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Catalytic Epoxidation of Unfunctionalized Alkenes by Dinuclear Nickel(II) Complexes[1]

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Abstract: The synthesis, crystal and molecular structure and catalytic activity in epoxidation reactions of new dinuclear nickel(II)-complexes, octahedral μ-diacetato-μ-[2,6-bis[*N*-2-(2'-pyridylethyl) formimidoyl]phenolato]bisnickel(II)·perchlorate·methanol (**6**) and square planar (μ-hydroxo-μ-[2,6-bis[*N*-((*S*)-1-benzyl-2-yl-pyrrolidine)formimidoyl]phenolato]bisnickel(II)·bisperchlorate (**7**), are described. For the preparation of **7** a new 5-step route for homochiral bisamine (*S*)-benzyl-2-aminomethyl-pyrrolidine (**19**) was developed starting from (*S*)-proline. Epoxidation of unfunctionalized alkenes with sodium hypochlorite and *tert*-butyl hydroperoxide as terminal oxidants was effectively catalyzed with bisnickel(II)-complexes **6** and **7**, and a turnover of 165 was reached using *trans*-β-methylstyrene (**34**). The epoxidations probably proceed *via* a radical intermediate (such as OCl·) and no enantioselectivity is obtained under phase transfer conditions. In epoxidation reactions employing *tert*-butyl hydroperoxide as terminal oxidant a turnover of 43 was obtained with *trans*-stilbene (**30**) as substrate. Unexpectedly in the case of styrene (**29**) 1,2-bis-(*tert*-butylperoxy)ethylbenzene (**59**) was isolated as the major product.

INTRODUCTION

Single oxygen transfer is an essential transformation in nature and results from the catalytic activity of various metal containing enzymes, such as the iron containing Cytochrome P-450, methane monooxygenase,[2] or the copper containing monooxygenase tyrosinase.[3] The development of models for these enzymes and the design of new catalysts to achieve selective oxygenation, are important goals in synthetic chemistry. Particularly challenging problems are the stereoselective epoxidation of unfunctionalized alkenes and the hydroxylation of alkanes.[4] Mononuclear, as well as dinuclear metal centres are commonly found in the active site of various oxygenases[5] and information on key structural features and factors governing the oxygenase activity is rapidly growing.[6] We have reported the use of dinuclear copper complexes in phenol oxidation, oxidative demethylation, arene hydroxylation and catalytic dehydrogenation in an approach to achieve bimetallic - oxygenase type - catalysis.[7]

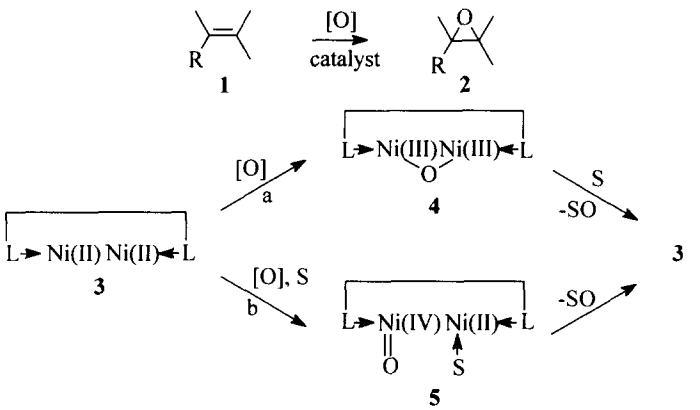
A number of highly successful catalytic epoxidations have been developed, based on mononuclear metal complexes[8] mimicking heme and non-heme oxygenases, giving excellent enantioselectivities.[5,9] A major breakthrough in this respect was the discovery by Jacobsen and co-workers of the enantioselective epoxidation of unfunctionalized alkenes by chiral manganese salen catalysts.[10] The application of dinuclear metal catalysts in stereoselective epoxidations has had only limited attention[7,11,12] despite the fact that the activity of enzymes capable of oxygen atom transfer is often due to cooperation between two metal centres.

Several nickel complexes show promising catalytic activity in oxidation reactions. Catalytic alkene

epoxidations employing mononuclear nickel complexes have been developed by Koola and Kochi,[13] Burrows and co-workers[14] and several other groups.[15] Terminal oxidants used in these oxidations are iodosylbenzene,[13,14e] sodium hypochlorite[14b,c,15b] or molecular oxygen in combination with aldehydes.[12,15a] Iodosylbenzene appears to be more appropriate for alkyl substituted alkenes whereas sodium hypochlorite is better suited for aryl substituted alkenes.[12-15] We focused on dinuclear nickel complexes as new epoxidation catalysts,[7] realizing that well defined dinuclear nickel centres with bridging μ-hydroxo, μ-aryloxo or μ-acetato units can be formed.[16]

Metal mediated oxidations using oxygen donors such as hypochlorite, hydrogen peroxide, alkyl hydroperoxides or iodosylbenzene are expected to proceed *via* a "shunt" or "rebound"[13,14,17] mechanism, in which the terminal oxidant transfers an oxygen atom to the metal centre and the resulting metal-oxo species oxidizes the substrate. Binding of the oxygen atom to the nickel centre can occur in various ways; postulated structures include a nickel(IV)-oxo-complex, a nickel(III)-hypochlorite-complex and a μ-oxo-bis(nickel(III))-complex,[13,18] possibly formed from a nickel(IV)-oxo and a nickel(II) species.

If a bimetallic catalyst is used, both nickel centres could be involved in a intramolecular fashion if incorporated in the complex at a predefined distance to facilitate, for instance, μ-oxo-binding as shown in **4** (scheme 1; route a).

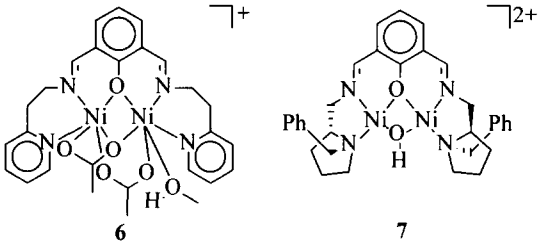


Scheme 1. Bimetallic shunt or rebound mechanism in catalytic epoxidation. (S = substrate, [O] = single oxygen donor).

In the case where the formation of the μ-oxo-intermediate or the oxygen transfer from a μ-oxo-species is the rate determining step, increase of the reaction rate can be expected, compared to the reaction rate of the proposed μ-oxo-bisnickel(III) complexes formed in an intermolecular fashion.[13] Alternatively, if oxygenation occurs at one nickel centre to form the Ni(IV)-oxo-species, the second nickel atom is available for substrate coordination. Thus activated oxygen and alkene are organized in an intramolecular arrangement as in **5**, and enhancement of the epoxidation rate and/or selectivity can be expected (scheme 1; route b). The oxygen transfer to the alkene occurs in both cases in the vicinity of the ligand. The use of chiral ligands capable of coordinating two metal centres, to achieve asymmetric oxygenation by dinuclear nickel complexes is therefore another attractive feature of the approach described here.

We present here the results of our study on the epoxidation of unfunctionalized alkenes using structurally well characterized dinuclear nickel complexes. Two bisnickel(II)-complexes, μ-diacetato-μ-[2,6-

bis[*N*-2-(2'-pyridylethyl)formimidoyl]phenolato] bisnickel(II)·perchlorate·methanol (**6**) and μ-hydroxy-μ-[2,6-bis[*N*-((*S*)-1-benzyl-2-yl-pyrrolidine) formimidoyl]phenolato]bisnickel(II)bisperchlorate (**7**), containing octahedral and square planar coordinated nickel centres, respectively, have been synthesized (figure 1).



6 **7**

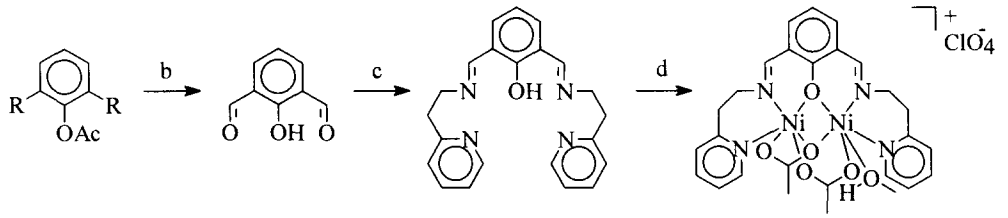
Figure 1.

Catalytic epoxidation experiments with **6** and **7** using sodium hypochlorite (phase transfer conditions) and *tert*-butyl hydroperoxide (phase transfer and homogeneous conditions) will be presented.

RESULTS AND DISCUSSION

Synthesis of the dinuclear nickel(II)catalysts.

a. Dinuclear nickel(II) catalyst 6. The ligands, capable of coordinating two metal centres, described here consist of an "upper part" or bridging unit, which in both cases is derived from 2-hydroxy-benzene-1,3-dicarbaldehyde (**10**) and the "lower part" comprised of two amine moieties (schemes 2 and 6).



a: **8**: R = Me; **9**: R = $CHBr_2$ **10** **12** **6**

Scheme 2. a. *hν*, Br_2, CCl_4, 64 %; b. KOH/H_2O Δ, 73 % c. 2-pyridin-2-yl-ethylamine (**11**), MeOH, Δ, 100 % d. $Ni(OAc)_2·4H_2O$, $Na(ClO_4)·H_2O$, MeOH, Δ, 67 %.

Since the literature synthesis of **10**[19] proceeds in only 22 % yield starting from 2-formylsalicylic acid (**13**), we devised a route to **10** starting from 2,6-dimethylphenyl acetate (**8**). Acetyl protected phenol **8** was converted to the tetrabromo derivative **9** employing radical bromination in 64 % yield. If the unprotected phenol was brominated, bromination also occurred at the aromatic ring, which is common for unprotected phenols.[20] The hydrolysis of **9** with 20 % aqueous potassium hydroxide under reflux conditions gave dialdehyde **10** in an overall yield of 47 %. Hydrolysis under basic conditions showed no trace of *para*-brominated product as was reported for acid hydrolysis.[21] Dialdehyde **10** was easily converted to bisimine

12 by condensation with 2 equivalent of 2-pyridin-2-yl-ethylamine (**11**). When ligand **12**, prepared *in situ*, was allowed to react with two equivalents of $Ni(OAc)_2 \cdot 4H_2O$ followed by anion exchange using one equivalent of $NaClO_4 \cdot H_2O$, a dark green crystalline nickel complex **6** was isolated (scheme 2).

Elemental analysis indicated a formula of $C_{26}H_{27}ClN_4Ni_2O_9 \cdot MeOH$, suggesting the binding of two nickel(II)-ions by ligand **12**. In order to establish unequivocally the structure of bisnickel(II)-complex **6** an X-ray analysis was undertaken. The molecular structure of **6** is depicted in figure 2.

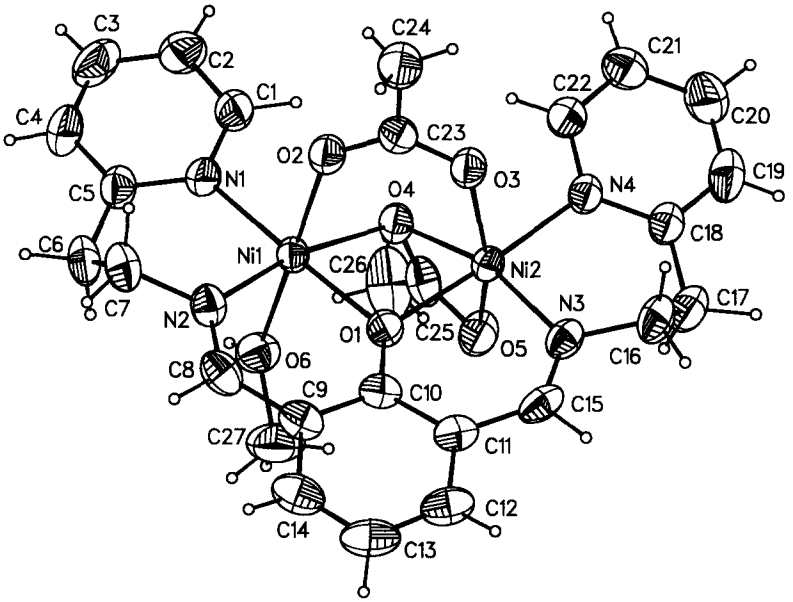
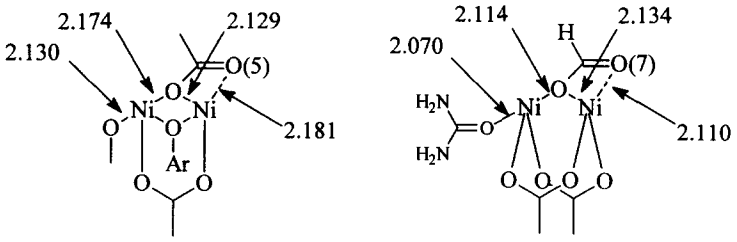


Figure 2. Molecular structure of **6** (ORTEP) with adopted numbering scheme.

Selected bond distances (Å) and angles (deg) (standard deviations in parentheses): Ni(1)-Ni(2): 3.075(2); Ni(1)-O(1): 2.012(3); Ni(1)-O(2): 2.047(3); Ni(1)-O(4): 2.174(3); Ni(1)-O(6): 2.130(3); Ni(1)-N(1): 2.076(3); Ni(1)-N(2): 2.018(4); Ni(2)-O(1): 2.026(3); Ni(2)-O(3): 2.019(3); Ni(2)-O(4): 2.129(3); Ni(2)-O(5): 2.181(3); Ni(2)-N(3): 1.992(3); Ni(2)-N(4): 2.078(4); O(1)-Ni(1)-O(2): 90.05(11); O(1)-Ni(2)-O(4): 80.95(11); O(1)-Ni(1)-O(4): 80.16(11); O(1)-Ni(2)-O(5): 90.77(11); O(1)-Ni(1)-O(6): 92.45(11); O(3)-Ni(2)-O(4): 97.53(11); O(2)-Ni(1)-O(4): 90.24(11); O(3)-Ni(2)-O(5): 158.00(11); O(2)-Ni(1)-O(6): 175.63(11); O(4)-Ni(2)-O(5): 61.02(10); O(4)-Ni(1)-O(6): 86.66(12); Ni(1)-O(1)-Ni(2): 99.18(11); O(1)-Ni(2)-O(3): 90.47(11); Ni(1)-O(4)-Ni(2): 91.21(11).

The complex shows slightly distorted octahedral geometries at the two nickel(II)-centres with a Ni-Ni separation of 3.075(2) Å. The two nickel(II)-ions are bridged by a μ-phenoxo, a symmetric μ-acetato and an asymmetric μ-acetato moiety. The octahedral coordination sphere of one of the metal centres (Ni(1)) is completed by coordination of a molecule of methanol. The average Ni-N distance of 2.041 Å is typical for octahedral nickel(II) complexes.[22] The distances between both Ni(1) and Ni(2) atoms and the μ-phenoxo (2.012(3) and 2.026(3)) and μ-acetato (2.047(3) and (2.019(3)) oxygen atoms are in the range of those reported in the literature for related dinuclear nickel complexes.[23] Furthermore, the distances between both nickel atoms and O(4) (Ni(1)-O(4): 2.174(3) Å, Ni(2)-O(4): 2.129(3) Å) resemble the Ni-O distances in a bis-acetato-bridged dinuclear nickel complex $[Ni_2(OAc)_3(urea)(tmen)_2](OTf)$ (tmen = *N,N,N',N'*-tetramethyl-ethylene diamine) **14** (Ni-O resp. 2.114(2) and 2.134(2)) reported by Lippard *et al.* (figure 3).[23c]



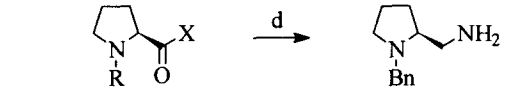
6 **14**

Figure 3. Core of complex **6** and **14**.[23c] (bond distances in Å, other ligands omitted for clarity)

The distance between the pendant O(5) and Ni(2) in **6** is 2.181(3) Å and is comparable to the distance between pendant O(7) and Ni(1) in complex **14** (2.110(2) Å). However, the Ni-Ni distance in **6** (μ-phenoxo-μ-acetato bridged) is 3.075(2) Å and is considerably shorter than the 3.4749(6) Å in **14** (bis-μ-acetato bridged). It should be noted that methanol coordination to nickel(II) complexes has been observed in a limited number of complexes.[24]

b. Chiral dinuclear nickel(II) catalyst 7. An important feature of biomimetic epoxidation catalysis is oxygen transfer in an enantioselective fashion, allowing the introduction of two stereogenic centres in a single transformation.[9] We decided to use a C_2-symmetric chiral catalyst[25] employing a chiral ligand in which the stereogenic centres are in close proximity to the metal centres, as exemplified by complex **7** in figure 1.

In order to synthesize the chiral complex **7**, a route to chiral bisamine (*S*)-*N*-benzyl-2-aminomethylpyrrolidine (**19**) was devised, based on (*S*)-proline (**15**), a readily available and cheap material. The first route that was followed is shown in scheme 3. In the first step (*S*)-proline (**15**) was alkylated using benzylchloride and NaOH to provide the corresponding *N*-benzylated proline **16**.[26] After esterification **17** was converted to the amide **18** using NH_3 at 80 °C in a Carius tube, in analogy to a literature procedure.[27] Subsequent reduction by $Li[AlH_4]$ yielded the amine **19** as a colorless oil.



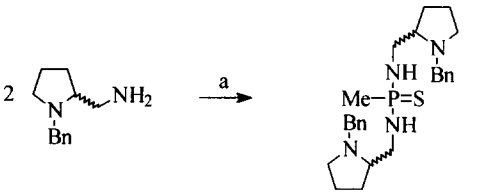
a **15**: R = H, X = OH
b **16**: R = Bn, X = OH
c **17**: R = Bn, X = OMe
18: R = Bn, X = NH_2

19

Scheme 3. a. $PhCH_2Cl$ (BnCl), NaOH, H_2O, 80 %; b. H_2SO_4, MeOH, 95 %; c. NH_3, MeOH, 80 °C, 80 %; d. $Li[AlH_4]$, THF, 81 %.

The enantiomerical purity of **19** was established using a facile enantiomeric excess (e.e.)-determination method that has been developed in our laboratory.[28] It is based on ^1H decoupled ^{31}P NMR analysis of diastereoisomers of phosphorous derivatives **21**, **22** and **23**. The advantage of this method is the use of an achiral derivatization agent ($MePSCl_2$[29] (**20**)) to form diastereoisomers with large differences in chemical shifts. This method has now been extended to bifunctional primary amines (scheme 4). Thus

reaction of $MePSCl_2$ (**20**) with racemic **19** in the presence of Et_3N affords diastereomeric thiophosphonic amides **21-23**. It appeared that the derivatizing agent only reacts with the primary amine functionality in **19**. In case of a racemic mixture of **19** three well separated singlets are observed in the ratio 1 : 2 : 1 corresponding to the racemate (*R,R*-**22** and *S,S*-**22**) and the two meso diastereoisomers (*S,R*-**21** and *R,S*-**23**) with a (*R,R*, *S,S*) : (meso) ratio of 1 : 1. In case of enantiomerically pure *R*-**19** (or *S*-**19**) only *R,R*-**22** (or *S,S*-**22**) is expected to be formed. Using **19** synthesized as described above (scheme 3) the ^1H decoupled ^{31}P NMR spectrum of derivatives **21-23** indicated that partial racemization (20 %) had occurred.

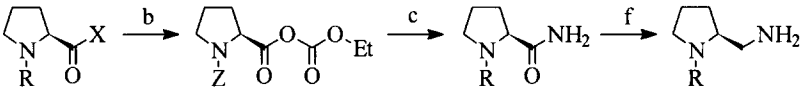


19

21: *S,R* (meso 1)
22: *S,S* and *R,R*
23: *R,S* (meso 2)

Scheme 4. a. $MePSCl_2$ (**20**), Et_3N, $CDCl_3$.

Therefore an alternative route to bisamine **19** had to be developed. In the previous route, the formation of the amide seems to be the critical step as elevated temperatures and basic conditions are employed. If this step could be carried out under milder conditions racemization might be suppressed (scheme 5).



a → **15**: R = H, X = OH; **24**: R = Z, X = OH

25

d → **26**: R = Z; **27**: R = H

e → **18**: R = Bn

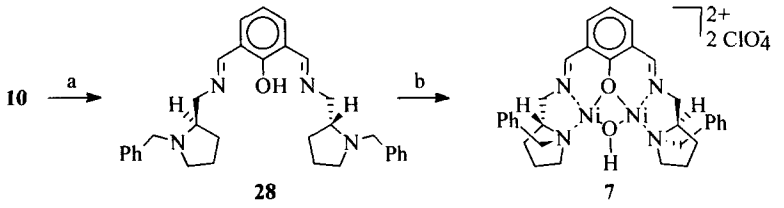
19

Scheme 5. a. $PhCH_2OCOCl$ (ZCl), NaOH, H_2O, 92 %; b. *N*-methylmorpholine, $ClCO_2Et$, CH_2Cl_2; c. NH_3, CH_2Cl_2, -25 °C, total of 2 steps: 92 %; d. Pd/C. H_2, MeOH, 83 %; e. BnBr, CH_2Cl_2/MeOH 4/1, 70 %; f. $Li[AlH_4]$, THF, 81 %.

(*S*)-Proline (**15**) was protected with the benzyloxycarbonyl group (Z-group) under Schotten Baumann conditions.[30] The next step, introduction of the amide, was conducted in a one pot two step procedure, using a "mixed anhydride" method.[31] Z-Protected proline **24** was modified to mixed anhydride **25** using ethyl chloroformate and *in situ* converted to amide **26** using gaseous NH_3 at low temperature (-25 °C). Deprotection of amide **26** was easily achieved using Pd/C under a H_2-atmosphere. The (*S*)-proline amide (**27**) obtained showed identical physical data (^1H NMR, ^{13}C NMR, m.p. and rotation, see experimental section) to those reported.[32] The pyrrolidine moiety was subsequently *N*-benzylated to provide tertiary amine **18**. In the last step **18** was reduced using $Li[AlH_4]$ to bisamine **19** (overall yield 40 %, scheme 5). In order to establish the enantiomeric purity of **19** the same procedure previously described was used. ^{31}P NMR analysis of the possible thiophosphonic amides **21-23** showed only one singlet corresponding to the

(*S*,*S*)-phosphonic amide **22**, indicating that **19** obtained *via* this route was enantiomerically pure (e.e. > 98 %).

Bisaldehyde **10** was easily converted to bisimine **28** using 2 equivalent of amine **19** in methanol. The ligand was reacted *in situ* with 2.0 equivalent of $Ni(OAc)_2 \cdot 6H_2O$ and 2.0 equivalent NaOH to yield bisnickel(II)complex **7** (scheme 6).



Scheme 6. a. 2 equivalent **19**, MeOH; b. $Ni(ClO_4)_2 \cdot 6H_2O$, NaOH, MeOH, overall 41 %.

Elemental analysis revealed formula $(C_{16}H_{19}ClNiN_2O_5)_n$, indicating that two nickel ions are bound by the ligand. Crystallization of **7** from a mixture of methanol and *iso*-propylether gave red crystals suitable for X-ray analysis. The molecular structure of **7** is given in figure 4.

The complex adopts C_2-symmetry in the solid state except for the *N*-benzyl groups. One benzyl group points above the Ni(1)-O(1)-Ni(2) plane towards the phenol moiety whereas the other benzyl group, below the Ni(1)-O(1)-Ni(2) plane, points away from the bridging phenol group. This is probably due to a packing effect which could be caused by steric hindrance of the ClO_4^- counter ions. It is reasonable to assume that in the molecule in solution C_2-symmetry is present due to conformational freedom of the benzyl groups. The geometry around each nickel(II)-ion in **7** is slightly distorted square planar (max. deviation from the mean plane is 0.162 Å), with a Ni-Ni separation of 2.849(1) Å. The dinuclear nickel core shows bridging phenolate and hydroxy moieties whereas the coordination sphere of each nickel(II)-ion is completed by an imine and a tertiary amine donor ligand. In figure 4b, viewing along the Ni(1)-O(1)-Ni(2)-O(2) plane it is seen that at the two nickel centres the pyrrolidine and benzyl moieties are in a *trans*-orientation with respect to each other. The configuration around each pyrrolidine nitrogen is tetrahedral and in this sense the nitrogen atoms have become stereogenic centres. The *N*-benzylpyrrolidine groups of the ligand are brought in an asymmetric arrangement in close proximity to the metal ions. Furthermore, the pyrrolidine nitrogen metal bond distance (1.941(6) and 1.928(6)) are longer than the imine metal distances (1.826(6) and 1.847(6)), despite the fact that amine nitrogen atoms usually show stronger coordination than imine nitrogen atoms.[33] This effect, however, is probably caused by enhanced steric hindrance of the tertiary amine nitrogen compared to the mono substituted imine nitrogen.

Epoxidation studies.

Square-planar nickel(II)-complexes have shown catalytic activity in the epoxidation of alkenes using various oxidants.[12-15] The structurally well defined complexes **6** and **7** enable us to explore the possibilities of dinuclear nickel catalysis in epoxidation. Using dinuclear nickel(II) complexes **6** and **7**, three oxidation systems were examined: i) sodium hypochlorite under phase transfer conditions, ii) *tert*-butyl hydroperoxide under phase transfer conditions and iii) *tert*-butyl hydroperoxide under homogeneous conditions.

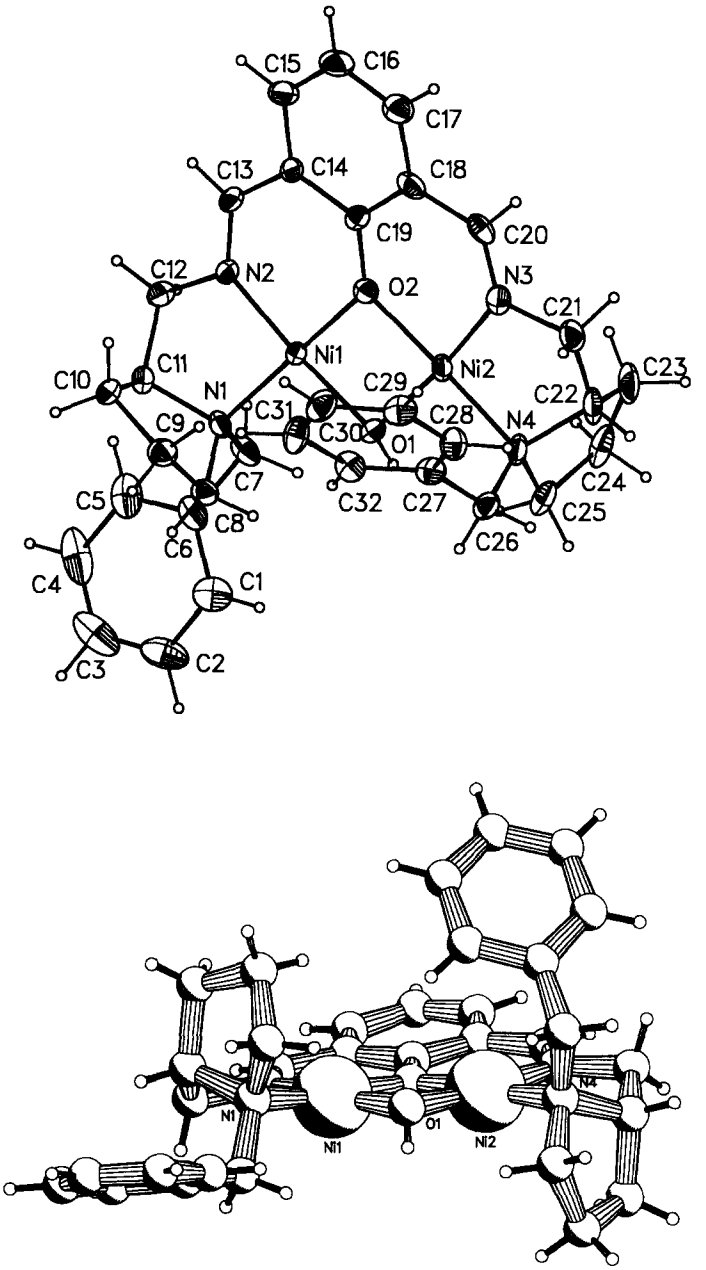
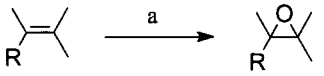


Figure 4. a. Molecular structure of **7** (ORTEP) with adopted numbering scheme: b. A view along the Ni(1) - O(1) - Ni(2) - O(2) plane of **7** (PLUTO; counter ions are omitted for clarity).

Selected bond lenghts (Å) and angles (deg) (standard deviations in parentheses): Ni(1)-O(1): 1.881(5); Ni(1)-O(2): 1.864(5); Ni(1)-N(1): 1.941(6); Ni(1)-N(2): 1.826(6); Ni(2)-O(1): 1.883(5); Ni(2)-O(2): 1.865(5); Ni(2)-N(3): 1.847(6); Ni(2)-N(4): 1.928(6); Ni(1)-Ni(2): 2.849(1); O(1)-Ni(1)-O(2): 81.0(2); O(1)-Ni(2)-O(2): 81.0(2); Ni(1)-O(1)-Ni(2): 98.4(2); Ni(1)-O(2)-Ni(2): 99.6(2);

i) Sodium hypochlorite (phase transfer conditions). In the first procedure sodium hypochlorite is used as the terminal oxidant in a two phase solvent system (dichloromethane (CH_2Cl_2)/H_2O) using benzyltriethylammonium bromide or chloride as phase transfer catalysts (PTC) (scheme 7).



1 2

Scheme 7. a. NaOCl, PTC ([$BnEt_3N$]Cl or [$BnEt_3N$]Br), catalyst **6** or **7**, CH_2Cl_2, H_2O .

Complexes **6** and **7** are both only soluble in CH_2Cl_2 and therefore the complexes presumably operate as catalyst in the organic layer. This is supported by the bright green or orange color of the organic layer containing **6** or **7** respectively, in comparison with the colorless H_2O layer. This was confirmed by UV-Vis measurements for complex **7** (figure 5b, λ_{max} 229 ($\varepsilon = 2.2*10^4$ $M^{-1}cm^{-1}$), 252 ($\varepsilon = 2.3*10^4$) and 384 nm ($\varepsilon = 5.7*10^3$); figure 5c, λ_{max} 228 ($\varepsilon = 2.4*10^4$), 248 ($\varepsilon = 2.3*10^4$) and 400 nm ($\varepsilon = 4.9*10^3$)).[34]

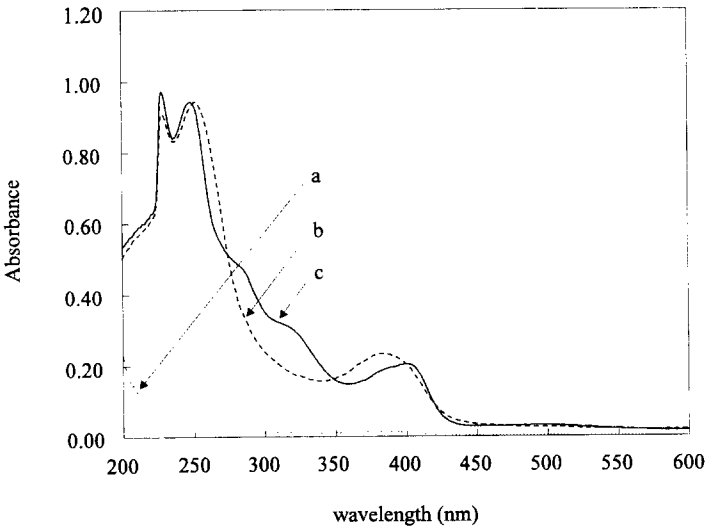


Figure 5. UV-Vis spectra of catalyst **7** (see scheme 7): a. H_2O phase; b. CH_2Cl_2 phase; c. **7** in CH_2Cl_2.

The epoxidation conditions were as follows: 1 mmol alkene, 1.5 mol% nickel catalyst and 10 mol% phase transfer catalyst were dissolved in 10 mL CH_2Cl_2, and 2.5 mL commercial bleach dissolved in 10 mL H_2O (pH = 12.5 ± 0.1) was added. The oxidation was conducted under vigorous stirring for 16 h at room temperature. The products were analyzed after workup using ^1H NMR (see experimental section, general procedure a.) The results are summarized in tables 1 and 2.

When dinuclear nickel(II)-complex **6** was used as the catalyst in the epoxidation of styrene (**29**), analysis of the oxidation products after 16 h showed 15 % epoxy styrene (**31**) and 50 % unreacted alkene **29** (table 1, entry 1). The remainder of the products consist of benzaldehyde (**32**) (8 %) and undefined

Table 1. Epoxidation with Complexes **6** and **7** and Hypochlorite as Oxidant (pH = 12.5 ± 0.1).

entry	catalyst	mol%	substrate[a]	conv.[b] (%)	epoxide (%)	t.o.[c]
1	**6**	2.0	**29**	50	15	7.5
2	**6**+py[d]	2.0	**29**	60	t[c]	t[c]
3	**7**	1.5	**29**	50	23	15
4	**7**	1.5	**30**	46	35	23

[a] **29**: styrene; **30**: *trans*-stilbene.

[b] conversion is based on alkene consumed.

[c] turnover (16 h.) is based on amount of catalyst used; t = trace.

[d] py = pyridine (**33**) (10 mol% with respect to the alkene).

compounds. The use of an additional nitrogen donor ligand (pyridine, **33**) leads to a dramatic decrease in the yield of epoxide (table 1, entry 2). Presumably styrene (**29**) is converted to chlorinated product(s) under these conditions. When catalyst **7** was used in the epoxidation of styrene (**29**) and *trans*-stilbene (**30**) at a pH of 12.5 low turnovers were obtained (table 1, entries 3 and 4)

As sodium hypochlorite oxidations are usually pH-dependent,[14a] a study of the influence of the pH on the amount of epoxide generated in the epoxidation of several alkenes was undertaken with a view to increase the reaction rate (see experimental section, general procedure b). The products were analyzed by GC employing an internal standard (hexadecane) and ^{1}H NMR. The results are summarized in table 2 and figure 6.

The optimum pH for epoxidation was found to be 9.0 in most cases. A turnover of 59 in the epoxidation of *trans*-β-methylstyrene (**34**) was observed (table 2, entry 3). It was shown that the catalyst was still active after complete conversion of the alkene, since renewed addition of alkene resulted in further conversion to epoxide. If the amount of catalyst **7** was decreased to 0.375 mol% the maximum turnover reached 165 providing 62 % isolated yield of epoxide (table 2, entry 4). The blank reaction (no nickel complex present) in this case resulted in formation of 9.3 % epoxide. The equilibrium between NaOCl and HOCl at pH = 9.0 is partially shifted to HOCl and therefore the solubility is increased in the organic phase. This is in accordance with previous observations by Burrows *et al.*[14a] who reported an enhancement of the epoxidation for *trans*-β-methylstyrene (**34**), cyclohexene (**36**) and norbornene (**40**), using a nickel(II)salen complex, when the pH was lowered from 12.5 to 9.3. Styrene (**29**) and *trans*-stilbene (**30**) give rise to considerable turnovers for the epoxidation. The higher reactivity of *trans*-β-methylstyrene (**34**) (table 2, entry 3) compared to styrene (**29**) (table 2, entry 1) is consistent with addition of an electrophilic oxygen to a more electron rich double bond.[14c] However, in the cases of α-methyl styrene (**35**) (table 2, entry 5) and cyclohexene (**36**) (table 2, entry 6) the turnover numbers are quite low. Apparently an aryl substituent is necessary to give rise to substantial epoxidation, as is clearly seen when cyclohexene (**36**) and *trans*-β-methylstyrene (**34**) are compared (table 2, entries 3 and 6). Although the aliphatic alkene appeared to be very reactive (table 2, entry 6), mainly chlorinated products were formed with nickel catalysts **6** and **7**. This is consistent with the formation of 1,2-dichloroethylbenzene (**37**) as major side product in the epoxidation of styrene (**29**) (*vide infra*).

Table 2. Nickel(II) catalyzed epoxidation[a] of selected alkenes at different pH's (conversion(%)[b]/ epoxide(%)[c]/turnover[d]).

entry	substrate	pH: 8	9	10	11	12
1	styrene (**29**)	100/35/23	96/39/26[e]	79/18/12	40/14/9	5/2/1
2	*trans*-stilbene (**30**)	100/78/52	100/78/52	50/56/37[f]	29/18/12	0/0/0
3	*trans*-β-methylstyrene (**34**)	100/78/52	100/89/59	69/59/39	59/33/22	28/6/4
4	*trans*-β-methylstyrene (**34**)[g]	n.d.	93/62/165	n.d.	n.d.	n.d.
5	α-methylstyrene (**35**)	100/21/14	100/24/16	91/26/17	64/20/13	29/8/5
6	cyclohexene (**36**)	100/14/9	92/11/7	74/8/5	65/8/5	46/3/2

[a] Conditions: 1.5 mol% catalyst 7; 1 mmol alkene; 10 mol% $BnEt_3NCl$ (PTC); NaOCl (2.0 eq.) in H_2O (10 mL) buffered with $Na_2B_4O_7$ and adjusted to the required pH with either 4 N NaOH or concentrated HCl; room temperature; 16 h; compounds were analysed by GC employing hexadecane as internal standard.
[b] Conversion based on alkene consumed.
[c] Chemical yield epoxide.
[d] Turnover : amount of epoxide / amount of catalyst.
[e] According to GCMS the major side product was 1,2-dichloro-ethylbenzene (**37**).
[f] In a similar experiment with *cis*-stilbene (**38**) only *trans*-stilbene oxide (**39**) was formed. (^{1}H NMR, GC).
[g] 0.375 mol% catalyst 7.

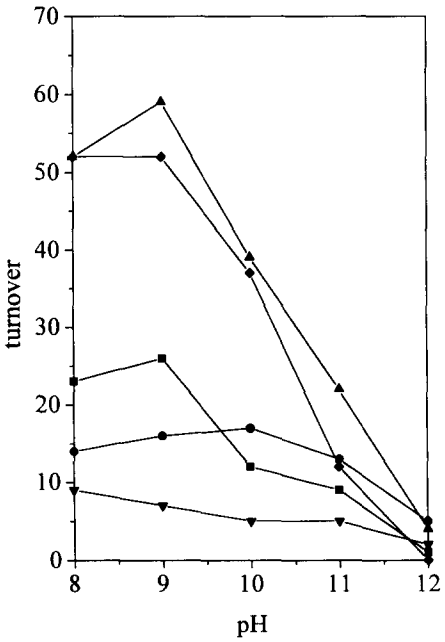


Figure 6. pH-Dependency of the epoxide formation using **7** as catalyst. (for conditions, see experimental). ■: styrene (**29**); ◆: *trans*-stilbene (**30**); ▲: *trans*-β-methylstyrene (**34**); •: α-methylstyrene (**35**); ▼: cyclohexene (**36**).

To broaden the scope of this epoxidation several alkenes (**40-47**) were tested at pH = 9.0 (see table 3). Despite the fact that conversions were often high, modest yields of epoxides were found. The best result was obtained for 2,3-dimethylbut-2-ene (**46**) with 67 % epoxide formed (table 3, entry 7), which could point to an electrophilic metal-oxo site involved[13] (see however following discussion, scheme 9). The nickel(II)-complex of the tetraazamacrocycle cyclam has been reported to give 85 % yield of epoxide with the same substrate.[13]

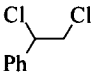
Table 3. Nickel(II) catalyzed epoxidation[a] of selected alkenes.

entry	substrate	conversion (%)[b]	epoxide (%)[c]	t.o.[d]
1	oct-1-ene (**41**)	44	20	14
2	oct-2-ene (**42**)	67	31	21[e]
3	dec-1-ene (**43**)	57	21	14
4	norbornene (**40**)	97	24	16
5	1,2-dihydronaphthalene (**44**)	92	38	25
6	allylbenzene (**45**)	48	20	13
7	2,3-dimethylbut-2-ene (**46**)	100	67	45
8	hex-3-ene (**47**)	73	15	10

[a] For conditions, see table 2.
[b] Conversion based on alkene consumed.
[c] Yield of epoxide by GC.
[d] Turnover : amount of epoxide / amount of catalyst.
[e] According to GC 76 % *trans*-epoxide (**48**) was formed.

To monitor the progression of the epoxidation of two alkenes, *trans*-β-methylstyrene (**34**) and allylbenzene (**45**), the reaction was followed using GC and the results are depicted in figure 7a and 7b. For reactive alkenes such as *trans*-β-methylstyrene (**34**) complete conversion was obtained after 50 minutes. Again it is shown that the conversion as well as the yield of epoxide improve by using aromatic alkenes whereas aliphatic alkenes give rise to low yields (see also table 3).

Comparable results were obtained for cyclohexene (**36**) and norbornene (**40**), using mononuclear nickel salen complexes.[14c] Increase of the reaction time did not result in higher yields of epoxide due to catalyst degradation. When the pH was lowered the yields drop because of competing side reactions, i.e. chlorinations are accelerated stronger than the epoxidation reaction. GCMS analysis as well as comparison by GC and NMR of possible chlorinated products based on independent synthesis[35] revealed the major side product in the reaction of styrene to be 1,2-dichloroethylbenzene (**37**).



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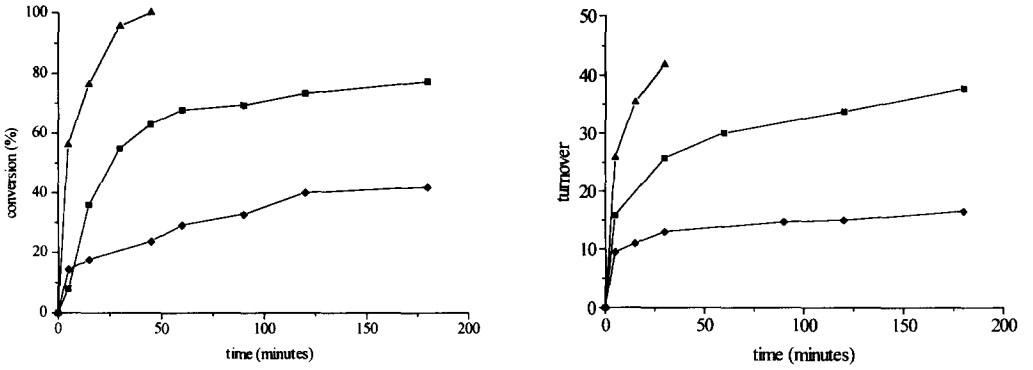
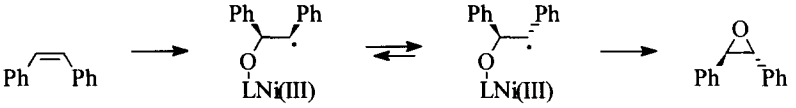


Figure 7. a. Conversion of *trans*-β-methylstyrene (**34**) with 4.0 equivalent NaOCl (▲), 2.0 equivalent NaOCl (■), and allylbenzene (**45**) with 2.0 equivalent NaOCl (◆) followed in time. b. Epoxide yield of *trans*-β-methylstyrene (**34**) with 4.0 equivalent NaOCl (▲), 2.0 equivalent NaOCl (■), and allylbenzene (**45**) with 2.0 equivalent NaOCl (◆) followed in time.

It should be noted that bromobenzene was converted to chlorobenzene under the reaction conditions employed using bisnickel catalyst **7**. A similar aryl-halogen exchange in nickel(II)salen and nickel(II)cyclam catalyzed epoxidation was observed by Burrows and co-workers.[36]

When the epoxides of alkenes **29**, **30**, **34** - **36** were analyzed by chiral GC, no enantiomeric excess was detected. A reason for the lack of enantioselectivity could be the radical nature of the oxygenation. An indication for such a radical or conversely a stepwise mechanism in this epoxidation is provided by the observation that *cis*-stilbene (**38**) was converted to *trans*-stilbene oxide (**39**) (table 2, entry 2) and the formation of an excess (76 %) *trans*-oct-2-ene oxide (**48**) starting from a mixture of *trans*- and *cis*-2-octene (**42**) (table 3, entry 2). Another indication is the fact that when dimethyl sulfide (**49**), a two electron acceptor, was added all reactivity ceased. The addition of 2,6-di-*tert*-butyl-4-methylphenol (**50**), a one electron acceptor, resulted in the suppression of the epoxidation favouring chlorination.

A possible sequence could involve the addition of a nickel-oxo-complex to the alkene, as was suggested by Burrows[14c] for mono nickel systems, and in analogy to the known chromium(V)-oxo-complex.[37] A radical intermediate **51** is formed which could subsequently undergo rotation around the C-C bond before ring closure to the epoxide **39** (scheme 8). Such a mechanism does not exclude π-face selection in the first C-O bond formation and could be responsible for induction of the asymmetric epoxide formed.[38]

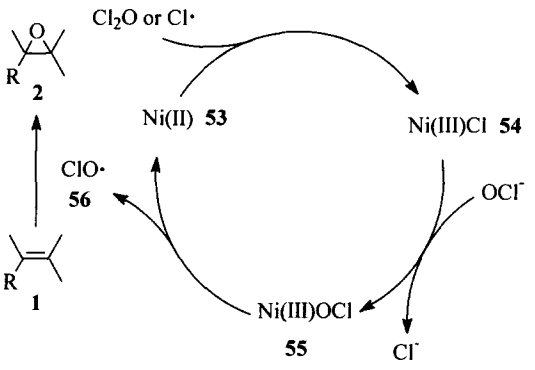


38 **51** **52** **39**

Scheme 8. Formation of *trans*-stilbene oxide (**39**) from *cis*-stilbene (**38**).

A more appropriate scheme to rationalize the epoxidation results is the mechanism shown in scheme 9.[14a] A nickel(III)hypochlorite complex **55** converts to a nickel(II) complex **53** resulting in the formation

of an hypochlorite radical (**56**). The hypochlorite radical (**56**) in turn epoxidizes the alkene (**1**) and as a consequence no stereochemical control by the chiral nickel complex is exerted. Our results are consistent with such a scheme, as no enantioselectivity during the epoxide formation is observed.

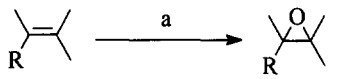


Scheme 9.

Comparison between the dinuclear nickel catalysts **6** and **7**, and results from mononuclear nickel salen complexes,[14a,c] (using NaOCl as oxidant) shows similar activity in the epoxidation of both styrene (**29**) and *trans*-β-methylstyrene (**34**). Oxidation of *trans*-stilbene (**30**), using **7**, proceeded in higher yields compared to results with mononuclear nickelsalen catalysts,[14c] whereas the activity in the epoxidation of α-methylstyrene (**35**) and cyclohexene (**36**) is strongly reduced. Comparison with a mononuclear $[Ni(bipy)_2Cl_2]$ catalyst (**57**),[15] shows enhanced activity in the epoxidation of *trans*-β-methylstyrene (**34**) and cyclohexene (**36**), whereas styrene (**29**) and α-methylstyrene (**35**) show reduced activity. Because of these contradicting observations a comparison between mononuclear and dinuclear nickel catalysts, with respect to the role of the second metal in the dinuclear complexes in the catalytic cycle, awaits further detailed mechanistic studies.[39]

ii) tert-Butyl hydroperoxide (two phase conditions). Oxidations with *tert*-butyl hydroperoxide in combination with metalloporphyrins[40] and the epoxidation of allylic alcohols,[9] have been highly successful. Hill has extensively studied transition metal-substituted polyoxometalate catalyzed oxidations with *tert*-butyl hydroperoxide.[41] This oxidant has only been used in a limited number of other catalytic systems. For instance, molybdenum catalyzed reactions have been described,[42] in which the catalyst preferentially epoxidizes the more substituted double bond of isoprene (**58**) and gives the corresponding epoxides in good yield.[43] The epoxidation of styrene (**29**) with copper complexes and *tert*-butyl hydroperoxide was reported to provide modest yields of epoxide **31**.[44] Ruthenium catalyzed epoxidation of stilbenes (**30** and **38**) has also been described.[45] Nickel catalyzed epoxidation using *tert*-butyl hydroperoxide as terminal oxidant has less precedent. A nickel boride binary complex as catalyst for *tert*-butyl hydroperoxide epoxidation[46] and the use of nickel in metal-substituted polyoxometalate catalysts[47] have been claimed. In the second system we investigated, *tert*-butyl hydroperoxide was used as the terminal oxidant under phase transfer conditions (scheme 10; see experimental section, general procedure c).

Typical epoxidation conditions were as follows: 1 mmol alkene and 1.5 - 2.0 mol% catalyst **6** or **7** were dissolved in 10 mL CH_2Cl_2 and a solution of 4 mmol NaOH and 7 mmol *tert*-butyl hydroperoxide in



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Scheme 10. a. *tert*-butyl hydroperoxide, NaOH, catalyst **6** or **7**, CH_2Cl_2, H_2O.

10 mL H_2O was added. The reaction was conducted with vigorous stirring for 20 h at room temperature. The reaction products were analyzed by either GC or ^1H NMR spectroscopy. The results are summarized in table 4.

Table 4. Epoxidation of alkenes using dinuclear nickel(II)catalysts **6** and **7** and *tert*-butyl hydroperoxide as oxidant.[a]

entry	catalyst	mol%	substrate[b]	conv.[c] (%)	epoxide (%)	t.o.[d]
1	**6**	2.0	**29**	90	11	13
2	**6**	2.0	**38**	30	10	5
3	**7**	1.5	**29**	50	3	2[e]
4	**7**	1.5	**30**	75	65	43
5	**7**	1.5	**34**	100	25	17
6	**7**	1.5	**35**	100	-[e]	-[e]

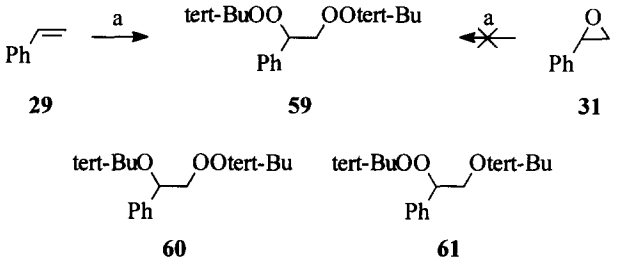
[a] Conditions: 1.5 mol% catalyst; 1 mmol alkene; 10 mL CH_2Cl_2; 7 mmol *tert*-butyl hydroperoxide in 10 mL H_2O; 100 mg NaOH; 20 h; room temperature; compounds were analyzed by GC or ^1H NMR.
[b] **29**: styrene; **30**: *trans*-stilbene; **34**: *trans*-β-methylstyrene; **35**: α-methylstyrene; **38**: *cis*-stilbene.
[c] Conversion is based on alkene consumed.
[d] Turnover is based on amount of catalyst used.
[e] See text.

Control experiments using $Ni(ClO_4)_2 \cdot 6H_2O$ as a catalyst did not give rise to epoxide formation, showing that nickel activation by complexation of an appropriate ligand, as in **6** or **7**, for the oxidation with *tert*-butyl hydroperoxide is essential.

When *cis*-stilbene (**38**) (table 4, entry 2) was epoxidized using catalyst **6** only *trans*-stilbene oxide (**39**) was obtained, pointing to a mechanism shown in scheme 8 (*vide supra*). *Trans*-stilbene (**30**) (table 4, entry 4) was epoxidized using 1.5 mol% **7**, 7 equivalent of *tert*-butyl hydroperoxide and 4 equivalent NaOH. After reductive workup, to remove the excess of peroxide, 65 % epoxide **39** was found as well as 9 % benzaldehyde (**32**) and starting material. Only the *trans*-epoxide **39** was detected. The base proved to be essential, and is probably involved in deprotonating the peroxide, since no epoxide was found in the absence of sodium hydroxide.

Oxidation of styrene (**29**) under these conditions (table 3, entries 1 and 3) gave rise to a rather unexpected product (**59**) (scheme 11). Although alkene conversion was 50 % in case of catalyst **7**, besides starting material and benzaldehyde, only 3 % epoxide **31** was detected. The major product (25 % isolated yield) consisted of the 1,2-bis-(*tert*-butylperoxy)ethylbenzene **59** (^1H NMR, ^{13}C NMR). MS(EI) did not give a molecular ion, but employing a D.C.I. (Desorption Chemical Ionization) method resulted in a parent

molecular ion peak of 300 ($M(NH_4^+)$). The formation of **59** is related to the formation of perethers **60** and **61** in the manganese porphyrin catalyzed epoxidation of styrene.[48] 1,2-Bis-(*tert*-butylperoxy)ethyl benzene **59** could not be a degradation product of styrene epoxide (**31**), since in control experiments using the epoxidation conditions **31** could not be converted in the 1,2-bis-(*tert*-butylperoxy)ethylbenzene (**59**).

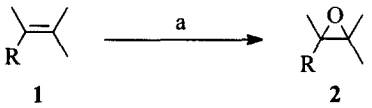


Scheme 11. a. *tert*-butyl hydroperoxide, 1.5 mol% **7**, CH_2Cl_2/NaOH/H_2O, 25 %.

Epoxidation of *trans*-β-methylstyrene (**34**) (table 4, entry 5) yielded 25 % epoxide **62**, with 100 % observed conversion. When α-methyl styrene (**35**) (table 4, entry 6) was used, only acetophenone (**63**) was isolated in 70 % yield. The formation of **63** and substantial amounts of aldehydes in the epoxidation of styrene (**29**) and stilbene (**30**) point to a radical nature of the intermediate species in this process.[14a] Passing oxygen through the solution as radical trapping agent had no influence on the product distribution indicating the absence of radical intermediates or the inability of oxygen to trap them. No free radicals could be detected in a temperature range of -130 °C to +25 °C by E.P.R. measurements, performed during the oxidations.

When the epoxides obtained were analyzed no enantioselectivity was detected.

iii) t-Butyl hydroperoxide (homogeneous conditions). In the third procedure that was briefly investigated, *tert*-butyl hydroperoxide was used as terminal oxidant employing homogeneous (H_2O free) conditions (scheme 12). The reaction was performed in CH_2Cl_2 using 3 equivalent *tert*-butyl hydroperoxide in *iso*-octane and 2 equivalent of pyridine (**33**) as a base (see experimental section, general procedure d). The results are summarized in table 5.



Scheme 12. a. *tert*-butyl hydroperoxide, pyridine, catalyst **6** or **7**, CH_2Cl_2.

Styrene (**29**) and *trans*-stilbene (**30**) did not react in the presence of nickel catalysts **6** or **7** (table 5, entries 4 and 5), therefore the activated alkene *para*-methoxy-*trans*-β-methylstyrene (anathol, **64**) (table 5, entry 1) was used resulting in a turnover of 53 (c.y. 80 %) of epoxide **65**, as well as 15 % *para*-methoxy-benzaldehyde (**66**). The control reaction (table 5, entry 2) gave rise to 20 % epoxide **65**. When *trans*-β-methylstyrene (**34**) (table 5, entry 3) was used only 4 % epoxide (**62**) was found. Due to the low activity of complexes **6** and **7** these catalysts are of limited use in homogeneous epoxidation using *tert*-butyl hydroperoxide as oxidant.

Table 5. Epoxidation of alkenes with catalyst **6** and **7** and *tert*-BuOOH as oxidant under homogeneous conditions.

entry	eatalyst	mol%	substrate[a]	conv.[b] (%)	c.y. (%)	t.o.[c]
1	**7**	1.5	**64**	100	80	53
2	-	-	**64**	30	20	[d]
3	**6**	1.5	**34**	5	3	(2)
4	**6**	1.5	**29**	-	-	-
5	**6**	1.5	**30**	-	-	-

[a] **29**: styrene; **30**: *trans*-stilbene; **34**: *trans*-β-methylstyrene; **64**: anathol.
[b] Conversion is based on alkene consumed.
[c] Turnover is based on amount of catalyst used (mol / mol catalyst).
[d] No catalyst is used.

CONCLUSIONS

It has been demonstrated in this study that the new dinuclear nickel(II) complexes **6** and **7** are active in the epoxidation of unfunctionalized alkenes. New octahedral and square planar bis(nickel(II))complexes have been synthesized, fully characterized and their catalytic activity established. Epoxidation of unfunctionalized alkenes using the bisnickel(II)complex **7** with sodium hypochlorite as oxidant is highly pH-dependent. An optimum is reached at a pH of 9, at higher pH the reactivity is diminished, whereas at low pH alkene chlorination becomes a competitive side reaction. The highest turnover so far (165) has been reached for *trans*-β-methylstyrene (**34**) at pH 9. Epoxidation of alkenes using *tert*-butyl hydroperoxide gives varying results, depending on the alkene, with almost quantitative epoxidation with *trans*-stilbene (**30**) or the formation of di-*tert*-butylperoxy ether **59** with styrene (**29**) as major reactions. Catalytic oxidation with *tert*-butyl hydroperoxide under homogeneous conditions was only possible for an activated substrate (anathol **64**). Further insight into the possible cooperative effects of the two nickel centres in these catalysts awaits additional mechanistic study. Significant enantioselectivity in the epoxidation using the enantiomerically pure dinuclear nickel complex **7** was not achieved.

EXPERIMENTAL SECTION

General remarks.

All experiments were performed under an inert (N_2) atmosphere when necessary. Melting points are uncorrected. IR spectra were recorded neat or as KBr pellet. ^{1}H NMR spectra were recorded at 200 or 300 MHz. $CDCl_3$ was used as a solvent unless stated otherwise. Chemical shifts are denoted in ppm relative to TMS. Coupling constants *J* are denoted in hertz. ^{13}C NMR spectra were recorded at 50.32 or 75.43 MHz. Chemical shifts are determined relative to the solvent and converted to the TMS scale. ^{1}H decoupled ^{31}P NMR spectra were recorded at 121.42 MHz. Chemical shifts are determined relative to phosphoric acid. HRMS mass spectra were recorded on a AEI-MS-902 mass spectrometer (E.I.) and GCMS spectra were

recorded on a RIBERMAG R 10-10C mass spectrometer (E.I.). Elemental analysis were performed in the Microanalytical Department of this laboratory. Flash chromatography was performed using Merck silica gel 60. Nitrogen was deoxygenated using a copper column. All reagents and solvents were purified, dried and stored under N_2 when necessary using standard procedures. 2-pyridin-2-yl-ethylamine was obtained from Aldrich Chimica. (*S*)-proline amide was obtained from Aldrich Chimica. $MePSCl_2$ was synthesized as reported previously.[28a]

X-ray determination

X-ray Structure Determination of complex 6. Crystal Data: Empirical formula: $C_{27}H_{31}ClN_4Ni_2O_{10}$; molecular mass 724.40; the dimensions of the unit cell were *a* (pm) = 877.6(1); *b* (pm) = 1369.7(1); *c* (pm) = 1406.4(1); α (°) = 69.147(7); β (°) = 72.754(7); γ (°) = 79.454(7); *V* (pm^3) = 1503.1(3) x 10^6; *Z* = 2; *d*(calcd) (g/cm^3) = 1.600; crystal system, triclinic; space group, $P\bar{1}$. Data Collection: crystal size (mm), 0.20 x 0.25 x 0.40, diffractometer, Nonius CAD-4F interfaced to a VAX-11/730 computer; monochromator, graphite; radiation Mo $K\bar{\alpha}$; μ(Mo $K\bar{\alpha}$) = 14.1 cm^{-1}, *F*(000) = 748, T = 295 K, $\omega/2\theta$ scan, $\Delta\omega = 0.75 + 0.34$ tg θ, $1.60 < \theta < 28.0$, total unique data 7265, No. of observations [$I \geq 2.5\ \sigma(I)$] 4807, observations/variables 9.23, $R = 0.041$, $R_w = 0.042$. The structure was solved by Patterson methods and subsequent partial structure expansion (SHELXS). Final refinement on F_0 by full matrix least-squares techniques (*Xtal*) with anisotropic thermal displacement parameters for the non-hydrogen atoms and isotropic thermal displacement parameter for the hydrogen atoms. The final difference Fourier map did not show any significant residual features. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

X-ray Structure Determination of complex 7. Crystal Data: Empirical formula: $C_{32}H_{38}Cl_2N_4Ni_2O_{10}$; molecular mass 826.96; the dimensions of the unit cell were *a* (pm) = 878.8(2); *b* (pm) = 1099.0(2); *c* (pm) = 3477.2(3); *V* (pm^3) = 3358.3 x 10^6; *Z* = 4; *d*(calcd) (g/cm^3) = 1.636; crystal system, orthorhombic; space group, $P2_12_12_1$. Data Collection: see X-ray determination complex **6** (*vide supra*) μ(Mo $K\bar{\alpha}$) = 13.49 cm^{-1}, crystal size (mm), 0.52 x 0.25 x 0.20; *F*(000) = 1712, T = 130 K, $\omega/2\theta$ scan, $\Delta\omega = 0.80 + 0.35$ tg θ, $1 < \theta < 30$, total unique data 5419, No. of observations [$I \geq 3.0\ \sigma(I)$] 4112, observations/variables 9.10, $R = 0.056$, $R_w = 0.064$. Structural Analysis and Refinement: see X-ray determination complex **6** (*vide supra*). Enantiomorph selection was made by knowledge of the precursor compound stereochemistry. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

Synthesis

2,6-Bis(dibromomethyl)phenyl acetate (9). In a three necked flask, fitted with a reflux condenser, connected with a watertrap, **8** (10 g, 60 mmol) was dissolved in CCl_4 (100 mL) and some glass pearls were added. Bromine (12.3 mL, 240 mmol, 1.0 equivalent) was added dropwise over a period of 2 h under continuous irradiation with a Philips IR133372E/44*E9 photolamp, while the solution was gently under reflux. After the addition was completed the solution was heated and irradiated for an additional 12 h, by which time the bromine had completely disappeared. The solvent was removed *in vacuo* and the residue purified by crystallization from hexane/$CHCl_3$, affording **9** (20.0 g; 70 %) as white crystalline material: mp

142.6-143.4 °C; ^{1}H NMR: δ 2.43 (s, 3H), 6.60 (s, 2H), 7.20-7.56 (m, 1H), 7.90 (d, *J* = 7.2, 2H); ^{13}C NMR: δ 20.77, 32.87, 127.60, 131.74, 134.19, 139.70, 167.66. HRMS calcd for $C_{10}H_8Br_4O_2$ 475.726, found 475.727. Anal. Calcd for $C_{10}H_8Br_4O_2$: C, 25.03; H, 1.68; Br, 66.62. Found: C, 25.01; H, 1.63; Br, 66.82.

2-Hydroxy-benzene-1,3-dicarbaldehyde (10). A slurry of **9** (18.15 g, 38 mmol) and KOH (17.7 g) in H_2O (150 mL) was heated under reflux for 3 h. The resulting red mixture was cooled to room temperature and filtered into 20 % aqueous HCl (250 mL). The precipitate was isolated and crystallized from H_2O yielding **10** (3.81 g; 67 %) as white needles: mp 120.3-121.5 °C (lit.[19] 125 °C), ^{1}H NMR: δ 7.02-7.33 (m, 1H), 8.03 (d, *J* = 7.6, 2H), 10.56 (s, 2H), 12.00 (s, 1H); ^{13}C NMR (50 °C): δ 119.79, 123.18, 137.43, 163.53, 191.79; HRMS calcd for $C_8H_6O_3$ 150.032, found 150.031.

2,6-Bis(2-pyridin-2-yl-ethylimino-methyl)-phenol (12). A solution of **10** (208 mg, 1.39 mmol) and 2-pyridin-2-yl-ethylamine (**11**) (341 mg, 2.80 mmol, 1.01 equivalent) in MeOH (25 mL) was heated under reflux for 1 h. The resulting orange solution was dried over Na_2SO_4. Filtration and evaporation of the solvent gave pure **12** (498 mg, 100 %) as an orange semi-solid. ^{1}H NMR (DMSO-*d*6): δ 3.08 (t, *J* = 7.1, 4H), 3.97 (t, *J* = 7.1, 4H), 6.82 (t, *J* = 7.7, 1H), 7.20 (m, 2H), 7.28 (d, *J* = 7.7, 2H), 7.66 (m, 4H), 8.51 (m, 2H), 8.57 (s, 2H). ^{13}C NMR (DMSO-*d*6): δ 20.46, 58.52, 117.38, 121.07, 121.41, 123.31, 132.02, 136.32, 149.03, 159.07, 161.05, 162.28; HRMS calcd for $C_{22}H_{22}N_4O$ 358.179, found 358.178.

μ-Diacetato-μ-[2,6-bis(2-pyridin-2-yl-ethylimino-methyl)-phenolato]bisnickel(II)·perchlorate ·methanol (6). A solution of **10** (464 mg, 3.10 mmol) and **11** (797 mg, 6.53 mmol, 1.05 equivalent) in MeOH (20 mL) was heated under reflux for 1 h followed by addition of $Ni(OAc)_2 \cdot 4H_2O$ (1.55 g, 6.22 mmol, 1.0 equivalent). After 2 h reflux $NaClO_4 \cdot H_2O$ (436 mg, 3.10 mmol, 1.0 eq.) was added to the dark green solution. After heating under reflux for an additional hour, **6** (1.50 g, 67 %) could be isolated from the reaction mixture by cooling and subsequent filtration as a blue green powder. Recrystallization (twice) from methanol gave green crystals suitable for X-ray analysis. Anal. Calcd for $C_{26}H_{27}ClN_4Ni_2O_9 \cdot CH_3OH$: C, 44.77; H, 4.31; N, 7.73; Ni, 16.20; Cl, 4.89. Found, C, 44.51; H, 4.38; N, 7.57; Ni, 15.41; Cl, 4.90.

(*S*)-1-Benzyl-pyrrolidine-2-carboxylic acid (16). This compound was prepared according to a literature procedure.[26] Starting from (*S*)-pyrrolidine-2-carboxylic acid (**15**) (9.2 g, 0.08 mol), **16** (5.3 g, 32 %) was obtained as a white solid: mp 163.7-165.7 °C; $[\alpha]_D^{18}$ = -26.9 (c 1.0, EtOH) (lit.[26] mp 164-165 °C, $[\alpha]_D^{18}$ = -28.4 (c 1.0, EtOH)); ^{1}H NMR: δ 1.70-2.00 (m, 2H), 2.07-2.28 (m, 2H), 3.77 (m, 1H), 3.53-3.63 (m, 1H), 4.18 (dd, *J* = 50, *J* = 12, 2H), 7.20-7.40 (m, 5H), 8.20 (br s, 1H); ^{13}C NMR: δ 22.67, 28.72, 53.13, 57.56, 67.48, 128.86, 129.19, 130.32, 130.69, 170.85.

(*S*)-1-Benzyl-pyrrolidine-2-carboxylic acid methylester (17). Aqueous HCl (1 N, 50 mL) was added to **16** (3.6 g, 18 mmol) and this mixture was evaporated to dryness. This procedure was repeated once more. The remaining H_2O was stripped using MeOH (2 x 25 mL) and the residue was dissolved in MeOH (50 mL). Concentrated H_2SO_4 (1 mL) was added and the solution was heated under reflux for 16 h. The mixture was poured into 1 N Na[HCO_3] (200 mL). The H_2O layer was extracted with $CHCl_3$ (3 x 50 mL). The combined chloroform layers were washed with H_2O (25 mL), dried on $MgSO_4$ and the solvent evaporated in vacuo. The residue was distilled (130 °C, 1 mm Hg) using bulb to bulb distillation yielding

17 (2.4 g, 61 %) as a colourless oil. $[\alpha]_D^{18}$ = -85.7 (c 4.0, $CHCl_3$); ^1H NMR: δ 1.65-2.15 (m, 5H), 2.35 (m, 1H), 2.97-3.06 (m, 1H), 3.16-3.25 (m, 1H), 3.59 (s, 3H), 3.68 (dd, J = 95, J = 13, 2H), 7.15-7.30 (m, 5H); ^{13}C NMR: δ 22.74, 29.12, 51.43, 53.02, 58.48, 65.01, 126.82, 127.89, 128.96, 137.96, 174.25. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.23; H, 7.76. Found: C, 70.99; H, 7.79.

(*S*)-Pyrrolidine-1,2-dicarboxylic acid, 1-benzyl ester (24) (Z-(*S*)-proline). This compound was prepared analogous to a literature procedure.[30] Starting from **15** (57.0 g, 0.5 mol), **24** (99.6 g, 80 %) was isolated as a colourless oil which crystallized upon standing in a desiccator over P_2O_5. ^1H NMR: δ 1.80-2.30 (m, 4H), 3.40-3.64 (m, 2H), 4.32-4.45 (m, 1H), 5.05-5.12 (m, 2H), 7.20-7.38 (m, 5H), 10.70 (br s, 1H); ^{13}C NMR: δ 23.07, 23.89, 29.36, 30.49, 46.21, 46.60, 58.38, 58.87, 66.84, 66.99, 127.18, 127.30, 127.45, 127.64, 128.00, 128.09, 136.00, 154.28, 155.07, 176.26, 176.84 (lit: ^{13}C NMR: δ 176.60, 176.20, 155.05, 154.30, 135.95, 128.05, 127.40, 127.10, 66.90 (2x), 58.80, 58.25, 46.60, 46.05, 30.45, 29.25, 23.85, 23.00).[49]

(*S*)-2-(Aminocarbonyl)-1-pyrrolidinecarboxylic acid, phenylmethyl ester (26).[31] A solution of **24** (50 g, 0.20 mol) in CH_2Cl_2 (300 mL) was cooled to 0 °C. To this solution *N*-methyl-morpholine (21.0 g, 0.21 mol, 1.05 equivalent) was added at such a rate that the temperature remained below 5 °C. The resulting mixture was cooled to -15 °C and subsequently ethyl chloroformate (22.8 g, 0.21 mol, 1.05 equivalent), dissolved in CH_2Cl_2 (50 mL), was added at such a rate that the temperature did not rise above -15 °C. After stirring for 2 h at -20 °C to -15 °C the solution was cooled to -25 °C. Subsequently, gaseous NH_3 was bubbled through during 1 h at such a rate that the temperature did not exceed -20 °C. Stirring was continued for 1 h while the temperature was allowed to rise to 0 °C. Next the solution was poured into H_2O (200 mL). The separated CH_2Cl_2 layer was washed successively with 1 N HCl (2 x 50 mL), 1 N $NaHCO_3$ (2 x 50 mL) and brine (50 mL). After drying over Na_2SO_4 the solvent was evaporated *in vacuo* yielding **26** (44 g, 88 %) as a colourless oil which crystallized upon standing in a desiccator over P_2O_5. ^1H NMR: δ 1.83-2.37 (m, 4H), 3.40-3.58 (m, 2H), 4.26-4.38 (m, 1H), 5.07-5.20 (m, 2H), 5.74 (br s, 1H), 7.25-7.45 (m, 5H), 7.75 (br s, 1H); ^{13}C NMR: δ 23.44, 24.26, 28.75, 30.94, 46.79, 47.18, 58.26, 60.00, 60.28, 66.99, 126.32, 127.51, 127.79, 128.25, 128.92, 130.47, 133.25, 136.15, 174.39, 175.13.

(*S*)-Pyrrolidine-2-carboxylic acid amide (27). A mixture of **26** (10 g, 0.04 mol) and 5 % Pd/C (100 mg) in MeOH (100 mL) was shaken for 5 h in a Parr apparatus under a H_2 atmosphere (40 psi). After this time the Pd/C was filtered over Celite and the methanol was evaporated *in vacuo*. After crystallization from toluene pure **27** (4.0 g, 87 %) was obtained as a white crystalline material: mp 94.6-96.2 °C; $[\alpha]_D^{20}$ = -99.5 (c 2.0, EtOH); (lit.[32] mp 95-97 °C; $[\alpha]_D^{20}$ = -100.0 (c 2.0, EtOH)); ^1H NMR (CD_3OD): δ 1.90-2.05 (m, 3H), 2.28-2.41 (m, 1H), 3.06-3.16 (m, 1H), 3.17-3.27 (m, 1H), 3.83-3.90 (m, 1H); ^{13}C NMR (CD_3OD): δ 26.89, 32.17, 47.92, 61.32, 179.34 ppm. HRMS calcd for $C_5H_{10}N_2O$ 114.079, found 114.079.

(*S*)-1-Benzyl-pyrrolidine-2-carboxylic acid amide (18) (first route). A solution of *N*-benzyl-(*S*)-proline methylester **17** (2.1 g, 9.6 mmol) in MeOH (10 mL) was saturated with NH_3(g) by bubbling through for 15 min in a Carius tube. The mixture was heated at 80°C for 40 h. After removal of the solvent the residue was purified by crystallization from benzene yielding **18** (0.60 g, 49 %) as a white solid. Analytical data: *vide infra*.

(*S*)-1-Benzyl-pyrrolidine-2-carboxylic acid amide (18) (second route). A solution of (*S*)-prolinamid **27** (5.7 g, 50 mmol) and benzylbromide (8.55 g, 50 mmol) in CH_2Cl_2/MeOH (4 : 1, 50 mL) was stirred for 16 h. After this period the solvent was removed in vacuo and the residue dissolved in CH_2Cl_2 (100 mL). The CH_2Cl_2 layer was washed successively with aqueous 1 N $NaHCO_3$ (2 x 50 mL) and H_2O (50 mL) and dried over $MgSO_4$. Filtration and evaporation of the solvent in vacuo yielded a colourless oil which was purified by bulb to bulb distillation (160 °C, 0.05 mm Hg). The resulting oil solidified upon standing. Compound **18** (6.7 g, 66 %) was obtained as white crystalline material: mp 61.1-62.7 °C, $[\alpha]_D^{20}$ = -81.4 (c 1.0, $CHCl_3$); ^{1}H NMR: δ 1.65-1.78 (m, 2H), 2.11-2.34 (m, 2H), 2.82-2.96 (m, 1H), 2.92-3.00 (m, 1H), 3.08-3.17 (m, 1H), 3.66 (dd, *J* = 155, *J* = 14, 2H), 6.94 (br s, 1H), 7.17-7.35 (m, 6H); ^{13}C NMR: δ 23.68, 30.24, 53.35, 59.36, 67.05, 126.84, 128.06, 128.31, 138.20, 178.18; HRMS calcd for $C_{12}H_{16}N_2O$ 204.126, found 204.124. Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.58; H, 7.84; N, 13.73; Found C, 70.42; H, 8.06; N, 13.68.

(*S*)-2-Aminomethyl-1-benzyl-pyrrolidine (19). A solution of **18** (8.0 g, 39 mmol) in THF (50 mL) was added, under a N_2 atmosphere, to a suspension of $Li[AlH_4]$ (4.0 g, 105 mmol, 5.4 equivalent) in THF (100 mL). This mixture was heated under reflux for 16 h and subsequently cooled to 10 °C. Next 10 % aqueous KOH (6 mL) was carefully added and the resulting mixture was heated under reflux for 1 h until the salts were coloured white. After cooling to room temperature the salts were removed by filtration. These salts were again heated under reflux for 1 h with THF (100 mL) and H_2O (2 mL). After removing the salts by filtration the THF layers were combined and dried over Na_2SO_4. Filtration and evaporation of the solvent and bulb to bulb distillation (150 °C, 0.3 mm Hg) of the residue yielded **19** (6.0 g, 81 %) as a colourless oil. ^{1}H NMR: δ 1.28 (br s, 2H), 1.54-1.70 (m, 3H), 1.79-1.90 (m, 1H), 2.14 (m, 1H), 2.43-2.54 (m, 1H), 2.61-2.76 (m, 2H), 2.85-2.93 (m, 1H), 3.57 (dd, *J* = 204, *J* = 13, 2H), 7.13-7.34 (m, 5H); ^{13}C NMR: δ 22.74, 27.71, 43.92, 54.32, 58.81, 65.28, 126.61, 127.91, 128.40, 139.60. $[\alpha]_{578}^{20}$ = -91.9 (c 1.0, CH_2Cl_2); HRMS calcd for $C_{12}H_{18}N_2$: 190.147, found 190.146. Anal. Calcd for $C_{12}H_{18}N_2$: C, 75.74; H, 9.53; N, 14.72; Found C, 75.43; H, 9.45; N, 14.45. Racemic **19** was prepared starting from racemic proline *via* the above described procedures. This resulted in an overall yield of 21 % of racemic **19**, pure by ^{1}H and ^{13}C NMR spectroscopy.

Enantiomeric excess determination of 19. To a stirred solution of amine **19** (190 mg, 1 mmol) and NEt_3 (101 mg, 1.0 mmol) in $CDCl_3$ (2 mL) at -20 °C a solution of $MePSCl_2$ (**20**)[29] (74.5 mg, 0.5 mmol, 1.0 eq.) in 1 mL $CDCl_3$ was added. The resulting solution was stirred for 10 min and transferred to a NMR tube. The ^{1}H decoupled ^{31}P NMR spectrum showed 3 singlets at δ 66.43, 66.40 and 66.19 ppm in a ratio of 1 : 2 : 1 in the case of racemic **19**, whereas for enantiomerically pure (*S*)-**19**, obtained *via* the route given above, a single absorption at δ 66.40 ppm was found, indicating an enantiomeric excess ≥ 98 %.

μ-Hydroxo-μ-[2,6-bis[*N*-((*S*)-1-benzyl-2-yl-pyrrolidine)-formimidoyl]phenolato] bisnickel(II) bisperchlorate (7). A solution of dialdehyde **10** (150 mg, 1.0 mmol) and (*S*)-2-aminomethyl-1-benzyl-pyrrolidine (**19**) (380 mg, 2.0 mmol, 1.0 equivalent) in MeOH (50 mL) was stirred for 1 h at room temperature. Next, NaOH (80 mg, 2.0 mmol, 1.0 equivalent) and $Ni(ClO_4)_2 \cdot 6H_2O$ (732 mg, 2.0 mmol, 1.0 eq.) were added and the mixture was refluxed for 2.5 h. After precipitation from a CH_2Cl_2/Et_2O solvent mixture **7** (640 mg, 0.77 mmol, 77 %) of an orange solid was obtained. This material was purified by diffusion crystallization using a MeOH/di-*iso*propyl ether bilayer system to give **7** (329 mg, 40 %) as red-

orange crystalline material suitable for X-ray analysis. Anal. Calcd for $C_{32}H_{38}Cl_2N_4Ni_2O_{10}$: C, 46.48; H, 4.63; Cl, 8.57; N, 6.77; Ni, 14.19. Found: C, 46.31; H, 4.62; Cl, 8.42; N, 6.74; Ni, 14.06.

UV-Vis measurements. Complex **7** (5.1 mg, 6.2 μmol) dissolved in 5.0 mL CH_2Cl_2 and 5.0 mL H_2O (pH = 9.0) was stirred vigorously for 10 min. The CH_2Cl_2 phase was diluted 30 times with CH_2Cl_2. The H_2O phase was diluted 30 times with H_2O (pH = 9.0). Similar complex **7** (5.1 mg, 6.2 μmol) was dissolved in CH_2Cl_2 (5.0 mL) and diluted 30 times. UV-Vis spectra were recorded at 25 °C.

Epoxidation reaction - general remarks. Domestic bleach was used for the preparation of NaOCl solutions and was titrated before use by iodometric methods.[50] Aqueous *tert*-butyl hydroperoxide (70 %) and *tert*-butyl hydroperoxide (3 M) in *iso*-octane were purchased from Aldrich and analyzed by titration following literature procedures.[51] Chemical yields are given on basis of GC analysis or on basis of ^1H NMR analysis. Furthermore the epoxides were purified by flash chromatography on silica gel (CH_2Cl_2/hexane mixtures as eluens). In the cases were styrene oxide, *trans*-stilbene oxide and *para*-methoxy-*trans*-styrene oxide were isolated, they proved to be identical to authentic samples purchased from Aldrich and Duphar (^1H and ^{13}C NMR). Other epoxides were characterized with ^1H and ^{13}C NMR. The enantioselectivity of the epoxidation was analyzed either by chiral GC analysis (CP-cyclodextrin-β-2,3,6 M-19 (df = 0.25 μm) column) or by ^1H NMR using a chiral shift reagent Tris[3-(heptafluoropropylhydroxy methylene)-d-camphorato]europium ($Eu(hfc)_3$).

Epoxidation of alkenes using NaOCl and 6 or 7 (general procedure a). To a solution of alkene (1 mmol), **6** or **7** (1.5 - 2.0 mol%) and $[BnEt_3N]Br$ (30 mg) in CH_2Cl_2 (10 mL) was added NaOCl (3 mL bleach, 1.2 mmol ± 0.1 mmol) and H_2O (7 mL). This mixture was stirred vigorously at room temperature for 16 h whereafter a black precipitate was observed. The layers were separated and the organic layer was washed with H_2O (2 x 10 mL). After drying the organic layer on $MgSO_4$, filtration and removal *in vacuo* the product mixture was obtained as an oil. In a typical example starting from stilbene (**30**, 180 mg) pure (according to ^1H and ^{13}C NMR) *trans*-stilbene oxide (**39**) (70 mg, 0.36 mmol, 36 %) was obtained. Further data are collected in tables. When **7** was used, the e.e. of styrene oxide (**31**) was determined by ^1H NMR (*vide supra*): an e.e. of ≤ 5 % was found. The optical purity of *trans*-stilbene oxide (**39**) was determined by polarimetry. However, no rotation was observed.

Epoxidation of alkenes using NaOCl and 6 or 7 (general procedure b). To a solution of alkene (1 mmol), **6** or **7** (1.5 - 2.0 mol%), $C_{16}H_{34}$ (226 mg, internal standard) and $[BnEt_3N]Cl$ (30 mg) in CH_2Cl_2 (10 mL) NaOCl (3 mL bleach, 1.2 mmol ± 0.1 mmol) and H_2O (7 mL) were added. The H_2O layer was prepared beforehand, buffered with $Na_2B_4O_7$ and adjusted to the required pH with either 4 N NaOH or concentrated HCl. This mixture was stirred vigorously at room temperature for 16 h. The layers were separated and the organic layer was washed with H_2O (2 x 10 mL), filtrated over Al_2O_3 and analyzed by GC.

Epoxidation of alkenes using NaOCl and 6 or 7 employing trapping agents. See general procedure b. Either methyl sulfide **49** (10 mmol; 10 equivalent) or 2,6-di-*tert*-butyl-4-methylphenol **50** (10 mmol; 10 equivalent) was added at the start of the epoxidation.

Epoxidation of alkenes using *tert*-butyl hydroperoxide (70 % in H_2O) and catalyst 6 or 7 (phase transfer conditions, general procedure c). To a solution of alkene (1 mmol) and **6** or **7** (1.5 mol%) dissolved in CH_2Cl_2 (10 mL) was added a mixture of NaOH (100 mg) and *tert*-butyl hydroperoxide solution (1 mL, approximately 7 mmol) in H_2O (9 mL). This mixture was stirred vigorously for 20 h, the layers were separated and the organic layer was washed with 1 M Na_2SO_3/NaOH (2 x 10 mL) to remove the excess peroxide. Drying over $MgSO_4$, filtration and removal of the solvent *in vacuo* yielded an oil, which was analyzed by ^1H NMR. Data are collected in table 3. From the product mixtures, epoxides were isolated by chromatography. With styrene as substrate two products were obtained. Styrene epoxide (**31**) (5 %): ^1H NMR: δ 2.73 (dd, J = 6.0, J = 2.4, 1H), 3.07 (dd, J = 6.0, J = 4.6, 1H), 3.80 (dd, J = 4.6, J = 2.4, 1H), 7.30 (s, 5H). This proved to be identical to an authentic sample. PhCH[OO*t*-Bu]CH_2[OO*t*-Bu] (**59**) (26 %): ^1H NMR: δ 1.23 (s, 9H), 1.27 (s, 9H), 3.97 (m, 1H), 4.20 (m, 1H), 5.20 (m, 1H), 7.33 (s, 5H). ^1H NMR: δ 1.23 (s, 9H), 1.25 (s, 9H), 4.08 (dd, J = 4.0, J = 12.0, 1H), 4.23 (dd, J = 12.0, J = 8.0, 1H), 5.21 (dd, J = 8.0, J = 4.0, 1H), 7.24-7.38 (m, 5H); ^{13}C NMR: δ 26.21, 26.27, 76.69, 80.32, 80.47, 83.19, 126.86, 127.75, 128.09, 138.46. MS (RIBERMAG R 10-10C mass spectrometer (D.C.I.)): m/e 300 ($M(NH_4^+)$). When product **59**, was analyzed by GCMS (injection temperature 160 °C) styrene oxide (**31**), benzaldehyde (**32**) and *tert*-butanol were detected as decomposition products. In all other cases quantitative isolation of the epoxides proved to be difficult. However, samples of stilbene oxide (**39**) (65 %) and *trans*-β-methylstyrene oxide (**62**) (31 %) were obtained by chromatography which were pure by ^1H NMR spectroscopy and identical to an independent sample. Compound **39**: ^1H NMR: δ 8.89 (s, 2H), 7.27-7.41 (m, 10H); Compound **62**: ^1H NMR: δ 1.35 (d, J = 5, 3H), 2.94 (dq, J = 5, J = 2, 1H), 3.47 (d, J = 2, 1H), 7.12-7.27 (m, 5H).

Epoxidation of alkenes using *tert*-butyl hydroperoxide in isooctane (homogeneous conditions, general procedure d). A mixture of alkene (1 mmol), **7** (1.5 mmol%), pyridine (0.1 mL) and 3 M *tert*-butyl hydroperoxide (1 mL) in isooctane, dissolved in CH_2Cl_2 (10 mL) was stirred for 48 h at room temperature. For workup, see procedure c. Data are collected in table 4. Styrene (**29**) and stilbene (**30**) were recovered quantitatively after workup. Pure *para*-methoxy-*trans*-β-methylstyrene oxide (**65**) was isolated in 60 % overall yield by chromatograpy. This product was analyzed by ^1H NMR with $Eu(hfc)_3$ as chiral shift reagent and proved to be racemic. The reaction of **64** under the same conditions, without catalyst, yielded 20 % of epoxide (**65**) (^1H NMR).

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