Mechanistic studies on the epoxidation of alkenes with molecular oxygen and aldehydes catalysed by transition metal–β-diketonate complexes †

Bastienne B. Wentzel, Patricia A. Gosling, Martin C. Feiters and Roeland J. M. Nolte *

Department of Organic Chemistry/Nijmegen SON Research Center, University of Nijmegen, 6525 ED Nijmegen, The Netherlands

The scope, mechanism and kinetics of the aerobic epoxidation of alkenes with an aldehyde and substituted β-diketonate–transition metal complexes as catalysts were studied. β-Diketonate complexes of nickel(II) proved to be among the best catalysts for this reaction. The epoxidation is not dependent on substrate concentration and is first order in aldehyde, catalyst concentration and oxygen partial pressure. It was shown by reactivity studies and EPR experiments that the reaction is radical in nature. Additional evidence for this was obtained from stereochemical investigations. The metal catalyst is not only an efficient initiator of the reaction, but is also believed to enhance the reactivity of intermediate species in the oxidation process by allowing these to co-ordinate to the metal center. A mechanism is proposed for the catalytic reaction.

Molecular oxygen as a cheap, clean and readily available oxidant has received much attention in recent years.[1] Mukaiyama and co-workers[2–7] and others[8–11] have reported that molecular oxygen can be used as the terminal oxidant in the epoxidation of alkenes with an aldehyde or primary alcohol as coreactant and a metal β-diketonate as a catalyst (Scheme 1). There has been discussion in the literature about the mechanism of the 'Mukaiyama' catalytic system and the role of the transition-metal catalyst in it, which can be omitted as was shown by Kaneda *et al.*[12] Since peroxyacids, which are formed in the autoxidation of aldehydes, are powerful epoxidizing reagents, the reaction in Scheme 1 might proceed through the peroxyacid as the actual epoxidizing agent. The only role of the transition-metal catalyst in this scenario is to catalyse the formation of the peracid as shown in Scheme 2.

Another possible mechanism proposed in the literature[10] is the formation of a metal–oxygen complex which reacts to form an oxometal species, similar to species described for manganese or vanadium.[13,14] In Scheme 3 this mechanism is outlined for a transition-metal(II)–β-diketonate complex.

A combination of the mechanisms in Schemes 2 and 3 was considered by Nam *et al.*[15] They investigated the 'Mukaiyama' system using cyclam-type transition-metal complexes and concluded from indirect evidence that the epoxidation reaction in their system is radical in nature. The peroxyacid and the oxometal mechanisms in Schemes 2 and 3 were believed to play no role. An acylperoxy radical, rather than a peroxyacid, was proposed to react with the alkene to form an epoxide. Alternatively, the acylperoxy radical could co-ordinate to the metal first, and this complex subsequently epoxidizes the alkene. The same authors reported shortly after[16] that cyclam complexes of NiII are inhibitors of this radical reaction. These complexes were believed to be sufficiently good reducing agents to react with an acylperoxy radical and form an unreactive acylperoxy anion and a nickel(III) complex.
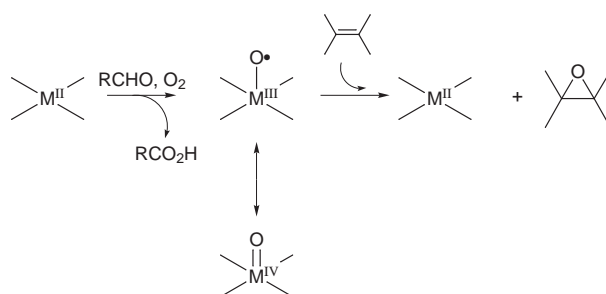
In the present paper we further explore the scope, kinetics and mechanism of the epoxidation of alkenes by the 'Mukaiyama' system. The most effective catalysts for this reaction reported so far, *viz.* second-row transition-metal complexes of
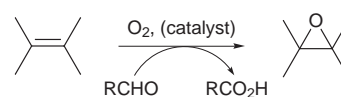
Scheme 1
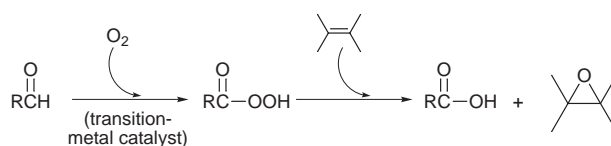
Scheme 2 Peracid epoxidation mechanism

Scheme 3 Oxo–metal epoxidation mechanism

β-diketonates, are used. In spite of the extensive discussions in the literature the role of the metal complex is still not entirely clear. This issue will be addressed as well.

Experimental

Materials

Dichloromethane was dried over CaCl₂, distilled from CaH under dry nitrogen and stored over molecular sieves. Acetonitrile was HPLC grade. All other solvents and isobutyraldehyde were distilled before use. Oxygen was obtained from Hoek-Loos and dried over calcium chloride. All alkene substrates were commercial samples (Aldrich) and were purified by column chromatography over basic alumina with CH₂Cl₂ as eluent or by vacuum distillation. An exception is *S*-limonene [1-methyl-4-(1-methylethenyl)cyclohexene] (Aldrich, 96%) which was used as received. Epoxide products were identified

with gas chromatography. The metal complexes were commercial products or were synthesized according to literature procedures.[17,18] Their physical properties were consistent with their structures and with literature values.[17,18]

Instrumentation

The GC analyses were performed on a Varian 3700 instrument with a fused-silica capillary column (25 m length, 25 μm diameter) with a CP-sil stationary phase or a 15 m × 35 μm diameter column with an FFAP stationary phase. The instrument was equipped with a flame-ionization detector and coupled to a Hewlett-Packard 3395 integrator. The UV/VIS spectra were taken on a Perkin-Elmer Lambda 5 spectrometer, IR spectra on a Bio-Rad FTS-25 spectrometer, low-temperature EPR spectra on a Bruker Electron Spin Resonance ER-220D-LR spectrometer and room-temperature spectra on a Bruker ESP-300 instrument. The NMR analyses were performed on a Bruker AC-300 or WH-90 instrument; the solvent was CDCl$_3$.

The catalytic system

The standard conditions used in the epoxidation of alkenes by nickel(II)–β-diketonate complexes in the presence of an aldehyde were as follows. 0.1 mol l^{-1} Alkene, 0.3 mol l^{-1} aldehyde and 1 mmol l^{-1} catalyst were stirred (1000 revolutions min^{-1}) in CH$_2$Cl$_2$ at 25.0 ± 0.5 °C under 1.0 atm of oxygen. Unless indicated otherwise, kinetic experiments were carried out with α-pinene as the alkene substrate, isobutyraldehyde as the coreagent and bis[3-(p-tert-butylbenzyl)pentane-2,4-dionato]-nickel(II) **1c** as the catalyst. Errors were estimated to be less than 5%. The catalytic reaction was followed by monitoring the disappearance of the substrate and the appearance of product(s) as a function of time with gas chromatography; the internal standard was dmf (100.0 μl). Adding dmf in small quantities did not affect the reaction.

Determination of CO$_2$ evolved from the epoxidation reaction[19]

A standard reaction mixture (see above) was prepared with [Ni(acac)$_2$] **1a** as the catalyst and S-limonene as the substrate. The exhaust gas of the reaction was bubbled though a BaCl$_2$ solution [in 4 mol l^{-1} NaCl (aq)–ethanol–glycol (1.5:2:1 v/v/v) at pH 11], and the CO$_2$ formed precipitated as BaCO$_3$. The turbidity of regularly taken samples from the barium solution was measured with UV spectroscopy at 360 nm, and the amount of CO$_2$ that had evolved was calculated from a calibration curve.

Results

Scope of the epoxidation reaction

A number of substrates were tested in the epoxidation reaction using the 'Mukaiyama' conditions and compound **1c** (M^{II} = Ni^{II}) as the catalyst. The results are collected in Table 1. Substituted alkenes, especially α-pinene, limonene and norbornene (bicyclo[2.2.1]hept-2-ene) gave very good yields as was expected based on other studies (see for example Yamada et al.[4] and Fdil et al.[11]). Also styrene is a very good substrate for this epoxidation reaction. Doubly substituted and electron-rich alkenes such as cis-stilbene, cyclohexene, β-pinene, trans-β-methylstyrene and camphene gave poorer but still respectable yields of epoxides between 23 (β-pinene) and 61% (camphene).

We also tested a variety of other metal complexes and metal salts in the epoxidation of α-pinene and S-limonene (see SUP 57387). In agreement with literature studies, nickel and cobalt complexes gave the highest epoxide yields (e.g. Fdil et al.[11]). It is noteworthy in this respect that Nam et al.[15,16] found nickel cyclam-type complexes to be inactive in their epoxidation reactions. These complexes were shown to reduce the generated acyl peroxy radical to the peroxy anion which is inactive as an oxidant.

**Table 1** Epoxidation of alkene substrates *

Substrate	Conversion (%)	Yield epoxide (%)
α-Pinene	93	86
β-Pinene	27	23
S-Limonene	77	72
Norbornene	100	96
Styrene	98	79
trans-β-Methylstyrene	51	47
Camphene	68	61
Allylbenzene	16	12
cis-Stilbene	41	36
trans-Stilbene	6	5
Cyclohexene	49	45
Oct-1-ene	23	19

* Reaction conditions: 0.1 mol l^{-1} alkene, 0.3 mol l^{-1} isobutyraldehyde, 1.0×10^{-3} mol l^{-1} catalyst **1c**, 5.0 cm^3 CH$_2$Cl$_2$, 1.0 atm O$_2$, 25 °C, 4 h.

Table 2 Epoxidation of α-pinene catalysed by substituted nickel(II)–β-diketonate complexes[a]

Entry	Complex 1	Turnover number[b]
1	a	15
2	b	c
3	c	21
4	d	11
5	e	32
6	f	39
7	g	24
8	h	8
9	i	1

[a] Reaction conditions as in Table 1. [b] Estimated error: 5%. [c] 74% Yield in 4 h.
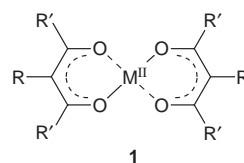
a R = H, R′ = CH$_3$
b R = H, R′ = p-methoxyphenyl
c R = p-tert-butylbenzyl, R′ = CH$_3$
d R = benzyl, R′ = CH$_3$
e R = p-methoxybenzyl, R′ = CH$_3$
f R = p-nitrobenzyl, R′ = CH$_3$
g R = p-fluorobenzyl, R′ = CH$_3$
h R = ethyl, R′ = CH$_3$
i R = H, R′ = CF$_3$

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Electronic and steric effects

In order to study electronic effects a new series of 3-substituted nickel(II)–β-diketonate complexes (**1a**–**1h**) was synthesized and tested as epoxidation catalysts. The results for the epoxidation of α-pinene are shown in Table 2. As can be seen in Table 2 there is a small but significant effect on the turnover rate of α-pinene by the catalyst when the para position of the benzene ring of the nickel complex is altered. Substitution of the benzene ring with an electron-withdrawing nitro group (entry 6) yields a catalyst with a relatively high turnover number (39) when compared to 11 turnovers found for the catalyst unsubstituted at the aromatic ring (entry 4). Remarkably, the catalyst substituted with an electron-rich methoxybenzyl group (entry 5) gives a high turnover number as well (32). Apparently, electronic effects do not play a major role in the reaction catalysed by the nickel(II) complexes **1**.

Aldehyde reactivity

The reactivity of a variety of aldehydes as coreactants in Scheme 1 was tested under standard conditions (see SUP 57387). Straight-chained and branched aldehydes such as pivaldehyde (68% α-pinene epoxide after 4 h) and isobutyraldehyde (91% epoxide) were the most active coreactants. Aromatic or conjugated aldehydes such as benzaldehyde and cinnamaldehyde were completely inactive under the reaction conditions. Investigations into a heterogeneous epoxidation system by Laszlo and
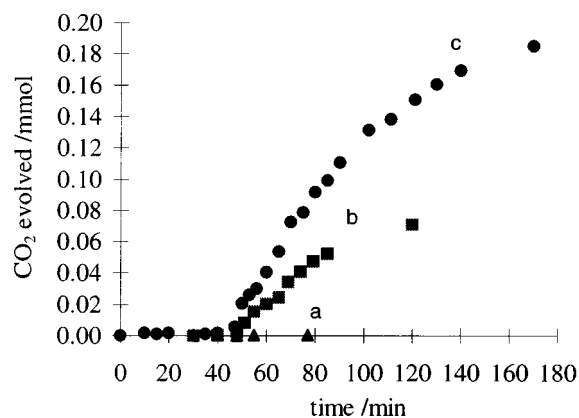
Fig. 1 Generation of CO_2 in the epoxidation of *S*-limonene. Reaction conditions: (a) 0.01 mmol [Ni(acac)$_2$] in CH_2Cl_2 (5 cm³); (b) 0.01 mmol [Ni(acac)$_2$] and 3 mmol isobutyraldehyde in CH_2Cl_2 (5 cm³); (c) 1 mmol *S*-limonene, 3 mmol isobutyraldehyde, 0.01 mmol [Ni(acac)$_2$], CH_2Cl_2 (5 cm³), 1 atm O_2, 25 °C

Levart,[20] using kaolinite and an aldehyde in the presence of O_2, yielded similar aldehyde reactivities.

If the acylperoxy radical is the active oxidizing agent, this radical might yield a carboxyl radical after epoxidation. The latter radical can decompose into CO_2 and an alkyl radical. As Lassila *et al*.[21] have suggested, epoxidation and decomposition may occur in a concerted process. A relatively stable alkyl radical is formed in the case of isobutyraldehyde and pivaldehyde, whereas the alkyl or aryl radicals generated from the other aldehydes will be less stable. This decomposition could create a driving force for the epoxidation reaction.

If decomposition of the carboxyl radical into carbon dioxide and an alkyl radical plays a major role in the reaction, it should be possible to detect this by measuring the amount of CO_2 evolving from the reaction; CO_2 was determined as described in the Experimental section. The results are shown in Fig. 1. After 3 h 67% of the aldehyde had reacted and only 10% had evolved as CO_2. Isopropyl hydroperoxide might be anticipated as an oxidation product of isobutyraldehyde.[21] Decomposition of this hydroperoxide would yield acetone or isopropyl alcohol, neither of which was detected by GC. Finally, only a part of the converted aldehyde was retrieved as isobutyric acid (approximately 10% by GC), indicating a difference in reaction mechanism of the present catalytic system and the systems reported by, for example, Mizuno *et al*.,[22] Yanai *et al*.[10] (the 'Mukaiyama' system) and Nam *et al*.[15] (see also Discussion).

Stereochemistry

In order to obtain information about the stereochemistry of the reaction we studied the epoxidation of *cis*-stilbene with various nickel(II) complexes and several oxidants. The results are shown in Table 3. From a comparison of the products obtained with *m*-chloroperbenzoic acid (entry 4) with the products obtained with the nickel(II) catalysts (other entries) it can be concluded that a free peroxyacid cannot be the main oxidizing species in our system; in that case the stereochemistry of the epoxide would have been retained, which is not observed. In the presence of a small quantity of pyridine the *cis*:*trans* ratio was shifted from 1:13 (entry 1) to 1:45 (entry 2), indicating that, although the main pathway for epoxidation is not concerted, a small fraction of the products are formed *via* a concerted pathway, which is inhibited by the presence of a co-ordinating ligand such as pyridine. We found that it is not possible to induce chirality in the epoxidation products by using chiral nickel(II)–β-diketonate complexes such as camphor {(1*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one} and carvone [2-methyl-5-(1-methylethenyl)-2-cyclohexen-1-one] derived complexes synthesized by Fdil *et al*.,[11] in agreement with their results.

Table 3 Stereoselectivity of the epoxidation of *cis*-stilbene with different oxidants and nickel complexes[a]

Entry	Catalyst	Conversion (%)	Epoxide (%)	*cis*:*trans* ratio
1	Complex **1c**	40	36	1:13
2	Complex **1c** and pyridine	47	46	1:45
3	Complex **1c** and *m*-ClC$_6$H$_4$CO$_3$H[b]	63	65	3:1
4	*m*-ClC$_6$H$_4$CO$_3$H[c]	60	60	100% *cis*
5	[Ni(salophen)][d]	70	53	1:10
6	[Ni(tpp)][e]	80	68	1:12
7	[Ni(O$_2$CMe)$_2$]	71	69	1:22

[a] Reaction conditions as in Table 1. [b] 0.1 mol l⁻¹ *m*-ClC$_6$H$_4$CO$_3$H under N$_2$. [c] 0.1 mol l⁻¹ *m*-ClC$_6$H$_4$CO$_3$H, no catalyst. [d] H$_2$ salophen = *N*,*N*′-Bis(salicylidene)-*o*-phenylenediamine. [e] H$_2$tpp = 5,10,15,20-Tetraphenylporphyrin.
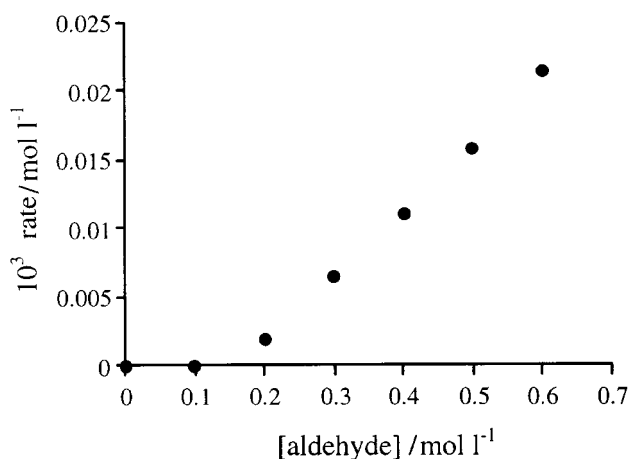

Fig. 2 Effect of aldehyde concentration on the initial epoxidation rate under standard conditions

Kinetics

The order in substrate concentration was determined for α-pinene in dichloromethane at 25 °C using complex **1c** as the catalyst and isobutyraldehyde as the coreactant. For aldehyde:alkene ratios >2:1 the order was zero. Below this ratio the reaction was first order.

The order in aldehyde concentration was calculated from the initial epoxidation rates measured at various aldehyde concentrations (0 to 0.6 mol l⁻¹ isobutyraldehyde) and the results are shown in Fig. 2. When the concentration of aldehyde was under 2.0 mol equivalents with respect to the substrate alkene little epoxide was formed. When it was equal to or greater than this a first-order dependence on the aldehyde was found. These results were observed regardless of the concentrations of the reactants. Therefore, it appears that the aldehyde must be present in the reaction mixture at a concentration of approximately twice that of the substrate for epoxidation to occur. The origin of this effect is not yet clear. The mechanism outlined in Scheme 4 does not, for instance, explain the need for *ca*. 2 equivalents of aldehyde in the reaction. A tentative explanation might be the following. For epoxidation to occur the alkene must be close to the active epoxidizing species, which we propose to be the acylperoxy metal complex. It is conceivable that the alkene first co-ordinates to the nickel center. In that case its position will be *trans* to that of the co-ordinated peroxy radical. When enough acid has been formed from the aldehyde one of the acetylacetonate ligands of the acylperoxy–nickel–alkene complex can dissociate allowing the alkene to move *cis* to the active oxidizing species. This displacement will not be possible when not enough acid formed by autoxidation of the aldehyde is present, and thus will not take place at low aldehyde concentrations. For a
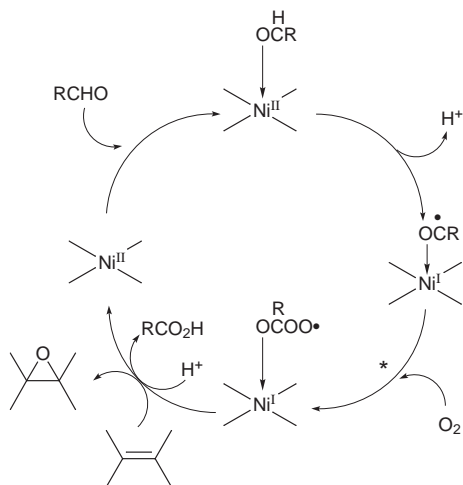
Scheme 4 Proposed mechanism for the epoxidation of alkenes with O$_2$ and an aldehyde, catalysed by nickel(II)–β-diketonate complexes; * = rate-determining step

Fig. 3 Influence of the catalyst concentration on the epoxidation rate under standard conditions

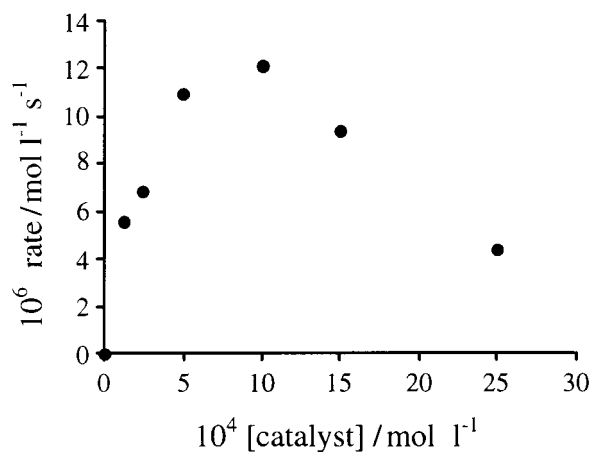related situation involving the dissociation of an acetylacetonate ligand from [Ni(acac)$_2$] see ref. 23.

The UV/VIS experiments revealed that isobutyraldehyde binds to the nickel center of complex **1c** as could be concluded from the change from pink to green and the disappearance of the broad band at 520 nm in the spectrum of **1c**. From a UV/VIS titration experiment the binding constant of the 1:1 **1c**–isobutyraldehyde complex was calculated to be $K_b = 0.68 \pm 0.08$ l mol^{-1}. The epoxide reaction could be inhibited by adding competing Lewis bases to the reaction mixture. Reactions carried out in the presence of pyridine (a strong Lewis base relative to isobutyraldehyde) slowed the reaction and changed the order in substrate concentration from one to zero if the aldehyde:alkene ratio was 2:1. This suggests that coordination of the aldehyde to the nickel complex is an important step in the reaction sequence.

The concentration of the catalyst was varied and the effect on the initial rate was determined, as shown in Fig. 3. The rate increases linearly with the concentration of catalyst up until a concentration of 5.0×10^{-4} mol l^{-1}. At higher than 10.0×10^{-4} mol l^{-1} (which is 1 mol% with respect to the alkene concentration) the rate decreased dramatically. Since this catalyst (**1c**) can only exist in the monomeric form under the reaction conditions used,[24] aggregation of the nickel complex into a trimer (as in the case of **1a**) is not a factor in the decrease in activity. It is possible that an increased amount of nickel catalyst acts as a radical trapping compound (see for example Nam *et al.*[16]), which would inhibit the reaction by preventing the formation of the nickel–peroxo radical species or converting it into a non-radical peroxy anion.

The epoxidation reaction was investigated at two different oxygen pressures, *viz.* 0.21 and 1.0 atm. No effect on the selectivity for epoxide was found. At both oxygen concentrations the reaction followed zero-order kinetics in substrate concentration with rate constants $k_0 = 1.73 \times 10^{-5}$ and 6.32×10^{-5} mol l^{-1} s^{-1}, respectively. Without O$_2$ the reaction did not proceed. Based on these data it can be concluded that the reaction is approximately first order in oxygen concentration. The epoxidation of α-pinene was carried out at various temperatures between 18 and 32 °C and found to follow Arrhenius behavior, with an activation energy $E_a = 48 \pm 6$ kJ mol^{-1}. Using the Eyring relationship the parameters $\Delta H^\ddagger$ and $\Delta S^\ddagger$ were calculated to be 46 ± 6 kJ mol^{-1} and -116 ± 6 J K^{-1} mol^{-1}, respectively. The large negative value of $\Delta S^\ddagger$ points to a rigid transition state for the rate-determining step.

Probes for a radical reaction mechanism

When a radical trapping compound such as 2-*tert*-butyl-4-methylphenol was added to the reaction mixture during the reaction epoxidation stopped immediately. When it was added at the beginning no epoxide was formed. These results indicate that the formation of a radical species in the reaction mixture is crucial for epoxidation to occur. Furthermore, in the presence of a radical inhibitor, no conversion of the substrate into other oxidation products was observed.

When cyclobutanol was used as the substrate in a reaction with complex **1c** as catalyst and isobutyraldehyde as reductant only 4-hydroxybutyraldehyde was produced, indicating an oxidizing species of a radical nature as opposed to a two-electron oxidant.[25]

Kaneda *et al.*[12] have found conditions (using temperatures slightly above ambient) under which a metal catalyst is not necessary in the epoxidation of alkenes with O$_2$ and aldehyde. Initiation in the absence of metal complex can only take place by light. We investigated these conditions and found that the observations of Kaneda were not valid for our reactions. The epoxidation under standard conditions (see Experimental section) did not proceed without a catalyst, even at higher temperatures (80 °C). In neat (freshly distilled) isobutyraldehyde the reaction did proceed but slower than with nickel catalyst present. For comparison reactions with conventional initiators were also performed. The exceptionally reactive radical initiator di-*tert*-butyl peroxalate[26] was tested in the epoxidation of *S*-limonene without catalyst under otherwise standard conditions.‡ The reaction proceeded much more slowly than with **1a** as the catalyst. The product distribution was identical, *i.e.* the *cis*:*trans* ratio of the epoxide was in both cases 2:3. The selectivity for epoxide was, however, much lower: 67% as opposed to 93% when **1a** was used. The epoxidation reaction did not proceed when either an initiator or a catalyst was present, although it was determined by iodide–thiosulfate titration[27] that the aldehyde used contained a small amount of peroxide (*ca.* 0.5%).

EPR studies using a spin trap

Electron spin spectroscopy using 'spin traps' can provide evidence for the presence of radicals in a reaction. We investigated the epoxidation of different alkenes by the nickel complexes **1a** and **1c** with the radical trap 5,5-dimethyl-1-pyrroline *N*-oxide **2**.[28]

‡ Di-*tert*-butyl peroxalate was synthesized according to a literature procedure.[26] For use in the epoxidation reaction a 16.4 mmol l^{-1} solution in CH$_2$Cl$_2$ was prepared, and 5 cm^3 of it was used as the solvent for the reaction. The amount of peroxide present was checked by iodide–thiosulfate titration.[27] Thus, in the reaction mixture 1.5% of peroxide with respect to the alkene was present.

Table 4 The EPR hyperfine splitting constants from spin-trap experiments with complexes **1a** and **1c** and compound **2** in CH_2Cl_2 at 25 °C

Entry	Sample	Isobutyraldehyde	O_2 present	a_N/G	a_{H_β}/G	a_{H_γ}/G
1	No substrate[a]	Yes	Yes	12.7	9.8	
2		Yes	No	13.35 ± 0.17	7.37 ± 0.12	0.3
3	α-Pinene[a]	Yes	Yes	13.3	8.7	
4		No	Yes	13.1	8.4	1.5
5	Stilbene[a]	No	Yes	No signal		
6	S-Limonene[b]	Yes	Yes	12.69 ± 0.35	8.03 ± 0.37	
7		Yes	No	13.30 ± 0.20	7.16 ± 0.12	0.3 ± 0.1
8		No	Yes	No signal		

[a] Catalyst **1c**. [b] Catalyst **1a**.
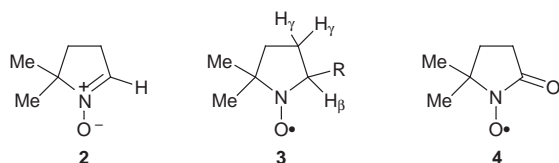
A solution containing compound **2** and complex **1a** (M^{II} = Ni^{II}) in dichloromethane was prepared. This did not give any signal (other than that of the cavity). To it were added the components of the reaction, *viz.* isobutyraldehyde and/or alkene substrate, so that the concentrations were identical to those of the standard reaction mixture (see Experimental section). No signal or only very broad signals were observed in a glass at 15 K. At 298 K signals were found when at least **2**, Ni^{II} and aldehyde or alkene were present. No signals were observed without **2**, strongly suggesting the presence of spin adducts **3** in the EPR-active samples. The nitrogen and hydrogen hyperfine splittings a_N and a_H observed for these samples are summarized in Table 4. Comparison of the a_N and a_H values with those reported in the literature[28] with benzene as the solvent allows a tentative identification of some of the spin adducts and therefore of the radicals trapped. Keeping the difference in solvent in mind, the resemblance of the set of hyperfine splittings of the signals in entry 1 to those reported for a benzoyloxy radical adduct with **2** in benzene (a_N and a_{H_β} of approximately 12.24 and 9.63 G, respectively) points to the trapping of an acyloxy radical[28] in our case.

Our trapping experiment cannot distinguish between an adduct derived from an acyloxy and an alkoxy radical. Alkoxy radicals are reported to have an a_N value of 13–13.5 G and an a_{H_α} value of 7–8 G.[28] The observed splitting parameters in entries 2, 3, 6 and 7 are very similar to these values, even without any O_2 present (entries 2 and 7), indicating the trapping of a radical derived from aldehyde, as an O- rather than a C-centered radical.

The hyperfine splitting constants of the EPR signals of the radical adducts in entries 1, 3, 4 and 6 are sufficiently different from each other to exclude the possibility that the same radical, derived, for example, from the acetylacetonate ligand, is trapped in these cases. The radical in entry 1 is likely to come from the isobutyraldehyde, *i.e.* it is probably the trapped acyl radical or, more likely, the trapped acylperoxy radical. The signals in entries 3, 4 and 6 might result from the alkene.

In the hematin/cumene hydroperoxide system reported previously[29] no radicals were trapped; all the EPR signals observed were due only to oxidation of the spin trap, resulting in 5,5-dimethylpyrrolidin-2-one N-oxyl, **4**.[30] The possibility that this compound was formed in our system could be ruled out, as the a_N and a_H values reported for this radical in solvents related in polarity to dichloromethane are different from those observed by us (benzene, a_N = 6.45 and a_H = 3.28; chloroform, a_N = 6.58 and a_H = 3.60 G[30]). It should be mentioned here that it was recently shown[31] that **4** is always formed when oxometal complexes are present as intermediate species, *e.g.* in the case of Mn. The absence of **4** in our experiments provides additional evidence against an oxometal epoxidation mechanism as shown in Scheme 3.

Discussion

From our results, and from those in the literature, we may conclude that the [Ni(acac)₂]–isobutyraldehyde–alkene system is a very useful catalytic system for the epoxidation of alkenes. The mechanism of the epoxidation reaction seems to be different from that of other epoxidations, such as peroxide-initiated reactions or reactions catalysed by other transition-metal complexes (*e.g.* salen or cyclam-type complexes).

First, an oxometal mechanism (Scheme 3) can probably be ruled out. No spectroscopic evidence was found for oxometal complexes in our reactions, and β-diketonate complexes do not form oxo-complexes easily. There is no evidence that Ni^{II}, when co-ordinated by oxygen ligands, is capable of directly binding molecular oxygen and forming an oxonickel species, based on the extensive studies carried out in this area.[14,32] In addition, as reported by Nam *et al.*,[15] the epoxidation reaction can proceed when it is initiated with a perester giving the same product distributions as the nickel(II)-catalysed reaction. If an oxometal species were to play an important role in the epoxidation reaction the perester-initiated reaction would most probably yield a different product distribution. Finally, no **4** was detected by EPR spectroscopy which can be taken as additional evidence that no oxometal complexes were generated in solution.

A second possibility is a mechanism in which peracid is formed *in situ*, which then oxidizes the alkene, as shown in Scheme 2. However, this would be at variance with the reactivity of the aldehydes as observed in our investigations as well as in those of Mukaiyama and co-workers.[2–7] Benzaldehyde, which has been reported to be easily converted into its corresponding peroxyacid in the presence of a number of transition metals,[33–37] is unreactive under the reaction conditions described here. Examination of the stereochemistry of the products (see Table 3) provides even stronger evidence discounting an *in situ* formed peroxyacid as the active epoxidizing agent. Peroxyacids normally carry out the epoxidation of alkenes by a concerted oxygen-transfer step,[33,34,38] so that the stereochemistry of the substrate is conserved in the product. We found that with *cis*-stilbene the opposite occurs: *trans*-stilbene oxide is formed almost exclusively. Thus peroxyacid epoxidation is not a major oxidation pathway in the system we studied, though it might very well be in the system Kaneda *et al.*[12] investigated. Their results regarding the stereochemistry and kinetics of the reaction are reminiscent of an autoxidation process.

The combined results of our kinetic and mechanistic studies lead us to conclude that the epoxidation reaction is radical in nature with the formation of a nickel-bound acyl radical as the first step and the formation of a nickel–acylperoxy intermediate, which might be cyclic for stability reasons, as the second important step. When compared to the literature (Nam *et al.*[15]), the most compelling, new evidence for a radical nature of the reaction intermediates was found with EPR spectroscopy. Our investigations pointed to the presence of two radical species. One is formed when the catalyst and isobutyraldehyde are present but oxygen is absent. We propose that this is the trapped acyl radical bound to the nickel center of the catalyst. The second radical species is observed when oxygen is added to the

reaction mixture; this may be the nickel–acylperoxy radical. Both radicals were trapped with **2** as oxygen-centered radicals.

Based on the data presented in the Results section the rate equation (1) holds, provided that the molar ratio of aldehyde to substrate is greater than 2:1. Here, k_{obs} is the observed rate

$$r = k_{obs}[O_2][Sub]^0[RCHO][Cat] \quad (1)$$

constant, [Sub] the concentration of alkene substrate, [RCHO] the concentration of isobutyraldehyde and [Cat] the concentration of nickel(II) complex. The reaction is first order in substrate concentration when the ratio of aldehyde to substrate is equal to or less than 2:1, changing to zero order when a Lewis base (pyridine) is added.

The overall rate law that usually applies to the autoxidation of aldehydes is given by equation (2),[39,40] provided that the

$$r = k \left(\frac{k_i}{2k_t}\right)^{\frac{1}{2}} [In]^{\frac{1}{2}}[RCHO] \quad (2)$$

oxygen and aldehyde concentrations are sufficiently high. Here k is the rate constant of the rate-limiting propagation reaction, k_i that of the initiation reaction, k_t that of the termination reaction and [In] is the initiator concentration. The rate-limiting step is hydrogen abstraction from the aldehyde. We assume that our epoxidation reaction (Scheme 1) is sufficiently fast as not to interfere with the autoxidation reaction. Our results do not conform to the rate law (2), because the order in catalyst concentration (assuming that its only role is initiating the reaction) is 1 instead of $\frac{1}{2}$. The rate law (2) depends on the type of termination step that is operative which may explain the dependence on oxygen pressure[40] of our reaction. The role of our metal catalyst is likely to be more than just an initiator of the reaction. If a radical chain mechanism, initiated by the nickel(II) complex, takes place an order of $\frac{1}{2}$ is expected, according to equation (3) where [Ni(acac)$_2$] is taken as an example.

$$[Ni^{II}(acac)_2] \longrightarrow [Ni^I(acac)] + acac^\bullet \quad (3)$$
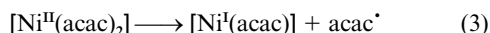
The mechanism we propose for the epoxidation of substituted alkenes with molecular oxygen and isobutyraldehyde, catalysed by nickel(II)–β-diketonate complexes, is a catalytic cycle in which the active oxidizing species is an acylperoxy radical which stays bound to the metal complex for stabilization (Scheme 4). Based on the observed rate equation, we may tentatively conclude that the rate-limiting step is the formation of the nickel acylperoxy species, formally a nickel(I) species (see Scheme 4). The products evolving from the aldehyde are small amounts of carboxylic acid and CO_2 (both *ca.* 10% with respect to converted aldehyde). Other aldehyde oxidation products could not be identified. It should be noted that Scheme 4 probably is a simplified picture of the actual process. Studies further to unravel the details of the reaction are currently in progress. The role of the metal complex is to promote both hydrogen abstraction from the aldehyde and acceleration of the oxidation reaction. The nickel(II) complex is proposed to take up an electron from the co-ordinated aldehyde which then loses a proton. Alternatively, one could imagine the formation of a nickel(III) hydride complex. These possibilities are currently under investigation.

Conclusion

We have proposed further details of the mechanism for the epoxidation of alkenes with molecular complex and an aldehyde, catalysed by β-diketonate complexes of Ni^{II}. It is shown that the mechanism is radical in nature, with the metal complex acting as an initiator of the reaction and a promoter of the oxidation. Our mechanism is in this respect different from that of Mukaiyama and others. The catalytic system is very useful to prepare a variety of multiply substituted epoxides from alkenes

under mild conditions. It is not yet clear what the fate of the aldehyde is, since neither large amounts of carboxylic acid nor of CO_2 could be detected. The proposed mechanism is consistent with the kinetic and EPR data and with the observed stereochemistry of the reaction.

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