



Development of protocols for the separation of Os catalysts from organic products in the catalytic dihydroxylation of olefins

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Abstract

Different approaches were investigated to achieve separation of osmium species from products in the course of the asymmetric dihydroxylation (AD) reaction. Prerequisite for these examinations was the development of a routine method for the detection of electrophilic osmium species in organic product solutions. For recycling of the catalyst an osmium alkaloid complex was immobilised by introducing an ionic group into the ligand and embedding the catalyst in a polyelectrolyte matrix. In addition, the native polymeric aminosugar chitin was used as ligand as well as a support in the dihydroxylation for the first time. These chitin-based catalysts showed good productivities and retention of osmium from the products was ensured using NMO as the oxidant. However, the catalytic reaction did not proceed enantioselectively.

Enantiomerically enriched diols were obtained in high yields without significant contamination of osmium applying a homogeneous AD with bleach as the oxidant with a downstream separation of the 1,2-diol from the catalyst by extraction. The remaining osmium-containing solution has been recycled up to eight times without loss of activity and enantioselectivity.

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1. Introduction

The catalytic asymmetric *cis*-dihydroxylation (AD) of olefins, discovered by Sharpless in 1988, is the most effective tool to obtain a wide range of chiral vicinal diols which are of interest for fine chemicals and pharmaceuticals [1]. Osmium tetroxide or potassium osmate as a precursor in combination with cinchona alkaloid-based ligands have been found to be a general class of chemo- and enantioselective catalysts. Due to the expensiveness and toxicity of osmium tetroxide various efforts have been launched to remove and recycle these catalysts effectively [2,3]. To achieve this aim most often functionalization of the alkaloid ligand with suitable groups has been performed in order to vary the solubility behaviour or to anchor it onto different supports. So far, both organic polymers as

well as inorganic materials have been examined as catalyst support. For example, the co-ordination of OsO₄ to poly-(4-vinylpyridine) [4], the embedding of OsO₄ alkaloid complexes into polymer chains [5–12] and microencapsulation [13–16] were reported. A more sophisticated system of homogeneous catalytic reaction followed by trapping OsO₄ in the pores of an Amberlite resin bearing residual vinyl groups was developed by Song et al. [17]. Also inorganic porous or layered supports such as silica [18–20], SBA-15 [21,22], hydrotalcites [23,24] and ion exchangers [25] were used to ensure a complete separation of the catalyst and product. In addition, soluble OsO₄ catalysts with PEG ether or hydroxyethyl sulfon chains in the alkaloid ligand have been recycled by extraction/precipitation after the reaction [26–32]. More recently an interesting method for Os recycling was published by Chandrasekhar et al. [33]. Here, polyethylene glycol was used as both an encapsulation and a reaction medium in the AD applying NMO as oxidant. Thus, the dihydroxylation reaction occurred at fast rate and a five-fold recycling of the catalyst without

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a significant decrease in yield and enantioselectivity was possible.

Despite the numerous efforts mentioned above there exists no general protocol for an easy separation of high valent osmium species and the organic products. Disadvantages are, from case to case, significant loss of osmium tetroxide, no reliable Os analyses and product contamination, insufficient stability of the support, as well as the decrease of activity and selectivity of the catalyst.

Here, we present the development and comparison of different approaches for the efficient separation of the organic products and the osmium catalyst in the AD. On the one hand, the encapsulation of dihydroxylation catalysts into polyelectrolytes [34] is shown. On the other hand, effective retention of the active catalyst is achieved by co-ordination of osmium tetroxide to the polyaminosugar chitin. Finally, the separation of 1,2-diols from the catalyst via an aqueous biphasic homogeneous system is demonstrated.

2. Experimental

General: ^1H and ^{13}C NMR spectra were recorded on a Varian UNITYPLUS 300 and 500 (300 and 500 MHz). Chemical shifts are given in ppm with respect to TMS, coupling constants are reported in Hz. Gas chromatograms were recorded on a Hewlett-Packard HP 5890 equipped with a HP5 column and a MSD 7673 detector. HPLC was operated on a Hewlett-Packard HP liquid chromatograph. The absolute configuration of the chiral 1,2-diols was determined by comparison with original samples prepared with AD-mix α and AD-mix β [1]. Optical rotations were measured on a

Perkin-Elmer 241 polarimeter. Mass spectra were obtained on an Autospec (Micromass). Elemental analyses were determined with an Optima 3000 XL (Perkin-Elmer) and a EA 1110 (CE Instruments). The polymer bond aminoalcohol and amines as well as the polymeric aminosugars were purchased from Argonaut Technologies, Polysciences and Aldrich and used as received.

2.1. Quantitative osmium analysis

Calibration curve (Fig. 1): Calibration samples were prepared by stirring 20 mg Argopore Trisamine MP (Argonaut Technologies) in 100 ml of dichloromethane solutions containing OsO_4 in the range of 0.027–1.08 mg (diluted from a stock solution) and 1 ml (0.01 mmol) of the standard $\text{PtCl}_2(1,5\text{-C}_8\text{H}_{12})$ (1.95 mg Pt). After 24 h, the loaded polymer was filtrated, washed with dichloromethane and dried on air. Then, the polymer sample was placed on a polycarbonate foil to record the X-ray fluorescence spectra (ED 2000, Oxford Instruments). The intensity ratio of fluorescent lines $\text{OsL}\alpha$ and $\text{PtL}\alpha$ was drawn as a function of the Os concentration in dichloromethane.

Leaching investigations of the reaction solutions: 1 ml of a 0.01 mol stock solution of $\text{PtCl}_2(1,5\text{-C}_8\text{H}_{12})$ (1.95 mg Pt) in dichloromethane was added to the dichloromethane solution which was obtained by extracting the reaction mixture. The volume of this solution was filled up to 100 ml with dichloromethane, and 20 mg of Argopore Trisamine MP was added, then the mixture was stirred for 24 h. The polymer was filtered off, air-dried, and the osmium content was determined by X-ray fluorescence spectroscopy (XRF) analysing the $\text{OsL}\alpha/\text{PtL}\alpha$ signal ratio.

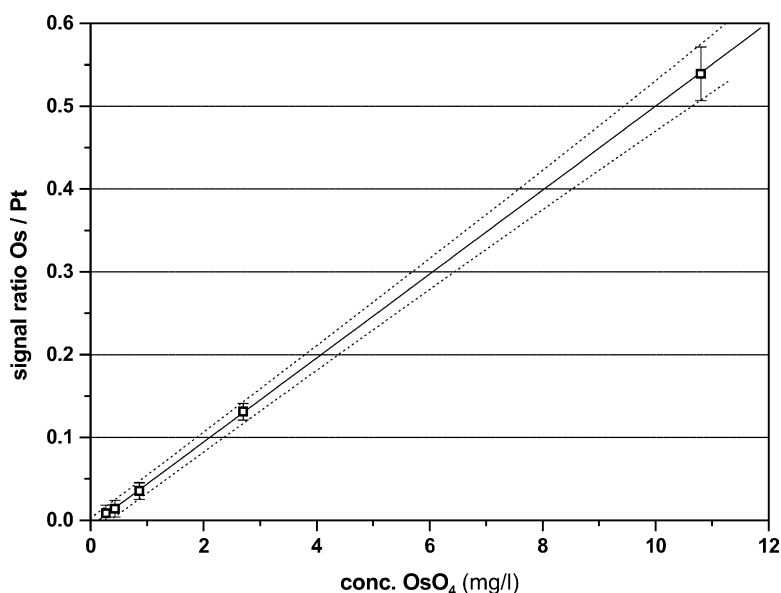


Fig. 1. Calibration curve of osmium content. Margins of error are shown by the dotted lines. An error of 6% was estimated for concentrations above 1 mg Os/l. At lower concentrations an increasing deviation should be expected which is caused by inhomogeneities of the Os polymer complex on the XRF target.

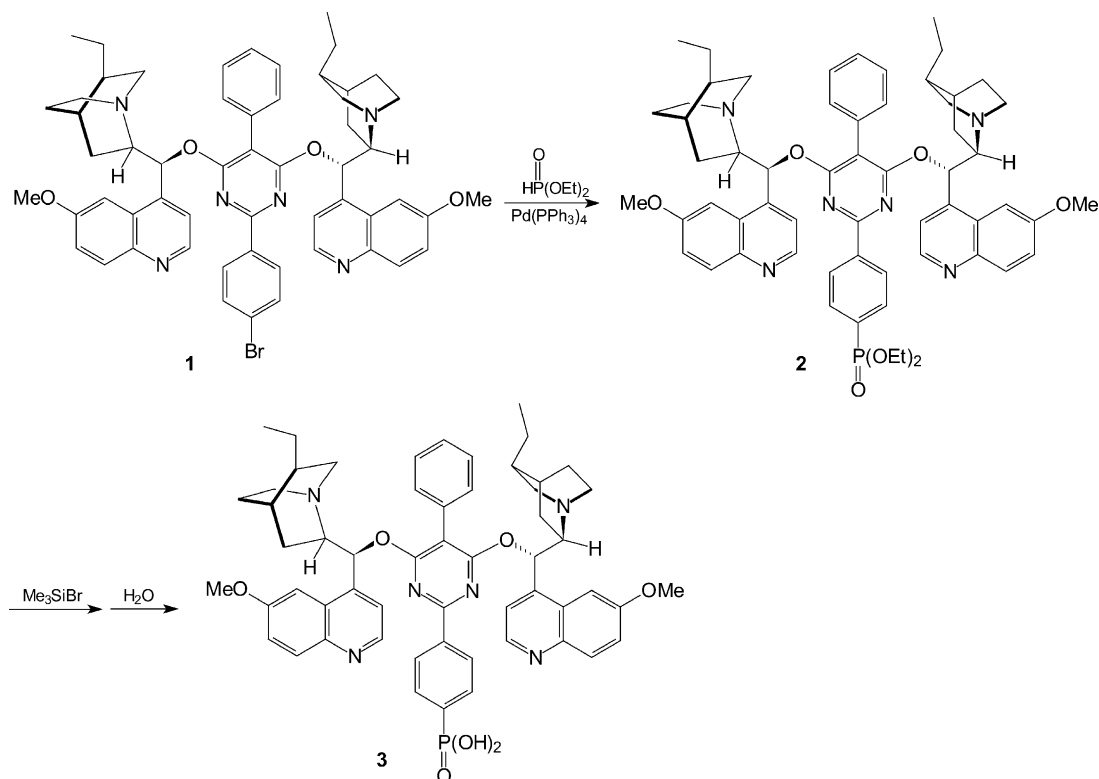


Fig. 2. Synthesis of (DHQD)₂PYR-P(O)(OH)₂ 3. The aryl bromide **1** was prepared according to a literature procedure [29].

2.2. Preparation of a polyelectrolyte-supported OsO₄-(DHQD)₂PYR catalyst

2.2.1. Synthesis of the ligand (DHQD)₂PYR-P(O)(OH)₂ 3 (Fig. 2)

2.2.1.1. (DHQD)₂PYR-P(O)(OEt)₂ 2. The palladium-catalysed introduction of the phosphonate group was realised by analogy with known procedures [35,36]. 6.03 g (6.3 mmol) of **1**, 0.87 g (6.3 mmol) diethyl phosphite, 0.71 g (7.0 mmol) triethylamine and 0.73 g tetrakis(triphenylphosphine)palladium (0) (0.63 mmol) in 10 ml toluene were heated under an inert atmosphere at 90 °C for 20 h. After cooling 50 ml dichloromethane was added and the reaction mixture was extracted three times with 10 ml H₂O each. The organic solution was dried over Na₂SO₄ and the solvent was evaporated. The residue was purified by column chromatography on silica gel (eluent: ethyl acetate/hexane/methanol 5:2:3). Yield: 1.9 g (30%); [α]_D²⁰ (methanol, c = 1.0): -284.8°; ³¹P NMR (CH₃OH): δ = 18.8; ¹H NMR (CD₃OD): δ = 0.67 (6H, m, CH₃), 1.24–1.30, (14H, m, CH₃CH₂OP + CH), 1.45–1.6 (6H, m, CH_{aliph}), 2.17 (2H, t, J = 11.5 Hz, CH_{aliph}), 2.50–2.90 (8H, m, CH_{aliph}), 3.09 (2H, t, J = 8.5 Hz, CH_{aliph}), 3.97 (6H, s, CH₃O), 4.02 (4H, dq, J = 6.8, 1.3 Hz, CH₂OP), 4.6 (2H, m, CH_{aliph}), 7.05 (2H, d, J = 1.9 Hz, CH_{arom}), 7.19–7.26 (2H, m, CH_{arom}), 7.37–7.41 (2H, m, CH_{arom}), 7.52–7.60 (4H, m, CH_{arom}), 7.67–7.77 (5H, m, CH_{arom}), 8.01 (2H, d, J = 9.3 Hz,

CH_{arom}), 8.68 (2H, d, J = 4.7 Hz, CH_{arom}); ¹³C NMR (CD₃OD): δ = 12.7, 16.6 (d, ³J_{CP} = 6.1 Hz, CH₃CH₂OP), 21.6, 25.4, 27.3, 27.5, 29.6, 38.2, 50.8, 52.2, 56.7, 60.0, 64.0 (d, ²J_{CP} = 5.8 Hz, CH₂OP), 78.3, 102.4, 107.4, 119.4, 123.9, 128.1, 128.9 (d, J_{CP} = 14.9 Hz), 129.8, 130.3, 131.7, 131.9, 132.1, 132.3, 141.5 (d, J_{CP} = 3.3 Hz), 145.1, 146.9, 148.4, 160.3, 160.9, 167.8. -C₆₀H₆₉N₆O₇P (961.44).

2.2.1.2. (DHQD)₂PYR-P(O)(OH)₂ 3. 1.2 g (1.25 mmol) **2** was stirred in 20 ml trimethyl bromosilane under an inert atmosphere at room temperature for 24 h. The excess silane and volatile compounds were removed carefully in vacuum (silyl ester: ³¹P NMR (DMSO): δ = 12.3) and the residue was dissolved in a mixture of 5 ml THF and 1 ml H₂O, stirred for 1 h and then the solvent was removed completely in vacuum.

Yield: 1.9 g (99%); MS (LSIMS, matrix “magic bullet”): m/z 961 [M + 1]⁺; [α]_D²⁰ (methanol, c=1.0): -324.1°; ³¹P NMR (CH₃OH): δ = 14.7; ¹H NMR (CD₃OD): δ = 0.72 (6H, m, CH₃CH₂), 1.62–1.99 (12H, m, CH_{aliph}), 2.32 (2H, t, J = 10.5 Hz, CH_{aliph}), 2.88 (2H, t, J = 10.4 Hz, CH_{aliph}), 3.15–3.71 (8H, m, CH_{aliph}), 4.02 (2H, t, J = 9.5 Hz, CH_{aliph}), 4.27 (6H, s, CH₃O), 7.24–7.31 (2H, m, CH_{arom}), 7.61–7.98 (7H, m, CH_{arom}), 8.17–8.21 (4H, m, CH_{arom}), 8.29–8.33 (4H, m, CH_{arom}), 9.00 (2H, d, J = 5.9 Hz, CH_{arom}); ¹³C

¹ J_{CP} could not be identified due to overlapping.

Table 1
Os chitin catalysts

Charge number	OsO ₄ in acetonitrile (mg)	OsO ₄ in acetonitrile (mmol)	mmol OsO ₄ /25 mmol chitin	mmol OsO ₄ /mmol chitin
I	508	2	0.34	0.0136
II	317.5	1.25	0.45	0.018
III	127	0.5	0.26	0.0104
IV	63.5	0.25	0.2	0.008
V	31.75	0.125	0.125	0.005

An additional catalyst (charge number VI) was prepared according to the general procedure except that 508 mg chitin (2.5 mmol) and 1.271 g OsO₄ (5.0 mmol) were added into 25 ml acetonitrile (24 h stirring). 8.4 mol% of the total OsO₄ amount was complexed (0.084 mmolOsO₄/1 mmol chitin).

NMR (CD₃OD):² δ = 12.2, 19.6, 23.9, 24.5, 26.0, 35.7, 50.3, 51.6, 59.2, 59.4, 73.3, 104.0, 107.7, 120.7, 124.6, 128.8 (J = 14.7 Hz), 129.4, 129.6, 130.5, 130.9, 131.0, 131.1, 131.5, 135.2, 135.8, 137.6, 139.2 (d, J = 3.0 Hz), 142.6, 153.2, 161.7, 162.8, 166.5. –C₅₆H₆₁N₆O₇P (961.44).

2.2.2. Preparation of the catalyst

1.034 g (6.4 mmol) poly(diallyldimethylammonium chloride) (PDADMAC) was dissolved in 50 ml H₂O. Under stirring 0.554 g (0.576 mmol) **3** was dissolved in 2 ml H₂O. Then 0.58 ml 2N NaOH and 23.6 mg (0.064 mmol) K₂[OsO₂(OH)₄] were added. This mixture was merged with the PDADMAC solution. The catalyst solution was stirred overnight at room temperature. It was filled into a syringe equipped with a 1/16 in. capillary made of stainless steel. Droplets with a diameter about 4–5 mm were formed by dropping the mixture on a polypropylene plate. They were dried in air to form plain lens-shaped catalyst particles (yield: 1.59 g). One-eighth of them was used in one catalytic run.

A catalyst with a higher molar ratio of PDADMAC was obtained by the same procedure except that the following components were used: 10.336 g (64 mmol) PDADMAC, 276.8 mg (0.288 mmol) **3**, 0.29 ml 2n NaOH, 11.8 mg (0.032 mmol) K₂[OsO₂(OH)₄]. A quarter of the catalyst mass (yield 10.886 g) was employed in one run.

2.3. Preparation of OsO₄ chitin catalysts

General procedure: A series of catalysts was prepared by stirring of 5.08 g chitin (25 mmol) in 100 ml acetonitrile (containing different amounts of OsO₄ in the range of 0.125–2.0 mmol) for 24 h. The chitin catalysts were filtered off, washed with acetonitrile and dried in air. The OsO₄ loading was determined by the weight increase and confirmed by determining uncomplexed OsO₄ in the solution. In Table 1, the prepared catalysts are listed.

2.4. Retention of OsO₄ with nucleophilic scavenger polymers

Twenty milligrams of the scavenger polymers **4–8** (Fig. 7) or chitin or chitosan were stirred in 100 ml of a solution of OsO₄ in dichloromethane (concentration 1 and 5 mg/l, respectively) for 24 h. The polymer was filtered off and 1.0 ml (0.01 mmol) of a solution of PtCl₂(1,5-C₈H₁₂) in dichloromethane was added to the filtrate. Then, the volume was filled up to 100 ml with dichloromethane. 20 mg of Argopore Trisamine MP was added and the mixture was stirred for 24 h. The polymer was filtered off and air-dried. The osmium content was determined with XRF.

2.5. Catalytic procedures

2.5.1. Dihydroxylation using heterogenised catalysts

Method A (PDADMAC catalyst): The appropriate amount of the PDADMAC catalyst (containing 0.008 mmol K₂[OsO₂(OH)₄], 0.072 mmol (DHQD)₂PYR-P(O)(OH)₂ and 0.8 mmol PDADMAC) and 2.0 mmol olefin were stirred in 7.5 ml *tert*-BuOH/7.5 ml buffer pH 12 at 25 °C using a Schlenck tube. NaOCl (3 mmol) was added and the stirring was continued for 1 h. The reaction solution was quenched with 2 g Na₂SO₃, stirred for 30 additional minutes and extracted three times with 10 ml dichloromethane each. The combined CH₂Cl₂ solutions were dried with Na₂SO₄. The drying agent was filtered off. Then, 1 ml of a 0.001 M solution of PtCl₂(1,5-C₈H₁₂) in CH₂Cl₂ was added to the filtrate. Finally, the volume was filled up to 100 ml with CH₂Cl₂. Conversion, yield, and enantioselectivity were determined by GC/MS and HPLC, osmium leaching by XRF according to the above mentioned method.

Method B: The experiments were performed similar to method A except applying another reaction medium. Instead of 7.5 ml *tert*-BuOH/7.5 ml buffer pH 12, a mixture of 7.5 ml *tert*-BuOH/ 7.5 ml H₂O and 4 mmol K₂CO₃ was used.

Method C: The experiments were run using method B with modified volume of the reaction medium (22.5 ml *tert*-BuOH/ 22.5 ml H₂O, 12 mmol K₂CO₃) and using a catalyst with a higher molar ratio of PDADMAC (16 mmol PDADMAC instead of 0.8 mmol).

Os chitin catalysts and NMO: 2.0 mmol α -methylstyrene and the appropriate amount of the Os-chitin catalyst were stirred in a mixture of 7.5 ml *tert*-BuOH/7.5 ml buffer pH 5 at 25 °C. 2.2 mmol NMO was added and the stirring was continued for 24 h. Then, the reaction solution was quenched with Na₂SO₃. The catalyst was filtered off and the filtrate was extracted three times with 10 ml dichloromethane. The combined organic solutions were dried using Na₂SO₄. Sodium sulphate was filtered off and 1 ml of a 0.001 M solution of PtCl₂(1,5-C₈H₁₂) in dichloromethane was added to the filtrate. The volume was filled up to 100 ml with dichloromethane. Conversion and yield were determined by GC/MS. Osmium leaching was investigated according to the procedure mentioned above.

² ¹J_{CP} could not be identified.

Os chitin catalysts and NaOCl: Instead of the *tert*-BuOH/buffer solvent a mixture of 7.5 ml *tert*-BuOH/7.5 ml H₂O/4 mmol K₂CO₃ was used as reaction medium. Apart from that, the procedure was carried out as described above applying NMO as oxidant.

2.5.2. Recycling of the active metal using a homogeneous dihydroxylation system

2.0 mmol α -methylstyrene, 0.01 mmol K₂[OsO₂(OH)₄], and 0.03 mmol (DHQD)₂PHAL were stirred in a mixture of 10 ml H₂O/10 ml *tert*-BuOH and 4.0 mmol K₂CO₃ at room temperature using a Schlenck tube. 3.0 mmol NaOCl was added and stirring was continued for 2 h. Then, the reaction mixture was extracted twice with 10 to 45 ml dichloromethane. The organic solution was used for the product analysis. Ten millilitre *tert*-BuOH, 2.0 mmol α -methylstyrene, 0.03 mmol (DHQD)₂PHAL and 3.0 mmol NaOCl were added to the aqueous catalyst solution and the mixture was stirred again for 2 h. Extractions with dichloromethane and reuses of the aqueous catalyst solution were repeated five to eight times until a decrease of conversion, product yield and selectivity was observed. Conversion, yield, chemo- and enantioselectivity were determined by GC/MS and HPLC.

2.5.3. Dihydroxylation of 1-phenylcyclohexene on 0.5 mol-scale

84.4 g (533 mmol) 1-phenylcyclohexene, 0.8 g (2.17 mmol) K₂[OsO₂(OH)₄], and 13.5 g (17.36 mmol) (DHQD)₂PHAL were stirred in a mixture of 2 l H₂O/ 2 l *tert*-BuOH and 147.5 g (1.07 mol) K₂CO₃ at room temperature. 800 mmol NaOCl was added and the stirring was continued for 1 h. Then, 533 g sodium sulphite was added and the stirring was continued for 30 min. Afterwards, the reaction mixture was extracted three times with 0.5 l dichloromethane each. The organic solution was dried with Na₂SO₄, filled up to 3500 ml and used for product analysis (conversion = 100%, yield_{diol} = 100%, ee = 92% (*R,R*)) and osmium analysis.

3. Results and discussion

3.1. Osmium XRF analysis

In order to evaluate the quality of heterogeneous Os catalysts, a simple and suitable analytical method for the determination of osmium contents in the product solutions must be available. So far, methods for quantitative analyses of osmium compounds have been reported mostly in the scientific or patent literature concerning samples from geological or metallurgical sources. Typically, the osmium compounds exist in ionic form, which makes it possible to dissolve them in strong acidic aqueous media [37–45]. In the case of the OsO₄-catalysed dihydroxylation of olefins the analysis of the Os species is more difficult, which prevents the application of the previously used customary analytical

methods. During the oxidative digestion, osmium species in lower oxidation states will be oxidised to OsO₄, and the determination of its content may be inaccurate because of the volatility of OsO₄. Applying ICP-MS or ICP-OES memory effects [46] in the sample introduction systems cause faulty and non-reproducible results. Obviously, organic solvents complicate the determination of osmium. Because of these difficulties only few studies have been reported to determine Os leaching into product solutions in the heterogeneous dihydroxylation. A widespread method is the separation of the catalyst from the product solution after the reaction and the reuse of the solution with fresh olefin and fresh oxidant. Here, the conversion of olefin in the catalytic reaction was used as an indicator for the osmium content. If no further conversion of olefin is observed it is claimed that no osmium will be leached into the solution. Clearly, this conclusion is invalid. Iodometric titration [14,25] was also used to determine the amount of osmium leaching. In our experiences this method has a low sensitivity. In the range of low osmium concentrations (<3 ppm) an overlapping with the blank value obstructs correct results.

Therefore, we developed a more suitable method for the determination of osmium leaching in dihydroxylation mixtures. We thought that X-ray fluorescence spectroscopy, which can be applied for the analysis of metal compounds in solutions, should solve the problem. Khomutova and Sinityn [47] used XRF for the detection of osmium in solutions, but the detection sensitivity was about 5 mg/l.

Indeed, when OsO₄ or other electrophilic Os species in the product solution were concentrated on the surface of a macroporous nucleophilic scavenger resin, the detection limit of Os applying XRF was typically 0.1–0.05 mg/l OsO₄. In some measurements, the lowest concentration was 0.02 mg/l. Especially, the macroporous polymer bound tris(2-aminoethyl)amine (e.g. Argopore Trisamine MP) has been proven to be a suitable scavenger resin. In an easy procedure, 20 mg of this polymer was added to a defined amount of the organic solution obtained by extracting the products from the reaction mixture. The scavenger resin was stirred in the solution for 24 h, filtered, air-dried and transferred on the sample target of the energy-dispersive X-ray spectrometer. PtCl₂(1,5-C₈H₁₂) was used as an internal standard because the small amount of polymer powder could not be consistently prepared on a polycarbonate foil target. Usual methods like pressing pellets are also not applicable. Therefore, the absolute signal intensities of the osmium and the platinum fluorescent lines depend on the sample consistence and the target covering. But the ratio of the absolute Os and Pt intensities is independent from those influences.

In addition, a series of solvents, which were used for the extraction, was checked to find out the most suitable for the method. In order to determine the accuracy of the method 100 ml of solutions with OsO₄ concentrations of 1 and 5 mg/l were submitted to the scavenging procedure. A dependence of the Os retrieval rate on the kind of solvent was observed.

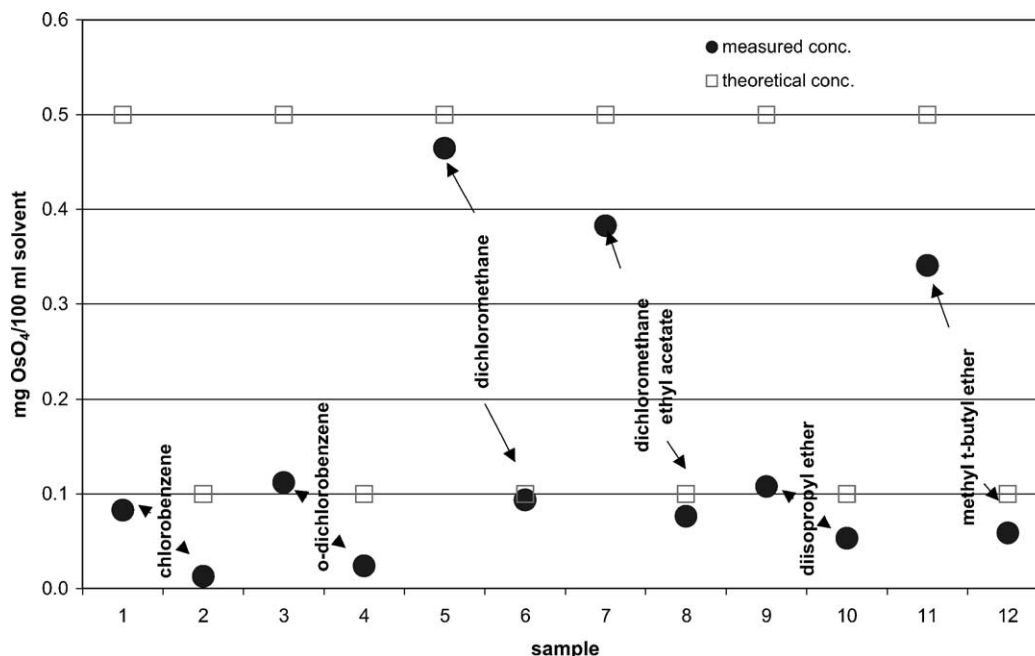


Fig. 3. Determination of the most suitable extraction solvent.

Best results were obtained using dichloromethane as solvent. Here, at least 92% of the available osmium species can be recovered (Fig. 3).

Although the coverage of the target foil varies, only a very low standard deviation of about 2.2% was observed in the experiment which is documented in Table 2. Based on the calibration shown in Fig. 1, the Os content and thus leaching of Os can be determined in a sufficient manner.

3.2. Dihydroxylation reactions with immobilised Os catalysts

Recently, some of us reported an encapsulation method of hydrogenation and hydroformylation catalysts into polyelectrolytes [34]. The retention of the catalyst is caused by electrostatic interaction between the ligand with an ionic anchoring group and the ionic polyelectrolyte backbone. In the meantime, we found that these interactions are strong enough to employ these polyelectrolyte catalysts even if they

are dissolved in an aqueous/alcoholic system [48]. The separation of the products from the reaction solution can be carried out by extraction with a non-miscible organic solvent like ethyl acetate or dichloromethane. Schwab and Mecking [49] described the separation of a similar soluble hydroformylation catalyst by ultrafiltration.

A schematic representation of the PDADMAC-based polyelectrolyte catalyst is shown in Fig. 4. We thought that the high symmetry in the (DHQD)₂PYR ligand developed by Sharpless et al. [50] should be kept as far as possible from this flexible system.

The preparation of the phosphonic acid-substituted (DHQD)₂PYR-P(O)(OH)₂ **3** started from the aryl bromide **1** (Fig. 2). Palladium-catalysed introduction of the phosphonate group [51,52] and cleavage of the ester via the silylester led to the corresponding phosphonic acid **3**. For a better dosage of the catalyst components lens-shaped catalyst particles were prepared which dissolved easily in the reaction mixture.

Table 2
Variation of amount and position of the polymer on the XRF foil

Amount of sample	Position of sample	Intensity Os signal	Intensity Pt signal	Ratio Os/Pt signals
Approximately 20 mg ^a	Sample on the edge distributed at random	105	773	0.136
Approximately 20 mg	Sample statistically distributed	291	2226	0.131
Approximately 250 mg ^a	Sample on the edge distributed at random	790	6060	0.130
Approximately 250 mg	Sample distributed at random	865	6383	0.136
Approximately 250 mg	Sample statistically distributed	905	6693	0.135
	Average value			0.134
	Standard deviation			0.003
	Relative standard deviation (%)			2.239

^a The 250 mg sample was loaded with the 12.5-fold amount of OsO₄ and Pt standard compared with the 20 mg sample.

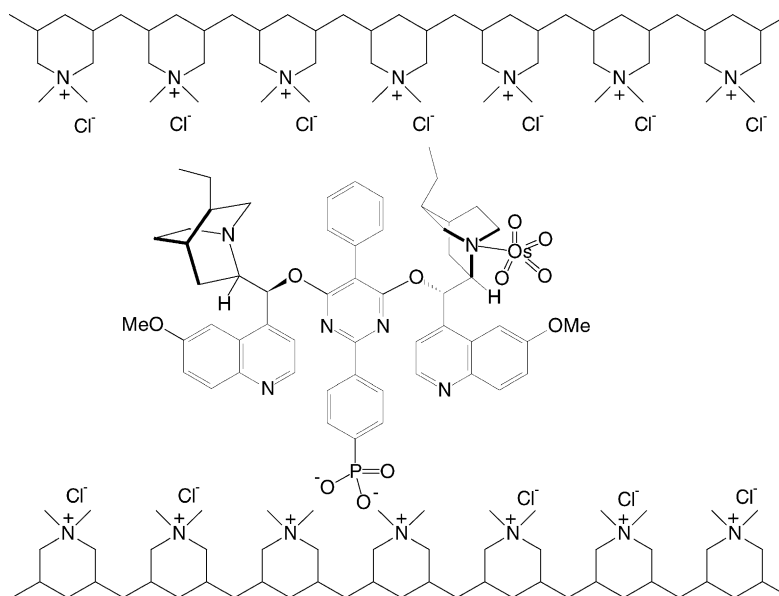


Fig. 4. Scheme of the embedded $\text{OsO}_4\text{-(DHQD)}_2\text{Pyr-P(O)(OH)}_2$ catalyst.

In general, the AD of different olefins (1-octene, styrene, 1-phenylcyclohexene, β -methylstyrene) was conducted with bleach as the oxidant following the homogeneous AD procedure (Table 3) [53]. The strong basic pH value was adjusted either by adding a buffer (Table 3, method A) or by using an aqueous solution of potassium carbonate (Table 3, method B and C). For the most part, better conversions and selectivities were attained using method B. Compared with the homogeneous AD, particularly with regard to enantioselectivity, the obtained results are unsatisfactory. Raising of the molar ratio of PDADMAC (method C) effected a nearly complete retention of osmium but, unfortunately, a significant decrease of the catalyst activity. Obviously, the presence of such long-chained ionic polymers interferes with the

enantioselection step in the dihydroxylation cycle probably by strong dipolar interactions.

Another approach to ensure an easy separation of dihydroxylation products from a heterogeneous Os catalyst is the co-ordination of osmium tetroxide to chitin. Chitin (Fig. 5) is a chiral biopolymer based on *N*-acetylglucosamine. Apart from the stereogenic carbon atoms in each amino sugar unit the helix shape of polymer chain introduces an additional asymmetric element into the polymer.

The idea to choose chitin as a ligand as well as a support was influenced by the recent results of the groups of Sharpless et al. [54] and Jacobs et al. [55]. Both groups demonstrated that the Os catalyst can be permanently co-ordinated to the ligand during the whole catalytic cycle (Fig. 6).

Table 3
Dihydroxylation using $\text{OsO}_4\text{-(DHQD)}_2\text{Pyr-P(O)(OH)}_2\text{/PDADMAC}$ catalysts

Olefin	Method ^a	X (%)	Y_{diol} (%)	S_{diol} (%)	ee (%)	TOF (h^{-1})	c_{Os} (mg/l) ^b
1-Octene	A	75	72	96	5	209	1.5
	B	77	77	100	8	181	0.3
	C	49	6	13	n.d. ^c	16	0
Styrene	A	67	54	81	26	177	2.5
	B	76	57	75	20	149	0.8
	C	66	0	–	–	–	0
β -Methylstyrene	A	84	69	82	32	105	n.d. ^c
	B	94	78	83	21	201	0.2
	C	52	43	83	54	110	0.04
Phenylcyclohexene	A	60	21	36	33	54	5.9
	B	76	57	76	38	144	0.3
	C	19	6	31	n.d. ^c	15	0

Reaction conditions: olefin 2 mmol, NaOCl 3 mmol, $\text{K}_2[\text{OsO}_2(\text{OH})_4]$ 0.008 mmol, $(\text{DHQD})_2\text{Pyr-P(O)(OH)}_2$ 0.072 mmol, 25 °C, 1 h.

^a Method A: buffer pH 12 7.5 ml/*tert*-BuOH 7.5 ml, PDADMAC 0.8 mmol; method B: K_2CO_3 4 mmol, H_2O 7.5 ml/*tert*-BuOH 7.5 ml, PDADMAC 0.8 mmol; method C: K_2CO_3 12 mmol, H_2O 22.5 ml/*tert*-BuOH 22.5 ml, PDADMAC 16 mmol.

^b c_{Os} of the product solution.

^c Not determined.

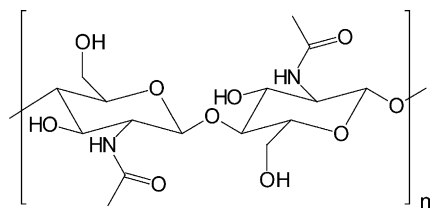


Fig. 5. Structure of chitin.

The commonly accepted reaction scheme of the osmium-catalysed dihydroxylation of olefins is shown in Fig. 6. The composition of different Os chitin catalysts and the results of the dihydroxylation are summarised in Tables 1 and 3. When a double molar surplus of OsO_4 was employed only 8.4 mol% of Os was complexed on the support. At a molar ratio of OsO_4 /chitin of 0.005, the whole metal oxide was co-ordinated to the nucleophilic acetyl amino and hydroxy groups of chitin. Applying higher molar ratios (charge numbers I–IV, Table 1), the OsO_4 amount was partly complexed. Most likely only the surface and outer pores of the chitin particles are accessible to the osmium tetroxide. As test reaction for the different Os chitin catalysts the dihydroxylation of β -methylstyrene in the presence of *N*-methyl morpholine *N*-oxide in a weakly acidic milieu (pH 5) and with bleach in a basic reaction medium was studied (Table 4). All prepared OsO_4 chitin catalysts showed catalytic activity in this reaction. The more active and selective catalysts were those with higher loadings of OsO_4 per molar unit of the amino sugar (e.g. runs 1 and 10). Even at a OsO_4 contents of 0.06–0.065 mol% (runs 6 and 7) active catalysts were obtained. In run 6, a turnover number of 1205 was observed which is comparably high for a heterogeneous Os catalyst. Unfortunately, an enantiomeric excess of only 3–4% ee was obtained. The osmium leaching in the NMO dihydroxylation was found to be lower than the detection limit in most cases. Nevertheless, catalyst recycling was not successful, the conversion and yield dropped dramatically in the second and third run in the dihydroxylation of β -methylstyrene.

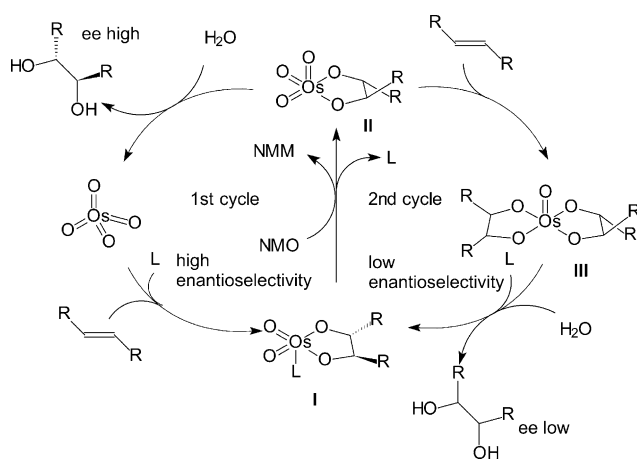


Fig. 6. Scheme of the AD of olefins with NMO as an oxidant.

Conversion and selectivity decreased when NaOCl was used as the oxidant. In the reactions with bleach (runs 11–15), the catalyst was not stable and a significant leaching was observed. Here, the partial cleavage of the amide C–N bond in the basic reaction conditions may be the reason for the unsatisfactory results. In addition to chitin also chitosan was tested as a catalyst support but the OsO_4 -complexed chitosan catalysts showed no activity in the test reaction, most likely due to the higher binding constant of amino groups in chitosan.

The excellent retention of the active metal both with chitin and tris(2-aminoethyl)amine bound to a polymer (Argopore Trisamine MP) led us to the idea to use such nucleophilic polymers for removal of osmium contaminations from product solutions. Various commercially available nucleophilic scavenger resins were tested for this purpose (Fig. 7).

As shown in Fig. 8, the synthetic resins 4–8 effected an excellent elimination of electrophilic osmium species from organic solutions. Interestingly, also the significantly cheaper natural polymer chitin and its derivative chitosan 9 are able to reduce the osmium content below the detection limit of our analytical method. However, a larger amount of polymer was needed in the latter case. In general, 20 mg or 100 mg of the polymer was stirred in 100 ml of dichloromethane solutions containing concentrations of 1 mg/l or of 5 mg/l osmium respectively for 24 h. After filtration of the scavenger resins the residual osmium content in the dichloromethane solutions was determined as described for the osmium leaching. This method of scavenging osmium contaminations enables an interesting alternative to the heterogeneous dihydroxylation. Advantageously, the reaction can be carried out homogeneously followed by removal of Os from the product solution via addition of a nucleophilic polymer.

3.3. Recycling of the active metal in a homogeneous dihydroxylation system

Within the scope of the investigations on the osmium leaching using heterogenised catalysts we became also interested in the leaching of homogeneous Os catalysts in the organic product phase. Usually, the homogeneous dihydroxylation procedure is performed in a biphasic mixture of a basic water phase and an organic *tert* butanol phase. After full conversion an extraction of the products from the water phase using organic solvents, e.g. ethyl acetate is done. Applying this procedure about one-third of the osmium can be found in the product. Surprisingly, we discovered that the extraction of the reaction mixture with selected solvents lead to a significant decrease of the osmium concentrations in product solution (Table 5). The most suitable solvents for extraction are halogenated ones but in the case of chlorobenzene and *o*-dichlorobenzene one should have in mind that the retrieval rate of osmium was about one-fifth of the concentration (Fig. 3). So we recommend to use dichloromethane for such extractions.

It is important to note that these low osmium leaching rates could only be found up to now in the dihydroxylation using

Table 4
Dihydroxylation using chitin catalysts with different OsO₄ loadings

Run	Charge number	Oxidation	<i>N</i> _{ligand} (mmol) ^a	<i>n</i> _{OsO₄} (mmol)	<i>n</i> _{OsO₄} / <i>n</i> _{ligand}	Os (mol%)	X (%)	Y (%)	S (%)	TON	<i>n</i> _{Os} / <i>n</i> _{product} (ppm)
1	VI	NMO	0.1 ^b	0.0084	0.084	0.42	100	100	100	242	0
2	V	NMO	1.6	0.008	0.005	0.4	67	53	79	132	0
3	IV	NMO	0.8	0.006	0.0075	0.3	83	64	78	224	0
4	III	NMO	0.4	0.004	0.01	0.2	82	78	94	395	0
5	II	NMO	0.16	0.003	0.019	0.15	89	78	88	521	0
6	I	NMO	0.1	0.0013	0.013	0.065	91	78	86	1205	0
7	V	NMO	0.25	0.0012	0.0048	0.06	86	34	40	584	0
8	IV	NMO	0.25	0.002	0.008	0.1	82	71	87	723	14
9	III	NMO	0.25	0.0026	0.0104	0.13	87	85	98	675	0
10	I	NMO	0.25	0.0033	0.0132	0.165	100	100	100	628	0
11	V	NaOCl	1.6	0.008	0.005	0.4	66	48	74	126	604
12	IV	NaOCl	0.8	0.006	0.0075	0.3	84	71	85	242	321
13	III	NaOCl	0.4	0.004	0.01	0.2	82	64	79	348	191
14	II	NaOCl	0.16	0.003	0.019	0.15	77	60	78	461	84
15	I	NaOCl	0.1	0.0013	0.013	0.065	75	67	90	1126	84

Reaction conditions: 2 mmol β -methylstyrene, 2.2 mmol oxidant, r.t., 24 h., NMO: 7.5 ml *tert*-BuOH/ 7.5 ml buffer (pH 5); NaOCl: 7.5 ml *tert*-BuOH/7.5 ml H₂O, 4 mmol K₂CO₃.

^a Related to monomeric units.

^b Catalyst with the highest observed OsO₄ loading.

bleach as oxidant. For example, applying molecular oxygen as oxidant for the dihydroxylation [56–59] a contamination of 5.4 mg/l osmium was determined in a comparable product solution.

In order to demonstrate the usefulness of the procedure we carried out the homogeneous dihydroxylation of 1-phenylcyclohexene with subsequent aqueous two-phase separation of the product from the catalyst on 0.5 mol scale (4 l reaction solution). To our delight, even in this

experiment, the resulting 1,2-diol (>99% yield) was contaminated with only 5 ppm of osmium. The enantiomeric excess of (*R,R*)-1-phenyl-1,2-hexanediol was found to be 92%, which was nearly the same as in the 2 mmol reaction.

These results encouraged us to investigate the possibility to recycle the active metal containing aqueous solution. This recycling was tested in the homogeneous dihydroxylation of α -methylstyrene. After the extraction of the reaction

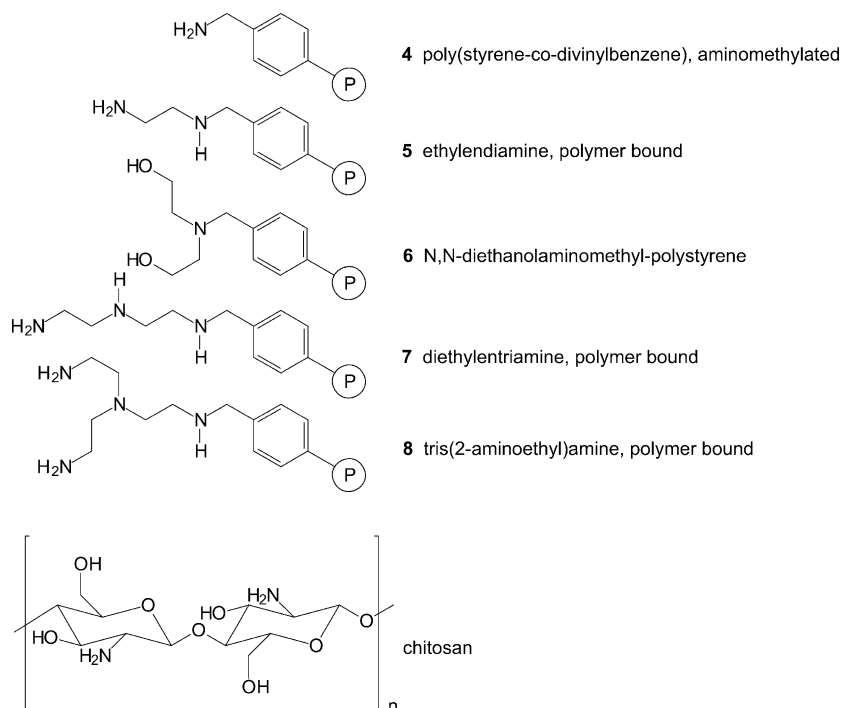


Fig. 7. Nucleophilic scavenger polymers.

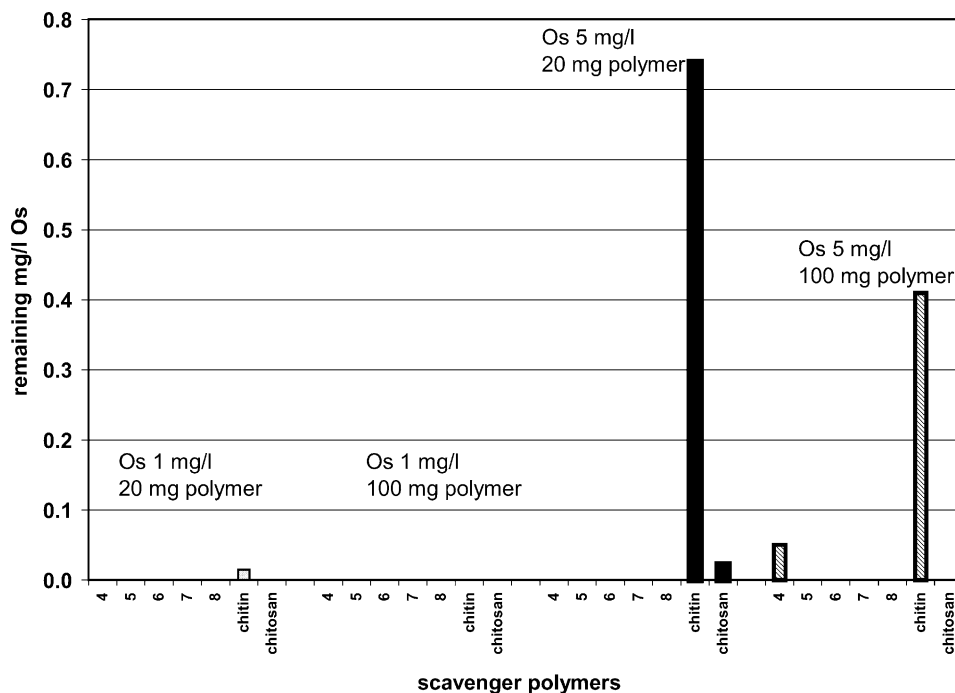


Fig. 8. Ability of scavenger polymers to remove osmium from solutions.

solution with dichloromethane, 2 mmol α -methylstyrene, 3 mmol bleach, 0.03 mmol (DHQD)₂PHAL and *tert*-BuOH (10 ml) were added and the reaction was carried out again. This reaction/separation cycle could be on average repeated up to four times, in one case up to eight times, without

decrease of conversion, yield and enantioselectivity (Table 6). Hence, the catalyst productivity increased up to turnover number of 1440 (eight-fold recycling).

It should be mentioned here, that the reuse of the aqueous active metal solution is limited by the deterioration of

Table 5

Comparison of the extraction with different solvents

Extraction solvent	mg Os/l extraction solvent	n_0 Os (%)	mg Os/kg product [ppm]	$n_{Os}/n_{product}$ [ppm]
Dichloromethane	0.05	0.33	13.0	13.1
2-Methyltetra-hydrofuran	0.09	0.59	23.4	23.6
MTBE	0.08	0.53	20.8	21.0
Chlorobenzene	0 ^a	0	0	0
<i>o</i> -Dichlorobenzene	0 ^a	0	0	0

Reaction conditions: 2 mmol 1-phenylcyclohexene, 3 mmol NaOCl, 0.008 mmol K₂[OsO₂(OH)₄], 0.1 mmol (DHQD)₂PHAL, 1 h, r.t., 7.5 ml H₂O/7.5 ml *tert*-BuOH, 4 mmol K₂CO₃.

^a Lower than the detection limit.

Table 6

Dihydroxylation of α -methylstyrene applying reuse of the aqueous reaction phase

Run	Addition osmate (mmol)	Addition ligand (mmol)	Extraction 1 (ml)	Extraction 2 (ml)	Conversion (%)	Yield _{diol} (%)	Selectivity (%)	ee (%)
1	0.01	0.03	20	10	100	83	83	72
2	0	0.03	20	10	100	88	88	65
3	0	0.03	20	10	100	95	95	78
4	0	0.03	23	10	100	89	89	82
5	0	0.03	25	10	100	89	89	82
6	0	0.03	45	10	100	87	87	84
7	0	0.03	45	10	100	91	91	84
8	0	0.03	45	10	51	34	66	83

Reaction conditions: Schlenk tube, stirrer, r.t., reaction time 2 h; start: 2 mmol α -methylstyrene, 0.01 mmol K₂[OsO₂(OH)₄], 0.03 mmol (DHQD)₂PHAL, 3 mmol NaOCl, 4 mmol K₂CO₃, 10 ml H₂O/10 ml *tert*-BuOH; after each run: extraction with CH₂Cl₂ (2×), reuse of the aqueous phase in the next run with addition of 2 mmol α -methylstyrene, 3 mmol NaOCl, 0.03 mmol (DHQD)₂PHAL and 10 ml *tert*-BuOH.

the phase separation owing to the enrichment of ionic components in the aqueous phase and the changing distribution balance between the phases. Nevertheless, the repeated use of the homogeneous osmium catalyst is remarkable because of the ease of handling and high catalyst productivity and should be further investigated in the dihydroxylation with other oxidants and other substrates.

4. Conclusions

Different approaches for an effective separation of the products (1,2-diols) from the osmium catalyst in the catalytic dihydroxylation of olefins have been described. As a precondition for such investigations, a routine method for the osmium analysis in organic reaction solutions was developed. Water-soluble phosphonic acid-substituted alkaloid ligands were synthesised for the immobilisation of the catalysts into polyelectrolytes. Unfortunately, these polyelectrolyte catalysts showed reduced activity and selectivity. Chitin was used for the first time both as the ligand and support in the catalytic dihydroxylation. The osmium retention of these catalysts was excellent with NMO as the oxidant but, unfortunately, no enantiomeric excess was observed. However, the results provided an opportunity to eliminate osmium traces from product solutions by catching them with nucleophilic scavenger polymers. This principle could be realised in a technical scale by passing the product solution through a column packed with this type of polymers. The best and most simple solution to an effective retention of catalytically active osmium species in the dihydroxylation with bleach was discovered in the method of homogeneous catalysis/heterogeneous separation of products and the reuse of the aqueous catalyst phase. This method of recycling of the aqueous catalyst phase ought to be transferred to dihydroxylation using other oxidants than bleach under mild reaction conditions.

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