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# Recycling of the homogeneous Co-Jacobsen catalyst through solvent-resistent nanofiltration (SRNF)

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**The Co-Jacobsen complex, catalysing a hydrolytic kinetic resolution, was recycled in a semi-continuous operation using a laboratory prepared polymeric SRNF-membrane.**

The use of enantiomerically pure components in the agrochemical, pharmaceutical and food industries will become more and more important in the future.[1] These compounds can be synthesized through the use of homogenous transition metal complexes (TMC). These TMCs however are often expensive and difficult to recycle. A lot of research has thus been done to heterogenize these complexes, but the anchoring on for instance inorganic supports[2] or organic polymers[3] often results in a loss of activity and selectivity.

The recent development of SRNF[4] provides an alternative to the classic heterogenisation of homogeneous complexes. The SRNF-membrane is used to separate the homogeneous catalyst from reaction mixture and thus recycle the homogenous complex. This approach was realized on an unmodified TMC for the first time by De Smet *et al.*[5] in the recycling of Ru-Binap and Rh-DUPHOS catalysts dissolved in methanol using a MPF-60 membrane (KOCH). However, the use of less polar solvents, such as diethyl ether and toluene, with these commercial membranes remains problematic, because of strong swelling of the membranes in these solvents. The molecular weight cutoff then increases drastically, making recycling of rather small complexes ( < 800 Da) inefficient. Therefore, a laboratory prepared SRNF membrane (COK M2, a silicon based membrane with an inorganic filler[6,7]) was especially developed for the recycling of the Co-Jacobsen catalyst (626 Da) in diethyl ether ($Et_2O$). This versatile catalyst is often used in chiral catalysis and is currently the best available for the hydrolytic kinetic resolution (HKR) of epoxides.[8] The reaction studied was the HKR of 1,2-epoxyhexane[9] in which one of the two epoxide enantiomers reacts with water to form the diol, while the other enantiomer remains untouched (Fig. 2).

The reported process of catalyst recycling involves a dead end filtration cell (60 ml) which is used both as a reactor and as a filtration unit (Fig. 1). The SRNF-membrane should retain the catalyst while it allows the formed product to permeate. The reaction is carried out using $Et_2O$ as a solvent at room temperature. During the SRNF process, the reactor is pressurized using $N_2$.

The Co-Jacobsen catalyst retention in $Et_2O$ for several commercially available polymeric NF-membranes[10] was screened first. The tests where performed in a cross-flow filtration cell at room temperature with a pressure of 5 bar $N_2$. The obtained retentions[11] for the complex and the permeabilities are shown in Fig. 3.

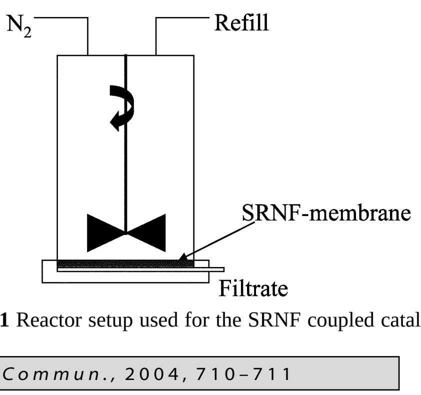

**Fig. 1** Reactor setup used for the SRNF coupled catalysis.

In spite of the wide selection of NF-membranes commercially available, 82% retention was the highest possible (TFC-SR2 membrane), which is still far too low to allow a (semi-)continuous operation. Moreover, this was combined with a very low permeability (0.005 g h$^{-1}$ cm$^{-2}$ bar$^{-1}$). The two laboratory prepared membranes provided much higher fluxes with retentions that were comparable or even higher. A PDMS SRNF-membrane had a retention of 78% combined with a permeability of 0.11 g h$^{-1}$ cm$^{-2}$ bar$^{-1}$, which was very high compared to TFC-SR2. With the COK M2 membrane a retention of 83% was obtained combined with a permeability of 0.02 g h$^{-1}$ cm$^{-2}$ bar$^{-1}$. By changing the filtration conditions to 30 bar in a dead end filtration cell, the PDMS membrane showed an increased retention of 86% and the COK M2 membrane an even higher retention of 98%, which should be sufficient for a semi-continuous combination with catalysis. The best commercial membrane, TFC-SR2, was also tested at 30 bar but compaction fully reduced the pressure to zero.

The reactor experiments were carried out in a dead end filtration cell at a pressure of 30 bar with the COK M2 NF-membrane. This membrane combined a high retention for the Co-Jacobsen complex with a required low retention for the substrate and product

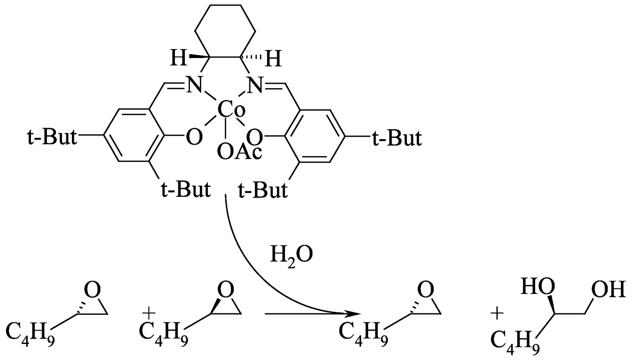

**Fig. 2** HKR of 1,2-epoxyhexane using the (*S*,*S*)-Co(III)-Jacobsen complex.

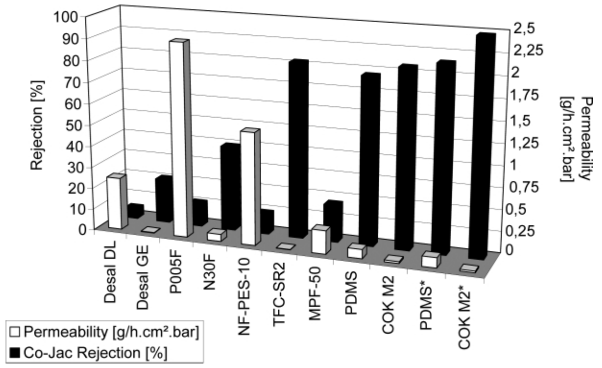

**Fig. 3** Retentions and permeabilities for several tested polymeric membranes (* dead end, 30 bar).

($R_{1,2\text{-epoxyhexane}} = 3\%$ , $R_{1,2\text{-hexanediol}} = 4\%$).[12] The permeate was collected in a cooled flask (0 °C) and analyzed to check the retention for the Co-Jacobsen catalyst. The reactor was filled with a 40 ml ether solution containing (±)-1,2-epoxyhexane (0.675 M), $H_2O$ (0.375 M) and 165.2 mg (*S*,*S*)-Co-Jacobsen catalyst, resulting in a substrate/catalyst ratio of 100 and a $H_2O$/substrate ratio of 0.56. After 30 h, the reactor was pressurized to 30 bar with $N_2$ until half of the reactor volume had permeated. Subsequently, 20 ml of a fresh reactant solution was added to restore the original volume. This procedure was repeated three times. Fig. 4 shows the conversion, the enantioselectivity (ee) of *S*-1,2-epoxyhexane, the ee of *R*-1,2-hexanediol[12] and the volume of the reactor as a function of time.

During the different reactions, a slight decrease in conversion is observed. This can be attributed to the incomplete retention of the complex and possibly to the reduction of a small part of the catalyst.[8] The decrease in conversion solely due to the incomplete catalyst retention by the membrane would however be less significant as shown in Fig. 4 by the dotted line, representing the theoretical decrease in conversion due to the loss of 2% catalyst in each filtration cycle. The catalyst has thus partly deactivated by reduction of the active Co(III) form to the inactive Co(II) form. According to literature, such deactivated catalyst can be reactivated by acid treatment.

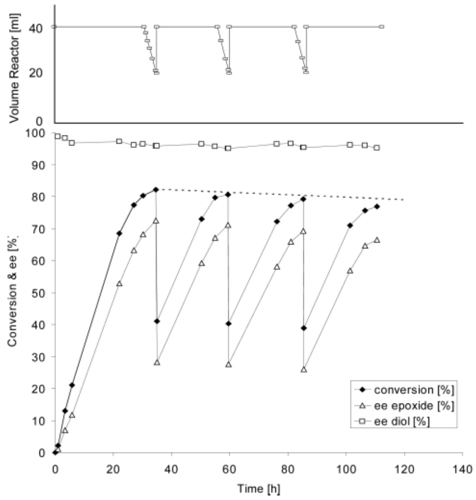

**Fig. 4** Reactor volume, conversion, ee for the diol and the epoxide as a function of time for the HKR of 1,2-epoxyhexane with Co(III)-Jacobsen.

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6 Preparation of COK-M2: 6 g of USY (CBV 780, PQ Corporation) was dispersed in 80 g hexane. After 1 h ultrasonic treatment, 1,9 g cross-linker (RTV 615 B, General Electric) was added to the zeolite dispersion and this mixture was stirred for 2 h at 40 °C. Finally, 12.1 g of the prepolymer (RTV 615 A, General Electric) was added and the mixture was stirred for another hour at 60 °C. The PAN support was fixed on a glass plate, saturated with water and treated with the adhesion promotor (SS-4155, General Electric), before being tilted over an angle of 30°. The polymer solution was then poured over the PAN support. After evaporation of the hexane, cross-linking was completed in an oven at 100 °C.

7 Pressure driven separations of liquid feeds, L. E. M. Gevers, I. F. J. Vankelecom and P. A. Jacobs, patent pending.

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9 1,2-epoxyhexane is an intermediate for the synthesis of certain fragrance components. US 2002/0119909 A1, Rhodia ChiRex, Inc., 2002.

10 Desal DL, Desal GE: Osmonics; P005F, N30F, NF-PES-10: NADIR; TFC-SR2, MPF-50: KOCH.

11 The concentration of the Jacobsen complex was determined with UV-VIS spectroscopy (Perkin Elmer Lambda 900) at 420 nm, the high pressure experiments and the TFC-SR2 samples were analysed on a Jobin Yvon Ultima ICP at 238,892 nm.

$$R = \left(1 - \frac{C_{permeate}}{C_{feed}}\right) \times 100$$

12 The GC analysis was carried out on a RTX®-5 (Restek) and a Chirasil-DEX CB (Chrompack) with $H_2$ as a carrier.