidation of methylcyclohexane, with an overall TON of 54 and 3°:2° bond selectivity of 9:1 (the amounts of 1° products were negligible). The respective bond selectivity for adamantane was 19:1 for **Ni12** (ranging from 16:1 to 19:1 for this series of complexes). Oxidation of cyclohexane was conducted using a ten-times higher amount of *m*-CPBA (0.13 equivalents relative to substrate), allowing TONs of up to 974 to be obtained (for **Ni12**). The amount of chlorobenzene by-product was comparable to that for cyclohexanol, which is unambiguous evidence of *m*-CPBA homolysis as the main reaction route. Substantial amounts of ϵ -caprolactone and chlorocyclohexane (Scheme 4) were observed (the ratio cyclohexanol:cyclohexanone: ϵ -caprolactone:chlorocyclohexane was 127:14:1:7); the origin of chlorine (*m*-CPBA or CH_2Cl_2 from the solvent mixture) was not discussed. In general, the nature of anion X in the $[\text{Ni}^{\text{II}}(\text{L}^{12})\text{X}](\text{BPh}_4)$ catalysts did not greatly influence the yields of products or bond selectivity. The complexes bearing *m*-CBA and, especially, the NO_3 anion revealed significant induction periods, which could be associated with stronger binding of the respective anions to the nickel centers. The

kinetic isotope effect in the parallel oxidation of normal and d_{12} -deuterated cyclohexane was found to be 2.67 for the acetate complex $[\text{Ni}^{\text{II}}(\text{L}^{12})(\text{OAc})](\text{BPh}_4)$ (**Ni12a**) as catalyst. Oxidation of toluene catalyzed by the latter compound resulted in bibenzyl as one of the main reaction products (Scheme 12). Bibenzyl appears from the coupling of two long-lived benzyl radicals and, therefore, the catalytic system operates via a free radical mechanism. Such an observation suggests [57] that the catalyst **Ni12a** does not interfere with this mechanism and does not act as a trap for carbon-centered radicals [56]. CSI-MS and UV spectroscopies were employed to trap the reactive intermediates. Mixing of **Ni12a** with *m*-CPBA in CH_2Cl_2 immediately resulted in the formation of the adduct $[\text{Ni}^{\text{II}}(\text{L}^{12})(m\text{-CPBA})]^+$ with an absorption band at 398 nm, which disappeared within one day.

Figure 14. (Left) Schematic representation of the ligand H_3L^{12} . (Right) Molecular structure (CSD refcode HUPLIQ) of the complex $[\text{Ni}^{\text{II}}(\text{L}^{12})\text{Cl}](\text{BPh}_4)$ (**Ni12**) [56]. The hydrogen atoms and BPh_4 anion are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; Cl, green; C, grey.

Scheme 12. Oxidation of toluene with *m*-CPBA, catalyzed by **Ni12a**, with formation of bibenzyl as a main product [56].

The coordination compounds of nickel with rigid N- or N,O-donor ligands (terpyridine, bisoxazoline, substituted phenanthrolines and bipyridines) was applied for the catalytic hydroxylation of polyethylene with *m*-CPBA [58]. The model substrates comprised cyclohexane and *n*-octadecane. Despite the structural similarity, all the catalysts revealed a broad range of turnover numbers in the oxidation of cyclohexane (Scheme 4). The lowest efficiency (TON = 60) was found for $[\text{Ni}^{\text{II}}(\text{L}^{13\text{db}})_2(\text{OAc})](\text{BPh}_4)$, where $\text{L}^{13\text{db}} = 2,9$ -dimethylphenanthroline (Figure 15). The complex bearing the terpyridine ligand $[\text{Ni}^{\text{II}}(\text{L}^{13\text{b}})_3](\text{BPh}_4)_2$ was the least reactive (TON = 132) from the $\text{M}(\text{L})_3$ family. The highest turnover number of 5560 in cyclohexane oxidation, supported by the yield of cyclohexanol of 52%, was observed for $[\text{Ni}^{\text{II}}(\text{L}^{13\text{dc}})_3](\text{BPh}_4)_2$ (**Ni13**) (Figure 15) [58]. Then, the catalyst **Ni13** was tested towards the hydroxylation of *n*-octadecane at an elevated temperature of 80 °C (Scheme 13) to confirm the conditions required further for the polyethylene oxidation, since the latter is hardly soluble below this temperature. Using four equivalents of *m*-CPBA relative to *n*-octadecane and a catalyst loading of 0.4 mol%, *n*-octadecanol was obtained as the main reaction product (yield of 41% relative to the substrate), while the amount of ketone was two-times lower (21%). Significant amounts (20% of yield) of the chloro-derivative of *n*-octadecane were also detected. The dichloroethane solvent was shown to be the main source of chlorine. However, both *m*-CPBA and chlorobenzene could also serve as chlorine sources, as was demonstrated by the comparative tests. Oxidation of low-molecular-weight polyethylene (4.3 kg/mol) under

similar conditions using the catalyst **Ni13** resulted in the maximum degree of polyethylene functionalization of 5.5 (sum of all functionalized products) per 100 monomers, with selectivity towards alcohols of up to 88%. Functionalization of a high-molecular-weight polyethylene required the addition of 1,2,4-trichlorobenzene as a co-solvent, an increase in the reaction temperature up to 90 °C and a decrease in the substrate concentration. Notably, in the absence of a nickel catalyst, the molecular weight parameters of the functionalized polymers were considerably lower than those for nickel-catalyzed reactions, indicating the cleavage of the polyethylene chain under the catalyst-free conditions.

Figure 15. (Left) Schematic representation of the ligand family L¹³. (Right) Molecular structure (CSD refcode CEHWOE) of the complex [Ni^{II}(L^{13dc})₃](BPh₄)₂ (**Ni13**) [58]. The hydrogen atoms and BPh₄ anion are omitted for clarity. Color scheme: Ni, light green; N, blue; C, grey.

Scheme 13. Oxidation of *n*-octadecane (*n* = 14) and polyethylene (M_w ranges from 4.3 to 122.9 kg mol^{−1}) with *m*-CPBA, catalyzed by **Ni13** [58].

The chiral oxazoline-based compounds L¹⁴ (Scheme 14) were recently explored as ligands for nickel catalysts in C–H oxidation with *m*-CPBA [59]. This family of ligands has recognized applications in asymmetric catalysis due to the possibility of the introduction of various bulky groups in a chiral manner into their structure. Only one complex of this series was isolated, [Ni(L^{14bc}–H)₂] (**Ni14**) (Figure 16), where the ligand L^{14bc} was converted into the β-diketimate form [59]. The complexes with the other ligands (L^{14a}, L^{14ba–bb} and L^{14bd}) were not isolated and were used for catalysis *in situ*, where the catalyst was formed through the reaction of Ni(OAc)₂ with one equiv. of the respective ligand. Oxidation of cyclohexane (Scheme 4) afforded cyclohexanol as the main product in all cases. The highest activity (TON of 651 and yield of products of 65% relative to *m*-CPBA, which was in deficiency) was observed for the ligand L^{14ba} for the reaction performed under an inert atmosphere. Large amounts of chlorobenzene (31% relative to *m*-CPBA) were detected. The presence of air caused a decrease in the overall TON down to 322 and, at the same time, a decrease in the amounts of chlorobenzene down to 10%. The same behavior was observed for all *in situ*-formed catalysts in this series as well as the isolated compound **Ni14**. Oxidation of methylcyclohexane afforded 3°:2° bond selectivity ranging from 6:1 to 8:1 (the latter ratio was observed for **Ni14**). The use of nickel acetate as a catalyst resulted in 9:1 bond selectivity under the same conditions. Although the observed normalized bond selectivity unequivocally indicates the high activity of the catalytic systems towards the oxidation of tertiary C–H bonds, the authors suggested that the higher absolute amounts of secondary products may be due to the reduced hindrance of the secondary groups as

compared to the tertiary ones [59]. A plausible metal-mediated reaction mechanism similar to that depicted in Scheme 5 was proposed, where the Ni(I) species undergo oxidation with air oxygen. The $\text{ArC(O)O}\bullet$ and $\text{Ar}\bullet$ radicals formed during this reaction (Scheme 1) were presumed to react with an alkane. Very large amounts of chlorobenzene product, comparable to those for alcohols, highlight the high contribution of a free radical pathway to the overall mechanism and free radicals as C–H attacking species. The overall activity and selectivity parameters only weakly depended on the ligand's nature. Therefore, the O- and C-centered radicals formed from *m*-CPBA are likely the C–H attacking species in these catalytic systems. Unfortunately, no test for the presence of alkyl hydroperoxide was performed (nor through the direct detection nor by using the PPh_3 reductant); thus, it is not possible to evaluate the contribution of this compound, which is a typical product in free radical alkane oxidation.

Scheme 14. Schematic representation of the ligand family L¹⁴ [59].

Figure 16. (Left) Schematic representation of the ligand L^{14bc}–H. (Right) Molecular structure (no CSD refcode available for the moment) of the complex $[\text{Ni}^{\text{II}}(\text{L}^{14bc}\text{--H})_2]$ (Ni14) [59]. The hydrogen atoms are omitted. One of the coordinated ligands is shown in bleached form, for clarity. Color scheme: Ni, light green; O, red; N, blue; C, grey.

The presence of the chiral ligands L¹⁴ could lead to asymmetric hydroxylation in the event that the metal complex intermediate is a C–H attacking species. The *in situ*-formed nickel complexes with the ligands L^{14a}, L^{14ba} and L^{14bc} were tested as catalysts for ethylbenzene oxidation (Scheme 15). *R*- and *S*-2-phenylethanols were formed in a nearly 1:1 ratio, which is reflected by the negligible (ca. 1%) enantioenrichment (*ee*) value. The formation of a racemic mixture of products is expected if the H atoms are abstracted by a small organic radical rather than a bulky nickel-oxo or nickel-peroxide complex.

Scheme 15. Oxidation of ethylbenzene with *m*-CPBA, catalyzed by selected complexes of the ligand family L¹⁴. *ee* means enantioenrichment, calculated as $(S - R)/(S + R) \times 100$, where *S* and *R* are concentrations of the respective enantiomers of 1-phenylethanol.

The largest coordination compound of nickel, tested as a catalyst for this type of reaction, is the complex with silsesquioxane ligand [Ni^{II}₆Cl(L^{15a})₂(L^{15b})₂(diox)](Na)(diox)₁₃(H₂O)₂ (**Ni15**) (where (L^{15a})^{6−} = macrocyclic silsesquioxane anion formed *in situ*; L^{15b} = benzonitrile; diox = dioxane) (Figure 17) [60]. The compound features a planar hexanuclear Ni(II) core of the [M₆(μ-X)₁₂] molecular structure type. The complex was studied as a catalyst for the oxidation of alkanes with various oxidants, including *m*-CPBA. Cyclohexane was oxidized at a 24% yield (sum of cyclohexanol and cyclohexanone), supported by a TON of 64 and TOF of 256 h^{−1}. Oxidation of methylcyclohexane gave a mixture of products, with a total yield of 9%. Although the bond selectivity was not reported, the authors noted that the product ratio was different from those observed for TBHP and H₂O₂ oxidants. More importantly, the oxidation of *cis*-1,2-dimethylcyclohexane produced both *cis*- and *trans*-tertiary alcohols, providing strong evidence of the participation of free alkyl radicals within the catalytic cycle.

Figure 17. (Left) Schematic representation of the *in situ*-formed ligand (L^{15a})^{6−}. (Right) Molecular structure (no CSD refcode available for the moment) of the complex [Ni^{II}₆Cl(L^{15a})₂(L^{15b})₂(diox)](Na)(diox)₁₃(H₂O)₂ (**Ni15**). The uncoordinated anions and cations, as well as solvents and hydrogen atoms, are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; Si and C, grey.

As can be seen from Table 1, most of the catalysts **Ni1–Ni15** were proposed to oxidize C–H bonds by nickel-oxo species, mostly Ni^{II}–O• or Ni^{III}=O ones. While the formation of Ni(III) intermediates during oxidation with *m*-CPBA was confirmed by EPR (**Ni5**, **Ni9** and **Ni10**) and EXAFS (**Ni8**) spectroscopies as well as DFT calculations (**Ni4** and **Ni8**), the question of whether these species are in fact those attacking and breaking the C–H

bonds of the substrates remains open. The main concern is that the bond selectivities are roughly the same for catalysts bearing different ligands. Furthermore, most of the catalysts induce homolytic splitting of *m*-CPBA (as evidenced by large amounts of a chlorobenzene product), inevitably generating a series of O- and C-centered radicals. Therefore, there is a possibility that the metal complex catalyst and its high-valence intermediate act merely as activators of the oxidant, *m*-CPBA, generating other species (presumably O-centered radicals), which, in fact, are C–H attacking ones.

A series of nickel complexes with L^{13} and L^{16} ligand families (Scheme 16, Figures 15 and 18) was tested towards the oxidation of cyclohexane and adamantane with *m*-CPBA: $[Ni^{II}(L^{13dc})_2Cl_2]$ (**Ni16**), $[Ni^{II}(L^{13ca})_2Cl_2]$ (**Ni17**), $[Ni^{II}(L^{13a})_3](BPh_4)_2$ (**Ni18**), $[Ni^{II}(L^{13cb})_3](BPh_4)_2$ (**Ni19**), $[Ni^{II}(L^{16a})(CH_3OH)Cl]Cl \cdot CH_3OH$ (**Ni20**), $[Ni^{II}(L^{16b})_2Cl_2]$ (**Ni21**), $[Ni^{II}(L^{13db})_2(OAc)](BPh_4)$ (**Ni22**) [23]. The 3°:2° bond selectivity in the oxidation of adamantane catalyzed by **Ni16**–**Ni22** (and **Ni1** under the same conditions) varied from 33:1 to 44:1 for oxygenated products (alcohols and ketones) and from 14:1 to 19:1 for all products (oxygenated and chlorinated ones). Oxidation of *cis*- and *trans*-1,2-dimethylcyclohexanes proceeded with almost complete epimerization of the stereoconfiguration. The $ArC(O)OO\bullet$ radical, generated from the photosplitting of a benzyl with the subsequent reaction of the $ArCO\bullet$ acyl radical with O_2 , revealed a higher 3°:2° bond selectivity of 35:1 in the oxidation of adamantane. The participation of 3-chlorophenyl radical $Ar\bullet$ as the main attacking species was ruled out since the oxidation of deuterated cyclohexane afforded only small amounts of singly deuterated 3-chlorobenzene. The EPR spectra of a frozen solution of **Ni16** after the addition of five equivalents of *m*-CPBA revealed a broad isotropic line with $g = 2.007$, as expected for an organic radical (while the complex **Ni16** is EPR-silent), which is considerably different from the spectra of Ni(III) species (Figures 6, 11 and 13). The authors concluded that aroyl radical $ArC(O)O\bullet$ is the C–H attacking species in all these catalytic systems, where an alkyl radical formed after H abstraction reacts with *m*-CPBA with the formation of oxygenated products in the course of a chain reaction mechanism, where the role of the catalyst is in the generation of $ArC(O)O\bullet$ radicals only (Scheme 17).

Scheme 16. Schematic representation of the ligand family L^{16} .

An important observation was the complete absence of stereoselectivity when using *cis*-1,2-dimethylcyclohexane as a substrate (Scheme 3) [23]. This effect can be explained by the formation of a long-lived alkyl radical upon H abstraction by the $ArC(O)O\bullet$ radical.

The conclusion regarding the radical chain mechanism, however, contradicts some observations reported in the literature. The self-supporting free radical chain usually requires much higher concentrations of the reagents than reported ($[alkane]_0 = 0.06$ M and $[m\text{-CPBA}]_0 = 0.03$ M); otherwise, the side reactions break the chain [61]. In the present case, such side reactions are the decarboxylation of $ArC(O)O\bullet$ radical and the trapping of an alkyl radical with dioxygen (the reactions involving **Ni14**–**Ni18** were carried out in air). The rate of decarboxylation of $ArC(O)O\bullet$ is expected to be comparable to the rate of hydrogen abstraction from a substrate [14], and the rates of the reaction of alkyl

radicals with molecular oxygen are known to be very high. Large amounts of chlorinated products (up to ca. 50% based on the oxidant) as well as complete epimerization of alkanes' stereoconfiguration are strong evidence of the presence of free alkyl radicals. However, in the case of some catalytic systems, particularly those proceeding in the absence of a halogen-containing solvent (such as the reaction using **Ni8**), the significant retention of the stereoconfiguration of dimethylcyclohexane was observed. Oxidation catalyzed by **Ni8** did not afford chlorobenzene, which appears from the decarboxylation of the $\text{ArC(O)O}\bullet$ radical. Hence, at least for the case of **Ni8**, the C–H attacking species are $\text{Ni}^{\text{III}}\text{--O}\bullet$ high-valence metal oxo radicals, but not $\text{ArC(O)O}\bullet$ ones. Remarkably, the oxidation of adamantane by **Ni8** resulted in $3^\circ:2^\circ$ bond selectivity of 18:1, which completely falls within the region presumed for the $\text{ArC(O)O}\bullet$ radical, if one considers both oxygenated and halogenated products (Table 1). Therefore, the bond selectivity when used alone could not serve as a reliable marker for the discrimination of the type of *m*-CPBA activation mechanism.

Figure 18. Molecular structures of the complexes $[\text{Ni}^{\text{II}}(\text{L}^{13\text{dc}})_2\text{Cl}_2]$ (**Ni16**), $[\text{Ni}^{\text{II}}(\text{L}^{16\text{a}})(\text{CH}_3\text{OH})\text{Cl}]\text{Cl}\cdot\text{CH}_3\text{OH}$ (**Ni20**) and $[\text{Ni}^{\text{II}}(\text{L}^{16\text{b}})_2\text{Cl}_2]$ (**Ni21**) (CSD refcodes XAGJIC, XAGJUO and XAGJOI, respectively) [23]. The uncoordinated solvent molecules, as well as anions and hydrogen atoms, are omitted for clarity. Color scheme: Ni, light green; O, red; N, blue; Cl, green; Br, brown–green; C, grey.

Scheme 17. General reaction pathway of the oxidation of a substrate (RH) with *m*-CPBA catalyzed by nickel complexes, proposed in [23].

In view of the above data, very recently, the catalytic behavior of the complexes **Ni1** and **Ni2** (Figures 1 and 2) was reinvestigated and compared to that of two complexes, $[\text{Ni}^{\text{II}}(\text{H}_2\text{L}^{17\text{a}})(\text{OAc})_2]\cdot\text{CH}_3\text{CN}$ (**Ni23**) and $[\text{Ni}^{\text{II}}(\text{H}_2\text{L}^{17\text{b}})(\text{TMG})]\cdot\text{CH}_3\text{CN}$ (**Ni24**) (where TMG = 1,1,3,3-tetramethylguanidine), bearing similar ligands (Scheme 18 and Figure 19) [62]. Both **Ni23** and **Ni24** catalyzed the oxidation of cyclohexane, with *m*-CPBA producing cyclohexanol and cyclohexanone (as well as trace amounts of ϵ -caprolactone) with 86 and 25% yields, respectively [63]. The reaction rates in the oxidation of cyclohexane (under inert atmosphere) exhibited by the catalysts **Ni1**, **Ni2**, **Ni23** and **Ni24** are different: while the catalyst **Ni24** demonstrates a W_0 of $6 \times 10^{-6} \text{ M s}^{-1}$, the complex **Ni2** was found to be most active, with an almost six-times higher rate W_0 of $32 \times 10^{-6} \text{ M s}^{-1}$ [62]. Noteworthy,

although the product accumulations curves for all series (**Ni1**, **Ni2**, **Ni23** and **Ni24**) are linear in the time span studied (ca. 3–20 min), none of the extrapolated lines pass through the zero point, exhibiting a clear lag period of ca. 2 min. The oxidation of cyclohexane catalyzed by **Ni1** was found to be strongly dependent on the atmosphere: while, under N_2 , the yields of oxygenates and chlorobenzene reached 83 and 34%, respectively, when the same reaction was repeated under O_2 , the yields dropped to 36 and 1% [62]. It should be noted that catalyst-free oxidations with *m*-CPBA are also sensitive to air [14] and, therefore, the presence of O_2 most likely influences the non-catalytic part (e.g., free radical one) of the mechanism. The possibility of the generation of $Ni^{II}-O\bullet$ species from **Ni1** was established from the ESI-MS, Raman and UV/Vis data.

Scheme 18. Schematic representation of the ligand family L^{17} [62,63].

A relatively high value of the kinetic isotope effect (KIE; 6.7) was obtained for the competitive oxidation of normal and deuterated cyclohexanes catalyzed by **Ni1** [62]. This value is considerably higher than those observed earlier for **Ni1** (2.8 and 3.7) and **Ni12** (2.7) [35,56]. A plausible explanation for such a difference is in the methods used to calculate the KIE value: while the most recent value (6.7) is based on the reaction rates, all others were obtained by measuring the amounts of normal and deuterated products after 1 h. The KIE value may vary drastically depending on the time point at which the amounts of products are recorded; thus, measuring the reaction rates is a more accurate method and, therefore, 6.7 appears to be the true KIE value for **Ni1**. The authors concluded that while $ArC(O)O\bullet$ is the most plausible C–H attacking species, the participation of $Ni^{II}-O\bullet$ ones is also possible. One should note here that the values of 3°:2° bond selectivity in the oxidation of adamantane (ca. 13 for **Ni1**; Table 1) are close to those expected for $tBuO\bullet$ and 2-iodobenzoate ($Ar^2C(O)O\bullet$) radicals (Table 1). Moreover, the KIE of 6.7 is close to the values observed for Co/*m*-CPBA catalytic systems (6–8), suggesting that all these values are due to similar C–H attacking species.

Figure 19. Molecular structures of the complexes $[\text{Ni}^{\text{II}}(\text{H}_2\text{L}^{17\text{a}})(\text{OAc})_2] \cdot \text{CH}_3\text{CN}$ (**Ni23**) and $[\text{Ni}^{\text{II}}(\text{H}_2\text{L}^{17\text{b}})(\text{TMG})] \cdot \text{CH}_3\text{CN}$ (**Ni24**) (CSD refcodes UDOLI and UDOLOP, respectively) [62,63]. The uncoordinated solvent molecules are omitted for clarity. Color scheme: Ni, light green; N, blue; O, red; C, grey.

Table 1. Bond selectivity parameters and mechanistic details of the catalysts discussed.

Cat.	Adamantane ^a	MeCyH ^b	Proposed C–H Attacking Species	Proposed O–O Splitting Type	Reaction Media	Ref.
Ni1	13	– ^c	NiO^+	–	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[35]
Ni1	36 ^e / 14 ^f	–	$\text{ArC}(\text{O})\text{O}\bullet$	homo	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[23]
Ni1	13	–	$\text{ArC}(\text{O})\text{O}\bullet/\text{Ni}^{\text{II}}-\text{O}\bullet$	homo	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[62]
Ni2	–	–	$\text{Ni}^{\text{II}}-\text{O}\bullet$	homo	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[27]
Ni3	13–17	–	$\text{Ni}^{\text{II}}-\text{O}\bullet$	homo	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[37]
Ni4	11–12	–	$\text{Ni}^{\text{II}}-\text{O}\bullet$	homo	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[38]
Ni5	–	–	$\text{Ni}^{\text{III}}-\text{O}^-$	homo	CH_2Cl_2	[39]
Ni6	–	5:1	$\text{Ni}^{\text{II}}-\text{O}\bullet/\text{Ni}^{\text{III}}=\text{O}$	homo/concerted	CH_2Cl_2	[42]
Ni7	–	8:2:1	$\text{Ni7}(m\text{-CPBA})$ complex	–	$\text{CF}_3\text{C}_6\text{H}_5$, $\text{CH}_3\text{C}_6\text{H}_5$, or C_6H_6	[48]
Ni8	18	–	$\text{Ni}^{\text{III}}-\text{O}\bullet$	hetero	CH_2Cl_2	[49]
Ni9	–	–	$\text{Ni}(\text{III})$ or $\text{Ni}(\text{IV})$	homo/hetero	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^g	[50]
Ni10	–	–	$\text{Ni}(\text{III})$	homo/hetero	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^g	[51]
Ni11	–	–	–	homo/hetero	$\text{CH}_3\text{C}_6\text{H}_5$, CH_2Cl_2 , CH_3CN , or $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ ^h	[52]
Ni12	19	9:1	–	homo	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[56]
Ni13	–	–	–	–	DCE ⁱ or DCE/TCB ^{j,k}	[58]
Ni14	–	8:1	$\text{Ni}^{\text{II}}-\text{O}\bullet/\text{ArC}(\text{O})\text{O}\bullet/\text{Ar}\bullet$	homo	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^g	[59]
Ni15	–	–	–	–	CH_3CN	[60]
Ni16–Ni22	30–44 ^e / 13–21 ^f	–	$\text{ArC}(\text{O})\text{O}\bullet$	homo	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[23]
Ni23	–	–	$\text{ArC}(\text{O})\text{O}\bullet/\text{Ni}^{\text{II}}-\text{O}\bullet$	homo	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[62,63]
Ni24	–	–	$\text{ArC}(\text{O})\text{O}\bullet/\text{Ni}^{\text{II}}-\text{O}\bullet$	homo	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[62,63]
NiCl_2	35 ^e / 17 ^f	–	–	–	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[23]
$\text{Ni}(\text{OAc})_2$	–	8:1	–	–	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^g	[59]
cat. free ^l	44 ^a	9:1	–	–	$\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ ^d	[23,59]
other cat. ^m	2	6:3:1–26:7:1 ⁿ	$\text{HO}\bullet$	–	CH_3CN	[64,65]
other cat. ^m	10	60:10:1–150:15:1 ⁿ	$^t\text{BuO}\bullet$	–	CH_3CN	[64,66,67]

Table 1. Cont.

Cat.	Adamantane ^a	MeCyH ^b	Proposed C–H Attacking Species	Proposed O–O Splitting Type	Reaction Media	Ref.
cat. free. ^o	>6	–	Ar ² C(O)O● ^p	–	ClC ₆ H ₅	[68]
cat. free ^q	33 ^e	–	PhC(O)OO●	–	DCE	[23]

^a Normalized 3°:2° bond selectivity in adamantane oxidation. The numbers in the column show the prevalence of a tertiary product ($3 \times 3^\circ$ products/2° products); ^b normalized 3°:2° bond selectivity in methylcyclohexane oxidation (3° product/(2° products/10):(1° products/3)). In the cases where the 1° products were not detected (or their amounts were negligible), only the 3°:2° ratio is shown; ^c no data; ^d 3:1 ratio; ^e hydroxylation products only; ^f hydroxylation and halogenation products; ^g 1:1 ratio; ^h 95:5 or 6:9 ratios; ⁱ 1,2-dichloromethane; ^j 1,2,4-trichlorobenzene; ^k 3:1 or 1:1 ratios; ^l oxidation with *m*-CPBA in the absence of a catalyst; ^m the other types of catalysts, generating the respective RO● radicals; ⁿ the range of typical ratios; ^o radical chain reaction initiated by catalytic amounts of benzoyl peroxide at 100 °C; ^p Ar² = 2-iodobenzoate; ^q the radical PhC(O)OO● was generated by the homolytic photosplitting of benzil under O₂ atmosphere.

3. Concluding Remarks

The field of the metal-catalyzed oxidation of organic compounds with *m*-CPBA has attracted great attention due to the possibility of the selective functionalization of organic substrates under mild conditions. Complexes of nickel exhibit notable catalytic activity and, at the same time, form high-valence intermediates with a lifetime that is sufficient for their trapping using conventional spectroscopic methods. The establishment of ligand systems allowing the isolation of a stable Ni/*m*-CPBA adduct is remarkable. However, despite the significant improvements in the field, the details of the *m*-CPBA cleavage mechanism and factors that suppress the undesired free radical activity are still to be established. One of the principal problems is the lack of systematic mechanistic tests that would help in the discrimination between metal-based attacking species and organic radicals formed from *m*-CPBA. We summarize below a few observations that we believe could help to establish the type of *m*-CPBA action mechanism in a certain case.

Although many nickel catalysts demonstrate similar activity and selectivity (Table 1), those bearing planar ligands (e.g., pincer-like Ni8, or porphyrin Ni11) differ by elevated selectivity, supported by lower yields of chlorobenzene, indicating a greater contribution of *m*-CPBA O–O bond heterolysis. This could be associated with the diamagnetic singlet spin state of Ni(II) ions in these complexes or the impossibility of bidentate coordination of *m*-CPBA to a nickel center due to the sterical hindrance of the ligands.

Blank tests in the absence of catalysts are mandatory because *m*-CPBA is known to epoxidize olefines and even oxidize weak C–H bonds [14,69]. Hence, in the event that the catalyst shows low activity, the effect of a catalyst-free background reaction should be always considered. Another suggestion concerns the ¹⁸O-labeling tests: one should always keep in mind the possibility of direct oxygen exchange between H₂¹⁸O and the product(s) and/or oxidant. Ketones are known to rapidly exchange oxygen with water [44–47]; thus, the observation of their large ¹⁸O-enrichment may be misleading. Although alcohols are less prone to such activity, some tertiary alcohols (such as cumyl alcohol or 2,3-dimethyl-2-butanol) could accumulate notable amounts of ¹⁸O directly from H₂¹⁸O. Further, in contrast to H₂O₂, peroxyacids show very complex behavior and, therefore, the possibility of their catalyst-free ¹⁸O-enrichment should not be excluded. Neglecting these factors when performing mechanistic tests using H₂¹⁸O may lead to incorrect conclusions.

The formation of chlorobenzene is direct evidence of the *m*-CPBA O–O bond homolysis and the presence of highly reactive free radicals, primarily ArC(O)O● and Ar● [14]. Therefore, whenever significant amounts of chlorobenzene are observed, the proposal for HVMO intermediates as the principal attacking species should be made only after careful evaluation of the reaction between the substrate and organic radicals. Oxidation of dimethylcyclohexane is a simple and efficient test (Scheme 3) [31,32] that could be performed in this case, where epimerization of the initial stereoconfiguration is expected for hydrogen abstraction by R● species. However, one should keep in mind that even a radical rebound mechanism may lead to some degree of epimerization due to the “radical escape” [70], and some organic radicals, such as ArC(O)OO●, may oxidize substrates with rather high selectivity [14,71]. Finally, one should avoid using high concentrations of a

substrate and *m*-CPBA during mechanistic investigations to prevent the initiation of a radical chain reaction, which eventually may lead to the formation of ArC(O)OO•.

Despite the recognized promoting effect of acidic additives in catalytic oxidations with H₂O₂ [6,72], most of the catalytic investigations where *m*-CPBA is an oxidant still do not use this option. There is evidence that the presence of small amounts of an acidic promoter suppress the free radical reaction in the case of a cobalt catalyst and *m*-CPBA oxidant [33,34,73]. One may expect a similar effect to be exhibited for other kinds of catalysts.

As a final remark, the rapidly growing field of the catalytic oxidation of valuable organic substrates requires the use of abundant first-row metals (such as nickel) as catalysts [74], where polynuclear and heterometallic compounds may be of special interest [6,75]. Many mechanisms of oxidative functionalization with peroxides are still to be explored and further efforts are needed to fulfil the demands of the fine catalysis and chemical industry.

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