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Sustainable application and recycling of organocatalysts

Thesis booklet

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1. Introduction

Catalysis is present in all areas of the chemical industry. It is estimated that in the case of 90% of chemical products, catalysts are used at some stage in the manufacturing process. According to some estimates, catalysis accounts for more than 35% of world GDP.[1] The global catalyst market was estimated to be worth US$35.5 billion in 2020 and is expected to reach US$57.5 billion by 2030.[2] These illustrate the economic importance of using catalysts. During catalysis, the reaction rate is increased by the catalyst by reducing the activation energy of the reaction. This saves energy and resources and produces less waste during the catalysis process, thus contributing to the development of sustainable technologies. In addition to the need to develop new, selective, and highly active catalysts, catalysis research also needs to address a number of problems, including activity reduction, catalyst degradation and loss.

Organocatalysts are usually small organic molecules that do not contain a metal atom in the reaction centre and are able to increase the reaction rate of various chemical transformations. The first known organocatalytic reaction was reported by Liebig in 1860, using acetaldehyde as a Lewis acid catalyst in the hydrolysis of dicyan.[3] A special type of organocatalysis is asymmetric organocatalysis, which gained widespread interest with two publications in 2000: List showed that small chiral organic molecules can mimic the mechanism of action of enzymes,[4] and MacMillan created the concept of organocatalysis and presented a general activation method.[5] The subsequent rapid progress of organocatalysis is due to the early recognition of its many advantages: organocatalysts are readily available, not very expensive, can be modified in many ways, are robust and are generally insensitive to air and moisture, which also facilitates their industrial application. However, they can also have some drawbacks: high catalyst loadings, long reaction times and high reagent excesses.

The recycling of catalysts, and its different methods, is being widely investigated to increase the sustainability of organocatalytic processes. In my research, I aimed to investigate various methods of catalyst recycling: filtering after attachment to a solid support and membrane filtration after attachment to a central core.

During my work, I studied a wide variety of research topics within organocatalysis that could be of benefit from a green chemistry perspective. In the field of asymmetric organocatalysis, I have developed novel asymmetric crown ether-squaramide phase-transfer catalysts; and I have applied low-energy membrane-based catalyst separation, the efficiency of which has been greatly enhanced by central core attachment. Furthermore, I have established a plastic recycling method for the organocatalytic degradation of poly(ethylene terephthalate) and BPA polycarbonate, which can be particularly advantageous economically due to their extensive optimisation.

[1] Hagen, J. Industrial Catalysis: A Practical Approach, John Wiley & Sons, 2015, 459–462.
[2] Catalyst Market by Type, Process, and Application: Global Opportunity Analysis and Industry Forecast, 2021–2030
https://www.alliedmarketresearch.com (2023. december 4.)
[3] Liebig, J. *Liebigs Ann. Chem.* **1860**, *113*, 246–247.
[4] List, B.; Lerner, R. A.; Barbas, C. F. *J. Am. Chem. Soc.* **2000**, *122*, 2395–2396.
[5] Ahrendt, K. A.; Borths, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000**, *122*, 4243–4244.

2. Literature review

The industrial application of organocatalysts is not yet significant, but given the progress made by academic researchers and the potential benefits of organocatalysis, it can be argued that the use of organocatalysts could be extended to industry if their application is made sustainable. This can be achieved by finding a solution for recycling and reusing the catalyst. Since organocatalysts are small organic molecules, the first representatives were homogeneous catalysts, but heterogeneous variants soon followed. Nowadays, both types can be efficiently recycled, but the sustainable recycling of catalysts requires further development.[6]

Although the recycling of homogeneous catalysts can be achieved by chromatography, this method is only applicable on a laboratory scale as it does not meet sustainability requirements. Today, most industrial catalytic processes are carried out in a multi-phase system where the catalyst is heterogeneous. Although their activity and selectivity are often lower than the corresponding homogeneous alternative, heterogeneous catalysts have significant advantages, such as easy separation from the reaction mixture, allowing rapid and economical reuse. From an industrial point of view, this may be a greater advantage due to easy recycling than a disadvantage due to lower catalytic activity and/or selectivity.[7]

Heterogenisation of homogeneous organocatalysts is a commonly used method to recover them from the reaction mixture, which can be achieved either by precipitation of the homogeneous catalyst or by using a heterogeneous catalyst in the first place.[8] The immobilisation of organocatalysts to a support has a major impact on the activity of the catalyst: both the type of support and the linker play an important role. Catalysts thus heterogenised can be recycled by simple filtration or centrifugation, which is highly beneficial from a green chemistry perspective. Furthermore, by changing the linker, it is possible to optimise the performance of the heterogeneous catalyst.

A special type of modification of organocatalysts is the conversion into a phase-transfer catalyst. The homogeneous catalyst is either converted into a salt or a complexing unit is added. Phase-transfer catalysis is an efficient asymmetric synthetic method, as it is not only cheap and sustainable, but also involves simple procedures under mild reaction conditions. Due to these advantages, phase-transfer catalysis is widely used in industrial processes.[9] In the case of asymmetric phase-transfer catalysis, as in the case of catalysts grafted to a solid support, the linker also plays an important role, in this case connecting the chiral moiety and the unit providing the phase-transfer property.

Compared to conventional separation methods (distillation, extraction, evaporation, adsorption, chromatography), membrane technologies may be preferable due to their low energy and space requirements and easy scalability. Due to its many attractive properties, membrane separation is widely used in industry.[10] Organic solvent nanofiltration (OSN) can separate molecules between 50-2000 Da using only a pressure gradient. The sustainability of OSN has seen significant advances, from more environmentally friendly membrane production to process efficiency improvements and scale-up. Hence, OSN is a sustainable recycling method for homogeneous catalysts. During the filtration process, the catalyst accumulates in the retentate. The efficiency of the separation is highly dependent on the difference in molecular

[6] Bertelsen, S.; Jørgensen, K. A. *Chem. Soc. Rev.* **2009**, *38*, 2178–2189.
[7] Benaglia, M. Recoverable and Recyclable Catalysts, John Wiley & Sons, 2009, 301–340.
[8] Joshi, S. S.; Ranade, V. V. Industrial Catalytic Processes for Fine and Specialty Chemicals, Elsevier, 2016
[9] Tan, J.; Yasuda, N. *Org. Process Res. Dev*. **2015**, *19*, 1731–1746.
[10] Galizia, M.; Bye, K. P. *Front. Chem.* **2018**, *6*, 511.

weight between the catalyst and the other components and on the absolute retention of the catalyst on the membrane. The leakage of catalyst into the permeate and the resulting loss of conversion and selectivity cause serious difficulties.[11] Therefore, small catalysts require an increase in molecular size, for example by anchoring to a multifunctional central core.

Although the modification of catalysts, whether by grafting to a solid support or to a central core, allows efficient catalyst recovery, it is essential to investigate the effect of the modification on catalytic activity and selectivity. In my work, I have focused on organocatalysts containing basic or hydrogen bond donor units.

In the case of asymmetric organocatalysts, economic considerations make it preferable to choose a starting material from the "chiral pool". Therefore, commercially available quinine and its derivatives (cinchona alkaloids) containing several asymmetric centres are often chosen as building blocks for organocatalysts. They have the advantage of being easily modifiable at multiple sites and containing a strongly basic nitrogen atom. The cinchona skeleton has bifunctional properties, since its hydroxyl group at position 9, or with its modification by another hydrogen bond donor moiety (squaramide, thiourea, etc.), is capable of activating electrophiles, whereas the nitrogen atom of the quinuclidine ring is responsible for activating nucleophiles as a hydrogen bond acceptor (Fig. 1).[12] Another important feature of cinchonas is that catalysts prepared from molecules with opposite configurations in the molecular part responsible for the catalytic activity are often observed to give the product with the opposite configuration.

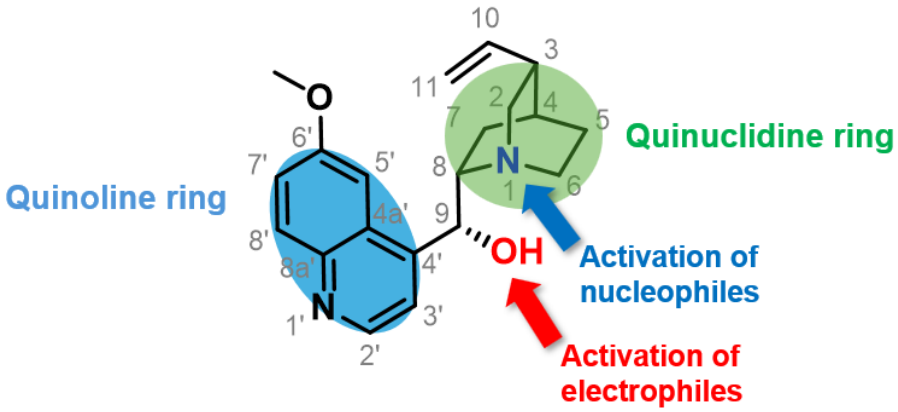


Fig. 1 Structure and conventional numbering of quinine

Nowadays, there is an increasing demand for sustainable plastic recycling methods as global plastic production is growing exponentially. One such sustainable method could be the chemical recycling of plastics, whereby the polymer is broken down into its building blocks, so that high quality, clean plastics can be produced again. Effective organocatalysts with basic and acidic character are used in academia, but their efficient recycling has not yet been solved, and therefore the development of recyclable catalysts is needed to make this method applicable to industry.

[11] Marchetti, P.; Jimenez Solomon, M. F.; Szekely, G.; Livingston, A. G. *Chem. Rev*. **2014**, *114*, 10735–10806.
[12] Nagy, S.; Fehér, Z.; Dargó, G.; Barabás, J.; Garádi, Z.; Mátravölgyi, B.; Kisszékelyi, P.; Dargó, Gy.; Huszthy, P.; Höltzl, T.; Balogh, G. T.; Kupai, J. *Materials* **2019**, *12*, 3034–3048.

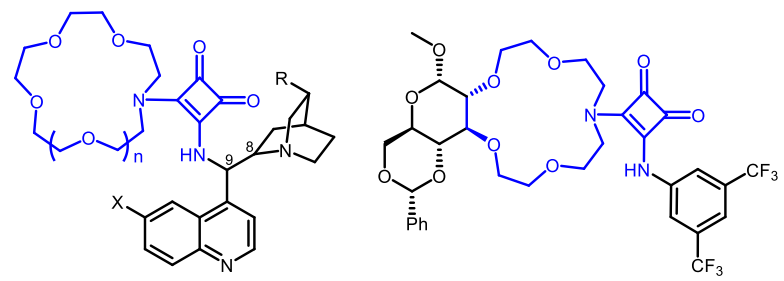
3. Experimental methods

The synthetic work was carried out using the methods of preparative organic chemistry. The progress of the reactions was monitored by TLC, NMR or HPLC-MS. The purification of the synthesised compounds was performed by column chromatography, thin layer chromatography or recrystallisation. Thin-layer chromatography, melting point measurement, optical rotation measurement and HPLC were used to check the purity of the compounds. The composition and structure of the compounds prepared were confirmed by spectroscopic methods (IR, ^{1}H, ^{13}C NMR, MS, HRMS, elemental analysis). Enantioselectivity in organocatalytic reactions was determined by chiral HPLC measurements. Membrane filtrations were carried out by Dr György Székely and his research group (King Abdullah University of Science and Technology). The results of the experimental designs were analysed using Statistica.

4. Results

4.1. Synthesis of novel crown ether-squaramides and their application as phase-transfer catalysts

Nowadays, an increasing number of asymmetric phase-transfer catalysts are being developed that include a hydrogen bond donor unit. Since no crown ether-based catalysts containing a squaramide unit have been used previously under phase-transfer conditions, we aimed to prepare new chiral crown ether-squaramide phase-transfer organocatalysts. Six different catalysts (**Q5**, **Q6**, **HQ5**, **C5**, **C6**, **G5**) were prepared using different chiral (quinine, hydroquinine, cinchonine and α-D-glucopyranoside) and crown ether units (1-aza-15-crown-5-ether, 1-aza-18-crown-6-ether) (Fig. 2). To the best of our knowledge, this was the first successful direct coupling of a squaramide unit to aza-crown ethers.



Q5: n=1, (8*S*,9*S*), X=OMe, R=vinyl (34%)
Q6: n=2, (8*S*,9*S*), X=OMe, R=vinyl (22%)
HQ5: n=1, (8*S*,9*S*), X=OMe, R=ethyl (76%)
C5: n=1, (8*R*,9*R*), X=H, R=vinyl (47%)
C6: n=2, (8*R*,9*R*), X=H, R=vinyl (49%)

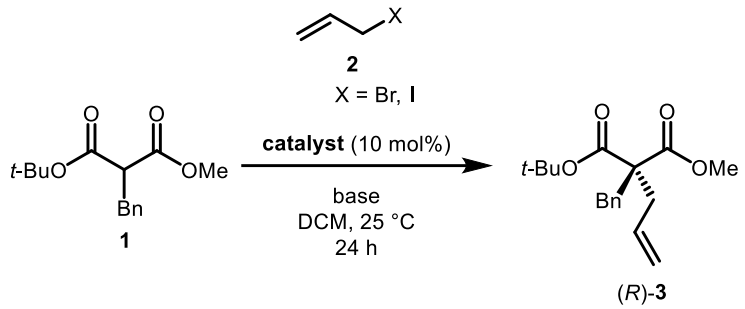
G5

Fig. 2 Cinchona alkaloid-based (**Q5**, **Q6**, **HQ5**, **C5**, **C6**) and D-glucose-based (**G5**) crown ether-squaramide phase-transfer catalysts.

The new phase-transfer catalysts were applied in the asymmetric α-alkylation of *tert*-butyl methyl α-benzyl malonate (**1**) with allyl halides (**2**) (Table 1), forming a quaternary carbon asymmetry centre in the product. The catalysts did not show significant enantioselectivity (≤9% ee). After extensive parameter studies (solvent, base, reagent, temperature), the achieved enantiomeric excess improved to only 15% using the catalyst with the highest selectivity (**C5**), but we obtained a product under appropriate conditions with excellent yield (98%), which can be further converted to α,α-disubstituted amino acids by Curtius rearrangement based on literature methods. Thus, it can be said that despite the poor selectivity, the new catalysts are

able to catalyse the formation of a quaternary carbon atom, which is often difficult to achieve due to steric hindrance.

Table 1 Comparison of catalysts in the α-alkylation of malonate **1**.



Entry	Catalyst	Base	Yield (%)	ee (%)
1	**Q5**	50% aq. NaOH	98	5
2	**Q6**	50% aq. KOH	59	<5
3	**HQ5**	50% aq. NaOH	93	<5
4	**C5**	50% aq. NaOH	73	9
5	**C6**	50% aq. KOH	37	<5
6	**G5**	50% aq. NaOH	86	5

The poor selectivity may be because the formed catalyst-substrate complex is not rigid enough, the catalyst is not able to coordinate malonate **1** sufficiently during the reaction. To address this problem, we have also used a reagent that is also able to form secondary interactions with the catalyst, thus increasing the selectivity. To investigate this, we reacted malonate **1** with benzyl acrylate reagent in Michael addition using the most selective **C5** catalyst, but we did not achieve enantioselectivity. In conclusion, the reason for the poor selectivity may be that since one amino group of the squaramide moiety in the catalysts is tertiary, only the other, secondary amino group can act as a hydrogen bond donor in the squaramide function, which our results suggest is not sufficient for efficient chiral induction. We hypothesize that a linker inserted between the crown ether moiety and the squaramide moiety may enhance enantioselectivity.

4.2. Synthesis of C_3-symmetric cinchona-based organocatalysts and their application in asymmetric Michael and Friedel–Crafts reactions

In our research group, we have previously studied several catalyst recycling methods, and in this work, we investigated the attachment of organocatalyst units to a central core (hub) to make recycling using OSN more efficient. Using different hubs and spacers, four different C_3-symmetric cinchona derivatives (**Hub$^{1–4}$-cinchona**) were prepared (Fig. 3).

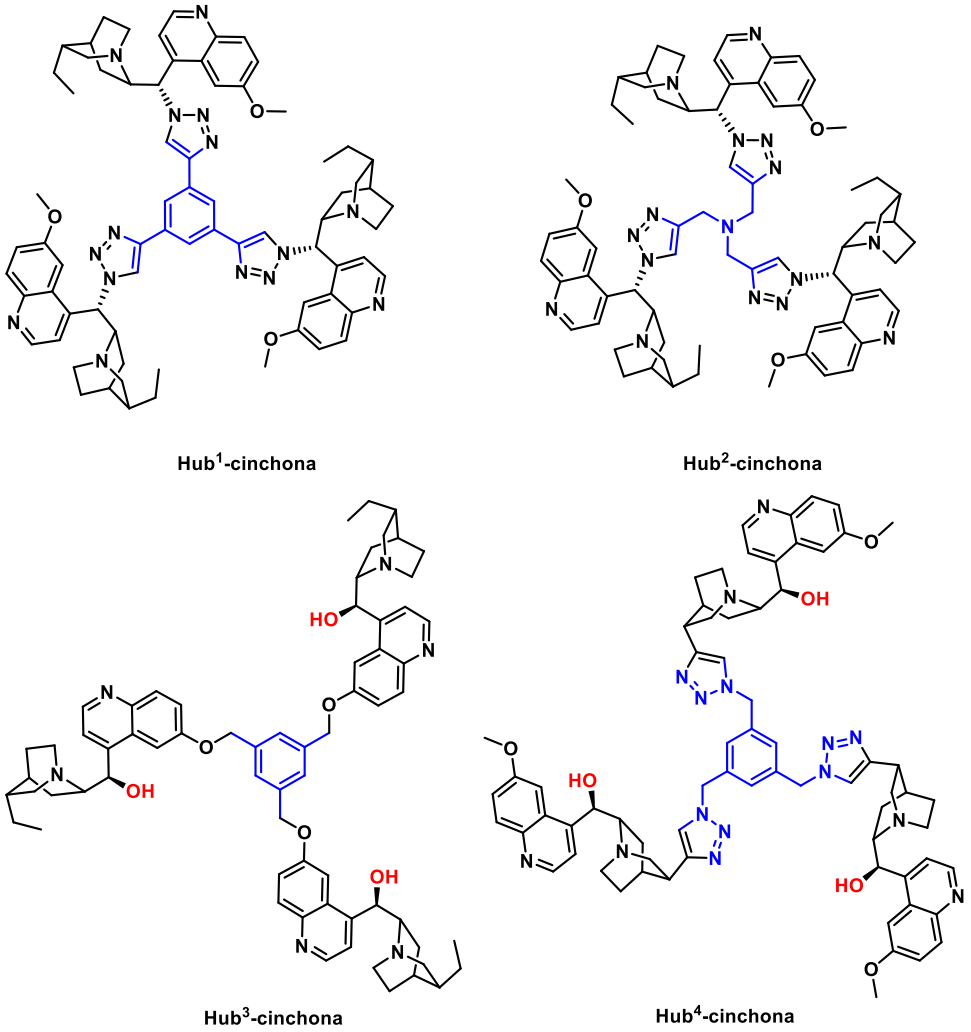
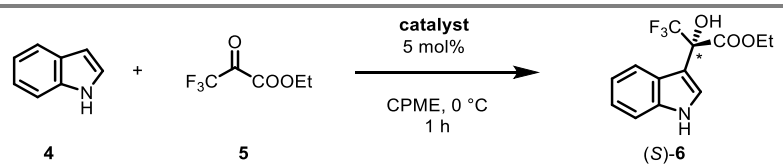


Fig. 3 Structure of the prepared C_3-symmetric cinchona derivatives.

The new cinchona derivatives were applied in the Friedel–Crafts alkylation reaction of indole with ethyl trifluoropyruvate (Table 2). First, the catalytic unit of the hub-bound organocatalysts, hydroquinine (**HQ**), was used as a catalyst to determine the best solvent (CPME) and the required reaction time. The new **Hub^X-cinchona** organocatalysts showed lower enantioselectivity (2–29% ee) than hydroquinine (73% ee).

Table 2 Friedel–Crafts alkylation of indole using hydroquinine (**HQ**) and **Hub^X-cinchona** catalysts.



4 **5** (*S*)-**6**

Entry	Catalyst	Yield (%)	ee (%)
1	**HQ**	87	72
2	**Hub^1-cinchona**	78	26
3	**Hub^2-cinchona**	77	<5
4	**Hub^3-cinchona**	69	18
5	**Hub^4-cinchona**	72	29

The reason for the lower selectivity may be that the catalytic units may also form secondary interactions with each other instead of coordinating substrates due to their spatial proximity. This hypothesis is supported by the fact that catalysts with longer spacers and stiffer cores provided better enantioselectivity than the others.

By developing new organocatalysts, we aimed to achieve their recycling by nanofiltration. By anchoring them to the hub, we increased the molecular size of the catalysts so that the membranes tested (DM900, DM500 and 20PBI.X) were able to fully retain them (Figure 4a). Membrane filtration was performed in PolarClean solvent at 10 bar pressure in a crossflow membrane cell. The DM900 membrane was found to be the most suitable for the recycling of **Hub^{X}-cinchona** catalysts, as it had the lowest retention of starting material (**4**) and product (**6**) and the highest flux (6.7±0.24 l m^{-2} h^{-1}, Figure 4b). Furthermore, the difference between the retention of hydroquinine (**HQ**) and the product (**6**) is small and therefore hydroquinine cannot be effectively recycled in this way.

Subsequently, the **Hub^{3}-cinchona** organocatalyst was investigated in the Michael addition of pentane-2,4-dione and 1,3-diphenylpropane-1,3-dione with *trans*-β-nitrostyrene, and in the latter, an enantiomeric excess of ≤93% was achieved. This represents a significant improvement in selectivity compared to hydroquinine (6% ee). In conclusion, C_3-symmetric cinchona organocatalysts attached to a central core may show better selectivity than the catalytic unit because their bulkiness may increase the rigidity of their structure, thus reducing the number of diastereomeric transition states, or because an alternative catalyst-substrate interaction involving two or more cinchona units may be created.

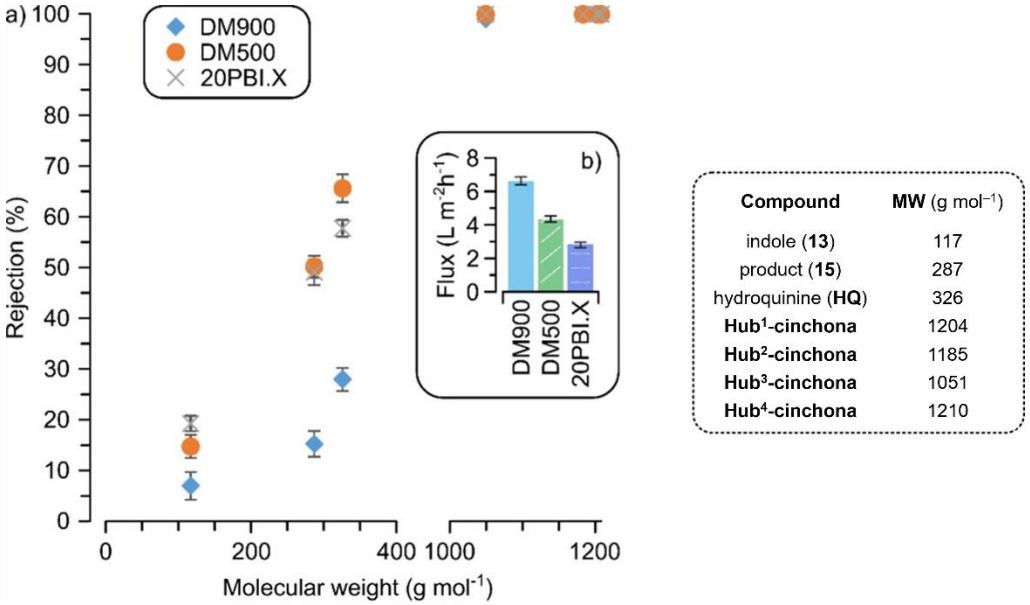


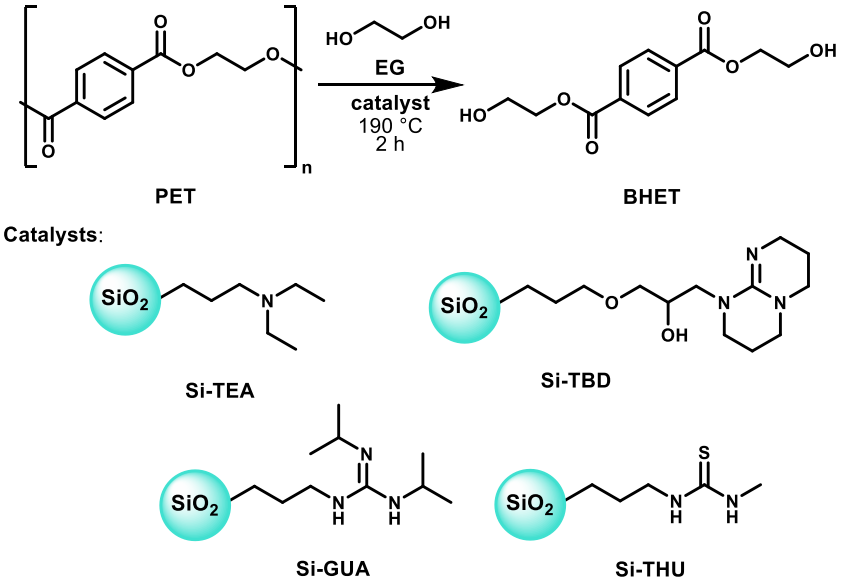
Fig. 4 Rejection (**a**) and flux (**b**) values for the three screened solvent-resistant membranes in PolarClean solvent at 10 bar in crossflow mode. The molecular weights (MW) of the tested compounds are shown on the right side of the figure, while the labels in (**a**) show the measurements on the different membranes.

4.3. Recyclable heterogeneous organocatalysts for PET glycolysis

Of the most significant plastics, poly(ethylene terephthalate) (PET) is the one that generates waste in the highest proportion, as it is mainly used for packaging. Due to its slow biodegradation and inadequate waste management, there is a need to develop recycling strategies to prevent its harmful effects on the environment and improve the sustainability of its

use. In my work, I aimed to develop a method for the chemical recycling of PET using recyclable organocatalysts. The depolymerisation of PET was carried out by glycolysis with ethylene glycol using organocatalysts supported on silica gel (Scheme 1). The advantage of glycolysis is that PET can be regenerated from the resulting bis(2-hydroxyethyl) terephthalate (BHET) in only one polycondensation step.

The reactions were carried out starting from ground post-consumer PET bottles in a closed glass vial. As catalysts, three commercially available modified silica gels (Si-TEA, Si-GUA, Si-THU) and a TBD-functionalised (1,5,7-triazabicyclo[4.4.0]dec-5-ene) silica gel (Si-TBD) prepared by us were used. In preliminary experiments, we compared the activity of the catalysts in glycolysis and also their thermal stability using TG-DSC. It was found that Si-TBD has the highest activity (92% BHET yield), but Si-TEA, which also has a relatively good catalytic activity (83% BHET yield), was found to be the most stable. As our aim was to recycle the catalysts, the more stable Si-TEA was used as catalyst for reaction optimisation.



Scheme 1 PET glycolysis with ethylene glycol.

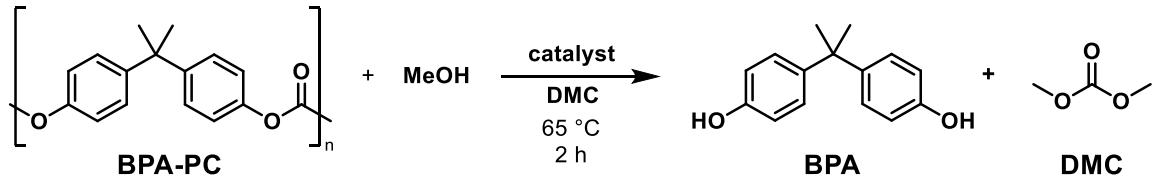
In order to optimise the reaction parameters, a 2^{4-1} fractional factorial design was developed to investigate the effects of temperature, catalyst loading, ethylene glycol:PET molar ratio and reaction time, with upper and lower levels chosen based on the preliminary parameter studies. Since our aim was to achieve the best possible BHET selectivity, a simple linear model for BHET yield was set up for the optimisation. We found that reaction temperature has the highest effect on BHET yield over the investigated parameter ranges, and that the interaction between catalyst and ethylene glycol amount, in addition to the main effects of the factors, has a statistically significant influence on the yield. Optimisation was performed using gradient method based on a reduced model with significant effects. As a result, the optimal reaction parameters are 190 °C, 15.5 mol% catalyst, 12.6:1 ethylene glycol:PET molar ratio, 1.7 h reaction time (for 0.38 g PET).

After determining the optimal conditions, the Si-TEA and Si-TBD catalysts were recycled for a total of 5 cycles each. The cumulative BHET yield for 5 reactions was 89% for the Si-TEA catalyst and 88% for the Si-TBD catalyst, indicating that despite the different stability measured with TG-DSC, there is no significant difference in the activity of the recycled catalysts. Reaction scale-up (6- and 18-fold) was also successfully achieved in a flask reaction with Si-TEA catalyst under optimal conditions with longer reaction times, during which

complete conversion was also observed. The experiments showed that further optimisation of the reaction time or stirring rate is required to improve yield, and this is being pursued after the submission of the present thesis.

4.4. A silica-supported organocatalyst for polycarbonate methanolysis under mild and economic conditions

As a continuation of our work on PET glycolysis, we also wanted to investigate the robustness of modified silica gels used in the chemical recycling of PET. Therefore, the next plastic of choice was bisphenol A based polycarbonate (BPA-PC), which can be depolymerised by a nucleophilic reagent in a similar way to PET. The importance of recycling BPA-PC lies in the fact that the BPA monomer, being a xenoestrogen, can have a harmful effect on the environment if waste BPA-PC is disposed of in landfills. Therefore, it is important to develop cost-effective solutions for the waste treatment and recycling of the polymer. Methanolysis of PC (Scheme 2) avoids the generation of carbon dioxide (unlike hydrolysis) and allows the use of BPA-PC as a source of carbonyl group to replace more expensive and hazardous reagents such as phosgene.



Scheme 2 Methanolysis of BPA-PC.

In our work, we applied the same organocatalysts grafted to silica gel as previously investigated in PET glycolysis (see Scheme 1). Among them, the Si-TBD catalyst synthesised by us has the highest catalytic activity in the methanolysis of PC (88% BPA yield). The reactions were carried out starting from pure BPA-PC granules to later degrade waste PC under optimised conditions; preliminary experiments were performed in a closed glass vial and optimisation was carried out in a round-bottomed flask.

The PC methanolysis process was also optimised by experimental design, in this case with 2^3 full factorial design (parameters: temperature, catalyst loading, MeOH:PC molar ratio), with the effect of reaction time being investigated separately. Statistically significant effects were temperature and MeOH:PC ratio. Optimisation was performed based on the resulting linear model. The optimal reaction conditions were 65 °C, 5 mol% Si-TBD, n(MeOH):n(PC) = 13:1, 2 h (for 2 g PC), in which case 96% BPA yield was obtained. The reaction kinetics was also investigated, and it was shown that Si-TBD-catalysed PC methanolysis is a pseudo-first-order reaction with an extremely low activation energy of 44.19 kJ mol^{-1}, which is the lowest of any PC methanolysis reaction published to date.

Si-TBD could be efficiently recycled in 10 reaction cycles after regeneration with KOH/MeOH solution, and although the activity of the regenerated catalyst was slightly lower than the native catalyst, good BPA yield (72±4%) was achieved. Furthermore, the effect of an inert atmosphere on catalyst recycling was investigated and its use was found not to be necessary, which facilitates industrial applicability. Even at room temperature, Si-TBD was able to catalyse the depolymerisation of PC in 2 days without stirring, with excellent BPA yield (94%), and using waste PC as starting material, the same results were obtained.

5. Theses

1) I prepared six novel crown ether-squaramide phase-transfer organocatalysts, incorporating distinct chiral units, through the unprecedented direct coupling of squaramide and aza-crown-ether components. These catalysts were applied in asymmetric *C*-alkylation and Michael addition under appropriate conditions with excellent or good yield (98% and 74%, respectively) but limited enantioselectivity (up to 17% ee). Despite the low selectivity, the catalysts demonstrated effectiveness in constructing quaternary carbon centres. [FZS-2]

2) I prepared four C_3-symmetric cinchona organocatalysts anchored to a trifunctional central core (hub) and investigated their catalytic performance in Friedel–Crafts alkylation of indole and Michael addition reactions. While the hub-cinchona catalysts exhibited reduced enantioselectivity (up to 29% ee) in the Friedel–Crafts reaction, structural–selectivity correlations highlighted the importance of more rigid and extensive spacers. In contrast, the **Hub^3-cinchona** catalyst demonstrated enhanced selectivity in the Michael addition reaction, achieving 93% ee with a bulkier substrate. Membrane recovery was facilitated by the hub-cinchona catalysts' increased molecular weight, showcasing potential for these sustainable catalytic processes. [FZS-1]

3) I demonstrated the efficacy of silica-supported organocatalysts Si-TBD and Si-TEA in the glycolysis of PET (polyethylene terephthalate). I employed experimental design and gradient method to optimise reaction conditions, revealing that Si-TEA achieves optimal performance (89% yield) at 190 °C, 15.5 mol% catalyst concentration, an ethylene glycol to PET molar ratio of 12.6, and a 1.7-hour reaction time. The recyclability of Si-TEA and Si-TBD was demonstrated through five reaction cycles with high BHET yields (89%, and 88% cumulative yields, respectively), and relatively low environmental energy impact was indicated compared to other PET glycolytic methods. [FZS-3]

4) I introduced a 'proof of concept' for the application of solid-supported organocatalysts in PET glycolysis, showing the efficiency of Si-TEA and Si-TBD catalysts. A scale-up of the reaction was achieved, with a 6-fold and 18-fold increase using Si-TEA, demonstrating the potential for industrial application. [FZS-3]

5) I established that the silica-supported TBD (Si-TBD) is a highly effective and economically viable heterogeneous organocatalyst for BPA-PC (poly(bisphenol A carbonate)) methanolysis. The optimisation of reaction conditions, including temperature, catalyst concentration, and MeOH:PC molar ratio, was achieved through experimental design, culminating in an economically optimised process with remarkable BPA yield (96%). The catalyst was recycled in 10 consecutive reaction cycles (72±4% average yield for the recycled catalyst in 9 reactions). [FZS-4]

6) The kinetic studies reveal that Si-TBD-catalysed PC methanolysis follows a pseudo-first-order reaction with an unprecedentedly low activation energy (44.19 kJ mol^{-1}). The catalyst's exceptional performance, demonstrated by depolymerisation of BPA-PC at room temperature without stirring, positions Si-TBD as a cost-efficient and potentially industrially significant catalyst. [FZS-4]

6. Possible applications

For the crown ether-squaramide phase-transfer catalysts, we proposed the introduction of a linker between the crown ether and the squaramide units, which could promote stronger hydrogen bonding and thus higher enantioselectivity, offering a promising avenue for future research. Investigation of different linkers, evaluation of catalyst recyclability and wider application could be key to optimising the new catalyst type in the future. The potential scaling-up of these catalysts for industrial applications could further help the development of the field.

The C_3-symmetric organocatalysts bound to a central core were efficiently recycled by organic solvent nanofiltration for Friedel–Crafts alkylation of indole. This environmentally friendly recycling method could be widely applied after improving selectivity by optimising the catalyst structure (e.g., incorporating a sufficiently long and rigid linker). This could contribute to the development of sustainable and economical processes in the future. For Michael additions, a positive effect of the C_3-symmetric structure on stereoselectivity was observed, which could provide valuable guidance for the design and optimisation of organocatalysts for various reactions.

In the case of chemical recycling (solvolysis) of PET and PC, our aim was to investigate the solvolytic applicability and robustness of organocatalysts attached to a solid support. Based on the comparisons reported in the dissertation, the methods we have developed have the potential to be applied in industry, although further development is needed in real scale-up. However, the experience we have described could contribute to a more sustainable management of plastic waste. Although our ongoing research suggests that in the scaled-up, thus longer-time depolymerisation of PET, the catalysts degrade at high temperatures, leading to a decrease in activity after 4-5 reaction cycles, it is expected that a solution to reduce the required reaction temperature could extend the lifetime of the catalysts. In the methanolysis of PC, Si-TBD could be an extremely cost-effective catalyst, as it is particularly suitable for industrial implementation due to its applicability at room temperature without stirring.

7. Publications

7.1. Publications serving as the basis for the dissertation

[FZS-1] Kisszékelyi, P.; **Fehér, Z.**; Nagy, S.; Bagi, P.; Kozma, P.; Garádi, Z.; Dékány, M.; Huszthy, P.; Mátravölgyi, B.; Kupai, J.: Synthesis of C_3-Symmetric Cinchona-Based Organocatalysts and Their Applications in Asymmetric Michael and Friedel–Crafts Reactions. *Symmetry* **2021**, *13*, 521. DOI: 10.3390/sym13030521, IF: 2.940; Citations: 3, Independent citations: 1. Participation share: 85%.

[FZS-2] **Fehér, Z.**; Richter, D.; Nagy, S.; Bagi, P.; Rapi, Z.; Simon, A.; Drahos, L.; Huszthy, P.; Bakó, P.; Kupai, J.: Synthesis of novel crown ether-squaramides and their application as phase-transfer catalysts. *Molecules* **2021**, *26*, 6542. DOI: 10.3390/molecules26216542, IF: 5.110; Citations: 4, Independent citations: 4. Participation share: 75%.

[FZS-3] **Fehér, Z.**; Kiss, J.; Kisszékelyi, P.; Molnár, J.; Huszthy, P.; Kárpáti, L.; Kupai, J.: Optimisation of PET glycolysis by applying recyclable heterogeneous organocatalysts. *Green Chem.* **2022**, *24*, 8447–8459. DOI: 10.1039/D2GC02860C,

IF: 9.8; Citations: 18, Independent citations: 16. Participation share: 70%.

[FZS-4] **Fehér, Z.**; Németh, R.; Kiss, J.; Balterer, B.; Verebélyi, K.; Iván, B.; Kupai, J.: A silica-supported organocatalyst for polycarbonate methanolysis under mild and economic conditions. *Chem. Eng. J.* **2024**, *485*, 149832. DOI: 10.1016/j.cej.2024.149832, IF (2022): 15.1. Participation share: 75%.

Other publications

In English:

[FZS-5] Nagy, S.; **Fehér, Z.**; Kisszékelyi, P.; Huszthy, P.; Kupai, J.: Cinchona derivatives as sustainable and recyclable homogeneous organocatalysts for aza-Markovnikov addition, *New J. Chem*. **2018**, *42*, 8596–8602. DOI: 10.1039/C8NJ01277F, IF: 3.269; Citations: 8, Independent citations: 4. Participation share: 20%.

[FZS-6] Nagy, S.; Dargó, G.; Kisszékelyi, P.; **Fehér, Z.**; Simon, A.; Barabás, J.; Höltzl, T.; Mátravölgyi, B.; Kárpáti, L.; Drahos, L.; Huszthy, P.; Kupai, J.: New enantiopure binaphthyl-cinchona thiosquaramides: synthesis and application for enantioselective organocatalysis, *New J. Chem*. **2019**, *43*, 5948–5959. DOI: 10.1039/C8NJ06451B, IF: 3.288; Citations: 17, Independent citations: 10. Participation share: 5%.

[FZS-7] Nagy, S.; **Fehér, Z.**; Dargó, G.; Barabás, J.; Garádi, Z.; Mátravölgyi, B.; Kisszékelyi, P.; Dargó, G.; Huszthy, P.; Höltzl, T.; Balogh, G. T.; Kupai, J.: Comparison of Cinchona Catalysts Containing Ethyl or Vinyl or Ethynyl Group at Their Quinuclidine Ring, *Materials* **2019**, *12*, 3034–3048. DOI: 10.3390/ma12183034, IF: 3.057; Citations: 8, Independent citations: 2. Participation share: 15%.

[FZS-8] Nagy, S.; **Fehér, Z.**; Kárpáti, L.; Bagi, P.; Kisszékelyi, P.; Koczka, B.; Huszthy, P.; Pukánszky, B.; Kupai, J.: Synthesis and Applications of Cinchona Squaramide-Modified Poly(Glycidyl Methacrylate) Microspheres as Recyclable Polymer-Grafted Enantioselective Organocatalysts, *Chem. Eur. J.* **2020**, *26*, 13513–13522. DOI: 10.1002/chem.202001993, IF: 5.236; Citations: 6, Independent citations: 3. Participation share: 20%.

[FZS-9] Kisszékelyi, P.; Nagy, S.; **Fehér, Z.**; Huszthy, P.; Kupai, J.: Membrane-Supported Recovery of Homogeneous Organocatalysts: A Review, *Chemistry* **2020**, *2*, 742–758. DOI: 10.3390/chemistry2030048, IF: 2.1; Citations: 7, Independent citations: 5. Participation share: 5%.

[FZS-10] Nagy, S.; Richter, D.; Dargó, G.; Orbán, B.; Höltzl, T.; Bagi, P.; **Fehér, Z.**; Kupai, J.: Cinchona-based hydrogen-bond donor organocatalyst metal complexes: asymmetric catalysis and structure determination, *ChemistryOpen* **2024**, e202300180. DOI: 10.1002/open.202300180, IF (2022): 2.3. Participation share: 5%.

In Hungarian:

[FZS-11] Kisszékelyi, P.; Nagy, S.; **Fehér, Z.**; Huszthy, P.; Kupai, J.: Membránszűréssel visszaforgatható homogén organokatalizátorok előállítása és alkalmazása, *Magy. Kém. Foly.* **2020**, *126*, 110–120., IF: 0. Participation share: 5%.

7.3. Presentations

International presentations:

1. **Fehér, Z.**; Németh, R.; Kiss, J.; Kupai, J.: Depolymerisation of polycarbonate applying silica gel-supported organocatalysts, International Symposium on Synthesis and Catalysis, Évora, Portugal, September 5–8, 2023
2. **Fehér, Z.**; Kiss, J.; Kisszékelyi, P.; Nagy, S.; Kárpáti, L.; Huszthy, P.; Kupai, J.: Application of heterogeneous organocatalysts in PET glycolysis, 10th European Young Engineers Conference, Warsaw, Poland (online), April 4–6, 2022
3. **Fehér, Z.**; Kiss, J.; Daicu, D.; Kisszékelyi, P.; Nagy, S.; Kárpáti, L.; Huszthy, P.; Kupai, J.: Poli(etilén-tereftalát) bontása visszaforgatható organokatalizátorok segítségével, XXVI. International Conference on Chemistry, online, October 30, 2020
4. **Fehér, Z.**; Nagy, S.; Kisszékelyi, P.; Kárpáti, L.; Pukánszky, B.; Huszthy, P.; Kupai, J.: Synthesis and application of a cinchona squaramide organocatalyst immobilized on poly(glycidyl methacrylate), 8th European Young Engineers Conference, Warsaw, Poland, April 8–10, 2019

National presentations:

5. **Fehér, Z.**; Kiss, J.; Németh, R.; Kupai, J.: Poli(etilén-tereftalát) és polikarbonát szolvolitikus depolimerizációja heterogén katalizátorok alkalmazásával, Meeting of the Working Committee of Heterocycle and Organometallic Chemistry of the Hungarian Academy of Sciences, Balatonszemes, Hungary, May 31 – June 2, 2023
6. **Fehér, Z.**; Németh, R.; Kiss, J.; Kupai, J.: Polikarbonát depolimerizációjának optimalizálása szilikagélhez rögzített organokatalizátorral, XXVI. Spring Wind Conference, Miskolc, Hungary, May 5–7, 2023
7. **Fehér, Z.**; Kiss, J.; Kisszékelyi, P.; Kárpáti, L.; Huszthy, P.; Kupai, J.: Heterogén organokatalizátorok alkalmazása PET glikolitikus lebontásában, XXV. Spring Wind Conference, Pécs, Hungary, May 6–8, 2022
8. **Fehér, Z.**; Kiss, J.; Kisszékelyi, P.; Kárpáti, L.; Huszthy, P.; Kupai, J.: PET lebontása szilikagélhez rögzített organokatalizátorokkal, XV. Szent-Györgyi Albert Conference, Budapest, Hungary, April 29–30, 2022
9. **Fehér, Z.**; Nagy, S.; Kisszékelyi, P.; Kárpáti, L.; Pukánszky, B.; Huszthy, P.; Kupai, J.: Poli(glicidil-metakrilát) hordozóhoz rögzített cinkona-négyzetamid organokatalizátor előállítása és alkalmazása, XLI. Chemistry Lectures, Szeged, Hungary, October 15–17, 2018
10. **Fehér, Z.**; Nagy, S.; Kisszékelyi, P.; Huszthy, P.; Kupai, J.: Bioaktív aza-Markovnyikov-adduktok szintézise fenntartható módon cinkona-alapú homogén organokatalizátorokkal, Meeting of the Working Committee of Alkaloid and Flavonoid Chemistry of the Hungarian Academy of Sciences, Mátrafüred, Hungary, April 12–13, 2018
11. **Fehér, Z.**; Nagy, S.; Kisszékelyi, P.; Huszthy, P.; Kupai, J.: Cinkonaalkaloid-alapú organokatalizátorok szintézise, alkalmazása aza-Markovnyikov-addíciókban és visszaforgatása szerves oldószeres nanoszűréssel, XL. Chemistry Lectures, Szeged, Hungary, October 16–18, 2017