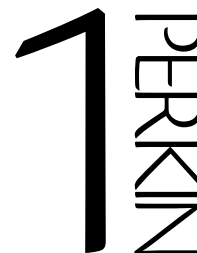# Aerobic epoxidation of alkenes using polymer-bound Mukaiyama catalysts

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Nickel(II) acetylacetonate bound to polybenzimidazole has been shown to be an efficient catalyst for the aerobic epoxidation of alkenes with an aldehyde as co-reactant. Rates of reaction and yields of epoxide are higher with this system than with dissolved Ni(II) acetylacetonate under otherwise identical conditions. The polymer-bound complex acts as a heterogeneous catalyst and can be recovered from the reaction mixture. Some loss of activity is observed upon re-use of the catalyst due to leaching of the metal complexes.

Introduction

The aerobic epoxidation of alkenes with a transition metal catalyst has been widely studied over the past decade. A well known, efficient method of alkene epoxidation in solution is the so-called 'Mukaiyama' procedure, in which an unfunctionalized alkene is epoxidized very efficiently using a transition metal β-diketonate complex as catalyst, molecular oxygen as oxidant and an aliphatic aldehyde as co-reactant.[1] For example, when bis(acetylacetonato)nickel(II) (Ni(acac)$_2$) is used as a catalyst, and isobutyraldehyde as a co-reagent, aliphatic and cyclic alkenes can be converted into the corresponding epoxides with yields ranging from 72% [(S)-limonene†] to 96% (norbornene†).[2] Other metal β-diketonate complexes, *e.g.* Co^{II}(acac)$_2$,[3] Mn^{II}(acac)$_2$,[3,4] and Fe^{III}(acac)$_3$[5] are effective as catalysts as well. Transition metal complexes such as Schiff's base complexes are also suitable for the aerobic epoxidation of alkenes with a co-reacting aldehyde. For example, cobalt(II) Schiff's bases give good results but these catalysts are not always selective for epoxidation.[6–12] Manganese–salen complexes have been used for the enantioselective aerobic epoxidation of alkenes with molecular oxygen and aldehydes as reagents. Enantiomeric excesses (ee's) as high as 92% are possible with this catalytic system.[13–17]

It has been reported in the literature that the epoxidation of alkenes by various oxidants can proceed very efficiently when a polymer-supported catalyst is used. For example, the epoxidation of propene, octene and other alkenes with hydroperoxide using a polymer-bound Mo^{VI}O$_2$(acac)$_2$ catalyst was shown to be possible with yields up to 100%.[18–22] A Jacobsen-type manganese catalyst has been anchored to various polymer supports and has been used with different oxidants to yield epoxides with ee's up to 95%.[23–25] The polymer-supported catalysts were thermo-oxidatively very stable and could be recycled without loss of activity.[26] An overview of polymer-supported alkene epoxidation catalysts has been published recently by Sherrington.[22]

In contrast to the oxidation reactions mentioned above, *aerobic* oxidations using polymer-bound catalysts are not widespread in the literature. A polyaniline-supported cobalt(II) catalyst was prepared by Das and Iqbal[27] and used for the aerobic epoxidation of alkenes. More recently, polystyrene-bound nickel complexes were synthesized by Han and Lei.[28] These catalytic systems showed activity in the aerobic oxidation of cyclohexene. A robust polymer-bound catalyst for the aerobic epoxidation of alkenes under Mukaiyama's conditions would be an interesting alternative for the epoxidation catalysts already described in the literature. It should have the high activity of a homogeneous catalytic system and the advantages of filtration and re-usability of a heterogeneous catalyst. As part of a project concerning the oxidation of terpenes for use in the flavors and fragrances industry we have used limonene as a model substrate. The oxidation of this compound is the first step in a synthetic route toward carvone, a spearmint flavor used in foodstuffs. We present our first studies aimed at the development of such a catalytic system in this paper.

Results and discussion

The results of limonene epoxidation after 4 hours are collected in Table 1. It can be seen that the polymer-bound catalyst PBI-Ni is more active (entry 1) than the homogeneous catalyst (entry 11) and also displays better selectivity toward formation of limonene oxide. PBI-Co is also very active but somewhat less selective (entry 2). PBI-Mo is not active at all with oxygen as an oxidant. No reaction was observed without catalyst at ambient temperature or with PBI resin without an attached metal complex. Neither did the reaction proceed when no aldehyde co-reactant was present. However, at 45 °C in the autoclave set-up, the reaction did proceed without catalyst after a variable induction period of approximately 50–100 minutes (entry 12). The main product of limonene epoxidation was in all cases the 1,2-epoxide, *i.e.* the endocyclic epoxide. The isopropenyl ring was found to be much less reactive toward epoxidation under the present conditions, in agreement with our earlier studies using the corresponding homogeneous nickel catalyst.[2] GC analysis showed the 1,2-epoxide to be a 60:40 mixture of the *cis* and *trans* isomers. In all cases the main by-product of the reaction

† The IUPAC name for limonene is 4-isopropenyl-1-methylcyclohexene, for norbornene is bicyclo[2.2.1]hept-2-ene and for carveol is 4-isopropenyl-1-methylcyclohex-6-en-2-ol.

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Table 1 Aerobic epoxidation of (S)-limonene with various polymer-bound catalysts[a]

| Entry	Catalyst	Substrate	Conversion (%)	Yield of epoxide[b] (%)
1	PBI-Ni	(S)-Limonene	93	74
2	PBI-Co		99	61
3	PBI-Mo		0	0
4	DowexA-Ni		51	31
5	DowexB-Ni		0	0
6	BP-Ni		0	0
7	PBI-Ni[c]		96	73
8	DowexA-Ni[d]		75 (100)	49 (25)
9	DowexB-Ni[d]		50 (100)	46 (73)
10	BP-Ni[d]		17 (100)	11 (44)
11	Ni(acac)$_2$		70	65
12	None[d]		94 (100)	45 (13)
13	PBI-Ni	α-Pinene	100	88
14	PBI-Ni	Oct-1-ene	88	52
15	PBI-Ni	Styrene[e]	43	23

[a] Reaction conditions: 5 ml CH$_2$Cl$_2$, 1 mmol substrate, 3 mmol isobutyraldehyde, 25.0 °C, O$_2$-filled balloon, 4 h. [b] In the case of limonene the 1,2-epoxide is formed as a 60:40 cis–trans mixture. In the case of α-pinene the reaction mixture was not analyzed for diastereomeric products. [c] At 25.0 °C in toluene, 7 bar pressure, 8% O$_2$ in N$_2$, 18 h. [d] At 45.0 °C in toluene, 7 bar pressure, 8% O$_2$ in N$_2$, ~2 h (in parentheses: 18 h). [e] 2,3-Dimethylvaleraldehyde was used instead of isobutyraldehyde.

was the 7,8-epoxide in yields to 10%, depending on the conditions. Diepoxide formation (at the cost of the 1,2-epoxide) was observed when the epoxidation was run for a long period of time (more than 5 hours). Otherwise, the diepoxide was formed in less than 1%. Some other by-products of the reaction included carveol† and unidentified isomers of carveol, all in small amounts up to 1%.

The differences between the various polymer resins used as the support are shown in entries 1 and 4–6. Apart from PBI, only the DowexA polymer **2** is a suitable support for the

1: PBI

2: DowexA

3: DowexB

4: BP
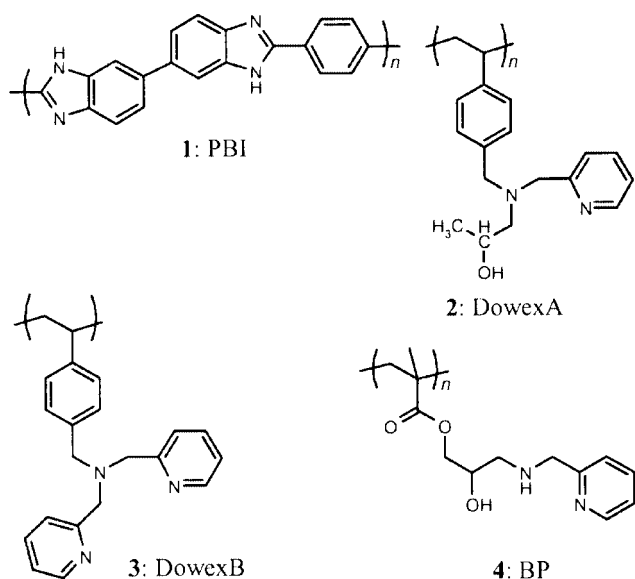
Ni(acac)$_2$ catalyst under ambient conditions, although the epoxidation reaction proceeds less selectively and more slowly than with PBI-Ni. It is understandable that the BP resin is not an effective support for the catalyst (entry 6) since it contains a secondary amine which has been observed to inhibit aerobic epoxidation using Ni^{II} and an aldehyde.[29] Why the DowexB resin **3** does not afford an active catalyst is not clear. Possibly the two pyridine ligands are both so tightly bound to the Ni^{II}
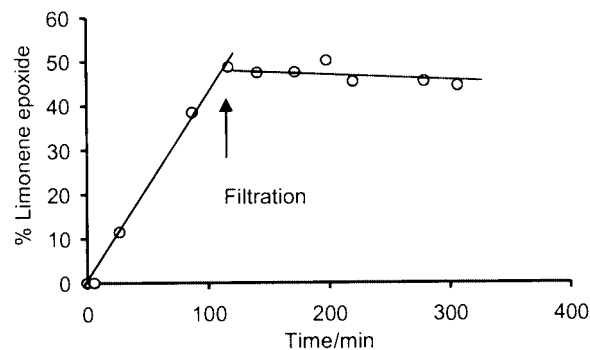
Fig. 1 Activity of the polymer-supported PBI-Ni catalyst after filtration. Conditions: 5 ml CH$_2$Cl$_2$, 1 mmol (S)-limonene, 3 mmol isobutyraldehyde, 1 mol% Ni^{II}, 25 °C, O$_2$-filled balloon. Filtration was carried out after 120 min (50% conversion) using a glass funnel.

center that the reaction is prevented. It is known that addition of an excess of pyridine to a reaction mixture containing Ni(acac)$_2$ completely inhibits the reaction[2] since two pyridine molecules are coordinated to the Ni^{II} center. The DowexA resin has only one pyridine ligand which seems to decrease the reactivity of the Ni center, but does not completely inhibit the reaction.

At higher pressure in the autoclave set-up the reactivity of the polymer-bound catalysts was quite different (Table 1, entries 7–10). Using PBI-Ni, (S)-limonene could be oxidized efficiently at 25 °C and 7 bar pressure (entry 7). Rather remarkably, the other three supported catalysts were not active at 25 °C and the temperature had to be raised to 45 °C in order to obtain some catalytic activity. The uncatalyzed (free radical) reaction at 45 °C (entry 12) displayed a similar epoxidation selectivity to DowexA-Ni (entry 8) whereas DowexB-Ni and BP-Ni (entries 9 and 10) were less active and selective. We therefore conclude that the latter two polymer supports inhibit the reaction as was suggested above (*vide infra*). The selectivity of these catalysts is very low at high conversions, which might also be due to the high temperature which favors uncatalyzed free radical oxidations at the expense of a catalyzed reaction.

Some other alkenes were tested as substrates for the aerobic epoxidation with the most active catalyst PBI-Ni (Table 1, entries 13–15). The epoxidation of α-pinene and oct-1-ene was very efficient. Styrene epoxidation however was slow, and probably polymers were also formed as reaction products.

The PBI-Ni catalyzed epoxidation of (S)-limonene was shown to be heterogeneous (Fig. 1) since the reaction stopped immediately when the polymer catalyst was filtered off. The filtered reaction mixture was analyzed for nickel content using atomic absorption spectroscopy (ICP). It appeared that ~20% of the original Ni^{II} present on the polymer had leached into the solution, but this unidentified Ni species was not active as an epoxidation catalyst. Clearly, the ligand environment of Ni^{II} is very important for the catalytic activity. ICP analysis of the used polymer confirmed the ~20% loss of nickel content. When the used PBI-Ni was washed with CH$_2$Cl$_2$ and tested again in a second epoxidation run, only 30% of the original epoxidation activity was left (Fig. 2). This is in contrast to a Mo^{VI} loaded PBI support which has been shown to be very thermo-oxidatively stable and retains activity on recycling.[21,26] The Ni^{II} loaded resin described here appears not to be as stable towards oxidative radical conditions.

The polymer-catalyzed epoxidation appears to display the same features as the homogeneous Ni(acac)$_2$ catalyzed reaction.[2] First, addition of a radical trapping compound (2-*tert*-butyl-4-methylphenol) during the reaction inhibited the epoxidation completely. The presence of this reagent at the start of the reaction prevented epoxidation from occurring at all.

Table 2 Analytical data of polymer-bound metal complexes

	Ni-**1**	Co-**1**	Mo-**1**	Ni-**2**	Ni-**3**	Ni-**4**
Metal loading (mmol g^{-1} resin)	0.33	0.28	1.78	1.36	1.26	0.44
Metal weight (mg g^{-1} resin)	19.4	16.5	26.8	79.8	74.0	25.8
% Metal	1.9	1.6	2.7	8.0	7.4	2.6
Ratio ligand : metal	9.8 : 1	11.6 : 1	1.8 : 1	2.6 : 1	2.5 : 1	9.1 : 1
%C						
Calculated[a]	77.9	77.9	77.9	76.57	79.97	62.4
Found	Nd	Nd	Nd	65.8	65.6	54.0
%H						
Calculated[a]	3.9	3.9	3.9	7.85	6.71	7.24
Found	Nd	Nd	Nd	7.0	6.1	7.0
%N						
Calculated[a]	18.2	18.2	18.2	9.92	13.33	11.2
Found	Nd	Nd	Nd	5.3	6.7	4.1

[a] Calculated for the *uncomplexed* polymer. Decreased weight percentages after complexation indicate that metal is complexed to the ligand.
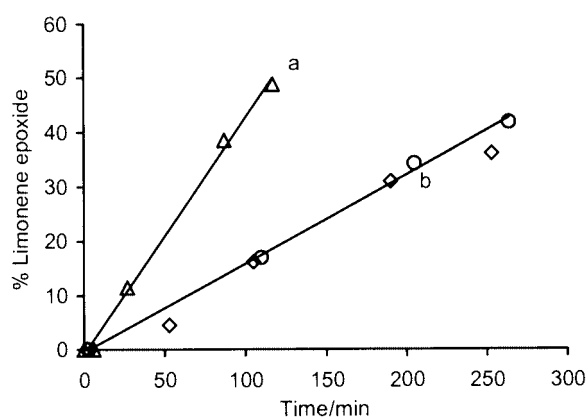

Fig. 2 Re-use of the PBI-Ni catalyst. Conditions: 5 ml CH$_2$Cl$_2$, 1 mmol (*S*)-limonene, 3 mmol isobutyraldehyde, 1 mol% Ni^{II}, 25 °C, O$_2$-filled balloon. a: fresh PBI-Ni catalyst, b: 2nd run with the same batch of PBI-Ni catalyst.

A mixture of *cis*- and *trans*-stilbene oxide was obtained when (*Z*)-stilbene was used as a substrate. This means that the epoxidation reaction takes place in two steps as observed with autoxidation chemistry, and not *via* a concerted peracid mechanism. Furthermore, the reaction did not proceed in the absence of a branched aliphatic aldehyde; without a Ni catalyst it proceeded only very slowly after addition of MCPBA. These factors point to a radical reaction *via* the same mechanism as the Ni(acac)$_2$-catalyzed reaction in homogeneous solution. The experiments presented above have demonstrated that the ligand environment of the Ni^{II} catalyst in the aerobic epoxidation using the Mukaiyama system is crucial. This leads us to believe that the reaction largely proceeds in the coordination sphere of Ni^{II}, as we have proposed earlier.[2]

Conclusions

The polymer-supported nickel(II) complex PBI-Ni turns out to be a very active and selective catalyst for the epoxidation of alkenes under 'Mukaiyama's conditions'. The epoxidation of (*S*)-limonene proceeds more efficiently and gives a higher yield when it is catalyzed by PBI-Ni than by the soluble Ni(acac)$_2$ catalyst. The reaction is heterogeneous and the catalyst can be recovered from the reaction mixture. Unfortunately, upon regeneration of the polymer-supported nickel complex, the catalyst loses some activity which is due to leaching of some inactive metal complex. Further studies will be aimed at reducing this leaching effect.

Experimental

Materials

CH$_2$Cl$_2$ was dried over CaCl$_2$ and distilled from CaH$_2$ under dry nitrogen and stored over molecular sieves. All other solvents and aldehydes were distilled before use. Oxygen was obtained from Air Liquide. All alkene substrates were commercial samples (Aldrich or Fluka, 96–98%) and were purified by vacuum distillation. Epoxide products were identified using gas chromatography and were compared to authentic samples. Ni(acac)$_2$ was purchased from Fluka (95%). PBI resin **1** was a gift from Hoechst-Celanese, DowexA and DowexB resins (**2** and **3**) were from the Dow Chemical company and BP resin **4** was from the BP company.

Instrumentation

GC analyses were performed on a Varian 3800 instrument with a Supelco fused-silica capillary column (15 m length, 35 μm ID, $d_f = 1.0$) with a FFAP stationary phase. Data were analyzed with Varian Star 5.2 software. Metal analyses were carried out using simultaneous/sequential inductively coupled plasma atomic emission spectroscopy (ICP-AES) on a Spectroframe instrument (Spectro Analytical Instruments). A 500 ppb nickel(II) nitrate solution in dilute nitric acid (Spectrosol, BDH Chemicals) was used as a standard.

Preparation of the polymer-supported complexes

The four resins (PBI **1**, DowexA **2**, DowexB **3** and BP **4**) were stirred overnight in aqueous 1 M NaOH, washed with H$_2$O until neutral, then extracted in a Soxhlet with acetone (24 h) and finally dried under vacuum. The attachment of the catalysts was achieved by refluxing a mixture of the resin with an excess of the appropriate M(acac)$_n$ complex in toluene (50 ml) for 48 h. The resulting resins were purified by extraction in a Soxhlet with toluene for 48 h and dried *in vacuo* at 40 °C (48 h). Metal contents were determined by microanalysis. The results of all metal analyses and microanalytical analyses are summarized in Table 2.

Description of the catalytic system

Epoxidation at ambient conditions. Alkene (1 mmol), aldehyde (3 mmol), and the appropriate amount of polymer complex corresponding to 0.01 mmol of metal as the catalyst, were stirred (1000 rpm) in CH$_2$Cl$_2$ (5 ml) at 25.0 ± 0.5 °C under 1.0 atm of oxygen. Unless indicated otherwise, the experiments were carried out with (*S*)-limonene as the substrate and iso-

butyraldehyde as the co-reagent. 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 using 1,2,4-trichlorobenzene as the external standard.

Epoxidation at high pressure. The epoxidation reactions at high pressure were performed in a Premex autoclave reactor with Hastelloy C276 wet parts, equipped with a HC276 Dean–Stark water separator, a 4-blade stirrer (1500 rpm), a sintered HC276 gas-inlet (5 µm frit) and a sampling tube. The temperature was regulated with a Premex C-M2 control unit to ± 0.1 °C. The nitrogen and oxygen gas inlet was regulated by mass-flow controllers (MFC's) and could be controlled to $\pm 0.1\%$ v/v O_2 in N_2. After depressurizing, the exhaust gas was cooled (-80 °C) to condense any vapor that was present. The gas was then analyzed for carbon dioxide and carbon monoxide with a Maihak Multor 610 CO_2/CO analyzer (IR detection) and for oxygen content with a Servomex 570A O_2 analyzer. Dipentene [60 mmol, a mixture of (R)- and (S)-limonene] and toluene (150 ml) were loaded into the autoclave and the Dean–Stark cooler was filled with toluene. This mixture was equilibrated for at least 1 h at 25.0 °C in an atmosphere of 8.5% v/v O_2 in N_2 (7 bar total pressure). No reaction was observed during this period. The autoclave was opened and the appropriate amount of polymer-bound catalyst (0.06 mmol, 0.1 mol% of metal catalyst), and isobutyraldehyde (180 mmol) were added quickly and the autoclave was closed and pressurized again. This was taken as time $t = 0$. During the reaction the pressure was maintained at 7.0 ± 0.1 bar and the temperature at 25.0 ± 0.1 °C. The stirring rate was 1500 rpm. Samples were taken regularly and analyzed with GC using 1,2,4-trichlorobenzene as the external standard and 2-*tert*-butyl-4-methylphenol as a stabilizer (radical trapping agent). The oxygen content of the exhaust gas was registered and the CO_2 and CO content monitored on-line in real-time using a personal computer.

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