Anodic aluminium oxide catalytic membranes for asymmetric epoxidation†

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Catechol-functionalized (salen)Mn complexes can be supported on mesoporous anodized aluminium oxide disks to yield catalytic membranes that are highly active in the enantioselective epoxidation of olefins when being deployed in a forced-through-flow reactor.

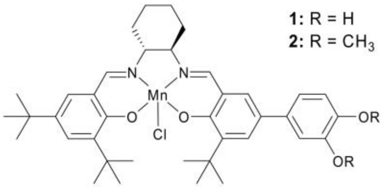
Catalytic membrane reactors have attracted much attention over the last decade due to practical advantages over other reactor designs. They can potentially reduce the size of conventional reactors and cost of operation by combining two essential processes, chemical reaction and separation of the resulting products from the catalyst, in one stage.[1] In particular, the catalytic membrane reactor configuration confers a significant advantage to oxidation reactions—the use of a catalytic membrane can provide a reactive interface for the oxidation to take place while avoiding long contact times of the desired product with catalysts, thereby minimizing over-oxidation.[2]

Recent developments in the synthesis of inorganic materials have allowed chemists to create single-site catalysts and catalyst supports that provide a uniform environment around each active catalyst center.[3] Among these inorganic materials, mesoporous anodic aluminium oxide (AAO) membranes have received great attention.[4] They contain well-ordered, densely packed, nanoscale pores that naturally form when aluminium films are anodized in an acidic electrolyte. Although AAO membranes can be brittle, they are used in a number of diverse applications such as bioreactors;[5a] sensors;[5b] templates for quantum dots,[5c] nanowires,[5d] nanotubes,[5e] and nanofibers;[5f] and supports for metals[5g] and catalysts.[5h]

An attractive potential use for AAO membrane would be as a support for the immobilization of asymmetric homogeneous catalysts to generate an enantioselective catalytic membrane. Heterogenized asymmetric catalysts are intrinsically more economical and convenient to use than their homogeneous counterparts since they can provide a direct route to chiral products without costly separations.[6] Among asymmetric homogeneous catalysts, chiral (salen)Mn complexes (Jacobsen–Katsuki catalysts)[7] for the asymmetric epoxidation of olefins comprise one of the most widely immobilized classes of homogeneous catalysts.[8] However, the ideal combination of activity, selectivity, and recyclability has not been achieved to date.

We have long been interested in the design of a catalytic system that can perform both a chemical transformation and a separation event within a single functionalized membrane material. To this end, we have explored the use of commercially available AAO membranes (Anodisc®, Whatman) as the supporting materials for chiral (salen)Mn complexes. Being non-compressible and possessing high chemical and thermal stability, the AAO membranes can serve as a stationary phase suitable for incorporation into catalytic membrane reactors. In addition, their mono-disperse pores provide well-defined surfaces upon which site isolation of the supported catalyst can be more carefully controlled than in cross-linked polymers or other inorganic solid supports.

Herein, we report the fabrication of a chiral (salen)Mn-immobilized AAO membrane and demonstrate its use in a catalytic membrane reactor for enantioselective epoxidation. As anchoring groups for the (salen)Mn complexes, we have chosen catechol (1,2-dihydroxyphenyl), which has great affinity for Al^{III} ions[9] and can adsorb strongly onto Al_2O_3.[10]



1: R = H
2: R = CH_3

Our catechol-functionalized unsymmetrical chiral salen ligand can be prepared easily from (1*R*,2*R*)-diaminocyclohexane in good yield and then metallated with $MnCl_2$/LiCl in air, resulting in complex **1**. Immobilization of **1** was accomplished by stirring its ethanolic solution with an AAO membrane‡ at 70 °C for 24 h, resulting in a brown membrane (**1-AAO**) (Fig. 1). The catalyst loading was determined by inductively coupled plasma (ICP) spectroscopy to be 4.1 μmol g^{-1}. The modified membrane was characterized by FT-IR, diffuse reflectance UV-Vis, and X-ray

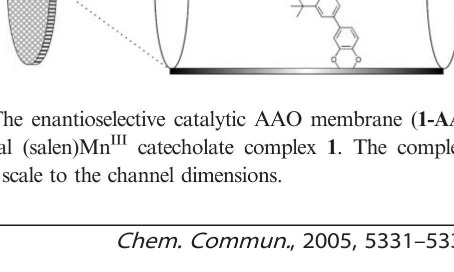


Fig. 1 The enantioselective catalytic AAO membrane (**1-AAO**) coated with chiral (salen)Mn^{III} catecholate complex **1**. The complex was not shown in scale to the channel dimensions.

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† Electronic supplementary information (ESI) available: Synthetic procedures and characterization data for complexes **1–2**; characterization data for **1-AAO**; general procedure for asymmetric epoxidations catalyzed by **1-AAO**. See http://dx.doi.org/10.1039/b507541f

Table 1 Catalytic performance of **1-AAO** *vs.* **2** in the asymmetric epoxidation of 2,2-dimethyl-2*H*-chromene[a]

Entry	Catalyst	Yield [%][b]	ee [%][c]	s [%][d]
1	**1-AAO**	79	81	100
2	**1-AAO** 2nd cycle	70	76	99
3	**1-AAO** 3rd cycle	62	73	97
4	**1-AAO** 4th cycle	51	69	95
5[e]	**2**	82	86	100

[a] Reaction performed in a shell vial under ambient conditions using magnetic stirring. Molar ratio olefin/oxidant/catalyst = 100/200/1. [b] GC yield after 1 h using undecane as an internal standard. [c] Determined using a Supelco β–DEX 120 chiral GC column. [d] Product selectivity of epoxide over ketone as measured by ^{1}H NMR spectroscopy. [e] Control experiment under homogeneous conditions using 1 mol% catalyst.

photoelectron spectroscopy to confirm the presence of surface-attached catalyst (see Supplementary Information†).

To provide a benchmark for the catalytic activity and selectivity of **1-AAO** in the homogeneous state, complex **2**[11] was also prepared. Catalytic epoxidations of 2,2-dimethyl-2*H*-chromene were carried out with both **1-AAO** and **2** using 2-(*tert*-butylsulfonyl)iodosylbenzene, **3**, as the oxidant (Table 1).[12] Although initial rates cannot be obtained,[13] under optimized batch reaction conditions **1-AAO** afforded the epoxide in yield and selectivities that are similar to those of **2** (Table 1, *cf.* entries 1 and 5).[14] These data suggest that reactant molecules have easy access to the supported active sites on the membrane, and that the sites retain structures that are similar to that of the free catalyst. This notion makes sense given the well-ordered, highly porous, and rigid morphology of AAO membrane and the large channel sizes (⩾20 nm), which define a readily accessible and unconstrained environment[15] for the immobilized catalyst.

Moreover, catalytic membrane **1-AAO** can be recovered and reused after a simple cleaning procedure (Table 1, entries 2–4). Although the recycled **1-AAO** membrane did exhibit a gradual decrease in activity,[16] it was still active with excellent chemoselectivity and good enantioselectivity after four cycles (85% of the original enantioselectivity). ICP analysis carried out on a membrane after the fourth cycle showed that 83–87% of the manganese still remained in the membrane.[17]

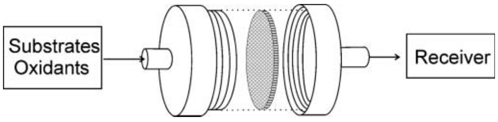

Fig. 2 Schematic diagram of the liquid-phase forced-through-flow catalytic membrane reactor for the enantioselective epoxidation of olefins.

Membrane **1-AAO** can also be used effectively in a simple catalytic membrane reactor (Fig. 2) where the substrate and oxidant are introduced *via* a syringe pump, which also controls the feed rate of reactants.[18] The catalytic results, obtained with the various fluxes, are presented in Table 2. Due to the membrane's compatibility with high flux (maximum flux for water = 4.9 mL min^{-1} cm^{-2}),[19] fluxes of up to 7.5 mL h^{-1} cm^{-2} were easily obtained with reactant mixture in dichloromethane, which is much less viscous than water. In this liquid phase forced-through-flow membrane reactor,[20] **1-AAO** exhibited extremely high activity and excellent chemoselectivity (Table 2, entries 1–2, 4). Furthermore, its enantioselectivity was similar to that of **2** under homogenous conditions. When the 7.5 mL h^{-1} cm^{-2} flux was applied, **1-AAO** provided unprecedented high turnover frequency (TOF) and one-pass conversion (Table 2, entry 4). Although not directly comparable to our present data, PDMS-membrane-occluded Jacobsen's catalyst only affords a TOF of 0.0438 h^{-1} for the styrene–NaOCl system[21] and [Al-MCM-41]-immobilized Jacobsen's catalyst only gave a TOF of 26 h^{-1} for the stilbene–iodosylbenzene system.[16a] Moreover, when **1-AAO** was reused after one cycle, it was still active and selective although the TOF had dropped off significantly[16c] (Table 2, entry 5). It is probable that at 2000 TON (total TON after 2 cycles at 10 mL h^{-1}, Table 2, entries 3–4) we are close to the limit of TON for **1-AAO** in the presence of **3**.

The product/reactant ratio can be further improved to 80% conversion (from 60%) by passing the initial permeate through another identical **1-AAO** membrane (Table 2, *cf.* entries 2 and 3). The leached-out Mn in the permeate side does not contribute to the overall activity as only a minimal increase (∼0.6%) in conversion was observed when the permeate was allowed to stir for an additional hour after being passed through the membrane.

The high activity and selectivity for asymmetric epoxidation obtained in the catalytic membrane reactor system can be ascribed to the two beneficial effects of the AAO membrane: (1) the well-ordered and unconstrained cylindrical pore structure of the membrane makes all active catalyst sites readily available to reactant molecules and (2) short catalyst contact time allows more turnovers while maintaining high selectivity and minimizing over-oxidation.

In summary, we have demonstrated, for the first time, that chiral catalysts can be immobilized onto mesoporous AAO

Table 2 Catalytic performance of **1-AAO** in a liquid phase forced-through-flow reactor for the asymmetric epoxidation of 2,2-dimethyl-2*H*-chromene

Entry	Cycle for membrane	Cycle for permeate	Flux [mL h^{-1} cm^{-2}][a]	Total TON[b]	Conversion [%][c]	TOF [min^{-1}][d]	ee [%][e]	s [%][f]
1	1	1	1.5	1174	47	20	86	100
2	1	1	4.5	1492	60	75	85	100
3	1[h]	2	4.5	1174 (1st) + 820 (2nd)	80	n/a	85	100
4	1	1	7.5	1670	67	134	84	100
5[g]	2	1	7.5	179	7	15	80	98

[a] Controlled by a syringe pump. [b] Total turnover number, based on conversion per catalyst. Molar ratio olefin/oxidant/catalyst = 10,000/2,500/1. [c] Based on oxidant as the limiting reagent. [d] Turnover frequency, based on conversion per catalyst per minute. [e] Determined using a Supelco β–DEX 120 chiral GC column. [f] Product selectivity of epoxide over ketone, measured by NMR spectroscopy. [g] After one cycle (entry 3), **1-AAO** was recovered, thoroughly washed with CH_2Cl_2, and reused with fresh reactants. [h] The permeate of entry 2 was passed through another freshly prepared **1-AAO**.

membranes, which can then be used effectively in enantioselective catalytic membrane reactors. The supported catalytic membrane provided easy catalyst separation and recycling with comparable activity and selectivity to homogeneous counterparts. When used in a forced-through-flow reactor, it offered great flexibility in the control of substrate feed and product separation from the catalyst. Under optimized conditions, unusually high activity (TON = 1670, TOF = 135 min^{-1}) with high enantioselectivity and excellent chemoselectivity can be observed for olefin epoxidation. This strategy likely can be extended to other catalytic reactions, allowing for straightforward inexpensive isolation of valuable products as well as minimization of side reactions.

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Notes and references

‡ **Preparation of 1-AAO.** Into a 15 mL Pyrex conical test tube (15 mm ID, Corning product #8060-15) equipped with a vaned magnetic stirbar were placed 20 membranes of Anodisc® 13 (Whatman, 13 mm diameter, 60 μm thickness, 20 nm front-end pore), each separated from the others by thin cylindrical polyethylene rings (12 mm ID × 1.5 mm H × 0.5 mm T). An ethanol solution (12 mL) of **1** (12 mg, 1.8×10^{-2} mmol) was added to the tube. The tube was capped with a rubber septum and the reaction was heated at 70 °C for 24 h. The membranes were then separated, thoroughly washed with EtOH (5 × 15 mL), and sonicated in EtOH (3 × 15 mL) for 5 min each. The resulting brown-colored membranes were air-dried for 15 min and baked at 70 °C in an oven for 10 min. They were then stored in the vacuum desiccator before use.

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11 Complex **2** is used in the control experiment instead of **1** because the latter is not very soluble in CH_2Cl_2 due to the exposed hydroxyl groups on the catechol moiety. In addition, the acidity of the phenolic protons of **1** can also cause side reaction with the epoxide products.

12 The use of excess oxidant was necessary because (*tert*-butylsulfonyl)-iodosylbenzene undergoes partial disproportionation to (*tert*-butylsulfonyl)iodoxylbenzene and (*tert*-butylsulfonyl)iodobenzene under our reaction conditions. See: D. Macikenas, E. Skrzypczak-Jankun and J. D. Protasiewicz, *J. Am. Chem. Soc.*, 1999, **121**, 7164–7165.

13 Under the reaction conditions shown in Table 1, the first 40% of conversion occurred within 1 min, rendering the measurement of initial rate *via* manual sampling impossible. This fast reaction rate is due to the high solubility of the oxidant (see ref. 12) as well as the high activity of the (salen)Mn^{V}=O intermediate towards olefins.

14 Due to phase-induced kinetic differences, the activities of salen-derived heterogenized catalysts for olefin epoxidation are often compared to those of their homogeneous counterparts in terms of TON or TOF, and not initial rate. See: (*a*) S. Keith and C.-H. Liu, *Chem. Commun.*, 2002, 886–887; (*b*) F. Bigi, L. Moroni, R. Maggi and G. Sartori, *Chem. Commun.*, 2002, 716–717.

15 Unlike AAO or mesoporous inorganic oxides with large pores, cross-linked polymer or small-pore zeolite supports may force the immobilized catalysts to adopt geometries that are significantly different from those of their homogenous counterparts due to the limited size of the supporting cavities in these latter materials. See: (*a*) L. Canali and D. C. Sherrington, *Chem. Soc. Rev.*, 1999, **28**, 85–93; (*b*) F. Bedioui, *Coord. Chem. Rev.*, 1995, **144**, 39–68.

16 A similar tendency toward the decline in activity and selectivity over recycling has been observed for other heterogenized epoxidation catalysts. See: (*a*) P. Piaggio, P. McMorn, C. Langham, D. Bethell, P. C. Bulman-Page, F. E. Hancock and G. J. Hutchings, *New J. Chem.*, 1998, **22**, 1167–1169; (*b*) S. B. Ogunwumi and T. Bein, *Chem. Commun.*, 1997, 901–902; (*c*) J. M. Fraile, J. I. Garcia, J. Massam and J. A. Mayoral, *J. Mol. Catal. A: Chem.*, 1998, **136**, 7–57. This decline in activity and selectivity is possibly a consequence of the catalyst leaching (see ref. 17), ligand decomposition, or site blockage by reactant or product molecules.

17 Although ICP analysis can yield the amount of manganese present in a membrane, not all of the Mn ions exist as supported (salen)Mn complex. The 83–87% of the initial Mn still present in the membrane after the 4th cycle represents an upper limit on the amount of active (salen)Mn complex that has not been leached out, decomposed, or blocked.

18 Direct comparison of the batch reactor (Table 1) and the forced-through-flow reactor (Table 2) cannot be performed due to the differences in reagent concentrations and mass transport (flow through *vs.* diffusion).

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