Preparation of Dendritic and Non-Dendritic Styryl-Substituted Salens for Cross-Linking Suspension Copolymerization with Styrene and Multiple Use of the Corresponding Mn and Cr Complexes in Enantioselective Epoxidations and Hetero-Diels–Alder Reactions

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Dedicated to Professor K. Barry Sharpless on the occasion of his 60th birthday

Abstract: Following work with TADDOLs and BINOLs, we have now prepared Salen derivatives (**2**, **3**, **14**, **15**, **18**, **19**, **20**, **21**) carrying two to eight styryl groups for cross-linking copolymerization with styrene. The Salen cores are either derived from (*R*,*R*)-diphenyl ethylene diamine (**3**, **15**, **19**, **21**) or from (*R*,*R*)-cyclohexane diamine (**2**, **14**, **18**, **20**). The styryl groups are attached to the salicylic aldehyde moieties, using Suzuki (cf. **1**) or Sonogashira cross-coupling (cf. **11**), and/or phenolic etherification (cf. **5**, **7**) with dendritic styryl-substituted Fréchet-type benzylic branch bromides. Subsequent condensation with the diamines provides the chiral Salens. Corresponding Salens lacking the peripheral vinyl groups (cf. **12**, **13**, **16**, **17**) were also prepared for comparison of catalytic activities in homogeneous solution with those in polystyrene. Cross-linking radical suspension copolymerization of styrene and the styryl Salens, following a procedure by Itsuno and Fréchet, gave beads (ca. 400 μm diameter) which were loaded with Mn or Cr (ca. 0.2 mmol of complex per g of polymer), with more than 95% of the Salen incorporated being actually accessible for complexation (by elemental analysis). The polymer-bound Mn and Cr complexes were used as catalysts for epoxidations of six phenyl-substituted olefins (*m*-CPBA/NMO; products **22a–f**), and for dihydropyranone formation from the Danishefsky diene and aldehydes (PhCHO, $C_5H_{11}CHO$, $C_6H_{11}CHO$, products **23a–c**). There are several remarkable features of the novel immobilized Salens: i) The dendritic branches do not slow down the catalytic activity of the complexes in solution; ii) the reactions with Salen catalysts incorporated in polystyrene give products of essentially the same enantiopurity as those observed in homogeneous solution with the dendritically substituted or with the original Jacobsen–Katsuki complexes; iii) some Mn-loaded beads have been stored for a year, without loss of activity; iv) especially the biphenyl- and the acetylene-linked Salen polymers (p-**2**, -**3**, -**20**, -**21**, Figure 2, 3) give Mn complexes of excellent performance: after ten uses (without re-charging with Mn!) there is no loss of enantioselectivity or degree of conversion under the standard conditions.

Keywords: asymmetric catalysis · cycloadditions · dendritic cross-linkers · epoxidations · polymer-bound Salen

Introduction

The preparation and application of polymer-supported reagents and catalysts is a rapidly growing field in modern synthetic chemistry. Solid-phase methodology plays a crucial role in combinatorial chemistry and led to a tremendous progress in this area.[1–3] Simultaneously, the importance of enantioselective synthesis has increased during the last decades, due to development of a great variety of highly effective catalysts for all kinds of enantioselective transformations.[4–6] Unfortunately, such catalysts are often very expensive and, in addition, have to be separated from the reaction mixture after use so that their application for the industrial production of chemicals is rather limited. In order to overcome these drawbacks, it is favorable to bind such catalysts to a polymer support which allows easy separation from the reaction mixture and reuse in many consecutive catalytic cycles.[7–14] In this way, even chemically sophisticated and expensive catalytic systems might become attractive for large-scale production. Also, chiral ligands or catalysts can be

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bound to a soluble support. In this case, the catalytic process can be performed under homogeneous conditions with the advantage that the desired micro-environment around the catalytic sites is generated, due to the very "flexible nature" of the supported catalyst; the major disadvantage is the recovery of the soluble catalyst from the reaction mixture. In contrast, immobilization of catalysts on heterogeneous supports allows easy separation from the reaction mixture by simple filtration and thus facilitates the handling of such catalysts tremendously. Unfortunately, heterogeneous catalysts prepared in this way are often less active than their homogeneous counterparts due to the fact that diffusion of substrates and products to and from the catalytic centers on the support is hindered. It should, however, also be pointed out that sometimes aggregation of several complexes leads to the actual catalytically most active species (in solution, cf. nonlinear effects[15]), and such aggregation is of course prevented on a very rigid polymer support, and especially with low degree of loading.

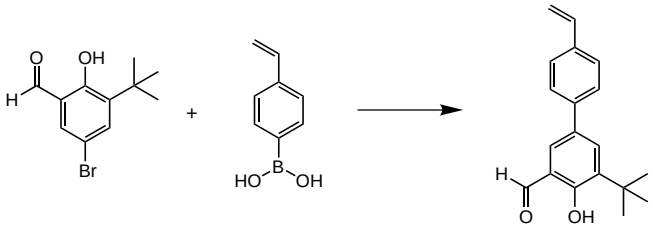
Several years ago, we have immobilized the TADDOL (TADDOL = $\alpha,\alpha,\alpha',\alpha'$-tetraaryl-1,3-dioxolane-4,5-dimethanol) on polystyrene, a versatile ligand for many enantioselective transformations,[16, 17] developed in our laboratory.[18] For practical reasons, suspension copolymerization of suitable TADDOL precursors with styrene and divinyl benzene (DVB) to give polymer beads, which are easy to handle, was our preferred way of immobilization at the time.[19] In 1997 we began to use dendritically modified TADDOLs with styryl groups at the periphery as cross-linkers in polystyrene, without the use of an additional cross-linker, as for example DVB.[20] This was in fact the first application of dendrimers as polymer cross-linkers. Having shown that TADDOLs, immobilized in this way, have an excellent catalytic activity,[21] we turned to the immobilization of 1,1′-bi-2-naphthol (BINOL) in the same way, confirming the high potential of this new way of immobilization in various Lewis acid mediated test reactions.[22] As already stated, we consider suspension copolymerization as a very useful way of binding a chiral ligand to a solid polymer support. Grafting of the desired ligand onto a commercially available polymer, as for example a Merrifield resin, or copolymerization of a mono-styryl substituted ligand with styrene/DVB requires a smaller synthetic effort, but immobilization "in our way" (i.e., copolymerization of a chiral cross-linking ligand with styrene) offers certain advantages: The polymers generated this way contain cavities around the catalytic sites within the polymer matrix that are likely to be chiral. Similar to the method of *molecular imprinting* in highly cross-linked polymer resins (developed by Wulff and his group[23, 24]) chiral cavities could lead—in an enzyme-like way—to an increase in catalytic performance of a polymer-bound catalyst in our case. In fact, a polymer-bound TADDOL, prepared by copolymerization of a cross-linking TADDOL dendrimer with styrene, showed a rate increase with respect to the homogeneous reaction in the Ti-TADDOLate mediated addition of Et_2Zn to PhCHO.[21] This was not the case with polymers prepared by copolymerization of a mono-styryl TADDOL with styrene/DVB. Furthermore, the C_2-symmetrical cross-linkers might serve as chiral templates for the polymerization of styrene to generate chiral polystyrene.[25]

In order to further extend this new and promising approach and motivated by the success with our TADDOLs and BINOLs, we have now immobilized Salen in the same way. There have already been quite a number of attempts of immobilizing Salen on inorganic supports,[26] as for example on zeolites, within a polysiloxane membrane[27] and on organic polymer supports, for use in Mn-Salen mediated enantioselective epoxidation of olefins[28–31] and kinetic resolution of terminal epoxides.[32] However, Salens immobilized on organic polymer supports have often given rather disappointing results in heterogeneous enantioselective epoxidations.[28–30] Quite recently, Sherrington reported for the first time on a polymer-bound Mn-Salen with a catalytic activity comparable to that of the homogeneous catalyst (epoxidation of 1-phenyl cyclohexene).[31]

In order to compare our approach of immobilization in a cross-linking fashion with other existing methods special focus was put on the use of dendritically modified Salen cross-linkers, especially in multiple use. Preparation of the Salen cross-linkers, copolymerization with styrene and application of the polymer-bound catalysts in various test reactions are the subjects of the present paper.

Results and Discussion

Preparation of Salen cross-linkers 2 and 3: The simplest way of generating a Salen cross-linker for styrene copolymerization is to introduce styryl groups at both aromatic units of the Salen core. Thus, the linear biphenyl branch **1** was generated by Suzuki cross-coupling of 3-*tert*-butyl-5-bromo salicylic aldehyde[33] and styrene boronic acid[34] (Scheme 1).[35] Very



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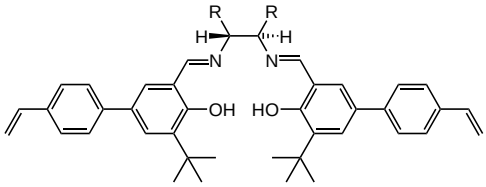

2 (R—R = -$(CH_2)_4$-)

3 (R = Ph)

Scheme 1. Preparation of the biphenyl arm **1** by Suzuki coupling. Conditions: [$Pd(PPh_3)_4$], 2 M Na_2CO_3, THF, 70 °C, 77%. The Salen monomers **2** and **3** were prepared by condensation of **1** with the corresponding diamines.

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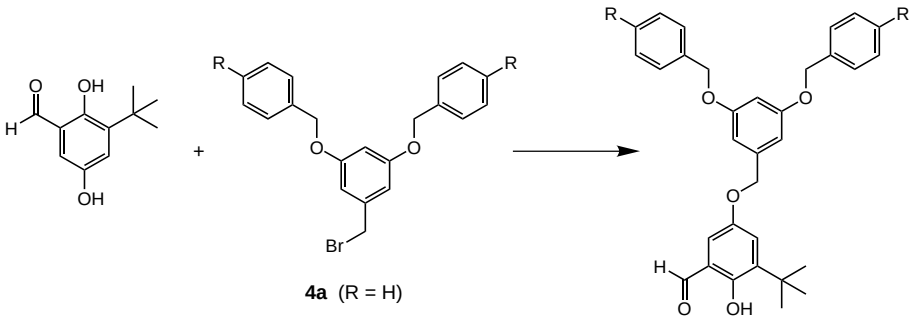
remarkably, no protection of the aldehyde or OH functions of the aldehyde was necessary. Condensation of **1** with (*R*,*R*)-1,2-cyclohexane diamine or (*R*,*R*)-1,2-diphenyl ethylene diamine under standard conditions afforded **2** and **3** in 83 and 91% yield, respectively.[28b, 29b] In contrast to this procedure, Suzuki cross-coupling of the Salen, prepared by condensation of 3-*tert*-butyl-5-bromo salicylic aldehyde with the diamine, and styrene boronic acid was not successful due to very slow conversion.

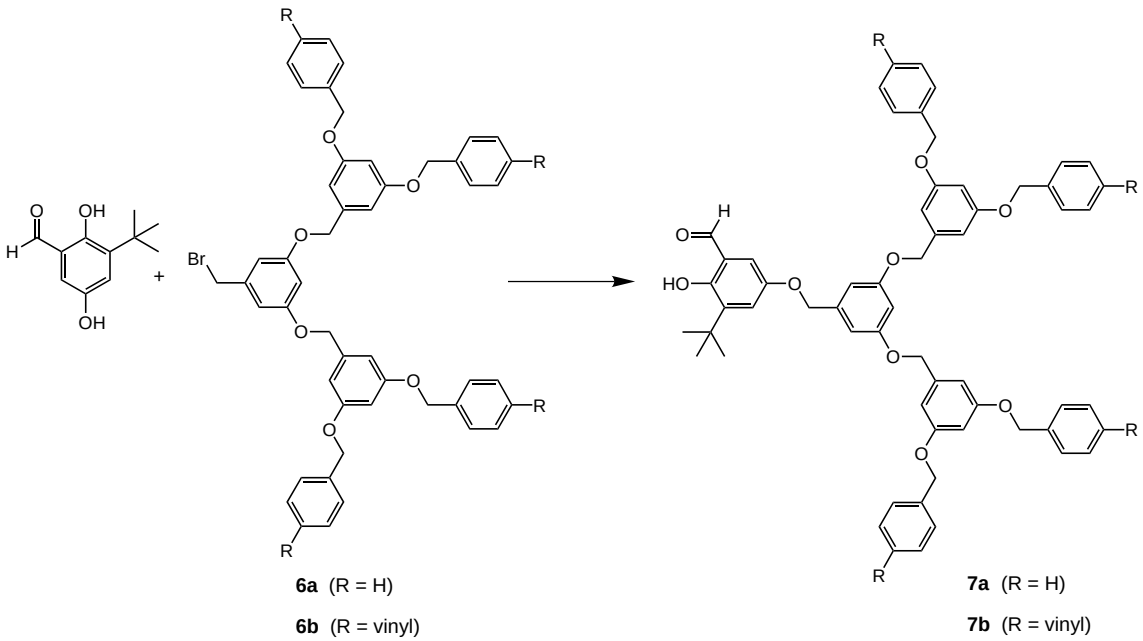
Preparation of first- and second-generation dendritic salicylic aldehyde branches: The main focus of this work was put on the investigation of dendritically cross-linked Salen copolymers. In order to compare the catalytic activity of the polymers to be prepared with the corresponding Salen dendrimers under homogeneous reaction conditions we also synthesized the analogous compounds lacking the vinyl groups. We decided to assemble the Salen cross-linkers by condensation of the corresponding dendritic salicylic aldehyde branches with the desired diamine. As described for the preparation of **2** and **3**, the strategy of first preparing the desired salicylic aldehyde derivative followed by condensation with the diamine appeared to be more promising than coupling of branches to a preformed Salen core structure. Thus, etherification of 3-*tert*-butyl-5-hydroxy-salicylic aldehyde[28d] with first-generation dendritic branches **4a**[36] and **4b**[22] afforded salicylic aldehyde derivatives **5a** and **5b** without and with vinyl groups in yields of 53 and 60%, respectively (Scheme 2).

Analogously, second-generation salicylic aldehyde branches **7a** and **7b** were prepared by mono-etherification of 3-*tert*-butyl-5-hydroxy-salicylic aldehyde with benzylic bromides **6a**[36] and **6b**[22] (Scheme 3).

One of the main applications of chiral Salen ligands is the manganese-mediated epoxidation of olefins.[37] We anticipated that Salen systems prepared from salicylic aldehyde branches **5a**,**b** and **7a**,**b** might be sensitive to oxidation under the reaction conditions due to the fact that they are hydroquinone derivatives. Therefore, we prepared the dendritic branch compound **11** with an acetylene linkage between the dendritic subunit and the salicylic aldehyde part which was expected to be much more stable under oxidative conditions than the branch compounds described above. The acetylene spacer moiety was introduced by Sonogashira cross-coupling[38] of 3-*tert*-butyl-5-bromo salicylic aldehyde[33] with



Scheme 2. Preparation of dendritic branches **5a** and **5b** by etherification reaction of 3-*tert*-butyl-5-hydroxy salicylic aldehyde with the benzyl bromides **4a** and **4b**. Conditions: K_2CO_3, KI, acetone, 70 °C, 6 h.



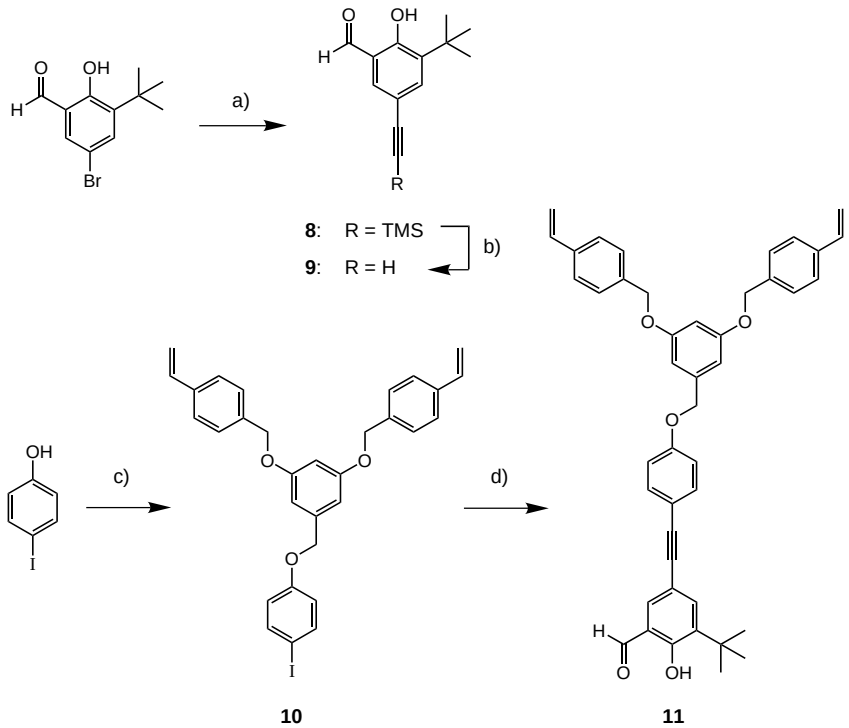
Scheme 3. Preparation of second-generation dendritic salicylic aldehyde branches **7a** and **7b**. Conditions: K_2CO_3, KI, acetone, 70 °C, 4 h.

ethinyl trimethyl silane to give the alkinyl derivative **8** in quantitative yield (Scheme 4). Again, no protection of functional groups was necessary. The desilylation of **8** caused problems: addition of TBAF to its solution in THF gave the deprotected product **9** in only 27% yield, due to oligomerization. The acetylene moiety reacts with the aldehyde group under these reaction conditions. Therefore, the deprotection was performed with TBAF in THF in the presence of 1N HCl, giving **9** in 82% yield after 20 h. Subsequent Sonogashira coupling with the dendritic aryl iodide branch compound **10**, prepared by etherification of **4b**[22] with commercial 4-iodo phenol, afforded the desired dendritically modified salicylic aldehyde derivative **11** (63%, Scheme 4).[38, 39]

Preparation of Salen dendrimers: The dendrimers **12**–**21** with and without peripheral vinyl groups were prepared by heating a solution of dendritic branches **5a**,**b**, **7a**,**b** or **11** and the desired diamine in EtOH for several hours (Scheme 5).[28b, 29b] In most cases, the dendrimers were obtained in yields between 75 and 95% after purification by flash column chromatography, and they were fully characterized by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy, by MALDI-TOF or Hi-Res-MALDI spectrometry, and by elemental analysis.

Epoxidation of olefins under homogenous conditions using dendritic Salen ligands 12, **13**, **16**, **and 17**: Before immobilizing dendritically substituted Salens in polystyrene and investigating the catalytic properties of their manganese complexes we had to check whether the dendritic modification gives rise to any change in the catalytic activity in solution. Thus, Salens **12**, **13**, **16**, and **17** were loaded with Mn by heating a solution of Salen and $Mn(OAc)_2 \cdot 4H_2O$ for several hours in EtOH/toluene, while air was bubbled through the reaction mixture, followed by stirring at room temperature for a further 12 h in the presence of LiCl (following published procedures[28, 29b, 33]). The epoxidation reactions were generally run with 20 mol% of Mn-Salen,[40] two equivalents of *m*-chloroperbenzoic acid (*m*-CPBA) as oxidant and five equivalents of 4-methylmorpholine-*N*-oxide (NMO) as additive in CH_2Cl_2 at $-20\,^\circ$C (Scheme 6).[41]

As shown in Scheme 6, we used several different phenyl substituted olefins as test substrates. The results are collected in Table 1. The selectivities and conversions obtained in the epoxidation of styrene (→ **22a**) with Salens **12** and **16** were comparable to those obtained with the corresponding (and commercially available) Jacobsen catalyst under identical conditions (*er* 75:25, conversion complete after 1 h). 3-Methyl styrene (→ **22b**) was oxidized in very similar selectivities and conversions. For both substrates, the enantiomer ratios in the epoxides formed using the diphenyl-ethylenediamine-derived Salens **13** or **17** were higher than those achieved with the cyclohexane diamine-derived Salens **12** and **16** (Table 1). The epoxidation of (*E*)-phenylpropene (→ **22c**) proceeded with lower enantioselectivities, in accordance with literature data.[37a] In contrast, enantiomerically highly enriched products and high degrees of conversions were observed with dendritically modified Salens **12**, **13**, **16**, and **17** in the epoxidation of 1-phenyl cyclohexene (→ **22d**), again comparable with the results obtained with the simple unsubstituted Jacobsen catalyst.[31, 42] Also, epoxidation of dihydronaphthalene (→ **22e**) gave rise to high enantioselectivities, again similar to the results obtained with unsubstituted Jacobsen catalyst under the same conditions (*er* 91:9, conversion complete after 15 minutes), whereas in the case of *trans*-stilbene (→ **22f**) the enantiomer ratios were poor. In summary, modification of Salen ligands with dendritic branches up to the second generation does not affect the catalytic performance in a negative way. The selectivities obtained in homogeneous solution using Salens **12**, **13**, **16**, and **17** are similar to those reported for the classical Jacobsen catalyst under comparable conditions. Furthermore, there seems to be no dependence of the catalytic activity from the size of the dendritic branches attached to the Salen core–second-generation Salens **16** and **17** gave, in most cases, similar results as the first-generation Salens **12** and **13**, in contrast to the observations made during our work on polymer-bound TADDOL[20] and BINOL[22]!



Scheme 4. Preparation of dendritic salicylic aldehyde branch **11**. Conditions: a) ethinyl trimethyl silane, $[PdCl_2(PPh_3)_2]$, CuI, THF, NEt_3, 70 °C, 12 h, quant.; b) TBAF · $3H_2O$, THF/1N HCl, 20 h, 82%; c) **4b**, K_2CO_3, 18-crown-6, acetone, 70 °C, 5 h, 92%; d) **9**, $[PdCl_2(PPh_3)_2]$, CuI, THF, NEt_3, 70 °C, 12 h, 63%.

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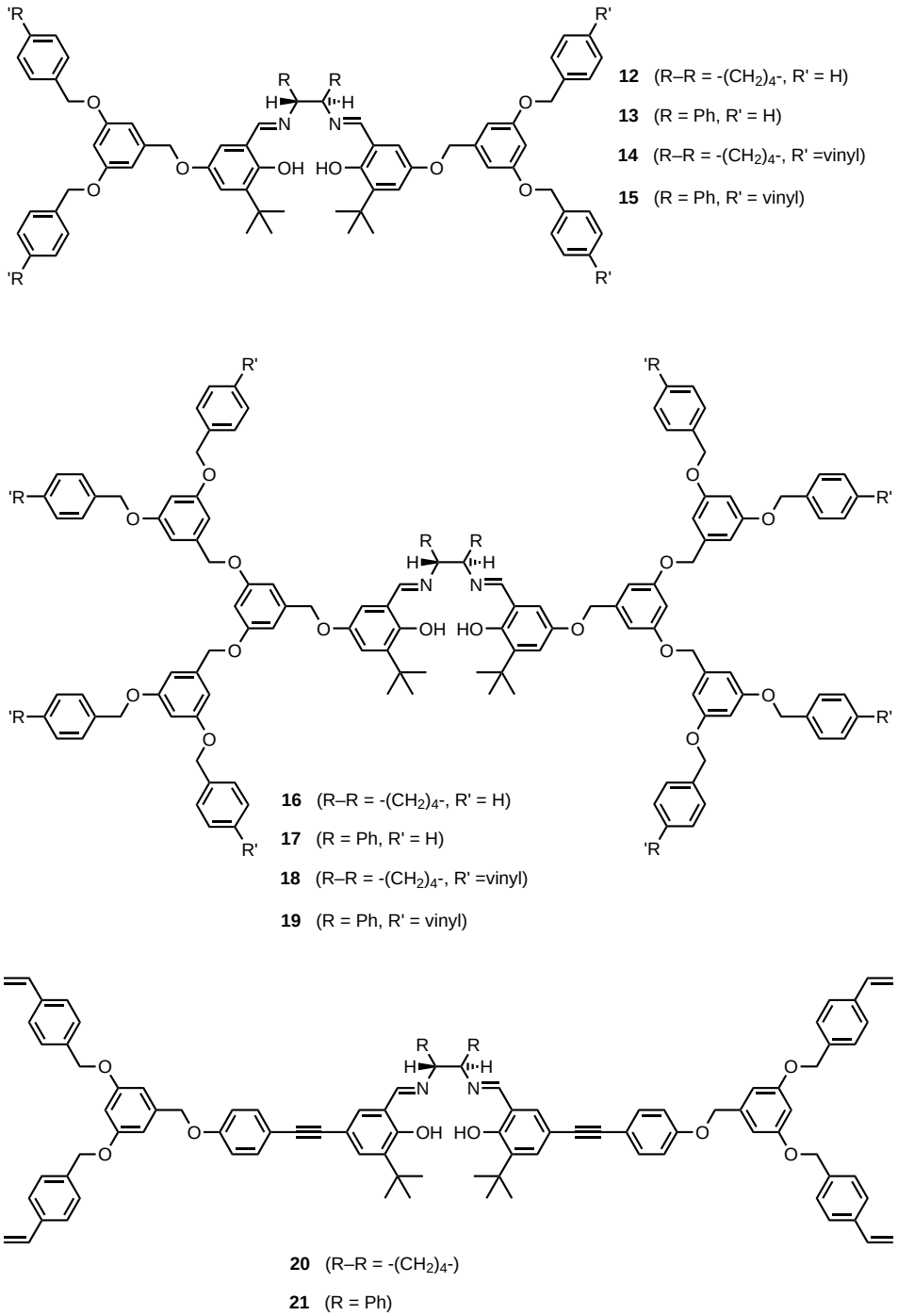
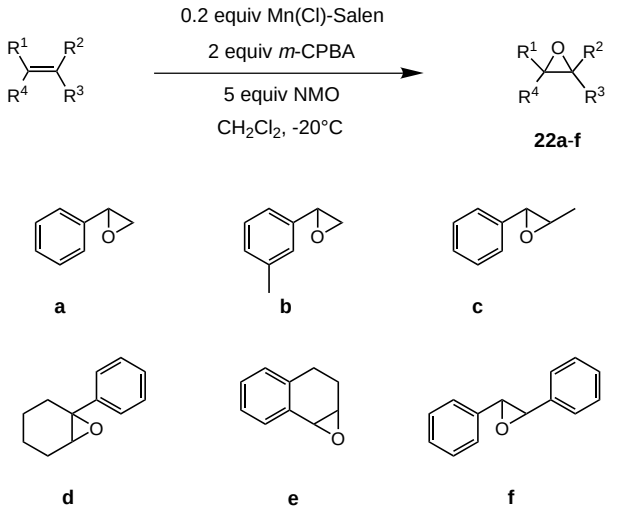


Scheme 5. Dendrimers **12**–**21** prepared by condensation of branches **5a**, **5b**, **7a**, **7b**, and **11** with the corresponding diamines.

Copolymerization of Salen cross-linkers with styrene to give polymer-bound Salen ligands and complexes thereof: Having shown that Salen ligands with attached dendritic branches are catalytically highly active, we have immobilized the styryl derivatives **2**, **3**, **14**, **15**, and **18**–**21** in polystyrene by suspension copolymerization using a procedure by Itsuno and Fréchet.[43] A solution of cross-linkers **2**, **3**, **14**, **15**, or **18**–**21**, styrene and azoisobutyronitrile (AIBN) in benzene and THF was mixed with an aqueous solution of poly(vinyl alcohol) (PVA) under constant stirring and heating at 85 °C for 24 h (Scheme 7). During this radical polymerization process spherical beads of cross-linked polystyrene were formed, with an average diameter of 500 μm and swelling factors between 2.5 and 4 in solvents such as toluene, CH_2Cl_2 or THF. After extensive washing with various solvents the polymer beads were collected by size, using a set of sieves with different mesh widths. In most cases the polymers were obtained in quantitative yield so that the loading (mmol Salen per g polymer) was directly calculated from the stoichiometric amounts of monomers used. Having experienced in our previous work[22] with the copolymerization of non-protected BINOL and styrene that the free phenolic OH groups

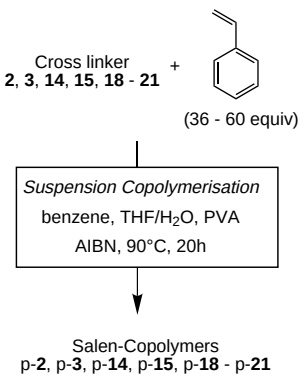


Scheme 6. Epoxidation of various olefins mediated by Mn-Salens **12**·, **13**·, **16**· and **17**·Mn(Cl) in homogeneous solution to give epoxides **22a**–**f**. The corresponding Mn-Salens were prepared according to literature procedures.[28, 29b, 33]

Table 1. Selectivities and conversions obtained in the epoxidation of various olefins, mediated by Mn complexes of Salens **12**, **13**, **16**, and **17** in homogeneous solution to give epoxides **22a**–**f** under the conditions outlined in Scheme 6. With the Jacobsen catalyst the following selectivities and conversions were obtained under the same conditions (conversion in both cases complete after 30 minutes): **22a**: *er* 75:25; **22e**: *er* 91:9.

Epoxide **22**	Salen	Conversion [%][a]	*er*
a	**12**	87	73:27
a	**13**	80	83:17
a	**16**	79	72:28
a	**17**	82	84:16
b	**12**	94	76:24
b	**13**	83	84:16
b	**16**	92	76:24
c	**12**	90	53:47
c	**13**	58	55:45
c	**16**	80	53:47
d	**12**	90	96:4
d	**13**	75	92:8
d	**16**	83	95:5
d	**17**	76	89:11
e	**12**	94	89:11
e	**13**	97	90:10
e	**16**	93	91:9
e	**17**	98	89:11
f	**12**	12	57:43
f	**13**	7	52:48
f	**16**	8	59:41

[a] After 30 min, determined by capillary gas chromatography (CGC).



Scheme 7. Suspension copolymerization of cross-linkers **2**, **3**, **14**, **15**, **18**–**21** with styrene to give Salen/styrene copolymers p-**2**, p-**3**, p-**14**, p-**15**, p-**18**–p-**21**. Conversions were complete in most cases so that ligand loadings were calculated by the relative amounts of monomers used. Loadings: 0.13–0.20 mmol g^{-1}.

the residues of the washing fractions no unpolymerized Salen derivatives or decomposition products were detected.

Epoxidation reactions of olefins catalyzed by polymer-bound Mn-Salens: For loading with Mn the beads were suspended in DMF/EtOH, in the presence of ten equivalents of Mn-$(OAc)_2 \cdot 4H_2O$; the beads changed color from yellow to black, immediately (Figure 1). Heating of the suspension under

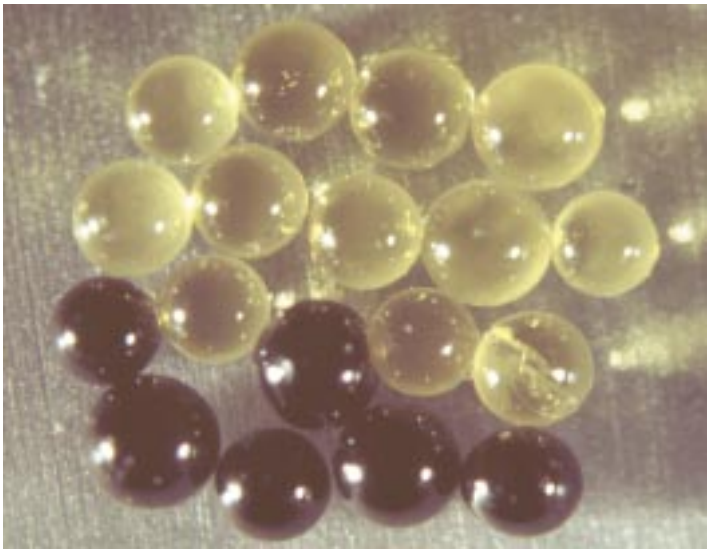


Figure 1. Polymer beads of p-**14** before (yellow) and after (black) loading with manganese.

suppressed the polymerization, we were surprised to see that in the case of the Salen derivatives (bearing a *tert*-butyl group at each phenolic moiety) no problems during copolymerization were encountered. After all, 2,6-di-*tert*-butyl-phenols are widely used as antioxidants (radical traps) in plastic materials.[44] Nevertheless, in order to make sure that all cross-linking Salen moieties were covalently incorporated into the resin and that no decomposition products from cross-linkers remained, the beads were extensively washed with THF, a solvent in which they swell well: by NMR measurements with reflux for 3 h, with air bubbling through the mixture, was followed by addition of 20 equivalents of LiCl and stirring at room temperature for 12 h, to give polymer-bound Mn-Salens p-**2**·, p-**3**·, p-**14**·, p-**15**·, p-**18**·, p-**19**·, p-**20**· and p-**21**·Mn(Cl).[28b, 31, 45] After the loading process, it was very important to wash the beads extensively with THF (to remove excess Mn salts and LiCl). The resulting supported Mn-Salens were stable to air, and even after storage for one year catalytically as active as directly after loading. Elemental analysis showed that in most charges the experimentally

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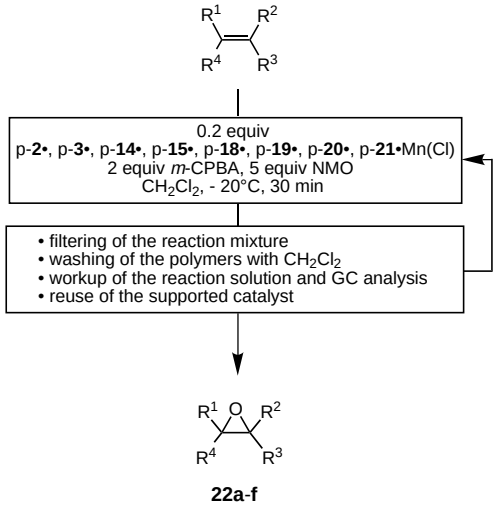
determined loading of the beads with manganese corresponded to the theoretical values, as shown in the following examples: p-**14**·Mn(Cl) (loading 0.2 mmol g^{-1}), theoretical Mn content 1.08%, found 1.03%; p-**15**·Mn(Cl) (loading 0.2 mmol g^{-1}), theoretical Mn content 1.08%, found 1.12%.

The epoxidation reactions were generally carried out by suspending the beads in CH_2Cl_2, adding an olefin and NMO, cooling to $-20\,^{\circ}C$ and finally adding *m*-CPBA (Scheme 8).



Scheme 8. Multiple application of polymer supported Mn-Salens in the epoxidation of olefins to give epoxides **22a–f** (see Scheme 6).

After 30 minutes, the reaction solution was withdrawn by syringe and the polymer beads were washed several times with CH_2Cl_2. Basic workup of the organic phases afforded the crude product which was analyzed by capillary gas chromatography (CGC) on a chiral column to provide the ratio of enantiomeric epoxides **22** as well as the content of unreacted olefin.[46]

The catalytic performance of the polymer-bound Mn-Salens was tested using the same substrates as in the homogeneous reaction (Scheme 6). The results are collected in Table 2. In the epoxidation of styrene and 3-methyl styrene to the epoxides **22a** and **22b** almost the same enantioselectivities were observed as in solution (see Table 1). As in the homogeneous reaction the complexes derived from Salens with a diphenyl ethylene diimine moiety (p-**3**·, p-**15**·, p-**19**· and p-**21**·Mn(Cl)) gave rise to higher enantioselectivities than the polymers containing cyclohexane diamine derived Salen cross-linkers (p-**2**·, p-**14**·, p-**18**· and p-**20**·Mn(Cl)). Furthermore, polymers p-**2**· and p-**3**·Mn(Cl), with the styryl groups directly attached to the Salen core, as well as p-**20**· and p-**21**·Mn(Cl), containing an acetylene spacer between Salen core and dendritic branches, showed complete conversion after a reaction time of 30 minutes. The results for the epoxidation of styrene are by far the best reported up until now for Mn-Salen complexes immobilized on organic supports. The epoxidation of (*E*)-phenylpropene (→ **22c**), mediated by p-**15**·Mn(Cl), proceeded with very low enantiomer ratios and with low conversions, as in homogeneous solution (Table 1). The reason for testing a substrate under heterogeneous conditions that gives rise to very poor enantioselectivities in solution was to check whether immobilization of Salen (site isolation of catalytic centers) has a positive effect on the catalytic performance (i.e., by change of the mechanism of epoxidation on solid support). This seemed not to be the case for **22c**. In contrast, ver good results were obtained for the epoxidations of 1-phenyl cyclohexene (→ **22d**) and dihydronaphthalene (→ **22e**). For **22d** almost the same enantiomer ratios (*er* up to 92:8) as in solution (*er* up to 96:4, Table 1) were observed whereas the enantioselectivities for **22e** (*es* up to 81%) were slightly reduced with respect to the homogeneous reaction (*es* up to 91%, Table 1). In both cases the best results were obtained with polymers p-**14**· and p-**18**·Mn(Cl) containing cyclohexane diamine derived Salen cross-linkers. However, *trans*-stilbene gave rise to very poor enantiomer ratios and very low conversions. Again, as in the case of (*E*)-phenylpropene, it was not possible to increase the catalytic performance by binding of Salen to a solid support.

In summary, the performance of Salen cross-linked polymers in epoxidation reactions was in all cases comparable to that observed under homogeneous conditions. According to our knowledge, the present work represents the first example of a Salen system immobilized on an organic support that exhibits a good catalytic activity towards a broad range of substrates. Placing the catalytic moiety at the cross-link of the polymer within a dendritic environment generates polymers that are catalytically highly active.

Multiple application of polymer-bound Mn-Salens in enantioselective epoxidations of olefins: Having shown that a variety of olefins can be epoxidized in very good enantiose-

Table 2. Selectivities and conversions obtained in the epoxidation of various olefins, mediated by Mn complexes of polymer-bound Salens p-**2**, p-**3**, p-**14**, p-**15**, p-**18**–p-**21** to give epoxides **22a–f** (see Scheme 6) under the conditions shown in Scheme 8. The loading of the polymers was 0.20 mmol g^{-1} unless otherwise stated.

Epoxide **22**	Salen-polymer	Conversion [%][b]	*er*
a	p-**2**	quant.	71:29
a	p-**3**	quant.	81:19
a	p-**14**	74	73:27
a	p-**15**	61	78:22
a	p-**18**	88	70:30
a	p-**19**	56	77:23
a	p-**20**[a]	quant.	72:28
a	p-**21**[a]	quant.	80:20
b	p-**2**	quant.	71:29
b	p-**3**	quant.	77:23
b	p-**14**	75	74:26
b	p-**15**	42	75:25
c	p-**15**	35	52:48
d	p-**14**	75	92:8
d	p-**15**	49	84:16
d	p-**18**	72	90:10
d	p-**19**	49	79:21
e	p-**14**	88	81:19
e	p-**15**	74	75:25
e	p-**18**	90	79:21
e	p-**19**	80	69:31
f	p-**14**	9	61:39
f	p-**15**	8	51:49

[a] Loading: 0.13 mmol Salen per g polymer. [b] After 30 min, determined by CGC.

lectivities and conversions we turned to the reusability of our catalysts. Due to the big synthetic effort of preparing a polymer-bound catalyst (first the synthesis of suitable polymerizable precursors, then the immobilization) it is of utmost importance to demonstrate its reusability in many catalytic cycles. Polymers p-**2**· and p-**3**·Mn(Cl) each were recycled ten times in the enantioselective epoxidation of styrene and 3-methyl styrene (Figure 2). The epoxides **22a** and **22b** were

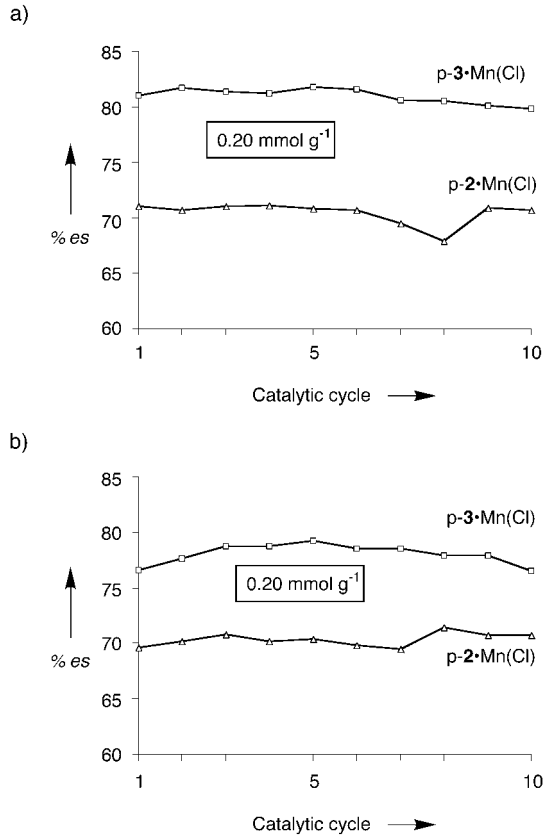


Figure 2. Multiple use of supported Mn-Salens p-**2**· and p-**3**·Mn(Cl) in the enantioselective epoxidation of a) styrene (→**22a**) and b) 3-methyl styrene (→**22b**), cf. Scheme 8.

obtained without any drop in enantioselectivity and conversion (always quantitative after a reaction time of 30 minutes) over ten cycles. This was the first time that a polymer-bound Salen could be recycled effectively without any loss in performance.

Encouraged by this fact, we also tried to reuse the dendritically cross-linked polymers p-**14**· and p-**15**·Mn(Cl), as often as possible, in the epoxidation of styrene (→**22a**) (Figure 3). Unfortunately the drop in selectivity and conversion was very pronounced in both cases, especially with polymer p-**15**·Mn(Cl), containing a diphenyl ethylene diamine derived Salen cross-linker, which, after ten cycles, gave rise to almost racemic product **22a**. Our first assumption was that loss in activity was due to leaching of manganese from the polymers. However, reloading of, for example, polymer p-**15**·Mn(Cl) with manganese after ten cycles, as described above, did not reinstall the original activity: **22a** was obtained with an enantiomer ratio of 52:48 instead of 51:49 before reloading, and the conversion decreased even further. This means that in repeated uses of manganese complexes of polymers p-**14** and p-**15** irreversible inactivation occurs. Probably the Salen units within these polymers are readily oxidized under the reaction conditions, due to the hydroquinone structure of the Salen cores. Very recently, Sherrington reported that recycling of a supported Mn-Salen, anchored to the resin via a benzyl ether linkage, failed.[31b] Furthermore, reloading of Sherrington's supported ligand with manganese did not reinstall the original performance of the catalyst, in accordance with our observations.[31b] Leaching of Salen from the polymer, a further possible reason for the decline in catalytic performance, could be excluded in our case as Salen or Salen-derived decomposition products were never detected by NMR spectroscopy of the crude reaction mixtures.

As we had not encountered recycling problems with polymers p-**2**· and p-**3**·Mn(Cl), bearing the original styryl groups directly attached to the Salen core, we concluded that it would probably be favorable to introduce an acetylene spacer between the dendritic branches and the Salen core in order to diminish the sensitivity to oxidation (as discussed above). It turned out that this approach was in fact very successful. Polymers p-**20**· and p-**21**·Mn(Cl) could be recycled ten times without significant loss in enantioselectivity and conversion (Figure 3). These results prove that loss in catalytic performance of polymers p-**14**· and p-**15**·Mn(Cl) is very likely due to oxidation of the Salen moieties under the reaction conditions.

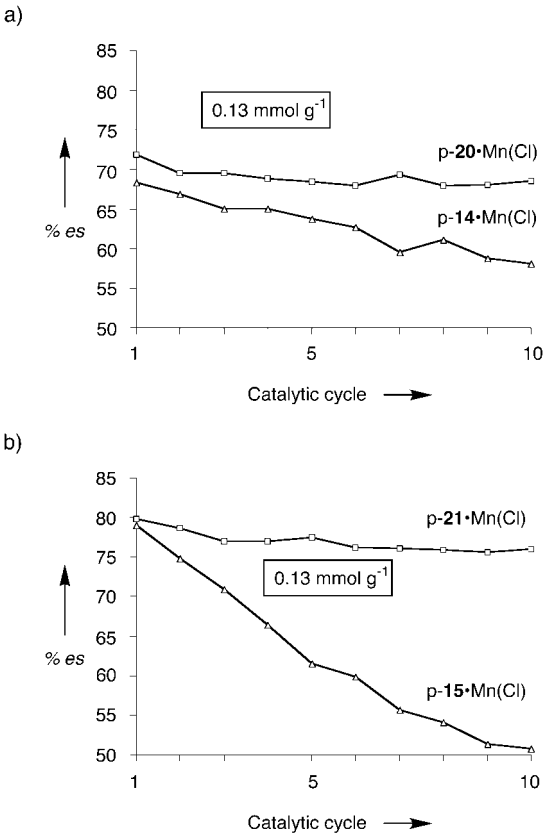


Figure 3. Comparison of polymer-bound Mn-Salens p-**14**· and p-**20**·Mn(Cl) (a) as well as p-**15**· and p-**21**·Mn(Cl) (b) during multiple use in the enantioselective epoxidation of styrene (→**22a**), cf. Scheme 8.

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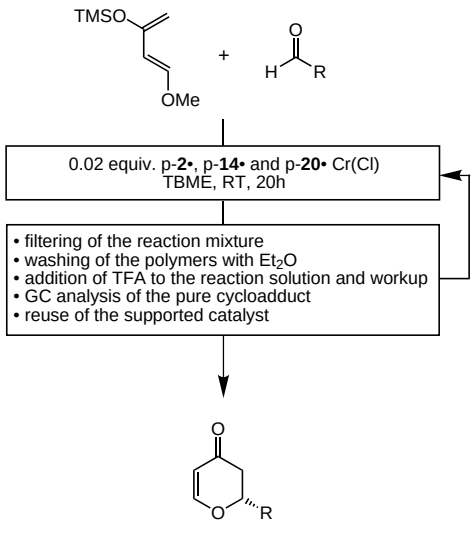
Hetero-Diels–Alder reaction of Danishefsky's diene with various aldehydes mediated by polymer-bound Salens: The growing importance of asymmetric hetero-Diels–Alder reactions can be attributed to the development of a number of very effective catalysts.[47] In 1998 Jacobsen demonstrated that Cr-Salen complexes can be employed for asymmetric hetero-Diels–Alder reactions of Danishefsky's diene with aldehydes to give dihydropyranones in good enantioselectivities.[48] We decided to test this reaction using polymers p-**2**, p-**14**, and p-**20** containing a cyclohexane diamine-derived Salen. For loading of the catalysts with chromium, the polymer beads were suspended in THF and $CrCl_2$ was added. The beads immediately changed color from yellow to brown. Stirring under Ar for 3 h and with contact to air for 12 h, followed by extensive washing with THF, afforded p-**2**·, p-**14**·, and p-**20**·Cr(Cl). The hetero-Diels–Alder reactions were generally performed using 0.02 equivalents of polymer-bound Cr(Cl)-Salen and one equivalent of diene and aldehyde, respectively (on the 1 mmol scale), in *tert*-butyl methyl ether (TBME) at room temperature (Scheme 9). After a reaction time of 24 h a sample was withdrawn from the reaction mixture for determination of the conversion by CGC. The reaction solution was filtered off and the beads were washed with Et_2O. After treatment of the combined organic fractions with trifluoro acetic acid (TFA) and purification by flash column chromatography the enantiomer ratios of cycloadducts **23a–c** were determined by CGC using a chiral column (Scheme 9).



23a-c

a: R = C_6H_5; **b**: R = pentyl, **c**: R = cyclohexyl

Scheme 9. Multiple application of polymer supported Cr-Salens p-**2**·, p-**14**· and p-**20**·Cr(Cl) in the hetero-Diels–Alder reaction of Danishefsky's diene with various aldehydes to give cycloadducts **23**.

The results for benzaldehyde, capronaldehyde and cyclohexane carboxaldehyde are summarized in Table 3. In all cases selectivities were achieved that were only slightly lower than in homogeneous solution under identical conditions.[49] For all three aldehydes tested, the lowest selectivities were obtained with p-**20**·Cr(Cl), the manganese analogue of which had given rise to the best results during multiple use in the epoxidation of styrene. Furthermore, the cycloadditions proceeded very slowly in the case of cyclohexane carboxaldehyde. Jacobsen had shown that the best enantioselectivities and conversions were obtained using a Salen-Cr(BF_4) complex.[48] This complex is prepared in solution by treatment of the corresponding Salen-Cr(Cl) complex with $AgBF_4$ to give a heterogeneous reaction mixture.[48] Generation of the polymer-bound Cr(BF_4)-Salen complex by exchange of the counterion in the supported Cr(Cl)-Salen was, thus, not possible. In order to circumvent this problem, p-**2**·Cr(BF_4) was generated by preforming **2**·Cr(BF_4) in solution, followed by copolymerization. The complex p-**2**·Cr(F) was prepared by addition of NaF to a suspension of p-**2**·Cr(BF_4) in acetonitrile/THF.[48] Unfortunately, p-**2**·Cr(BF_4) and p-**2**·Cr(F) did not give rise to better enantiomer ratios and conversions in the cycloaddition of capronaldehyde with Danishefsky's diene (Table 3).

Table 3. Hetero-Diels–Alder reaction of Danishefsky's diene with aldehydes, catalyzed by polymer-bound Cr-Salens, according to Scheme 9. The selectivities obtained with simple unsubstituted Cr(Cl)-Salen are the following: **23a**: *er* = 80:20; **23b**: *er* = 89:11; **23c**: *er* = 87:13.

Catalyst	Loading [mmol g^{-1}]	Cycloadduct **23**	*er* (**23**)	Conversion[a] [%]
p-**2**·Cr(Cl)	0.20	**a**	78:22	74
p-**14**·Cr(Cl)	0.13	**a**	79:21	67
p-**20**·Cr(Cl)	0.13	**a**	75:25	82
p-**2**·Cr(Cl)	0.20	**b**	85:15	79
p-**2**·Cr(F)	0.20	**b**	85:15	58
p-**2**·Cr(BF_4)	0.20	**b**	85:15	27
p-**14**·Cr(Cl)	0.13	**b**	86:14	70
p-**20**·Cr(Cl)	0.13	**b**	85:15	73
p-**2**·Cr(Cl)	0.20	**c**	85:15	60
p-**14**·Cr(Cl)	0.13	**c**	86:14	41
p-**20**·Cr(Cl)	0.13	**c**	82:18	36

[a] After a reaction time of 24 h.

Again, we turned our attention to the reusability of the catalysts. Figure 4 shows the enantioselectivities in the formation of cycloadducts **23a** and **b** by reaction of Danishefsky's diene with PhCHO or capronaldehyde in five consecutive catalytic cycles. Very surprisingly, in the case of p-**2**· and p-**14**·Cr(Cl), the enantioselectivity with which the dihydropyranones **23** were formed, steadily increased during multiple use to reach the values of the homogeneous reaction (Table 3) while the conversion gradually dropped. In contrast, p-**20**·Cr(Cl) could be recycled up to ten times without loss of conversion (only the first five cycles are shown in Figure 4) and with essentially constant enantioselectivity. Thus, also in case of the hetero-Diels–Alder reaction, the polymer p-**20**·Cr(Cl) prepared from a Salen cross-linker containing acetylene spacers between dendritic branches and Salen core exhibits a superior performance with respect to recycling compared with the corresponding polymer p-**14**·Cr(Cl), built from a Salen cross-linker with the dendritic branches directly attached to the core by etherification.

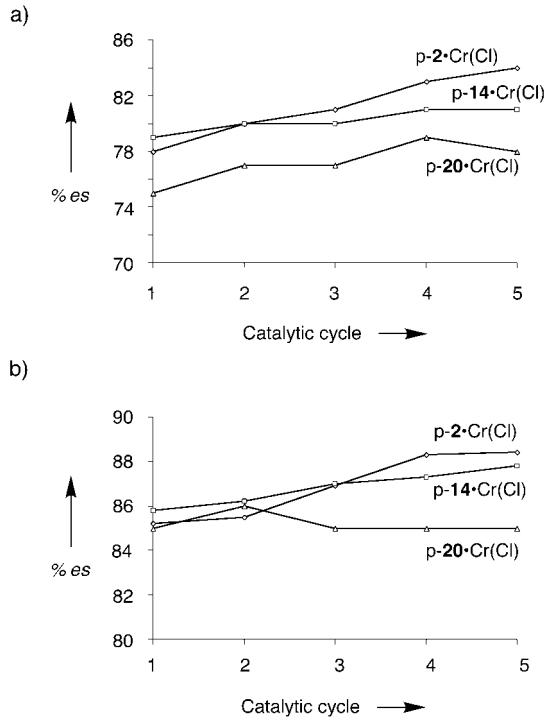


Figure 4. Multiple use of Cr-Salen polymers p-**2**•, p-**14**• and p-**20**•Cr(Cl) in the hetero-Diels–Alder reaction of Danishefsky's diene with a) benzaldehyde (→**23a**) and b) capronaldehyde (→**23b**), cf. Scheme 9.

Conclusion

In the present paper we have demonstrated that Salen ligands can be successfully immobilized on polystyrene by copolymerization of suitable cross-linking styryl derivatives with styrene. Polymer-bound manganese complexes were employed for the enantioselective epoxidation of various olefins giving rise to selectivities that were comparable with the results in solution. Furthermore, we have demonstrated for the first time that immobilized Salens can be recycled up to ten times without loss of activity in Mn-Salen mediated epoxidations. The high catalytic activity of the Salen copolymers was also shown in the Cr-Salen catalyzed hetero-Diels–Alder reaction of Danishefsky's diene with aldehydes. For the first time we have shown that this reaction can be performed using a polymer-bound Salen complex affording the corresponding cycloadducts in the same selectivities as under homogeneous conditions. In addition, multiple use of the supported Cr-Salen complexes in consecutive catalytic cycles is possible.

Experimental Section

General: *Starting materials and reagents*: The solvents used in the reactions were of p.a. quality or purified and dried according to standard methods. 4-Methylmorpholine-*N*-oxide monohydrate (NMO) was heated at 110 °C under reduced pressure for 24 h to remove water. *tert*-Butyl methyl ether (TBME), capron aldehyde ($C_5H_{11}CHO$) and benzaldehyde were distilled prior to use. All other chemicals were used as commercially available.

Equipment: TLC: precoated silica gel 25 Durasil UV_{254} plates (Macherey–Nagel); visualization by UV_{254} light, development using phosphomolybdic acid solution (phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot 4H_2O$ (10 g), H_2SO_4 (60 mL), H_2O (940 mL)). Flash column chromatography: SiO_2 60 (0.040–0.063 mm, Fluka), pressure 0.2–0.3 bar. M.p.: open glass capillaries, Büchi 510 (Tottoli apparatus), 50 °C range Anschütz thermometers, uncorrected. $[\alpha]_D$ at RT (ca. 20 °C) Perkin–Elmer 241 polarimeter (p.a. solvents, Fluka). Capillary gas chromatography (CGC): Carlo Erba GC 8000; column: Supelco β-Dex (30 m × 0.25 mm); injector temperature 200 °C, detector temperature 225 °C (FID); carrier gas: H_2. ^1H and ^{13}C NMR spectra: Bruker AMX-300, AMX-400, AMX-II-500, Varian XL-300, Gemini-200 or Gemini-300; δ in ppm downfield of TMS ($\delta = 0$). IR: $CHCl_3$ solutions; Perkin–Elmer FT-IR 1600; (s = strong, m = medium, w = weak). MS: Hitachi-Perkin–Elmer RMU-6M (EI), Ion Spec Ultima 4.7 FT Ion Cyclotron Resonance (ICR) mass spectrometer (Hi-Res-MALDI), matrix: 2,5-dihydroxy benzoic acid (2,5-DHB), fragment ions in *m*/*z* with relative intensities (%) in parentheses; MALDI-TOF-spectra: Bruker Reflex Spectrometer (N_2 laser, 337 nm), matrix: 2,5-dihydroxy benzoic acid (2,5-DHB). Elemental analyses were performed by the Microanalytical Laboratory of the Laboratorium für Organische Chemie (ETH Zürich).

Etherification reaction of 3-*tert*-butyl-5-hydroxy salicylic aldehyde with dendritic branch bromides to give dendritic salicylic aldehyde derivatives. General procedure I (GP I): K_2CO_3 (1 equiv) and KI (0.01 equiv) were subsequently added to a solution of 3-*tert*-butyl-5-hydroxy salicylic aldehyde[28d] (1 equiv) and dendritic branch bromide (1 equiv) in acetone and the suspension was heated under reflux for several hours. After cooling to room temperature, CH_2Cl_2, and H_2O were added, the layers were separated and the aqueous layer was extracted ($2 \times CH_2Cl_2$). After drying over $MgSO_4$ the solvent was evaporated under vacuum and the resulting residue was purified by flash column chromatography.

Preparation of dendritic Salens by condensation of diamines with dendritic salicylic aldehyde derivatives. General procedure II (GP II): Dendritic salicylic aldehyde derivative (2 equiv) and diamine (1 equiv) were heated in EtOH under reflux for several hours.[28b, 29b] The solvent was evaporated and the residue redissolved in Et_2O. After the organic layer was washed with H_2O and brine and dried over $MgSO_4$, the solvent was evaporated and the residue was purified by flash column chromatography.

Compound 1: Under Ar a solution of 3-*tert*-butyl-5-bromo salicylic aldehyde[33] (2.15 g, 8.4 mmol), 4-styrene boronic acid[34] (1.61 g, 10.9 mmol), $[Pd(PPh_3)_4]$ (290 mg, 0.25 mmol), Na_2CO_3 (2 M, 11.0 mL, 22.0 mmol) in THF (40 mL) was heated under reflux for 3 h.[35] The organic phase was separated and the aqueous layer was extracted with Et_2O (50 mL). After the combined organic phases were dried over $MgSO_4$ and evaporation of the solvent, the residue was redissolved in a minimum of Et_2O, the Pd salts were allowed to precipitate and were filtered off over Celite. Flash column chromatography (hexane/Et_2O 8:1) afforded **1** (1.80 g, 77 %) as a yellow solid. M.p. 109.0–110.0 °C; R_f (hexane/Et_2O 5:1): 0.37; ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 11.80$ (s, 1H; C*H*O), 9.96 (s, 1H, OH), 7.77–7.48 (m, 8H; 8arom. H), 6.76 (dd, J(H,H) = 17.6, 10.9 Hz, 1H; C*H*CH_2), 5.79 (dd, J(H,H) = 17.6, 0.9 Hz, 1H; 1vinyl. H), 5.28 (dd, J(H,H) = 10.9, 0.9 Hz, 1H; 1vinyl. H), 1.47 (s, 9H; 3CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 197.21$, 160.66, 139.44, 138.80, 136.54, 136.26, 132.95, 131.98, 129.85, 126.78, 126.74, 120.75, 114.01, 35.04, 29.23; IR ($CHCl_3$): $\tilde{\nu} = 2963$ (m), 1650 (s), 1514 (w), 1441 (m), 1416 (w), 1394 (m), 1363 (w), 1332 (m), 1270 (m), 1164 (m), 1074 (w), 989 (w), 912 (w), 842 cm^{-1}; MS (EI): *m*/*z* (%): 281.2 (10), 280.2 (47) $[M]^+$, 266.2 (9), 265.2 (46), 237.2 (7), 179.2 (4), 178.2 (4), 165.1 (5), 118.6 (8), 32.0 (30), 28.1 (100); elemental analysis calcd (%) for $C_{19}H_{20}O_2$ (280.36): C 81.40, H 7.19; found: C 81.41, H 7.31.

Compound 2: A solution of **1** (1.64 g, 5.9 mmol) and (*R*,*R*)-cyclohexane diamine (334 mg, 2.9 mmol) in EtOH (20 mL) was heated under reflux for 4 h, according to GP II.[28b, 29b] After workup of the reaction mixture, following GP II, and flash column chromatography (pentane/CH_2Cl_2 2:1), **2** (1.55 g, 83 %) was obtained as a yellow foam. R_f (pentane/CH_2Cl_2 2:1): 0.28; $[\alpha]_D^{RT} = +101.9$ ($c = 0.54$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 13.9$ (s, 2H; 2OH), 8.34 (s, 2H; 2imine H), 7.46 (d, J(H,H) = 2.3 Hz, 2H; 2arom. H), 7.42–7.38 (m, 8H; 8arom. H), 7.19 (d, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.76 (dd, J(H,H) = 17.6, 10.9 Hz, 2H; 2C*H*CH_2), 5.75 (dd, J(H,H) = 17.6, 0.9 Hz, 2H; 2vinyl. H), 5.23 (dd, J(H,H) = 10.9, 0.9 Hz, 2H; 2vinyl. H), 3.38–3.36 (m, 2H; 2CH_2C*H*N), 2.04–2.01 (m, 2H; 2cyclohexyl H), 1.90–1.89 (m, 2H; 2cyclohexyl H), 1.79–1.77 (m, 2H; 2cyclohexyl H), 1.57–1.50 (m, 2H; 2cyclohexyl H), 1.44 (s, 18H; 6CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 165.72$, 160.02, 140.47, 137.59, 136.49, 135.82, 130.39, 128.24, 127.99, 126.65, 126.53, 118.69, 113.43, 72.41, 34.94, 33.05, 29.36, 24.32; IR ($CHCl_3$): $\tilde{\nu} = 3008$ (w), 2939 (m),

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2862 (w), 1630 (s), 1513 (w), 1442 (s), 1392 (m), 1272 (m), 1170 (m), 1072 (w), 1000 (w), 910 cm^{-1}; Hi-Res-MALDI: *m/z* (%): 662.3833 (6), 661.3801 (12) $[M+Na]^+$, 641.4026 (11), 640.3984 (47), 639.3947 (100) $[M+H]^+$, 638.3862 ((5) $[M]^+$, calcd 638.3872), 525.2801 (14); elemental analysis calcd (%) for $C_{44}H_{50}N_2O_2$ (638.88): C 82.72, H 7.89, N 4.38; found: C 82.73, H 7.93, N 4.22.

Compound 3: According to GP II, a solution of **1** (1.53 g, 5.5 mmol) and (*R*,*R*)-diphenyl ethylene diamine (580 mg, 2.7 mmol) in EtOH (20 mL) was heated under reflux for 3 h.[28b, 29b] After workup and flash column chromatography (pentane/CH_2Cl_2 5:1 → 3:1), **3** (1.84 g, 91%) was obtained as a yellow foam. R_f (pentane/CH_2Cl_2 2:1): 0.70; $[\alpha]_D^{RT} = +34.7$ ($c = 0.87$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 13.85$ (s, 2H; 2OH), 8.41 (s, 2H; 2imine H), 7.46 (d, J(H,H) = 2.3 Hz, 2H; 2arom. H), 7.42–7.36 (m, 8H, 8arom. H), 7.25–7.17 (m, 12H, 12arom. H), 6.73 (dd, J(H,H) = 17.6, 10.9 Hz, 2H; 2C*H*CH_2), 5.75 (dd, J(H,H) = 17.6, 0.9 Hz, 2H; 2 vinyl. H), 5.23 (dd, J(H,H) = 10.9, 0.9 Hz, 2H; 2vinyl. H), 4.76 (s, 2H; 2PhCHN), 1.44 (s, 18H; 6CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 167.10$, 159.89, 140.39, 139.29, 137.65, 136.47, 135.84, 130.52, 128.61, 128.41, 128.25, 128.02, 127.64, 126.65, 126.52, 118.69, 113.45, 80.18, 34.97, 29.33; IR ($CHCl_3$): $\tilde{\nu} = 3008$ (m), 2960 (m), 1628 (s), 1514 (w), 1441 (s), 1393 (m), 1330 (w), 1268 (m), 1170 (m), 1048 (w), 1028 (w), 989 (w), 910 (m), 842 cm^{-1}; Hi-Res-MALDI: *m/z* (%): 760.3968 (6), 759.3918 (10) $[M+Na]^+$, 737.4099 ((10) $[M+H]^+$, calcd 737.4107), 654.3353 (13), 633.3551 (8), 632.3511 (16), 528.2975 (12), 527.2936 (28), 471.2318 (23), 415.1681 (11), 371.2197 (13), 370.2163 (45), 369.2041 (23), 368.2000 (86), 354.1845 (12), 313.1409 (22), 312.1376 (100), 302.1510 (19), 280.1688 (27), 106.0654 (31); elemental analysis calcd (%) for $C_{52}H_{52}N_2O_2$ (736.98): C 84.75, H 7.11, N 3.80; found: C 84.84, H 7.24, N 3.85.

Compound 5a: According to GP I, a suspension of 3-*tert*-butyl-5-hydroxy salicylic aldehyde[28d] (3.00 g, 15.4 mmol), **4a**[36] (5.92 g, 15.4 mmol), K_2CO_3 (2.13 g, 15.4 mmol), and KI (24 mg, 0.14 mmol) in acetone (60 mL) was heated under reflux for 6 h. Workup according to GP I and flash column chromatography (hexane/CH_2Cl_2 1:2) afforded **5a** (4.06 g, 53%) as a yellow solid. M.p. 117.0–118.0 °C; R_f (hexane/CH_2Cl_2 1:2): 0.58; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 11.52$ (s, 1H; C*H*O), 9.77 (s, 1H; OH), 7.42–7.32 (m, 10H; 10arom. H), 7.24 (dd, J(H,H) = 3.1, 0.4 Hz, 1H; 1arom. H), 6.81 (d, J(H,H) = 3.1 Hz, 1H; 1arom. H), 6.68 (d, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.59 (t, J(H,H) = 2.3 Hz, 1H; 1arom. H), 5.25 (s, 4H; 2OCH_2), 4.97 (s, 2H; OCH_2), 1.41 (s, 9H; 3CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 196.65$, 160.24, 156.39, 151.06, 140.21, 139.18, 136.72, 128.63, 128.07, 127.54, 124.60, 119.81, 113.23, 106.41, 101.62, 70.66, 70.15, 35.04, 29.13; IR ($CHCl_3$): $\tilde{\nu} = 3015$ (w), 2964 (m), 2872 (w), 1651 (s), 1595 (s), 1492 (w), 1446 (s), 1430 (s), 1374 (m), 1318 (s), 1154 (s), 1041 (s), 836 cm^{-1}; MS (EI): *m/z* (%): 496.2 (3) $[M]^+$, 304.2 (8), 303.2 (35), 179.1 (5), 105.1 (5), 92.1 (8), 91.0 (100); elemental analysis calcd (%) for $C_{32}H_{32}O_5$ (496.59): C 77.40, H 6.49; found: C 77.29, H 6.56.

Compound 5b: A mixture of 3-*tert*-butyl-5-hydroxy salicylic aldehyde[28d] (2.00 g, 10.3 mmol), **4b**[22] (4.48 g, 10.3 mmol), K_2CO_3 (1.42 g, 10.3 mmol), and KI (16 mg, 0.10 mmol) in acetone (40 mL) was heated under reflux for 12 h, according to GP I. After workup and flash column chromatography (pentane/CH_2Cl_2 1:1), **5b** (3.37 g, 60%) was obtained as a yellow solid. M.p. 109.0–110.0 °C; R_f (pentane/Et_2O 4:1): 0.51; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 11.52$ (s, 1H; C*H*O), 9.77 (s, 1H; OH), 7.40 (dd, J(H,H) = 21.3, 8.2 Hz, 8H; 8arom. H), 7.24 (dd, J(H,H) = 3.1, 0.4 Hz, 1H; 1arom. H), 6.81 (d, J(H,H) = 3.1 Hz, 1H; 1arom. H), 6.71 (dd, J(H,H) = 17.6, 10.9 Hz, 2H; 2C*H*CH_2), 6.67 (d, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.57 (t, J(H,H) = 2.3 Hz, 1H; 1arom. H), 5.75 (dd, J(H,H) = 17.6, 0.9 Hz, 2H; 2vinyl. H), 5.26 (dd, J(H,H) = 10.9, 0.9 Hz, 2H; 2vinyl. H), 5.03 (s, 4H; 2OCH_2), 4.96 (s, 2H; OCH_2), 1.41 (s, 9H; 3CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 196.62$, 160.18, 156.38, 151.05, 140.20, 139.18, 137.42, 136.39, 136.23, 127.73, 126.44, 124.56, 119.81, 114.19, 113.25, 106.42, 101.63, 70.65, 69.89, 35.03, 29.13; IR ($CHCl_3$): $\tilde{\nu} = 2994$ (w), 2954 (m), 2872 (w), 1651 (s), 1595 (s), 1508 (w), 1456 (m), 1430 (s), 1369 (m), 1323 (s), 1154 (s), 1035 (s), 1015 (w), 990 (w), 913 (m), 831 cm^{-1}; MS (EI): *m/z* (%): 549.3 (19) $[M]^+$, 548.3 (55), 356.3 (8), 355.2(26), 239.1 (6), 233.2 (10), 207.2 (6), 194.1 (8), 179.1 (11), 118.1 (11), 117.1 (100), 115.1 (9), 91.1 (6); elemental analysis calcd (%) for $C_{36}H_{36}O_5$ (548.67): C 78.81, H 6.61; found: C 78.69, H 6.61.

Compound 7a: According to GP I, a suspension of 3-*tert*-butyl-5-hydroxy salicylic aldehyde[28d] (0.72 g, 3.7 mmol), **6a**[36] (3.00 g, 3.7 mmol), K_2CO_3 (0.51 g, 3.7 mmol), and KI (6 mg, 0.04 mmol) in acetone (40 mL) was heated under reflux for 4 h. Workup according to GP I and flash column chromatography (pentane/CH_2Cl_2 1:1) afforded **7a** (1.65 g, 50%) as a yellow solid. M.p. 60.0–61.0 °C; R_f (hexane/CH_2Cl_2 1:1): 0.38; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 11.52$ (s, 1H; C*H*O), 9.77 (s, 1H; OH), 7.42–7.30 (m, 20H; 20arom. H), 7.24 (d, J(H,H) = 2.7 Hz, 1H; 1arom. H), 6.83 (d, J(H,H) = 3.1 Hz, 1H; 1arom. H), 6.68–6.66 (m, 6H; 6arom. H), 6.57 (t, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.56 (t, J(H,H) = 2.3 Hz, 1H; 1arom. H), 5.03 (s, 8H; 4OCH_2), 4.98 (s, 4H; 2OCH_2), 4.96 (s, 2H; OCH_2), 1.40 (s, 9H; 3CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 196.66$, 160.20, 160.15, 159.95, 156.39, 151.08, 140.22, 139.16, 136.74, 128.61, 128.05, 127.58, 124.56, 119.81, 113.27, 106.48, 106.42, 101.62, 101.55, 70.71, 70.14, 70.03, 35.04, 29.13; IR ($CHCl_3$): $\tilde{\nu} = 3006$ (w), 2984 (w), 2871 (w) 1651 (m), 1595 (s), 1497 (w), 1451 (s), 1374 (m), 1323 (m), 1297 (w), 1154 (s), 1051 (s), 836 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 923.5 $[M+2]^+$; elemental analysis calcd (%) for $C_{60}H_{56}O_9$ (921.08): C 78.24, H 6.13; found: C 78.21, H 6.32.

Compound 7b: A mixture of 3-*tert*-butyl-5-hydroxy salicylic aldehyde[28d] (1.50 g, 7.7 mmol), **6b**[22] (7.04 g, 7.7 mmol), K_2CO_3 (1.07 g, 7.7 mmol), and KI (19 mg, 0.07 mmol) in acetone (50 mL) was heated under reflux for 4 h, following GP I. After workup and flash column chromatography (pentane/CH_2Cl_2 1:2) **7b** (1.72 g, 22%) was obtained as a yellow solid. M.p. 55.0–56.0 °C; R_f (pentane/CH_2Cl_2 1:2): 0.57; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 11.51$ (s, 1H; C*H*O), 9.76 (s, 1H; OH), 7.37 (dd, J(H,H) = 25.06, 8.2 Hz, 16H; 16arom. H), 7.24 (d, J(H,H) = 3.1 Hz, 1H; 1arom. H), 6.82 (d, J(H,H) = 3.1 Hz, 1H; 1arom. H), 6.70 (dd, J(H,H) = 17.6, 10.9 Hz, 4H; 4C*H*CH_2), 6.66 (d, J(H,H) = 2.3 Hz, 6H; 6arom. H), 6.55 (t, J(H,H) = 2.3 Hz, 3H; 3arom. H), 5.74 (dd, J(H,H) = 17.6, 0.9 Hz, 4H; 4vinyl. H), 5.24 (dd, J(H,H) = 10.9, 0.8 Hz, 4H; 4vinyl. H), 5.01 (s, 8H; 4OCH_2), 4.97 (s, 4H; 2OCH_2), 4.95 (s, 2H; OCH_2), 1.41 (s, 9H; 3CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 196.63$, 160.15, 156.38, 151.09, 140.22, 139.20, 137.40, 136.43, 136.27, 127.75, 126.43, 126.39, 126.34, 124.55, 119.82, 114.14, 113.30, 106.50, 106.43, 101.64, 101.59, 70.72, 70.01, 69.89, 35.04, 29.14; IR ($CHCl_3$): $\tilde{\nu} = 3005$ (w), 2964 (w), 2872 (w), 1646 (m), 1595 (s), 1508 (m), 1451 (s), 1436 (m), 1405 (w), 1369 (m), 1323 (m), 1297 (w), 1154 (s), 1046 (s), 1015 (w), 990 (w), 913 (m), 831 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 1048.3 $[M+Na]^+$; elemental analysis calcd (%) for $C_{68}H_{64}O_9$ (1025.23): C 79.66, H 6.29; found: C 79.55, H 6.38.

Compound 8: $[PdCl_2(PPh_3)_2]$ (493 mg, 0.7 mmol) and CuI (272 mg, 1.4 mmol) were added to a solution of 3-*tert*-butyl-5-bromo salicylic aldehyde[33] (9.03 g, 35.3 mmol) in THF (20 mL)/NEt_3 (20 mL). To this suspension a solution of ethinyl trimethyl silane (5.13 mL, 37.0 mmol) in THF (7 mL) was slowly added over a period of 1 h, the reaction mixture thereby turning black.[38] After heating under reflux for 24 h, Et_2O (100 mL) and H_2O (50 mL) were added, the phases were separated and the aqueous phase was extracted with Et_2O (100 mL). Drying over $MgSO_4$ and purification by flash column chromatography (hexane/Et_2O 9:1) afforded **8** (9.60 g, 99%) as a yellow oil. R_f (hexane/Et_2O 4:1): 0.52; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 11.90$ (s, 1H; C*H*O), 9.83 (s, 1H; OH), 7.59 (d, J(H,H) = 2.2 Hz 1H; 1arom. H), 7.56 (d, J(H,H) = 2.2 Hz 1H; 1arom. H), 1.41 (s, 9H; 3CH_3), 0.26 (s, 9H; Si(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 196.64$, 161.35, 138.75, 137.35, 135.67, 120.32, 114.19, 104.01, 93.03, 34.94, 29.07, 29.00; IR ($CHCl_3$): $\tilde{\nu} = 3007$ (w), 2965 (m), 2151 (m), 1653 (s), 1605 (w), 1442 (m), 1414 (m), 1320 (m), 1268 (w), 1153 (m), 1030 (w), 981 (w), 930 (w), 888 (w), 857 cm^{-1}; MS (EI): *m/z* (%): 274.0 (16) $[M]^+$, 137.0 (35), 77.4 (10), 72.2 (15).

Compound 9: TBAF · 3H_2O (1.41 g, 4.5 mmol) was added to a solution of **8** (1.02 g, 3.7 mmol) in THF (10 mL)/1N HCl (3.7 mL, 3.7 mmol). After stirring at room temperature for 20 h, Et_2O (50 mL) and H_2O (50 mL) were added, the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). Drying of the combined organic phases over $MgSO_4$ and evaporation of the solvent gave the crude product which was purified by flash column chromatography (hexane/Et_2O 20:1) to afford **9** (620 mg, 82%) as a yellow solid. M.p. 58.0–59.0 °C; R_f (hexane/Et_2O 1:2): 0.53; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 11.94$ (s, 1H; C*H*O), 9.84 (s, 1H; OH), 7.62 (d, J(H,H) = 1.9 Hz, 1H; 1arom. H), 7.58 (d, J(H,H) = 2.2 Hz, 1H; 1arom. H), 3.02 (s, 1H; 1acetylene H), 1.41 (s, 9H; 3CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 196.58$, 161.57, 138.97, 137.44, 135.75, 120.35, 113.07, 82.68, 76.17, 34.95, 29.03; IR ($CHCl_3$): $\tilde{\nu} =$ 3304 (m), 2964 (m), 1654 (s), 1608 (w), 1441 (m), 1413 (m), 1394 (w), 1382 (w), 1364 (w), 1317 (m), 1270 (w), 1148 (m), 1029 (w), 970 (w), 889 cm^{-1}; MS (EI): *m/z* (%): 201.0 (4) $[M-H]^+$, 199.0 (14), 198.0 (7), 187.0 (5), 137.0 (34), 136.5 (5), 91.0 (7), 72.2 (4); elemental analysis calcd (%) for $C_{13}H_{14}O_2$ (202.25): C 77.20, H 6.98; found: C 77.27, H 6.91.

Compound 10: A suspension of **4b**[22] (4.95 g, 11.4 mmol), 4-iodo phenol (2.50 g, 11.4 mmol), K_2CO_3 (3.20 g, 22.8 mmol) and 18-crown-6 (0.60 g,

2.3 mmol) in acetone (150 mL) was heated under reflux for 5 h. After cooling to room temperature, K_2CO_3 was filtered off and acetone was evaporated. The residue was redissolved in Et_2O (100 mL), H_2O (50 mL) was added and the phases were separated. After the organic phase was dried over $MgSO_4$ and evaporation of the solvent, purification of the residue by flash column chromatography (hexane/CH_2Cl_2 1:1) afforded **10** (6.00 g, 92%) as a colorless oil. R_f (hexane/CH_2Cl_2 1:1): 0.53; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.54-7.52$ (m, 2H; 2arom. H), 7.38 (dd, J(H,H) = 23.8, 8.1 Hz, 8H; 8arom. H), 6.72 (dd, J(H,H) = 17.6, 10.9 Hz, 2H; 2vinyl. H), 6.69 (d, J(H,H) = 9.1 Hz, 2H; 2arom. H), 6.62 (d, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.54 (t, J(H,H) = 2.3 Hz, 1H; 1arom. H), 5.75 (dd, J(H,H) = 17.6, 0.9 Hz, 2H; 2vinyl. H), 5.26 (dd, J(H,H) = 10.9, 0.9 Hz; 2H; 2vinyl. H), 5.01 (s, 4H; 2CH_2O), 4.95 (s, 2H; CH_2O); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 160.13$, 158.48, 138.99, 138.22, 137.38, 136.40, 136.23, 127.71, 126.41, 117.31, 114.14, 106.28, 101.65, 83.10, 69.91, 69.86; IR ($CHCl_3$): $\tilde{\nu} = 3008$ (w), 1597 (s), 1514 (w), 1485 (s), 1458 (m), 1405 (w), 1373 (m), 1292 (m), 1154 (s), 1059 (w), 1046 (w), 1024 (w), 913 (m), 830 cm^{-1}; Hi-Res-MALDI: m/z (%): 598.0921 (5), 597.0898 ((15) $[M+Na]^+$, calcd 597.0903), 573.0922 (4), 563.3732 (4), 505.3360 (6), 470.1861 (6), 457.2933 (5), 456.2895 (16), 447.2931 (8), 274.0430 (14), 243.2877 (8), 242.2845 (42), 137.0240 (25), 91.0153 (8), 72.1908 (9); elemental analysis calcd (%) for $C_{31}H_{27}O_3I$ (574.45): C 64.82, H 4.74; found: C 64.80, H 4.88.

Compound 11: [$PdCl_2(PPh_3)_2$] (100 mg, 0.14 mmol) and CuI (55 mg, 0.29 mmol) were added to a solution of **10** (4.10 g, 7.1 mmol) in THF (4 mL)/NEt_3 (4 mL) under Ar. To the resulting orange suspension a solution of **9** (1.52 g, 7.5 mmol) in THF (3 mL) was slowly added over a period of 1 h whereupon the reaction mixture immediately turned black.[38] After heating under reflux for 12 h Et_2O (100 mL) and H_2O (50 mL) were added, the phases were separated and the aqueous phase was extracted with Et_2O (100 mL). Drying of the combined organic phases over $MgSO_4$ and evaporation of the solvent afforded the crude product which was purified by flash column chromatography (hexane/CH_2Cl_2 1:1) to give **11** (2.90 g, 63%) as a yellow foam. R_f (hexane/CH_2Cl_2 1:1): 0.39; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 11.89$ (s, 1H; C*H*O), 9.86 (s, 1H; OH), 7.65 (d, J(H,H) = 0.4 Hz, 1H; 1arom. H), 7.58 (d, J(H,H) = 2.1 Hz, 1H; 1arom. H), 7.45–7.35 (m, 10H; 10arom. H), 6.91 (d, J(H,H) = 9.0 Hz, 2H; 2arom. H), 6.72 (dd, J(H,H) = 17.6, 10.9 Hz, 2H; 2C*H*CH_2), 6.66 (d, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.56 (t, J(H,H) = 2.3 Hz, 1H; 1arom. H), 5.75 (dd, J(H,H) = 17.6, 0.9 Hz, 2H; 2vinyl. H), 5.25 (dd, J(H,H) = 10.9, 0.9 Hz, 2H; 2vinyl. H), 5.02 (s, 4H; 2CH_2O), 5.01 (s, 2H; CH_2O), 1.40 (s, 9H; 3CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 196.73$, 161.02, 160.16, 158.70, 139.06, 138.85, 137.41, 137.01, 136.43, 136.26, 134.91, 132.99, 127.74, 126.44, 120.51, 115.52, 115.01, 114.66, 114.15, 106.35, 101.67, 88.23, 87.10, 69.90, 34.98, 29.12; IR ($CHCl_3$): $\tilde{\nu} = 3008$ (m), 2964 (m), 2867 (w), 1653 (s), 1599 (s), 1508 (s), 1456 (s), 1409 (m), 1373 (m), 1332 (w), 1294 (m), 1157 (s), 1017 (w), 991 (w), 914 (w), 833 cm^{-1}; Hi-Res-MALDI: m/z (%): 671.2778 ((3) $[M+Na]^+$, calcd 671.2773), 274.0428 (13), 137.0237 (21), 136.5219 (6), 91.0151 (9); elemental analysis calcd (%) for $C_{44}H_{40}O_5$ (648.79): C 81.46, H 6.21; found: C 81.44, H 6.36.

Compound 12: A solution of **5a** (2.0 g, 4.0 mmol) and (*R*,*R*)- cyclohexane diamine (230 mg, 2.0 mmol) in EtOH (40 mL) was heated under reflux for 5 h, according to GP II.[28b, 29b] Workup and purification by flash column chromatography (pentane/CH_2Cl_2 1:1) yielded **12** (1.63 g, 75%) as a yellow foam. R_f (pentane/CH_2Cl_2 1:1): 0.62; $[\alpha]_D^{RT} = -125.9$ ($c = 0.53$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 13.50$ (s, 2H; 2OH), 8.21 (s, 2H; 2imine H), 7.42–7.30 (m, 20H; 20arom. H), 6.98 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 6.65 (d, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.56 (t, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.52 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 5.02 (s, 8H, 4OCH_2), 4.83 (s, 2H; OCH_2), 4.82 (s, 2H; OCH_2), 3.35–3.28 (m, 2H; 2CH_2C*H*N), 2.01–1.98 (m, 2H; 2cyclohexyl H), 1.91–1.88 (m, 2H; 2cyclohexyl H), 1.77–1.75 (m, 2H; 2cyclohexyl H), 1.50–1.45 (m, 2H; 2cyclohexyl H), 1.40 (s, 18H; 6CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 165.40$, 160.14, 150.32, 139.68, 138.71, 136.81, 128.58, 127.99, 127.55, 155.05, 119.03, 117.87, 112.69, 106.40, 101.60, 72.36, 70.65, 70.09, 34.95, 33.06, 29.30, 24.29; IR ($CHCl_3$): $\tilde{\nu} = 3036$ (w), 2944 (m), 2862 (m), 1631 (m), 1595 (s), 1446 (s), 1380 (m), 1328 (s), 1297 (w), 1277 (w), 1164 (s), 1046 (s), 836 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 1094.3 $[M+Na]^+$, 1072.4 $[M+H]^+$; elemental analysis calcd (%) for $C_{70}H_{74}N_2O_8$ (1071.38): C 78.48, H 6.96, N 2.61; found: C 78.40, H 7.04, N 2.66.

Compound 13: According to GP II, a solution of **5a** (2.0 g, 4.0 mmol) and (*R*,*R*)-diphenyl ethylene diamine (428 mg, 2.0 mmol) in EtOH (40 mL) was heated under reflux for 12 h.[28b, 29b] Workup and purification of the crude product by flash column chromatography (pentane/CH_2Cl_2 1:2) afforded **13** (1.79 g, 76%) as a yellow foam. R_f (pentane/CH_2Cl_2 1:1): 0.67; $[\alpha]_D^{RT} = -27.5$ ($c = 0.56$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 13.39$ (s, 2H; 2OH), 8.28 (s, 2H; 2imine H), 7.41–7.17 (m, 30H; 30arom. H), 6.98 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 6.65 (d, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.55 (t, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.50 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 5.01 (s, 8H; 4OCH_2), 4.81 (s, 4H; 2OCH_2), 4.70 (s, 2H; 2PhC*H*N), 1.41 (s, 18H; 6CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 166.75$, 160.14, 155.07, 150.38, 139.65, 139.42, 138.81, 136.80, 128.62, 128.58, 128.35, 128.02, 127.99, 127.55, 119.49, 117.83, 112.87, 106.38, 101.61, 80.18, 70.63, 10.09, 35.00, 29.29; IR ($CHCl_3$): $\tilde{\nu} = 3067$ (w), 3005 (m), 2954 (m), 2872 (m), 1631 (m), 1595 (s), 1497 (w), 1451 (s), 1435 (s), 1374 (s), 1328 (s), 1297 (w), 1272 (w), 1154 (s), 1046 (s), 836 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 1170.5 $[M+H]^+$; elemental analysis calcd (%) for $C_{78}H_{76}N_2O_8$ (1169.45): C 80.11, H 6.55, N 2.40; found: C 78.75, H 6.80, N 2.24.

Compound 14: According to GP II, a solution of **5b** (1.72 g, 3.1 mmol) and (*R*,*R*)-cyclohexane diamine (333 mg, 1.6 mmol) in EtOH (80 mL) was heated under reflux for 12 h.[28b, 29b] Workup and purification of the crude product by flash column chromatography (pentane/CH_2Cl_2 7:3) afforded **14** (1.46 g, 73%) as a yellow foam. R_f (pentane/CH_2Cl_2 1:2): 0.78; $[\alpha]_D^{RT} = -110.7$ ($c = 1.00$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 13.50$ (s, 2H; 2OH), 8.19 (s, 2H; 2imine H), 7.42–7.34 (m, 16H; 16arom. H), 6.97 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 6.71 (dd, J(H,H) = 17.6, 10.9 Hz, 4H; 4C*H*CH_2), 6.64 (d, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.53 (t, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.50 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 5.75 (dd, J(H,H) = 17.6, 0.9 Hz, 4H; 4vinyl. H), 5.24 (dd, J(H,H) = 10.9, 0.8 Hz, 4H; 4vinyl. H), 4.99 (s, 8H, 4OCH_2), 4.81 (s, 2H; OCH_2), 4.80 (s, 2H; OCH_2), 3.31–3.29 (m, 2H; 2CH_2C*H*N), 2.00–1.97 (m, 2H; 2cyclohexyl H), 1.89–1.87 (m, 2H; 2cyclohexyl H), 1.76–1.74 (m, 2H; 2cyclohexyl H), 1.49–1.45 (m, 2H; 2cyclohexyl H), 1.39 (s, 18H; 6CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 196.62$, 165.43, 160.10, 155.07, 150.34, 139.69, 138.73, 137.36, 136.46, 136.40, 136.35, 127.75, 127.73, 126.44, 126.41, 119.03, 117.88, 114.19, 114.10, 112.75, 106.46, 101.64, 70.67, 69.90, 69.85, 34.95, 29.31, 29.13; IR ($CHCl_3$): $\tilde{\nu} = 3005$ (w), 2944 (m), 2862 (w), 1631 (m), 1595 (s), 1436 (s), 1374 (m), 1328 (m), 1154 (s), 1046 (s), 1015 (m), 984 (w), 913 (m), 831 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 1176.7 $[M+H]^+$; elemental analysis calcd (%) for $C_{78}H_{82}N_2O_8$ (1175.53): C 79.70, H 7.03, N 2.38; found: C 79.83, H 7.03, N 1.81.

Compound 15: A solution of **5b** (1.72 g, 3.1 mmol) and (*R*,*R*)-diphenyl ethylene diamine (333 mg, 1.6 mmol) in EtOH (80 mL) was heated under reflux for 12 h, according to GP II.[28b, 29b] Workup and flash column chromatography (pentane/CH_2Cl_2 1:1) yielded **15** (1.46 g, 73%) as a yellow foam. R_f (hexane/CH_2Cl_2 1:2): 0.57; $[\alpha]_D^{RT} = -30.7$ ($c = 0.98$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 13.50$ (s, 2H; 2OH), 8.28 (s, 2H; 2imine H), 7.41–7.17 (m, 26H; 26arom. H), 6.98 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 6.70 (dd, J(H,H) = 17.6, 10.9 Hz, 4H; 4C*H*CH_2), 6.64 (d, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.53 (t, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.50 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 5.74 (dd, J(H,H) = 17.6, 0.9 Hz, 4H; 4vinyl. H), 5.24 (dd, J(H,H) = 10.9, 0.9 Hz, 4H; 4vinyl. H), 4.99 (s, 8H, 4OCH_2), 4.80 (s, 4H; 2OCH_2), 4.69 (s, 2H; 2PhC*H*N), 1.41 (s, 18H; 6CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 166.77$, 160.09, 155.07, 150.39, 139.63, 139.38, 138.82, 137.35, 136.44, 136.32, 128.35, 128.03, 127.75, 127.56, 126.41, 119.47, 117.84, 114.10, 112.87, 106.44, 101.61, 80.18, 70.63, 69.84, 35.00, 29.29; IR ($CHCl_3$): $\tilde{\nu} = 3087$ (w), 3005 (w), 2953 (m), 2861 (w), 1631 (m), 1594 (s), 1513 (m), 1451 (s), 1436 (s), 1405 (w), 1369 (m), 1328 (s), 1297 (w), 1277 (w), 1154 (s), 1046 (s), 1020 (m), 990 (w), 913 (m), 831 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 1296.5 $[M+Na]^+$, 1274.5 $[M+H]^+$; elemental analysis calcd (%) for $C_{86}H_{84}N_2O_8$ (1273.60): C 81.10, H 6.65, N 2.20; found: C 81.08, H 6.84, N 2.16.

Compound 16: A solution of **7a** (1.50 g, 1.6 mmol) and (*R*,*R*)-cyclohexane diamine (93 mg, 0.8 mmol) in EtOH (40 mL) was heated under reflux for 12 h, following GP II.[28b, 29b] Workup and purification by flash column chromatography (pentane/CH_2Cl_2 1:2) afforded **16** (1.18 g, 75%) as a yellow foam. R_f (hexane/CH_2Cl_2 1:2): 0.31; $[\alpha]_D^{RT} = -60.1$ ($c = 0.97$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 13.50$ (s, 2H; 2OH), 8.20 (s, 2H; 2imine H), 7.43–7.28 (m, 40H; 40arom. H), 6.98 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 6.66 (d, J(H,H) = 2.3 Hz, 8H; 8arom. H), 6.64 (d, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.56 (t, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.52 (t, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.50 (d, J(H,H) = 2.9 Hz, 2H; 2arom. H), 5.01 (s, 16H, 8OCH_2), 4.94 (s, 8H, 4OCH_2), 4.81 (s, 2H;

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OCH_2), 4.80 (s, 2H; OCH_2), 3.31–3.28 (m, 2H; $2CH_2CHN$), 2.00–1.96 (m, 2H; 2cyclohexyl H), 1.89–1.87 (m, 2H; 2cyclohexyl H), 1.74–1.72 (m, 2H; 2cyclohexyl H), 1.49–1.46 (m, 2H; 2cyclohexyl H), 1.39 (s, 18H; $6CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 196.65, 160.20, 160.16, 160.06, 155.07, 139.67, 139.22, 138.74, 136.78, 136.74, 128.61, 128.58, 128.04, 128.00, 127.57, 127.52, 106.47, 106.41, 101.61, 101.54, 70.13, 70.10, 70.02, 69.98, 34.95, 29.30, 29.13; IR ($CHCl_3$): $\tilde{\nu}$ = 3067 (w), 3005 (w), 2933 (m), 2872 (m), 1595 (s), 1492 (w), 1451 (s), 1374 (m), 1328 (m), 1297 (m), 1154 (s), 1051 (s), 836 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 1922.5 $[M+2]^+$; elemental analysis calcd (%) for $C_{126}H_{122}N_2O_{16}$ (1920.32): C 78.81, H 6.40, N 1.46; found: C 78.69, H 6.50, N 1.43.

Compound 17: A solution of **7a** (1.00 g, 1.1 mmol) and (*R*,*R*)-diphenyl ethylene diamine (212 mg, 0.5 mmol) in EtOH (40 mL) was heated under reflux for 12 h, according to GP II.[28b, 29b] Workup and purification by flash column chromatography (pentane/CH_2Cl_2 1:2) afforded **17** (0.80 g, 73%) as a yellow foam. R_f (hexane/CH_2Cl_2 1:2): 0.33; $[\alpha]_D^{RT}$ = −13.1 (c = 0.97 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 13.40 (s, 2H; 2OH), 8.26 (s, 2H; 2imine H), 7.42–7.28 (m, 50H; 50arom. H), 6.99 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 6.66 (d, J(H,H) = 2.3 Hz, 8H; 8arom. H), 6.64 (d, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.55 (t, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.52 (t, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.50 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 5.00 (s, 16H, $8OCH_2$), 4.93 (s, 8H, $4OCH_2$), 4.80 (s, 4H; $2OCH_2$), 4.68 (s, 2H; 2PhC*H*N), 1.40 (s, 18H; $6CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 166.78, 160.20, 160.15, 160.06, 155.09, 139.63, 139.38, 139.21, 136.77, 136.73, 128.60, 128.58, 128.34, 128.04, 128.00, 127.57, 106.46, 106.40, 101.60, 101.55, 76.70, 70.67, 70.13, 70.10, 70.02, 70.70, 35.60, 29.29, 29.13; IR ($CHCl_3$): $\tilde{\nu}$ = 3067 (w), 3015 (m), 2964 (w), 2871 (m), 1595 (s), 1497 (w), 1451 (s), 1374 (s), 1328 (s), 1292 (m), 1154 (s), 1051 (s), 836 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 2041.2 $[M+Na]^+$, 2019.3 $[M+H]^+$; elemental analysis calcd (%) for $C_{134}H_{124}N_2O_{16}$ (2018.42): C 79.74, H 6.19, N 1.39; found: C 79.69, H 5.98, N 1.22.

Compund 18: According to GP II, a solution of **7b** (0.84 g, 0.8 mmol) and (*R*,*R*)-cyclohexane diamine (47 mg, 0.4 mmol) in EtOH (40 mL) was heated under reflux for 4 h.[28b, 29b] Workup and purification of the crude product by flash column chromatography (CH_2Cl_2/pentane 2:1 → CH_2Cl_2) afforded **18** (0.61 g, 70%) as a yellow foam. R_f (pentane/CH_2Cl_2 1:2): 0.41; $[\alpha]_D^{RT}$ = −58.8 (c = 0.34 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 13.48 (s, 2H; 2OH), 8.17 (s, 2H; 2imine H), 7.36 (dd, J(H,H) = 20.6, 8.3 Hz, 32H; 32arom. H), 6.97 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 6.69 (dd, J(H,H) = 17.6, 10.9 Hz, 8H; 8C*H*CH_2), 6.65–6.63 (m, 12H; 12arom. H), 6.53 (t, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.51 (t, J(H,H) = 2.3 Hz, 2H; 2arom. H), 6.49 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 5.73 (d, J(H,H) = 17.6, 0.9 Hz, 8H; 8vinyl. H), 5.23 (d, J(H,H) = 10.9, 0.9 Hz, 8H; 8vinyl. H), 4.98 (s, 16H, $8OCH_2$), 4.92 (s, 8H, $4OCH_2$), 4.79 (s, 2H; OCH_2), 4.78 (s, 2H; OCH_2), 3.29–3.27 (m, 2H; $2CH_2CHN$), 2.00–1.96 (m, 2H; 2cyclohexyl H), 1.87–1.85 (m, 2H; 2cyclohexyl H), 1.73–1.70 (m, 2H; 2cyclohexyl H), 1.47–1.45 (m, 2H; 2cyclohexyl H), 1.38 (s, 18H; $6CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 165.47, 160.10, 160.05, 155.08, 150.35, 139.66, 139.25, 138.74, 137.34, 136.44, 136.30, 127.83, 127.76, 127.68, 126.41, 126.30, 119.00, 117.87, 114.09, 112.70, 106.50, 106.40, 101.63, 101.56, 72.30, 70.69, 69.96, 69.84, 34.95, 32.98, 29.30; IR ($CHCl_3$): $\tilde{\nu}$ = 3005 (w), 2933 (m), 2872 (w), 1595 (s), 1513 (w), 1451 (m), 1410 (w), 1374 (m), 1333 (m), 1297 (w), 1154 (s), 1051 (m), 1015 (w), 990 (m), 913 (m), 831 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 2129.1 $[M]^+$; elemental analysis calcd (%) for $C_{142}H_{138}N_2O_{16}$ (2128.62): C 80.12, H 6.53, N 1.32; found: C 79.99, H 6.60, N 1.17.

Compound 19: A solution of **7b** (0.88 g, 0.9 mmol) and (*R*,*R*)-diphenyl ethylene diamine (91 mg, 0.45 mmol) in EtOH (40 mL) was heated under reflux for 4 h, following GP II.[28b, 29b] Workup and purification by flash column chromatography (CH_2Cl_2/pentane 2:1 → CH_2Cl_2) yielded **19** (0.32 g, 34%) as a yellow foam. R_f (pentane/CH_2Cl_2 1:2): 0.39; $[\alpha]_D^{RT}$ = −16.2 (c = 0.85 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 13.41 (s, 2H; 2OH), 8.25 (s, 2H; 2imine H), 7.35 (dd, J(H,H) = 21.1, 8.2 Hz, 32H; 32arom. H), 7.21–7.15 (m, 10H; 10arom. H), 6.99 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 6.69 (dd, J(H,H) = 17.6, 10.9 Hz, 8H; 8C*H*CH_2), 6.64–6.63 (m, 12H; 12arom. H), 6.53–6.51 (m, 6H; 6arom. H), 6.49 (d, J(H,H) = 3.0 Hz, 2H; 2arom. H), 5.73 (dd, J(H,H) = 17.6, 0.9 Hz, 8H; 8vinyl. H), 5.23 (dd, J(H,H) = 10.9, 0.9 Hz, 8H; 8vinyl. H), 4.98 (s, 16H, $8OCH_2$), 4.92 (s, 8H, $4OCH_2$), 4.78 (s, 4H; $2OCH_2$), 4.67 (s, 2H; 2PhC*H*N), 1.40 (s, 18H; $6CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 166.81, 160.09, 160.04, 155.08, 150.41, 139.63, 139.35, 139.23, 138.84, 137.33, 136.43, 136.29, 128.58, 128.33, 128.03, 127.75, 127.56, 126.41, 119.45, 117.83, 114.09, 106.48, 106.39, 101.61, 101.56, 80.13, 70.67, 69.95, 69.83, 35.00, 29.29; IR ($CHCl_3$): $\tilde{\nu}$ = 3682 (w), 3005 (m), 2954 (w), 2872 (w), 1595 (s), 1513 (w), 1451 (s), 1374 (m), 1328 (m), 1292 (w), 1154 (s), 1051 (s), 990 (w), 913 (w), 831 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 2227.4 $[M]^+$; elemental analysis calcd (%) for $C_{150}H_{140}N_2O_{16}$ (2226.72): C 80.91, H 6.34, N 1.26; found: C 80.89, H 6.52, N 1.07.

Compound 20: A solution of **11** (1.40 g, 2.2 mmol) and (*R*,*R*)-cyclohexane diamine (123 mg, 1.1 mmol) in EtOH (25 mL) was heated under reflux for 2 h, following GP II.[28b, 29b] After workup and purification of the residue by flash column chromatography (pentane/CH_2Cl_2 1:1 → 1:2) **20** (1.25 g, 84%) was obtained as a yellow foam. R_f (pentane/CH_2Cl_2 1:1): 0.28; $[\alpha]_D^{RT}$ = +151.3 (c = 0.68 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 14.10 (s, 2H; 2OH), 8.24 (s, 2H; 2imine H), 7.42–7.34 (m, 22H; 22arom. H), 7.17 (d, J(H,H) = 2.0 Hz, 2H; 2arom. H), 6.89–6.88 (m, 4H; 4arom. H), 6.72 (dd, J(H,H) = 17.6, 10.9 Hz, 4H; 4C*H*CH_2), 6.65 (d, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.55 (t, J(H,H) = 2.3 Hz, 2H; 2arom. H), 5.75 (dd, J(H,H) = 17.6, 0.8 Hz, 4H; 4vinyl. H), 5.24 (dd, J(H,H) = 10.9, 0.8 Hz, 4H; 4vinyl. H), 5.02 (s, 8H; $4OCH_2$), 5.00 (s, 4H, $2OCH_2$), 3.35–3.33 (m, 2H; $2CH_2CHN$), 2.02–1.99 (m, 2H; 2cyclohexyl H), 1.91–1.89 (m, 2H; 2cyclohexyl H), 1.77–1.75 (m, 2H; 2cyclohexyl H), 1.50–1.47 (m, 2H; 2cyclohexyl H), 1.42 (s, 18H; $6CH_3$); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 165.08, 160.69, 160.15, 158.37, 139.18, 137.74, 137.40, 136.45, 136.30, 132.98, 132.85, 132.67, 127.74, 126.44, 118.38, 116.17, 114.90, 114.13, 112.73, 106.34, 101.71, 88.28, 87.11, 72.21, 69.90, 34.88, 32.89, 29.26, 24.23; IR ($CHCl_3$): $\tilde{\nu}$ = 3008 (w), 2942 (m), 2867 (m), 1630 (s), 1597 (s), 1508 (s), a443 (s), 1406 (w), 1373 (m), 1293 (m), 1157 (s), 1065 (m), 1016 (m), 990 (w), 914 (m), 832 cm^{-1}; Hi-Res-MALDI: m/z (%): 1377.6791 (17), 1376.6740 (32), 1375.6769 ((34) $[M+H]^+$, calcd 1375.6775), 1164.5344 (15), 1163.5267 (17), 1022.5306 (14), 1021.5225 (27), 1020.5157 (35), 1019.5102 (36), 903.4442 (32), 847.3792 (31), 667.3534 (44), 666.3447 (66), 665.3405 (100), 117.0702 (99); elemental analysis calcd (%) for $C_{94}H_{90}N_2O_8$ (1375.73): C 82.07, H 6.59, N 2.04; found: C 82.06, H 6.66, N 2.06.

Compound 21: A solution of **11** (1.11 g, 1.72 mmol) and (*R*,*R*)-diphenyl ethylene diamine (182 mg, 0.86 mmol) in EtOH (40 mL) was heated under reflux for 3 h, according to GP II.[28b, 29b] Workup and flash column chromatography (pentane/CH_2Cl_2 1:1 → 1:2) of the residue yielded **21** (1.18 g, 94%) as a yellow foam. R_f (pentane/CH_2Cl_2 1:1): 0.24; $[\alpha]_D^{RT}$ = +67.9 (c = 0.69 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 14.03 (s, 2H; 2OH), 8.27 (s, 2H; 2imine H), 7.42–7.22 (m, 32H; 32arom. H), 7.16 (d, J(H,H) = 2.0 Hz, 2H; 2arom. H), 6.90–6.88 (m, 4H; 4arom. H), 6.71 (dd, J(H,H) = 17.6, 10.9 Hz, 4H; 4C*H*CH_2), 6.65 (d, J(H,H) = 2.3 Hz, 4H; 4arom. H), 6.55 (t, J(H,H) = 2.3 Hz, 2H; 2arom. H), 5.75 (dd, J(H,H) = 17.6, 0.8 Hz, 4H; 4vinyl. H), 5.24 (dd, J(H,H) = 10.9, 0.8 Hz, 4H; 4vinyl. H), 5.02 (s, 8H; $4OCH_2$), 5.00 (s, 4H, $2OCH_2$), 4.73 (s, 2H; $2CH_2CHN$), 1.44 (s, 18H; $6CH_3$); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 166.44, 160.50, 160.15, 158.40, 139.18, 139.03, 137.82, 137.41, 136.45, 136.29, 133.24, 133.03, 132.85, 128.47, 127.98, 127.75, 126.44, 118.39, 116.14, 114.92, 114.14, 112.92, 106.35, 101.71, 88.22, 87.18, 80.05, 69.90, 34.95, 29.26; IR ($CHCl_3$): $\tilde{\nu}$ = 3007 (w), 2999 (w), 2872 (w), 1628 (s), 1597 (s), 1508 (s), 1453 (s), 1375 (m), 1293 (m), 1157 (s), 1050 (w), 1029 (w), 1016 (w), 990 (w), 913(w), 832 cm^{-1}; Hi-Res-MALDI: m/z (%): 1497.6843 (35), 1496.6777 (54), 1495.6748 ((48) $[M+Na]^+$, calcd 1495.6751), 1475.6987 (17), 1474.6972 (26), 1473.6933 ((25) $[M+H]^+$, calcd 1473.6932), 1391.6180 (34), 1390.6216 (39), 1369.6408 (44), 1368.6357 (36), 759.3336 (37), 758.3270 (39), 743.3156 (37), 739.3635 (49), 738.3609 (83), 737.3484 (56), 736.3456 (100); elemental analysis calcd (%) for $C_{102}H_{92}N_2O_8$ (1473.83): C 83.12, H 6.29, N 1.90; found: C 82.94, H 6.38, N 1.99.

Loading of Salens 12, 13, 16, and 17 with Mn. General procedure III (GP III): Detailed example for the preparation of **16**·Mn(Cl).[28, 29b, 33] A solution of **16** (500 mg, 0.26 mmol) in EtOH (15 mL)/toluene (15 mL) was treated with $Mn(OAc)_2 \cdot 4H_2O$ (638 mg, 2.6 mmol, 10 equiv) and heated under reflux for 6 h while air was bubbled through the reaction solution. Then LiCl (221 mg, 5.2 mmol, 20 equiv) was added and the mixture was stirred at room temperature for a further 12 h. Toluene (20 mL) and H_2O (20 mL) were added, the phases were separated and the organic layer was washed with H_2O (20 mL) again. After the organic phases were dried over $MgSO_4$, the solvent was evaporated and the crude product was purified by flash column chromatography (hexane/CH_2Cl_2 1:2) to give **16**·Mn(Cl) (78%) as a dark brown foam. IR ($CHCl_3$): $\tilde{\nu}$ = 3067 (w), 3035 (w), 3005 (w), 2944 (w), 3872 (w), 1595 (s), 1544 (m), 1497 (w), 1444 (s), 1415 (w), 1369

(m), 1338 (m), 1287 (m), 1154 (s), 1051 (m), 1036 (m), 831 cm^{-1}; MALDI-TOF-MS (2,5-DHB): 1974.2 $[M\text{-(HCl)}]^+$, 1944.3, 1922.1; elemental analysis calcd (%) for $C_{126}H_{120}N_2O_{16}ClMn$ (2008.70): C 75.34, H 6.02, N 1.39, Cl 1.76; found: C 75.35, H 6.07, N 1.28, Cl 1.92.

Epoxidation of olefins mediated by Mn-Salens 12·, 13·, 16· and 17·Mn(Cl) under homogeneous conditions to give epoxides 22. General procedure IV (GP IV): Detailed example for the epoxidation of styrene using **12**·Mn(Cl) to give styrene oxide (**22a**).[41] NMO (87 mg, 0.75 mmol, 5 equiv) was added to a solution of **12**·Mn(Cl) (36 mg, 0.03 mmol, 0.2 equiv) and styrene (17 μL, 0.15 mmol, 1 equiv) in CH_2Cl_2 (2.5 mL). After the reaction mixture was cooled to −20 °C, *m*-CPBA (51 mg, 0.3 mmol, 2 equiv) was added and the suspension was stirred at this temperature for 30 min. Et_2O (50 mL) and 1N KOH (50 mL) were added, the phases were separated and the organic phase was extracted with H_2O (50 mL). Drying of the organic phase over $MgSO_4$ and evaporation of the solvent gave the crude product mixture. The enantioselectivity of **22a** and the conversion were determined by CGC (*β*-CD; heating 90 °C/isothermal; pressure 1.0 bar H_2; t_R (styrene) ca. 3.2 min, t_R (first enantiomer (**22a**)) ca. 12.3 min, t_R (second enantiomer (**22a**)) ca. 12.8 min): *er* (**22a**): 73:27, conversion: 91%.

CGC methods for epoxides **22b**–**f**: **22b**: *β*-CD; heating 80 °C/isothermal; pressure 1.0 bar H_2; t_R (3-methyl styrene) ca. 7.1 min, t_R (first enantiomer (**22b**)) ca. 34.3 min, t_R (second enantiomer (**22b**)) ca. 35.7 min; **22c**: *β*-CD; heating 90 °C/isothermal; pressure 1.0 bar H_2; t_R ((*E*)-phenylpropene) ca. 4.6 min, t_R (first enantiomer (**22c**)) ca. 8.3 min, t_R (second enantiomer (**22c**)) ca. 8.7 min; **22d**: *β*-CD; heating: 120 °C/isothermal/10 min, 1.5 °C/min, 140 °C/isothermal/10 min; pressure 1.0 bar H_2; t_R (1-phenyl cyclohexene) ca. 18.3 min, t_R (first enantiomer (**22d**)) ca. 24.2 min, t_R (second enantiomer (**22d**)) ca. 24.5 min; **22e**: *β*-CD; heating 140 °C/isothermal; pressure 1.0 bar H_2; t_R (dihydronaphthalene) ca. 3.7 min, t_R (first enantiomer (**22e**)) ca. 10.2 min, t_R (second enantiomer (**22e**)) ca. 10.6 min; **22f**: *β*-CD; heating 160 °C/isothermal; pressure 1.0 bar H_2; t_R (*trans*-stilbene) ca. 21.1 min, t_R (first enantiomer (**22f**)) ca. 23.5 min, t_R (second enantiomer (**22f**)) ca. 24.8 min.

Suspension copolymerization of Salen cross-linkers 2, 3, 14, 15, and 18–21 with styrene to give polymers p-2, p-3, p-14, p-15, and p-18–p-21. General procedure V (GP V): Detailed example for the preparation of Salen/styrene copolymer p-**15**.[43] In a three-necked flask, equipped with a condenser and an overhead stirrer, a warm solution of poly(vinyl alcohol) (115 mg, degree of polymerization 100000, 86–89% hydrolyzed) in H_2O (10 mL), which was prepared by violent stirring at 40–50 °C and subsequent filtering to remove insoluble residues, was added to a solution of **15** (599 mg, 0.47 mmol), styrene (2.94 g, 28.2 mmol), and AIBN (130 mg) in THF (0.6 mL) and benzene (4.5 mL). After stirring at room temperature for 5 min to generate a homogeneous emulsion, the temperature was raised to 80–85 °C during one hour. Having stirred at this temperature for 20 h, the suspension was filtered over a glass filter (G2) and the resulting polymer beads were extensively washed with hot H_2O (400 mL), H_2O/MeOH 1:1 (200 mL), MeOH (200 mL), THF (300 mL), MeOH (200 mL) and pentane (200 mL). The beads were then dried under high vacuum for several hours to give polymer p-**15** (3.51 g, 99%, theoretical loading: 0.133 mmol g^{-1}). The beads were sieved through a sieve (mesh widths: 1000, 800, 630, 500, 400, 250, 160, 100) to give fractions of uniform size.

According to this general procedure, all polymers were prepared by stoichiometrically adjusting the amounts of organic solvents, AIBN, H_2O and poly(vinyl alcohol) to the amount of monomers used.

Loading of Salen polymers p-2, p-3, p-14, p-15, and p-18–p-21 with Mn to generate Mn-Salen polymers p-2·, p-3·, p-14·, p-15· and p-18·–p-21·Mn(Cl). General procedure VI (GP VI): Detailed example for the generation of polymer p-**15**·Mn(Cl).[28b, 31] $Mn(OAc)_2 \cdot 4H_2O$ (192 mg, 0.79 mmol, 10 equiv) was added to a suspension of p-**15** (590 mg, 0.079 mmol, loading: 0.133 mmol g^{-1}) in DMF (11 mL)/EtOH (5 mL) whereupon the polymer beads immediately turned black. The suspension was heated under reflux for 3 h while air was bubbled through the suspension, then LiCl (68 mg, 1.57 mmol, 20 equiv) was added. After stirring at room temperature for 12 h, the suspension was filtered over a glass filter (G2) and the polymer beads were extensively washed with THF (400 mL), MeOH (100 mL) and pentane (100 mL). After drying under high vacuum for several hours black polymer beads of p-**15**·Mn(Cl) (586 mg, 98%) were obtained with a new theoretical loading of 0.131 mmol g^{-1}.

Epoxidation of olefins mediated by polymer-bound Mn-Salens p-2·, p-3·, p-14·, p-15· and p-18·–p-21·Mn(Cl) under heterogeneous conditions to give epoxides 22. General procedure VII (GP VII): Detailed example for the epoxidation of styrene using polymer p-**21**·Mn(Cl) to give styrene oxide (**22a**). Polymer beads of p-**21**·Mn(Cl) (404 mg, 0.052 mmol, 0.2 equiv, loading: 0.128 mmol g^{-1}) were suspended in CH_2Cl_2 (4.4 mL). After addition of styrene (30 μL, 0.26 mmol, 1 equiv) and NMO (151 mg, 1.29 mmol, 5 equiv) the reaction mixture was cooled to −20 °C and *m*-CPBA (89 mg, 0.52 mmol, 2 equiv) was added. After stirring at this temperature for 30 min, a sample was taken from the reaction mixture, Et_2O and 1N KOH were added and the organic layer was analyzed by CGC: *er* (**22a**): 80:20, conversion: quantitative. The reaction solution was withdrawn by syringe and the polymer beads were washed with CH_2Cl_2 (3 × 5 mL). Et_2O (50 mL) and 1N KOH (50 mL) were added to the combined organic phases, the aqueous phase was separated and the organic layer was extracted with H_2O (50 mL). After drying of the combined organic layers over $MgSO_4$ and evaporation of the solvent, pure **22a** was obtained as a colorless oil. For multiple use of the catalyst p-**21**·Mn(Cl), the washed polymer beads were dried under high vacuum, resuspended in CH_2Cl_2 and the substrates were added as described above.

Loading of Salen polymers p-2, p-14, and p-20 with Cr to generate Cr-Salen polymers p-2·, p-14·, and p-20·Cr(Cl). General procedure VIII (GP VIII): Detailed example for the loading of polymer p-**20** with $CrCl_2$ to give polymer-bound Cr-Salen p-**20**·Cr(Cl). $CrCl_2$ (17 mg, 0.138 mmol, 1.1 equiv) was added under Ar to a suspension of polymer beads p-**20** (958 mg, 0.126 mmol, loading: 0.131 mmol g^{-1}) in THF (7 mL), the beads thereby immediately turning brown. After stirring under Ar for 3 h, the flask was opened and the suspension was stirred with contact to air for a further 12 h.[48] Washing of the beads with THF (600 mL) and toluene (100 mL) and drying under high vacuum afforded polymer p-**20**·Cr(Cl) (916 mg, 95%) as brown beads with a new theoretical loading of 0.130 mmol g^{-1}.

Hetero-Diels–Alder reaction of Danishefsky's diene with aldehydes to give cycloadducts 23, mediated by polymer-bound p-2·, p-14·, and p-20·Cr(Cl). General procedure IX (GP IX): Detailed example for the cycloaddition of Danishefsky's diene to capronaldehyde (→**23b**), catalyzed by p-**14**·Cr(Cl).[48] A suspension of polymer beads p-**14**·Cr(Cl) (150 mg, 0.02 mmol, 0.02 equiv, loading: 0.133 mmol g^{-1}), Danishefsky's diene (195 μL, 1.0 mmol, 1 equiv) and capronaldehyde (123 μL, 1.0 mmol, 1 equiv) in *tert*-butyl methyl ether (TBME) (1 mL) was stirred at room temperature under Ar for 24 h. The reaction solution was withdrawn by syringe and the polymer beads were washed with Et_2O (3 × 5 mL). TFA (two drops) was added to the combined organic fractions and the solvent was evaporated. Purification of the crude product by flash column chromatography (hexane/ethyl acetate 4:1) afforded **23b** (97 mg, 58%). The enantiomeric purity of **23b** was analyzed by CGC (*β*-CD; heating 120 °C/isothermal; pressure 1.0 bar H_2; t_R (*S*)-**23b** ca. 25.0 min, t_R (*R*)-**23b** ca. 25.7 min): (*R*)/(*S*)-**23b**: 86:14. In order to determine the conversion of the reaction a sample was taken from the reaction mixture prior to workup, diluted with Et_2O and treated with TFA (one drop). CGC analysis thereof (*β*-CD; heating 120 °C/isothermal; pressure 1.0 bar H_2; t_R (capronaldehyde) ca. 1.4 min, t_R (**23b**) as described above) showed a conversion of 70%. For multiple use of the polymer-bound catalyst, the beads were dried under high vacuum, resuspended in TBME and substrates were added as described above.

The reactions with benzaldehyde and cyclohexane carboxaldehyde were analogously performed. The enantiomer ratios of the corresponding cycloadducts **23a** and **23c** were determined according to literature.[48]

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[1] a) J. S. Früchtel, G. Jung, *Angew. Chem.* **1996**, *108*, 19–46; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 17–42; b) J. S. Früchtel, G. Jung, *Combinatorial Peptide and Nonpeptide Libraries*, VCH, Weinheim, **1996**.
[2] J. A. Ellman, *Chemtracts* **1995**, *8*, 1–4.

  0947-6539/01/0713-2886 $ 17.50+.50/0

[3] B. Jandeleit, D. J. Schaefer, T. S. Powers, H. W. Turner, W. H. Weinberg, *Angew. Chem.* **1999**, *111*, 2648–2689; *Angew. Chem. Int. Ed.* **1999**, *38*, 2476–2514.

[4] J. Seyden-Penne, *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, Wiley, New York, **1995**.

[5] R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**.

[6] H.-U. Blaser, *Chem. Rev.* **1992**, *92*, 935–952.

[7] E. C. Blossey, W. T. Ford in *Comprehensive Polymer Science. The Synthesis, Characterization, Reactions and Applications of Polymers, Vol.6* (Eds.: G. Allen, J. C. Bevington), Pergamon, New York, **1989**, pp. 81–114.

[8] P. Hodge in *Innovatives and Perspectives in Solid Phase & Combinatorial Libraries* (Ed.: R. Epton), Mayflower Scientific, Kingswinford, **1990**, pp. 273–292.

[9] S. Itsuno in *Polymeric Materials Encyclopedia*; *Synthesis, Properties and Applications, Vol. 10* (Ed.: J. C. Salamone), CRC Press, Boca Raton, **1996**, pp. 8078–8087.

[10] S. J. Shuttleworth, S. M. Allin, P. K. Sharma, *Synthesis* **1997**, 1217–1239.

[11] H.-U. Blaser, B. Pugin in *Supported Reagents and Catalysts in Chemistry* (Eds.: B. K. Hodnett, A. P. Kybett, J. H. Clark, K. Smith), The Royal Society of Chemistry, **1998**, pp. 101–109.

[12] L. Pu, *Tetrahedron: Asymmetry* **1998**, *9*, 1457–1477.

[13] P. Hodge, *Chem. Soc. Rev.* **1997**, *26*, 417–424.

[14] D. C. Sherrington, *Chem. Commun.* **1998**, 2275–2286.

[15] C. Girard, H. B. Kagan, *Angew. Chem.* **1998**, *110*, 3088–3127; *Angew. Chem. Int. Ed.* **1998**, *37*, 2922–2959.

[16] a) R. Dahinden, A. K. Beck, D. Seebach in *Encyclopedia of Reagents for Organic Synthesis, Vol. 3* (Ed.: L. Paquette), Wiley, Chichester, **1995**, pp. 2167–2170 and references therein; b) A. K. Beck, B. Bastani, D. A. Plattner, W. Petter, D. Seebach, H. Braunschweiger, P. Gysi, L. La Vecchia, *Chimia* **1991**, *45*, 238–244.

[17] D. Seebach, A. K. Beck, A. Heckel, *Angew. Chem.* **2001**, *113*, 96–142; *Angew. Chem. Int. Ed.* **2001**, *40*, 92–138, and references therein.

[18] a) D. Seebach, R. Marti, T. Hintermann, *Helv. Chim. Acta* **1996**, *79*, 1710–1740; b) P. J. Comina, A. K. Beck, D. Seebach, *Org. Proc. Res. Dev.* **1998**, *2*, 18–26. Besides our own work, TADDOL has also been immobilized by other groups: c) B. Altava, M. I. Burguete, B. Escuder, S. V. Luis, R. V. Salvador, J. M. Fraile, J. A. Mayoral, A. J. Royo, *J. Org. Chem.* **1997**, *62*, 3126–3134; d) J. Irurre, A. Fernandez-Serrat, F. Rosanas, *Chirality* **1997**, *9*, 191–197; e) J. Irurre, A. Fernandez-Serrat, M. Altayo, *Enantiomer* **1998**, *3*, 103–120; f) B. Altava, M. I. Burguete, J. M. Fraile, J. I. Garcia, S. V. Luis, J. A. Mayoral, M. J. Vincent, *Angew. Chem.* **2000**, *112*, 1563–1566; *Angew. Chem. Int. Ed.* **2000**, *39*, 1503–1506. TADDOL has recently also successfully been immobilized on silica by grafting: A. Heckel, D. Seebach, *Angew. Chem.* **2000**, *112*, 165–167; *Angew. Chem. Int. Ed.* **2000**, *39*, 163–165.

[19] a) A. Guyot in *Synthesis and Separations using Functional Polymers* (Eds.: D. C. Sherrington, P. Hodge), Wiley, Chichester, **1988**, pp. 1–42; b) P. Hodge, D. C. Sherrington in *Synthesis and Separations using Functional Polymers* (Eds.: D. C. Sherrington, P. Hodge), Wiley, Chichester, **1988**, pp. 469–478.

[20] P. B. Rheiner, H. Sellner, D. Seebach, *Helv. Chim. Acta* **1997**, *80*, 2027–2032.

[21] H. Sellner, D. Seebach, *Angew. Chem.* **1999**, *111*, 2039–2041; *Angew. Chem. Int. Ed.* **1999**, *38*, 1918–1920.

[22] H. Sellner, C. Faber, P. B. Rheiner, D. Seebach, *Chem. Eur. J.* **2000**, *6*, 3692–3705.

[23] G. Wulff, *Angew. Chem.* **1995**, *107*, 1959–1979; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1812–1832, and references therein.

[24] G. Wulff in *Templated Organic Synthesis* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **2000**, pp. 39–73, and references therein.

[25] G. Wulff, *Angew. Chem.* **1989**, *101*, 22–38; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 21–37, and references therein.

[26] a) D. E. De Vos, J. L. Meinershagen, T. Bein, *Angew. Chem.* **1996**, *108*, 2355–2357; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2211–2212; b) M. J. Sabater, A. Corma, A. Domenech, V. Fornés, H. Garcia, *Chem. Commun.* **1997**, 1285–1286; c) S. B. Ogunwumi, T. Bein, *Chem. Commun.* **1997**, 901–902; d) J. M. Fraile, J. I. Garcia, J. A. Mayoral, *J. Mol. Catal. A: Chem.* **1998**, *136*, 47–57; e) G.-J. Kim, J.-H. Shin, *Tetrahedron Lett.* **1999**, *40*, 6827–6830; f) X.-G. Zhou, X.-Q. Yu, J.-S. Huang, S.-G. Li, L.-S. Li, C.-M. Che, *Chem. Commun.* **1999**, 1789–1790; g) G.-J. Kim, S.-H. Kim, *Catal. Lett.* **1999**, *57*, 139–143.

[27] a) I. F. J. Vankelecom, D. Tas, R. F. Parton, V. Van de Vyver, P. A. Jacobs, *Angew. Chem.* **1996**, *108*, 1445–1447; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1346–1348; b) K. B. M. Janssen, I. Laquiere, W. Dehaen, R. F. Parton, I. F. J. Vankelecom, P. A. Jacobs, *Tetrahedron: Asymmetry* **1997**, *8*, 3481–3487.

[28] a) B. B. De, B. B. Lohray, P. K. Dhal, *Tetrahedron Lett.* **1993**, *34*, 2371–2374; b) B. B. De, B. B. Lohray, S. Sivaram, P. K. Dhal, *Macromolecules* **1994**, 27, 1291–1296; c) B. B. De, B. B. Lohray, S. Sivaram, P. K. Dhal, *Tetrahedron: Asymmetry* **1995**, *6*, 2105–2108; d) B. B. De, B. B. Lohray, S. Sivaram, P. K. Dhal, *J. Polym. Sci. Polym. Chem.* **1997**, *35*, 1809–1818.

[29] a) F. Minutolo, D. Pini, P. Salvadori, *Tetrahedron Lett.* **1996**, *37*, 3375–3378; b) F. Minutolo, D. Pini, P. Salvadori, *Tetrahedron: Asymmetry* **1996**, *7*, 2293–2302.

[30] M. D. Angelino, P. E. Laibinis, *Macromolecules* **1998**, *31*, 7581–7587.

[31] a) L. Canali, E. Cowan, H. Deleuze, C. L. Gibson, D. C. Sherrington, *Chem. Commun.* **1998**, 2561–2562; b) L. Canali, E. Cowan, H. Deleuze, C. L. Gibson, D. C. Sherrington, *J. Chem. Soc. Perkin Trans. 1* **2000**, 2055–2066.

[32] a) D. A. Annis, E. N. Jacobsen, *J. Am. Chem. Soc.* **1999**, *121*, 4147–4154; b) S. Peukert, E. N. Jacobsen, *Org. Lett.* **1999**, *1*, 1245–1248.

[33] J. F. Larrow, E. N. Jacobsen, Y. Gao, Y. Hong, X. Nie, C. M. Zepp, *J. Org. Chem.* **1994**, *59*, 1939–1942.

[34] J. Braun, H. Normant, *Bull. Soc. Chim. Fr.* **1966**, *8*, 2557–2564.

[35] N. Miyaura, T. Yanagi, A. Suzuki, *Synth. Commun.* **1981**, *11*, 513–519.

[36] C. J. Hawker, J. M. J. Fréchet, *J. Am. Chem. Soc.* **1990**, *112*, 7638–7647.

[37] Reviews: a) E. N. Jacobsen in *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), VCH, New York, **1993**, pp. 159–202; b) E. N. Jacobsen in *Comprehensive Organometallic Chemistry II* (Eds.: E. W. Abel, F. G. A. Stone, E. Wilkinson), Pergamon, New York, **1995**, pp. 1097–1135; c) T. Katsuki, *Coord. Chem. Rev.* **1995**, *140*, 189–214; d) L. Canali, D. C. Sherrington, *Chem. Soc. Rev.* **1999**, *28*, 85–93.

[38] a) S. Thorand, N. Krause, *J. Org. Chem.* **1998**, *63*, 8551–8553; b) J. Frackenpohl, W. M. Braje, H. M. R. Hoffmann, *J. Chem. Soc. Perkin Trans. 1* **2001**, 47–65.

[39] We also tried to synthesize **11** in an "inverse" way by first attaching a phenyl-acetylene moiety to **4b**, followed by coupling of the resulting dendritic acetylene branch to 3-*tert*-butyl-5-bromo salicylic aldehyde by Sonogashira coupling. Unfortunately, mainly homo-coupling of the dendritic acetylene moieties occurred under the coupling conditions, with **11** being formed in only minor amounts.

[40] In solution generally less than 5 mol% of Mn-Salen are used for the epoxidation reactions. We decided to use 20 mol% of catalyst both for homogeneous and heterogeneous reactions. With the heterogeneous catalysts being recyclable many times, the amount of catalyst employed is not as crucial as under homogeneous conditions!

[41] M. Palucki, G. J. McCormick, E. N. Jacobsen, *Tetrahedron Lett.* **1995**, *36*, 5457–5460.

[42] B. D. Brandes, E. N. Jacobsen, *J. Org. Chem.* **1994**, *59*, 4378–4380.

[43] S. Itsuno, Y. Sakurai, K. Ito, T. Maruyama, S. Nakahama, J. M. J. Fréchet, *J. Org. Chem.* **1990**, *55*, 304–310.

[44] H. Zweifel, *Stabilization of Polymeric Materials*, Springer, Berlin, **1998**.

[45] In most literature examples, polymer-bound Mn-Salens have been prepared by copolymerization or grafting of a suitable pre-formed Mn-Salen. References [28b] and [31] are examples for loading a polymer-bound Salen with manganese after copolymerization. In contrast to the procedures described in [28b] and [31], we had to use DMF as co-solvent, because our beads do not swell in pure EtOH.

[46] For determination of the degree of conversion, a sample was taken from the reaction mixture after 30 minutes, 1N KOH and Et_2O were added, and the organic phase was subjected to CGC analysis.

[47] A very recent review: K. A. Jørgensen, *Angew. Chem.* **2000**, *112*, 3702–3733; *Angew. Chem. Int. Ed.* **2000**, *39*, 3558–3588, and references therein.

[48] S. E. Schaus, J. Brånalt, E. N. Jacobsen, *J. Org. Chem.* **1998**, *63*, 403–405.

[49] For determination of the enantioselectivities under homogeneous conditions we used a Salen prepared by condensation of (*R*,*R*)-cyclohexane diamine and 3-*tert*-butyl-5-bromo salicylic aldehyde.

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