Immobilization of BINOL by Cross-Linking Copolymerization of Styryl Derivatives with Styrene, and Applications in Enantioselective Ti and Al Lewis Acid Mediated Additions of Et_2Zn and Me_3SiCN to Aldehydes and of Diphenyl Nitrone to Enol Ethers

Holger Sellner,[a] Claude Faber,[b] P. Beat Rheiner,[a] and Dieter Seebach*[a]

Abstract: The chiral ligand 1,1′-bi-2-naphthol (BINOL) has been succesfully immobilized on polystyrene. Several dendritic and non-dendritic BINOL derivatives (**3**, and **13**–**17**), bearing at least two polymerizable styryl groups, were prepared and fully characterized. Suspension copolymerization of the MOM- or TIPS-protected cross-linking BINOL ligands (MOM = methyloxymethyl, TIPS = triisopropylsilyl) with styrene, cleavage of the protecting-groups, and loading with a Lewis-acid afforded catalytically active polystyrene-supported BINOLates. The polymer-bound BINOLs p-**3**, and p-**13**–p-**16** were tested in the Ti-BINOLate-mediated addition of Et_2Zn to PhCHO. The enantioselectivities (up to 93%) and conversions obtained with the polymer-bound catalysts were in most cases identical (within experimental error) to those obtained with the unsubstituted 1,1′-bi-2-naphthol and with the non-polymerized BINOL cross-linkers under homogeneous conditions. Special focus was put on the reusability of the supported catalyst: the polymer-beads were used in up to 20 consecutive catalytic runs, with the best polymers showing no or only minor loss of selectivity. BINOL-polymers p-**17**, obtained by copolymerization of a 3,3′-distyryl-substituted BINOL **17a** with styrene, were used in the BINOL·AlMe-mediated cycloaddition of diphenyl nitrone with alkyl vinyl ethers. In all cases the *exo*/*endo* selectivity (≥92:8) and the enantioselectivities with which the *exo*-cycloadducts were formed (≥95%) correspond to those observed in the homogeneous reactions. A dendritically cross-linked BINOL-polymer was also employed in the Ti-BINOLate-mediated cyanosilylation of pivalaldehyde. The enantiopurity of the cyanohydrine obtained in the first run was as high as in the homogeneous reaction (72%); surprisingly the catalytic performance of the supported catalyst increased steadily during the first catalytic cycles to reach 83%. Thus, cross-linking BINOLs can be succesfully incorporated into a polystyrene matrix (without racemization!) to give polymer-bound BINOL ligands that give excellent performance over many catalytic cycles with catalytic activities comparable with those of soluble analogues.

Keywords: asymmetric catalysis · 1,1′-binaphthols · catalysts · dendritic cross-linkers · polymers

Introduction

During the last years, enormous progress has been achieved in the field of enantioselective catalysis. Catalysts and auxiliaries for a great variety of enantioselective reactions have been developed.[1–3] As the preparation of these chiral catalysts is often tedious and expensive, it is favorable to reuse them as often as possible. Besides the possibility of immobilizing chiral ligands on soluble polymer-supports, the ligands can also be bound to solid supports.[4–11] This approach offers the advantages of easy separation, recovery of the insoluble catalyst from the reaction mixture by simple filtration, and subsequent reuse (which makes these catalysts also attractive for industrial applications). For practical reasons, polystyrene is used as polymer support in many cases. The ligands can either be grafted to an existing cross-linked polystyrene resin or they can be immobilized by copolymerization of a polymerizable ligand with styrene and a cross-linker (for example divinyl benzene). In the latter case, suspension copolymerization offers a convenient method for the generation of polymer beads, which are easy to handle.[12, 13]

During the last years, we became interested in the immobilization of TADDOL (TADDOL = α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanol) ligands,[14] developed in our laboratory.[15] Three years ago, we started using dendriti-

[a] Prof. Dr. D. Seebach, H. Sellner, Dr. P. B. Rheiner
Laboratorium für Organische Chemie
der Eidgenössischen Technischen Hochschule Zürich
ETH Zentrum, Universitätstrasse 16
CH-8092 Zürich (Switzerland)
Fax: (+41) 1-632-1144
E-mail: seebach@org.chem.ethz.ch

[b] C. Faber
Visiting student at ETH Zürich (1999) from
Université Louis Pasteur, Strasbourg (France)

  0947-6539/00/0620-3692 $ 17.50+.50/0

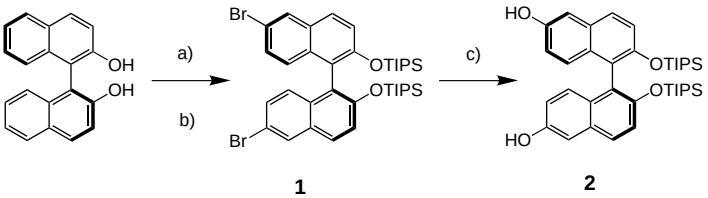
cally substituted, polymerizable TADDOLs as cross-linkers in polystyrene.[16] Thus, TADDOLs with dendritic branches, which have styryl groups at the periphery, underwent suspension copolymerization with styrene, without the use of an additional cross-linker, to give dendritically cross-linked TADDOL-polymers. The supported TADDOLs prepared in this way give an excellent catalytic performance with respect to stability (of enantioselectivity and conversion) during multiple use as catalyst ligands (in up to 20 catalytic cycles).[17]

In order to find out whether this approach is applicable to other ligands, we have now immobilized 1,1′-bi-2-naphthol (BINOL) in the same way. BINOL can be used as a chiral ligand in many stereoselective Lewis acid mediated transformations.[18] Surprisingly, it appears that there is no report up until now on the succesful immobilization of BINOL on polystyrene. Besides the work of L. Pu and his group on mainly soluble, so-called polybinaphthyl-polymers generated by repetitive Pd-mediated cross-coupling of BINOL-monomers to long-chain BINOL-polymers,[19] there is only one application of a polystyrene-bound BINOL-derivative used in a Mukaiyama aldol reaction,[20] and the immobilization of a BINOL-derived ligand (BINAPHOS) in a highly cross-linked polystyrene resin used for asymmetric hydroformylation of olefins.[21] Most recently there have also been examples of a BINAP-ligand supported on a Merrifield resin[22] and on a soluble polymer support.[23]

Preparation of the BINOL cross-linkers, copolymerization with styrene and first applications of the polymers in various test reactions are the subjects of this paper.

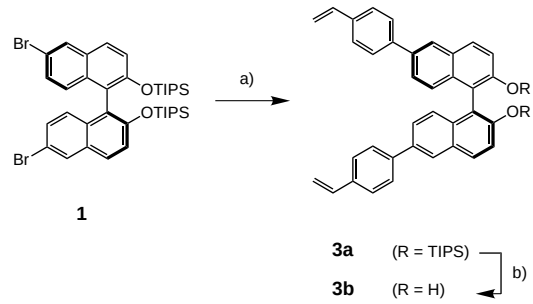
Results and Discussion

Preparation of BINOLs 1 and 2 used as core units of cross-linking BINOLs: The 6,6′-positions of the BINOL system were considered most favorable for the attachment of spacer groups to the BINOL core unit. Besides the synthetic accessibility of these positions within the BINOL molecule, the advantage was that branches attached to the core in this way would be situated at a large enough distance from the catalytic center so as not to cause any steric hindrance. For the preparation of BINOLs **1** and **2**, we optimized a synthetic route developed by Yoshida[24] for the preparation of dendritically substituted BINOL ligands (Scheme 1). Thus, BINOL was first brominated selectively in the 6- and 6′-position,[25] followed by TIPS-protection (TIPS = triisopropylsilyl) of the OH groups to give BINOL derivative **1**. Subsequent replacement of the Br atoms by OH groups (Br/Li exchange, addition of $B(OMe)_3$[26] and oxidative workup[27]) afforded BINOL derivative **2**.[28]



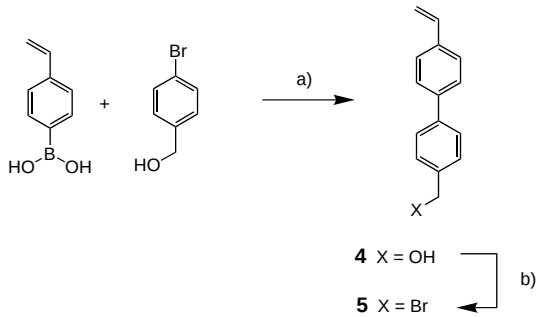
Scheme 1. Synthesis of the BINOL core building blocks **1** and **2**. Conditions: a) Br_2, CH_2Cl_2, −78 °C, 4 h, 90 %; b) Triisopropylsilyl chloride (TIPSCl), imidazole, DMAP, RT, 48h, 90 %; c) 1) *t*BuLi, THF, −78 °C, 30 min, 2) $B(OMe)_3$, THF, −78 °C → RT, 2 h, 3) H_2O_2, NaOH, THF, 89 %.

Preparation of BINOL cross-linkers with the spacer groups attached in 6,6′-positions: Several branches or spacer moieties were attached to the 6,6′-positions of the BINOL core unit in two different ways. In one method a styryl group was directly attached to the BINOL core by a Pd-mediated Suzuki cross-coupling reaction of **1** with styrene boronic acid[29] to give BINOL derivative **3a** (Scheme 2).[19i] Subsequent cleavage of



Scheme 2. Preparation of BINOL **3b** by Suzuki coupling and subsequent deprotection. Conditions: a) 4-styrene boronic acid, $[Pd(PPh_3)_4]$, 1 M K_2CO_3, THF, 70 °C, 16 h, 67 %; b) TBAF · $3H_2O$, RT, 1 h, quantitative yield.

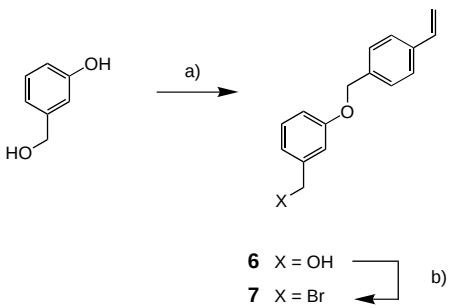
the TIPS protecting-groups afforded BINOL **3b**. In the second method derivatives were generated by etherification reactions of **2** with various branches and spacer molecules bearing a benzylic bromide functionality.[30] Thus, biphenyl spacer **5** with a vinyl group was obtained by Suzuki coupling[31] of styrene boronic acid and 4-bromo-benzyl alcohol (→ **4**) (no protection of the OH group was necessary!), followed by OH/Br substitution (Scheme 3).



Scheme 3. Preparation of the biphenyl arm **5**. Conditions: a) $[Pd(PPh_3)_4]$, 2 M Na_2CO_3, THF, 70 °C, 16 h, 77 %; b) PBr_3, Et_2O, RT, 1 h, 97 %.

A more flexible spacer moiety **7** was prepared by etherification of 3-hydroxy-benzyl alcohol with 4-vinyl-benzyl chloride (→ **6**) and OH/Br replacement under Appel conditions (Scheme 4).[32]

We also synthesized the styryl-substituted first- and second-generation Fréchet branches **10** and **12** starting from 3,5-



Scheme 4. Preparation of the spacer molecule **7**, starting from 3-hydroxybenzylic alcohol. Conditions: a) 4-vinyl-benzyl chloride, K_2CO_3, CH_3CN, 50 °C, 48 h, 92 %; b) CBr_4, PPh_3, THF, RT, 16 h, 90 %.

dihydroxy benzoic acid methyl ester and 4-vinyl-benzyl chloride, through the intermediates **8**, **9**, and **11** (Scheme 5).[33–35]

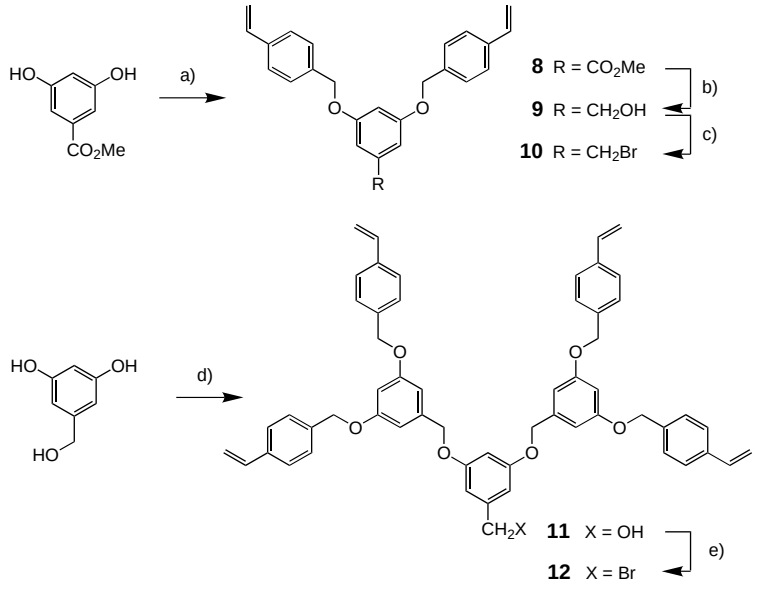
Coupling of the BINOL core unit **2** with the benzyl bromide branches and spacers was performed by using NaH as base in DMF at room temperature.[24] Workup of the reaction mixture and purification by flash-column chromatography afforded the pure TIPS-protected BINOL cross-linkers **13**, and **14a**–**16a**. The yields of the coupling reactions were only 40–50 %, due to migration of the silyl groups under the coupling conditions, as noticed previously by Yoshida et al.[24, 36] Cleavage of the TIPS protecting-groups afforded BINOLs **14b**–**16b** (Scheme 6).[37] All compounds were fully characterized by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy, by FAB- or MALDI-TOF-mass spectrometry, and by elemental analysis.

Preparation of a BINOL cross-linker with styryl spacers attached in the 3,3′-positions: 3,3′-Disubstituted BINOL derivatives have turned out to be useful for many types of enantioselective reactions.[18] Therefore, we have also prepared BINOL derivative **17a** by Suzuki cross coupling of MOM-protected (MOM = methyloxymethyl) 3,3′-diiodo-1,1′-bi-2-naphthol[38] with styrene boronic acid.[19j] Removal of the MOM protecting groups was achieved by addition of HCl in THF/MeOH to give **17b** (Scheme 7).

Addition of Et_2Zn to PhCHO mediated by Ti complexes[39, 40] of 3b and 14b–16b under homogeneous conditions: Before immobilizing the BINOL cross-linkers on polystyrene, we had to make sure that the branch and spacer moieties attached to the BINOL core had no negative effect on the catalytic performance in homogeneous solution. As a test reaction we chose the addition of Et_2Zn to PhCHO (Scheme 8).[41, 42] The reaction showed that by using 20 mol % of catalyst the selectivities and conversions were comparable in all cases with those obtained with the simple unsubstituted BINOLate (enantiomeric ratio (*er*) 94:6, conversion 90 % after 2 h) (Table 1).

A slight decrease in conversion was observed only in the case of BINOLs **14b** and **16b**. Thus, attachment of huge dendritic branches at the 6,6′-positions of the BINOL core unit has a minute influence on the catalytic performance; this confirms the previous observations by Yoshida et al.[43]

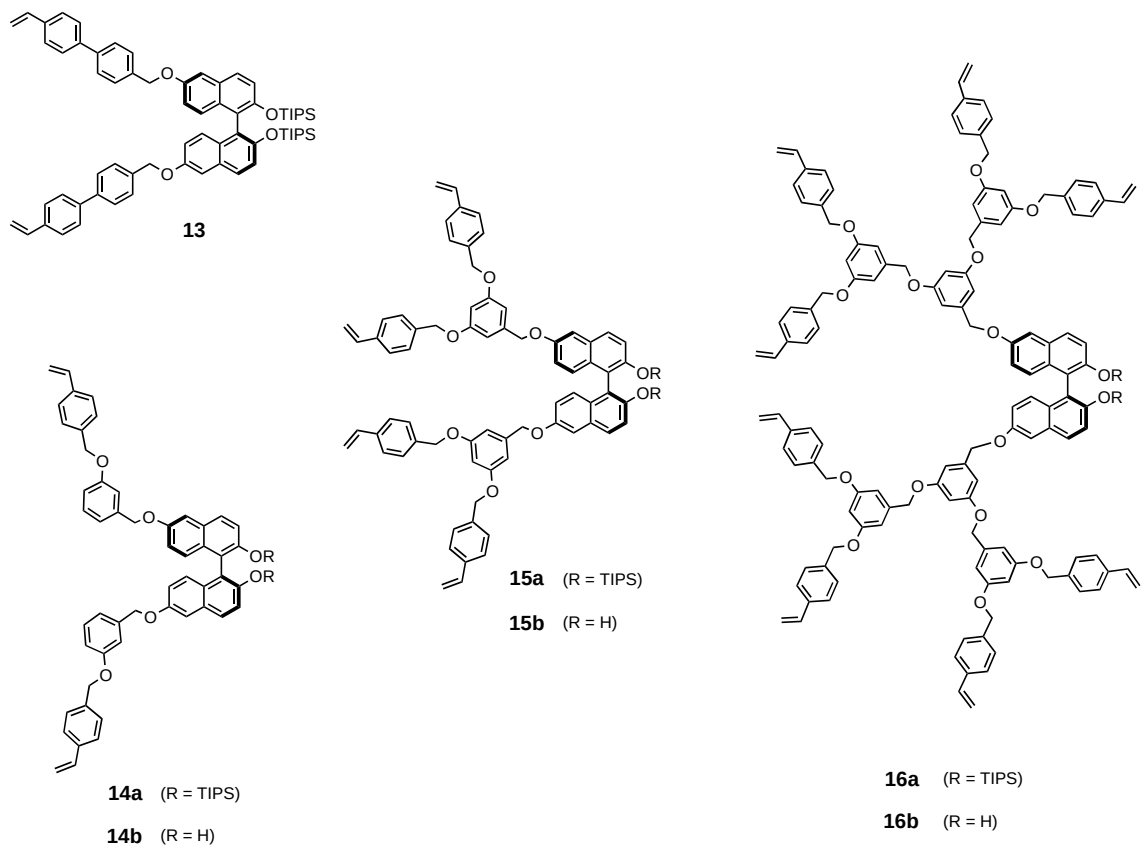
Copolymerization of the BINOL cross-linkers with styrene: One of the most convenient ways of immobilizing a chiral ligand is the suspension copolymerization of a suitable derivative, giving insoluble polymer beads. Following a procedure by Fréchet and Itsuno[44] (successfully used by us in our previous work[15–17]), a solution of styrene, BINOL cross-linker **3a**, **13**, and **14a**–**17a**, and α,α'-azobis(isobutyronitrile) (AIBN) in C_6H_6/THF was mixed with an aqueous solution of poly(vinyl alcohol) (PVA) under constant stirring and heating at 80 °C for 14 h (Scheme 9). During this process, cross linked, spherical polymer beads with an average diameter of 400 μm and swelling factors between 2.5 and 4 in toluene were formed. In order to prevent racemization of the BINOL core unit during the copolymerization process, the MOM- or TIPS-protected BINOLs **3a**, **13**, and **14a**–**17a** were employed and the protecting groups were cleaved from the polymer beads after copolymerization to give supported BINOLs p-**3** and p-**13**–p-**17** (Scheme 9).[45, 46]



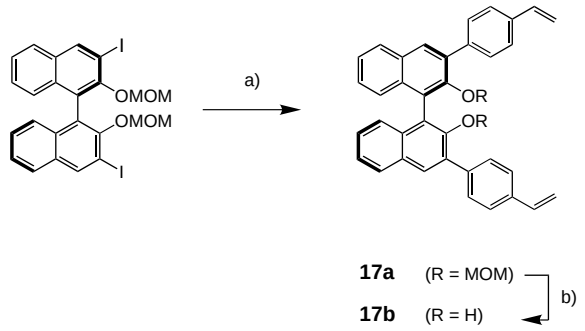
Scheme 5. Preparation of first- and second-generation Fréchet branches **10** and **12**. Conditions: a) 4-vinyl benzyl chloride, K_2CO_3, 18-crown-6, acetone, 70 °C, 48h, 86 %; b) $LiAlH_4$, THF, 70 °C, 4 h, 90 %; c) CBr_4, PPh_3, THF, RT, 20 h, 57 %; d) **10**, K_2CO_3, 18-crown-6, acetone, 70 °C, 48 h, 73 %; e) CBr_4, PPh_3, THF, RT, 48 h, 74 %.

Addition of Et_2Zn to PhCHO mediated by Ti complexes of polymer-bound BINOLs p-3 and p-13–p-16: The immobilized BINOLs p-**3** and p-**13**–p-**16** were first tested in the enantioselective addition of Et_2Zn to PhCHO with 20 mol % of Ti-BINOLate[39, 40] (Scheme 10).[41, 42] Addition of $Ti(OiPr)_4$ to a suspension of the beads in toluene afforded

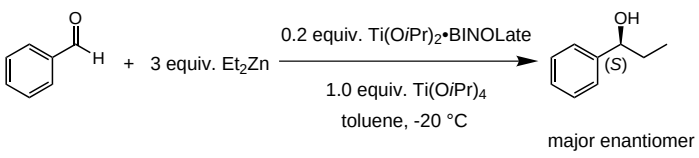
0947-6539/00/0620-3694 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 20



Scheme 6. TIPS-protected BINOL cross-linkers **13** and **14a**–**16a**, obtained by coupling of BINOL core unit **2** with the benzyl bromides **5**, **7**, **10**, and **12**, and deprotected BINOL derivatives **14b**–**16b**. Conditions for deprotection: TBAF · 3 H_2O, THF, RT, 1 h, quantitative yield.



Scheme 7. Preparation of TIPS-protected 3,3′-disubstituted BINOL cross-linker **17a** by Suzuki cross-coupling reaction and subsequent deprotection to give substituted BINOL **17b**. Conditions: a) 4-styrene boronic acid, [$Pd(PPh_3)_4$], 1M K_2CO_3, THF, 70 °C, 16 h, 62 %; b) HCl, THF/MeOH, RT, 2 h, 80 %.



Scheme 8. Addition of Et_2Zn to PhCHO mediated by Ti-BINOLates of **3b** and **14b**–**16b**.

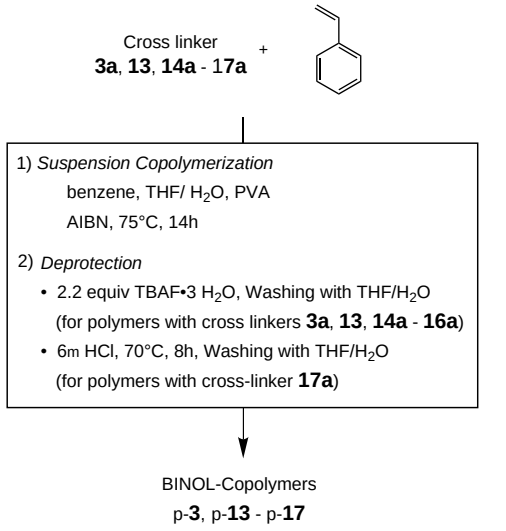
polymer-bound p-**3** · $Ti(OiPr)_2$ and p-**13** · $Ti(OiPr)_2$–p-**16** · $Ti(OiPr)_2$, the beads thereby turned orange (Figure 1). After stirring at room temperature for 12 h, followed by addition of PhCHO and $Ti(OiPr)_4$, the reaction mixture was cooled to −20 °C and Et_2Zn was added. After several hours of reaction (Table 2), the solution was separated from the beads by syringe, and the polymer beads were washed several times with toluene under Ar. The conversion of the reaction and the enantiopurity of 1-phenyl-1-propanol were determined by capillary gas chromatography (CGC) of the reaction solution after acidic workup. The beads were resuspended in toluene, charged with substrates, and used in a new catalytic run (Scheme 10). The results are given in Table 2.

Table 1. Selectivities and conversions obtained in the Et_2Zn addition to PhCHO, mediated by Ti complexes of BINOLs **3b** and **14b**–**16b** in homogeneous solution, with formation of enantioenriched 1-phenyl-1-propanol.

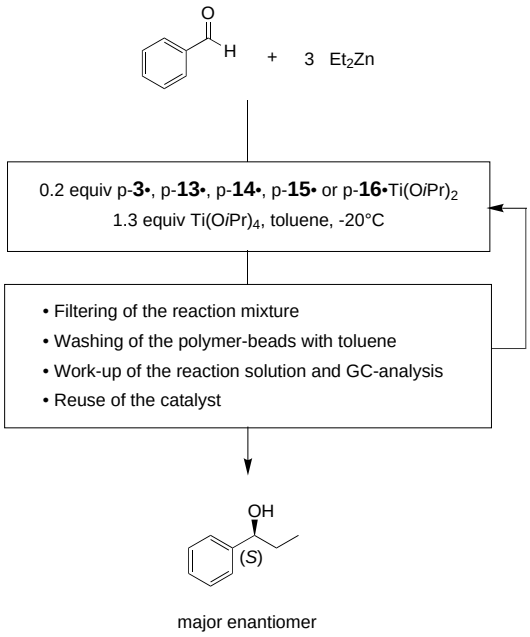
BINOL	*S*/*R*	Conversion [%][a]
3b	92.5:7.5	87
14b	91.5:8.5	79
15b	93.7:6.3	88
16b	93.1:6.9	78

[a] After a reaction time of 2 h, [PhCHO] = 0.1M.

In most cases, the selectivities were as good as those obtained with the cross-linkers in homogeneous solution (Table 1). Also, the conversions of the heterogeneous reactions were comparable with those observed under homogeneous conditions in most cases. In the case of polymers p-**3** · $Ti(OiPr)_2$ and p-**13** · $Ti(OiPr)_2$–p-**15** · $Ti(OiPr)_2$, the catalytic performance (with respect to enantioselectivity and conver-



Scheme 9. Copolymerization of cross-linkers **3a, 13**, and **14a**–**17a** with styrene and subsequent cleavage of the protecting groups to give BINOL cross-linked copolymers p-**3** and p-**13**–p-**17**. The loadings (mmol BINOL per gram of polymer) were calculated from the relative amounts of the components used in the copolymerization.



Scheme 10. Multiple use of polymer-bound p-**3**·Ti(O*i*Pr)$_2$ and p-**13**·Ti(O*i*Pr)$_2$–p-**16**·Ti(O*i*Pr)$_2$ in the Ti-BINOLate-mediated addition of Et_2Zn to PhCHO.

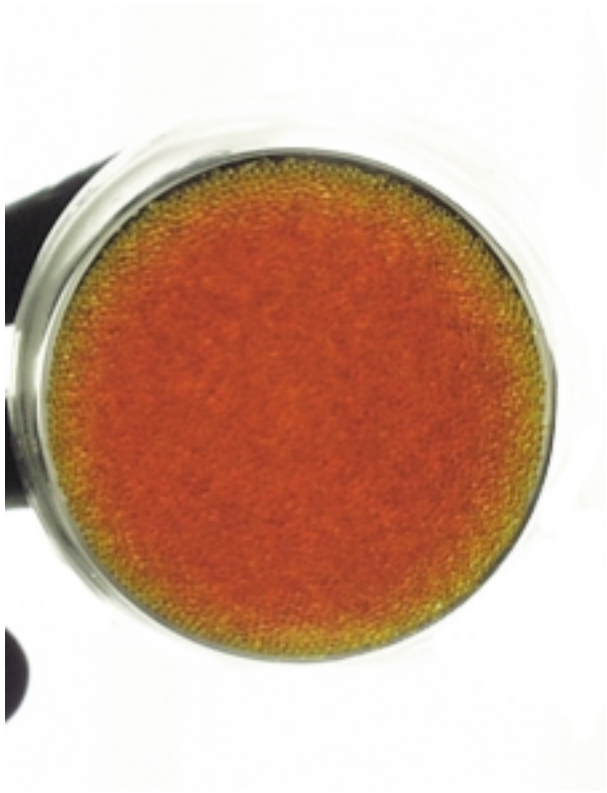


Figure 1. Round-bottomed flask containing a suspension of polymer beads (diameter 400 μm) p-**15**·Ti(O*i*Pr)$_2$ in toluene after loading with titanate.

Table 2. Enantioselectivities and conversions obtained in the addition of Et_2Zn to PhCHO mediated by p-**3**·Ti(O*i*Pr)$_2$ and p-**13**·Ti(O*i*Pr)$_2$–p-**16**·Ti(O*i*Pr)$_2$ with different loadings, with the formation of enantioenriched 1-phenyl-1-propanol (cf. Scheme 10).

	Loading [mmol g^{-1}]	*S*/*R*	Conversion [%] (reaction time)
p-**3**·Ti(O*i*Pr)$_2$	0.18	92.2:7.8	91 (4 h)[a]
	0.13	92.5:7.5	82 (4 h)[b]
p-**13**·Ti(O*i*Pr)$_2$	0.17	92.6:7.4	90 (4 h)[a]
	0.13	93.1:6.9	82 (3 h)[a]
p-**14**·Ti(O*i*Pr)$_2$	0.17	92.8:7.2	94 (4 h)[b]
	0.13	93.3:6.7	31 (3 h)[c]
p-**15**·Ti(O*i*Pr)$_2$	0.17	89.5:10.5	67 (4.5 h)[a]
	0.15	91.7:8.3	91 (4 h)[a]
	0.13	91.6:8.4	96 (4 h)[a]
p-*ent*-**15**·Ti(O*i*Pr)$_2$	0.13	7.2:92.8	99 (4.5 h)[a]
p-**16**·Ti(O*i*Pr)$_2$	0.07	91.3:8.7	66 (4 h)[b]
	0.05	90.0:10.0	22 (3 h)[c]

[a] [PhCHO] = 0.1 M. [b] [PhCHO] = 0.07 M. [c] [PhCHO] = 0.04 M.

sion,especially for polymer p-**15**·Ti(O*i*Pr)$_2$) increased slightly with decreased loading. This can be rationalized by the fact that, in our polymers, lower loading means lower degree of cross-linking and thus better accessibility for substrates and reactants. Only in the case of polymers p-**16**·Ti(O*i*Pr)$_2$ with a second-generation dendritic cross-linker, significantly lower selectivities were observed, although the loading of the polymers was the lowest of all.

The immobilization of a chiral catalyst on a polymer support is only suitable if the immobilized catalyst has an activity comparable with the soluble analogue and if multiple use of the polymer-bound catalyst with no or only minor loss of activity is possible. Having shown that the supported BINOLs, introduced into polystyrene as cross-linkers, perform as well as the homogeneous BINOLs, we focused our attention on multiple use of the catalyst (cf. our previous work on polymer-bound TADDOL[15, 17]). Following the procedure outlined in Scheme 10, we reused the supported Ti-BINOLates in up to 20 consecutive catalytic runs. The observed selectivities in the formation of 1-phenyl-1-propanol, by using

0947-6539/00/0620-3696 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 20

polymers p-**3** · Ti(O*i*Pr)$_2$ and p**13** · Ti(O*i*Pr)$_2$ – p-*ent*-**15** · Ti(O*i*Pr)$_2$ with a loading of 0.13 mmol BINOL per gram of polymer, are presented in Figure 2.

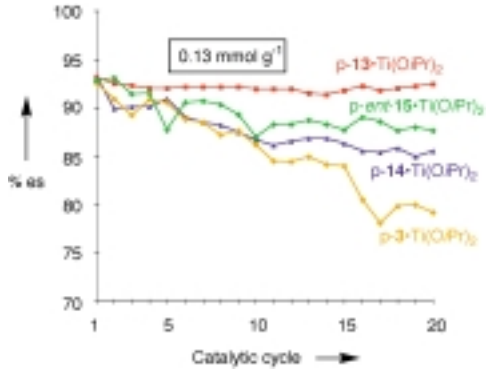


Figure 2. Enantioselectivities of 1-phenyl-1-propanol during multiple use of p-**3** · Ti(O*i*Pr)$_2$, p-**13** · Ti(O*i*Pr)$_2$, p-**14** · Ti(O*i*Pr)$_2$, and p-*ent*-**15** · Ti(O*i*Pr)$_2$ with a loading of 0.13 mmol g^{-1} (cf. Scheme 10).

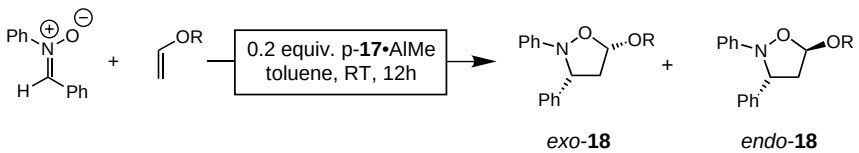
With polymer p-**13** · Ti(O*i*Pr)$_2$ no loss of enantioselectivity over 20 runs was observed, also p-*ent*-**15** · Ti(O*i*Pr)$_2$ and p-**14** · Ti(O*i*Pr)$_2$ showed only minor loss of activity (5 and 7% enantiomeric selectivity (*es*), respectively) after 20 cycles. In contrast, p-**3** · Ti(O*i*Pr)$_2$ was less stable. The same negative effect was also encountered with polymers of higher loading[47] and with polymer p-**16** · Ti(O*i*Pr)$_2$ carrying second-generation dendritic branches. It should be noted that in contrast to the situation with Ti-TADDOLates, multiple use of the supported Ti-BINOLates was difficult to achieve due to their sensitivity to air and moisture; it was important to avoid contact of the polymer-bound catalysts with air during multiple use!

1,3-Dipolar cycloaddition of diphenyl nitrone to vinyl ethers mediated by Al complexes of BINOL copolymers p-17: Recently, Jørgensen et al. reported about the 1,3-dipolar cycloaddition of various nitrones to vinyl ethers, mediated by Al-BINOLates;[48] only 3,3′-disubstituted BINOL derivatives gave rise to high selectivities in this cycloaddition. Encouraged by the fact that the reaction shows a linear correlation between enantiopurities of BINOL and product and that the reaction proceeds well with Pu's soluble polybinaphthols,[19o] we decided to test it with our polystyrene-bound BINOL p-**17**. Addition of $AlMe_3$ to a suspension of the polymer beads in toluene and stirring at room temperature for 2 h afforded the catalyst p-**17** · AlMe (Scheme 11), accompanied by a color change of the beads from colorless to yellow (Figure 3). Diphenyl nitrone and the corresponding vinyl ether were

Figure 3. Round-bottomed flask containing a suspension of polymer beads p-**17** · AlMe (diameter > 1000 μm) in toluene.

added, and the reaction mixture was stirred at rooom temperature for 12 h (Scheme 11). Isolation of cycloadducts **18** was achieved simply by washing of the beads with toluene and evaporation of the solvent. The *exo*/*endo* ratio in the crude product **18** was determined by ^{1}H NMR spectroscopy.[48] In every case, the conversion was complete as no signals of the nitrone were detected. The enantiopurity of *exo*-**18** was determined by HPLC analysis[48] of pure samples of the *exo*-cycloadducts on a chiral column (Table 3).

The selectivities obtained with p-**17** · AlMe correspond to those found in homogeneous solution.[48] In contrast to the results with the Et_2Zn addition to PhCHO, there seems to be no dependence of the performance of the polymer-bound catalyst from the degree of loading. Even highly loaded BINOL copolymers (0.39 mmol g^{-1}) give rise to the same selectivities found with low-loaded polymers (0.14 mmol g^{-1}). Moreover, the fact that in the case of the polymer with the lowest loading (better site isolation of the catalytic centers) the same selectivities are obtained as in solution, supports the proposed transition-state model involving a single Al-BINOLate.[48] Furthermore, it is remarkable that attachment of the polystyrene matrix to the 3,3′-positions of the BINOL core, close to the catalytic site, has no negative effect on the catalytic performance. Unfortunately, the copolymers p-**17** · AlMe could not be used in



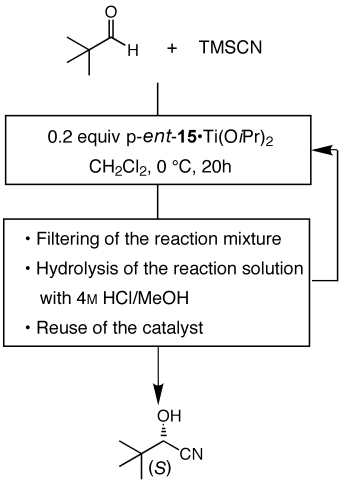
Scheme 11. 1,3-Dipolar cycloaddition of diphenyl nitrone to vinyl ethers to give cycloadducts **18**, mediated by BINOL copolymers p-**17** · AlMe. R = Et or *t*Bu.

Table 3. Selectivities obtained in the 1,3-dipolar cycloaddition of diphenyl nitrone with ethyl vinyl ether (R = Et) or *tert*-butyl vinyl ether (R = *t*Bu), mediated by p-**17** · AlMe with different loadings.

Loading of p-**17** [mmol g^{-1}]	Cycloadduct **18**	e*xo*/*endo* (**18**)	enantioselectivity (*exo*-**18**) [%]
0.39	R = Et	92:8	96
0.22	R = Et	93:7	96
0.14	R = Et	93:7	97
0.39	R = *t*Bu	> 95:5	95
0.22	R = *t*Bu	> 95:5	96
0.14	R = *t*Bu	> 95:5	95

further catalytic cycles. Neither direct application of p-**17** · AlMe in a new catalytic run nor hydrolysis of p-**17** · AlMe followed by re-loading with $AlMe_3$ were successful. This is in contrast to an observation with a polymer-bound TADDOL, an $Al(OEt)_3H^-$ complex of which could be hydrolyzed and regenerated.[15a]

Asymmetric cyanosilylation of pivalaldehyde mediated by a Ti complex of p-*ent*-15: (*i*PrO)$_2$Ti-BINOLate was employed by Nakai et al. for the asymmetric cyanosilylation of aliphatic aldehydes,[49] and we chose this transformation in a third test of our dendritically cross-linked BINOL copolymer. In this case, the p-*ent*-**15** material was loaded with Ti(O*i*Pr)$_4$, and the resulting complex (20 mol% Ti-BINOLate) used for the cyanosilylation of pivalaldehyde with trimethylsilyl cyanide (TMSCN), see Scheme 12.



Scheme 12. Multiple use of polymer-bound BINOL p-*ent*-**15** · Ti(O*i*Pr)$_2$ in the Ti-BINOLate-mediated cyanosilylation of pivalaldehyde. Loading of polymer: 0.13 mmol g^{-1}.

Again, the main focus of the investigation was put on multiple use of the catalyst. After each catalytic cycle, the reaction solution was separated from the beads. The enatiopurity of the cyanohydrine (after hydrolytic work-up) and the conversion of the reaction were determined by CGC by using a chiral column. The beads were resuspended in CH_2Cl_2, substrates were added and the catalyst was used again. In all cases the conversion after 20 h was above 90%. In the first run, the enantioselectivity was 72%, which corresponds to that found with the homogeneous reaction. Surprisingly, the enantioselectivity increased gradually during the following catalytic runs to reach a value of 83% after five runs (Figure 4).

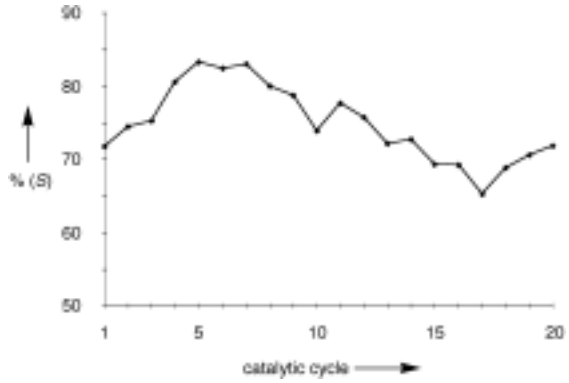


Figure 4. Enantiopurity of 2-hydroxy-3,3-dimethylbutanenitrile formed with multiple use of p-*ent*-**15** · Ti(O*i*Pr)$_2$ by cyanosilylation of pivalaldehyde, followed by acidic workup (for conditions see Scheme 12).

The slight decrease in selectivity from the 8th to the 15th run was probably due to leaching of the titanate from the catalyst: the polymer beads were treated with Ti(O*i*Pr)$_4$ after the 16th run to reload vacant catalytic sites, washed thoroughly with CH_2Cl_2 under Ar and used again. As can be seen from Figure 4, the enantioselectivity steadily increased again from the 17th to the 20th run.[50] Nevertheless, the polymer-bound Ti-BINOLates are remarkably stable over many catalytic runs and the possibility of simply reloading the catalyst with titanate to reinstall its performance offers a convenient method for multiple application.

Conclusions

In the present paper we have demonstrated that BINOL derivatives can be immobilized in polystyrene.[51] Cross-linking BINOL derivatives were prepared and incorporated into polystyrene by suspension copolymerization. The resulting copolymers were employed in three test reactions giving rise to identical performance as in homogeneous solution. Special focus was put on multiple use of the catalysts and showed that polymer-bound Ti-BINOLates, while being very sensitive to air, could be recycled many times without any loss of activity. Thus, incorporation of chiral ligands into polystyrene in a cross-linking manner seems to be a promising new approach to prepare polymer-bound catalysts of high stability and performance in multiple use.

Experimental Section

General: Starting materials and reagents: (*R*)- and (*S*)-1,1′-bi-2-naphthol were purchased from Kankyo Kagaku Center (5–1 Ookawa, Kanzawa-ku, Yokohama 236-8605, Japan). Et_2Zn (Witco AG, Germany) was used as received without further purification. A stock solution of Et_2Zn (2 M) was prepared from Et_2Zn (10.25 mL) and toluene (39.75 mL). (*i*PrO)$_4$Ti (Hüls

0947-6539/00/0620-3698 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 20

AG, Troisdorf, Germany), ethyl vinyl ether, *tert*-butyl vinyl ether, pivalaldehyde, and benzaldehyde (PhCHO) were distilled prior to use. The solvents used in the reactions were of p.a. quality or purified and dried according to standard methods. All other chemicals were used as commercially available.

Equipment: Thin-layer chromatography (tlc): precoated silica gel 25 Durasil UV_{254} plates (Macherey-Nagel); visualization by UV_{254} light, development with 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 (FC): 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 room temperature (approximately 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. HPLC: Waters 515 HPLC Pump, Waters 484 tunable absorbance detector, Waters automated gradient controller; column: Daicel Chiracel OD column; eluent: hexane/*iso*-propanol 99:1 to 99.5:0.5. ^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), VG ZAB2-SEQ (FAB); MALDI-TOF-spectra: Bruker Reflex Spectrometer (N_2 laser, 337 nm), matrices: α-cyano-4-hydroxy cinnamic acid (CCA), 2,5-dihydroxy benzoic acid (2,5-DHB), 2-(4-hydroxyphenylazo) benzoic acid (HABA), fragment ions in *m*/*z* with relative intensities (%) in parentheses. Elemental analyses were performed by the Microanalytical Laboratory of the Laboratorium für Organische Chemie (ETH Zürich).

Br/OH substitution of the benzylic branch alcohols. General procedure I (GP I): Under ice-bath cooling CBr_4 (1.5 equiv), then PPh_3 (1.5 equiv) were added to a solution of the benzylic alcohol (1 equiv), and the reaction mixture was stirred for 30 min at 0 °C. Aluminium foil was then wrapped around the flask to prevent exposure to light, and the mixture was stirred for an additional 20 h at room temperature to give a milky white suspension. Et_2O and H_2O were added, the layers were separated, and the aqueous layer was extracted (2 × Et_2O). After drying over $MgSO_4$, the solvent was evaporated under vacuum, and the resulting residue immediately purified by flash column chromatography.

Coupling of the benzylic branch bromides to the BINOL core 2. General procedure II (GP II):[24] NaH (2.5 equiv) was added to a solution of BINOL core **2** (1 equiv) in DMF under ice bath cooling. After stirring at room temperature for 10 min, the resulting green suspension was cooled to 0 °C again, and a solution of the benzylic branch bromide (2 equiv) in DMF was slowly added. Having stirred at room temperature for 1 h, the reaction mixture was cooled to 0 °C, diluted with Et_2O, and brine was added. After separation of the layers, the aqueous layer was extracted (5 × CH_2Cl_2). The combined organic layers were dried over $MgSO_4$, and the solvents were evaporated under reduced pressure. The resulting crude product was purified by flash column chromatography.

Deprotection of the BINOL cross-linkers. General procedure III (GP III): TBAF · $3H_2O$ (2 equiv) was added to a solution of the protected BINOL (1 equiv) in THF at 0 °C. After stirring at room temperature for 1 h, Et_2O and H_2O were added, the layers were separated, and the aqueous layer was extracted (3 × Et_2O). Drying over $MgSO_4$ and evaporation of the solvents under reduced pressure afforded the deprotected BINOLs that were purified by flash column chromatography.

Compound 1:[24] Compound **1** has been reported previously in a preliminary communication without experimental details or characterization.[24] Imidazole (5.33 g, 78.3 mmol), DMAP (9.56 g, 78.3 mmol) and TIPSCl (16.6 mL, 78.3 mmol) were added to a solution of 6,6′-dibromo-1,1′-bi-2-naphthol[25] (15.80 g, 35.6 mmol) in DMF (150 mL). After stirring at room temperature for 48 h, brine (200 mL) and CH_2Cl_2 (200 mL) were added to the suspension, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (4 × 100 mL). Drying of the combined organic phases over $MgSO_4$ and evaporation of the solvents afforded a yellow oil as crude product which was purified by flash column chromatography (CH_2Cl_2/hexane 1:5) to give **1** (20.92 g, 78%) as a white solid. M.p. 60.0–62.0 °C; R_f (hexane/acetone 2:1): 0.76; $[\alpha]_D^{20} = -10.3$ ($c = 1.02$ in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.72$ (d, J(H, H) = 7.5 Hz, 18H; $6CH_3$), 0.79 (d, J(H, H) = 7.5 Hz, 18H; $6CH_3$), 1.02 (m, 6H; $6CH(CH_3)_2$), 7.02 (dd, J(H, H) = 9.0, 0.5 Hz, 2H; arom. H), 7.20 (d, J(H, H) = 8.9 Hz, 2H; arom. H), 7.23 (dd, J(H, H) = 9.0, 2.0 Hz, 2H; arom. H), 7.70 (d, J(H, H) = 8.8 Hz, 2H; arom. H), 7.95 (d, J(H, H) = 2.0 Hz, 2H; arom. H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 12.72$, 17.66, 17.73, 116.88, 121.01, 121.23, 127.47, 127.88, 129.10, 129.61, 130.07, 133.03, 151.78; IR ($CHCl_3$): $\tilde{\nu} = 2946$ (s), 2867 (s), 1584 (s), 1490 (s), 1470 (m), 1347 (s), 1278 (s), 1248 (w), 1135 (w), 1066 (m), 1000 (m), 942 (m), 920 (w), 882 (m), 842 (w), 818 cm^{-1} (w); MS (EI): *m*/*z* (%): 756.0 (11) $[M]^+$, 754.0 (5), 555.9 (3), 158.2 (15), 157.2 (100), 115.1 (46), 87.1 (15), 73.1 (11), 59.1 (10); elemental analysis calcd (%) for $C_{38}H_{52}Br_2O_2Si_2$ (756.80): calcd: C 60.31, H 6.93; found C 60.14, H 6.89.

Compound 2:[24, 26–28] Compound **2** has been reported previously in a preliminary communication without experimental details or characterization.[24] *t*BuLi (15.2 mL, 21.2 mmol, 1.4 M in pentane) was added slowly to a solution of BINOL **1** (4.0 g, 5.3 mmol) in THF (60 mL) at −78 °C. The resulting yellow solution was stirred for 30 min at this temperature whereupon freshly distilled $B(OMe)_3$ (3.6 mL, 31.6 mmol) was added. After stirring at −78 °C for another 5 min, the solution was slowly allowed to warm to room temperature. After stirring at room temperature for 2 h, NaOH (15%, 5 mL) and H_2O_2 (30%, 5 mL) were added at 0 °C. Addition of Et_2O (200 mL) to the resulting violet solution, separation of the layers, washing of the organic layer with H_2O (3 × 100 mL), drying of the organic phases over $MgSO_4$, and evaporation of the solvent afforded a yellow oil as crude product. Flash column chromatography (CH_2Cl_2/Et_2O 20:1) yielded **2** (2.97 g, 89%) as a colorless foam, which had to be stored at −20 °C under Ar due to very ready decomposition. R_f (CH_2Cl_2/Et_2O 5:1): 0.50; ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.72$ (d, J(H, H) = 7.5 Hz, 18H; $6CH_3$), 0.79 (d, J(H, H) = 7.5 Hz, 18H; $6CH_3$), 1.02 (m, 6H; $6CH(CH_3)_2$), 4.80 (s, 2H; 2OH), 6.80 (dd, J(H, H) = 9.2, 2.5 Hz, 2H; arom. H), 7.08–7.15 (m, 6H; arom. H), 7.60 (d, J(H, H) = 8.8, 2H; arom. H); MS (EI): *m*/*z* (%): 633.5 (5), 632.5 (19), 631.5 (50), 630.5 (100) $[M]^+$, 629.5 (5), 431.3 (5), 430.3 (9), 157.2 (86), 129.2 (12), 115.1 (78), 101.1 (10), 87.1 (35), 86.0 (14), 84.0 (21), 73.1 (31), 59.1 (44), 49.0 (23). Due to the very unstable nature of this compound no further characterization was possible.

Compound 3a:[19i] A mixture of **1** (2.00 g, 2.64 mmol), 4-styrene boronic acid[29] (0.98 g, 6.6 mmol), $[Pd(PPh_3)_4]$ (183 mg, 0.16 mmol), K_2CO_3 (1 M, 13.2 mL, 13.2 mmol), and THF (60 mL) was heated at 70 °C for 16 h. After cooling to room temperature, Et_2O (200 mL) was added, and the layers were separated. Drying of the organic phase over $MgSO_4$ and evaporation of the solvents gave a yellow oil as crude product. The residue was redissolved in a minimum of Et_2O, and the Pd-salts were allowed to precipitate and were filtered off over Celite. Flash column chromatography (hexane/CH_2Cl_2 10:1) afforded **3a** (1.42 g, 67%) as a white foam. R_f (hexane/acetone 2:1): 0.60; $[\alpha]_D^{20} = +98.1$ ($c = 1.00$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.75$ (d, J(H, H) = 7.5 Hz, 18H; $6CH_3$), 0.81 (d, J(H, H) = 7.5 Hz, 18H; $6CH_3$), 1.02 (m, 6H; $6CH(CH_3)_2$), 5.25 (dd, J(H, H) = 10.9, 0.9 Hz, 2H; vinyl H), 5.76 (dd, J(H, H) = 17.6, 0.9 Hz, 2H; vinyl H), 6.75 (dd, J(H, H) = 17.6, 10.9 Hz, 2H; $2CHCH_2$), 7.23 (d, J(H, H) = 8.9 Hz, 2H; arom. H (BINOL)), 7.34 (d, J(H, H) = 8.8 Hz, 2H; arom. H (BINOL)), 7.47 (dd, J(H, H) = 8.8, 1.9 Hz, 2H; arom. H (BINOL)), 7.49 (dd, J(H, H) = 6.5, 1.7 Hz, 4H; arom. H), 7.66 (dd, J(H, H) = 6.6, 1.7 Hz, 4H; arom. H), 7.85 (d, J(H, H) = 8.8 Hz, 2H; arom. H (BINOL)), 8.03 (d, J(H, H) = 1.9 Hz, 2H; arom. H (BINOL)); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 12.83$, 17.72, 17.80, 113.62, 120.68, 121.33, 125.17, 125.37, 126.56, 126.64, 127.20, 128.93, 129.25, 133.96, 135.20, 136.25, 136.52, 140.84, 151.62; IR ($CHCl_3$): $\tilde{\nu} = 3007$ (w), 2945 (s), 2892 (m), 2867 (s), 1626 (w), 1593 (s), 1516 (m), 1490 (s), 1470 (s), 1406 (m), 1351 (m), 1285 (m), 1248 (m), 1137 (w), 1088 (w), 1042 (m), 1015 (s), 998 (s), 948 (m), 911 (w), 882 (m), 865 (w), 848 (m), 824 cm^{-1} (s); MS (FAB): *m*/*z* (%): 803.9 (100) $[M]^+$, 802.9 (83), 603 (10); elemental analysis calcd (%) for $C_{54}H_{66}O_2Si_2$ (803.29): C 80.74, H 8.28; found: C 80.84, H 8.50.

Compound 3b: according to GP III, TBAF · $3H_2O$ (250 mg, 0.78 mmol) was added to a solution of **3a** (300 mg, 0.37 mmol) in THF (20 mL) at 0 °C. Workup and flash column chromatography (CH_2Cl_2/hexane 1:1 → CH_2Cl_2) afforded **3b** (177 mg) as a white solid in quantitative yield. R_f (hexane/acetone 1:1): 0.50; $[\alpha]_D^{20} = +326.6$ ($c = 0.50$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 5.10$ (s, 2H; 2OH), 5.27 (dd, J(H, H) = 10.9, 0.9 Hz, 2H; vinyl H), 5.78 (dd, J(H, H) = 17.6, 0.9 Hz, 2H; vinyl H), 6.76 (dd, J(H, H) = 17.6, 10.9 Hz, 2H; $2CHCH_2$), 7.24 (d, J(H, H) = 8.7 Hz, 2H; arom. H (BINOL)), 7.40 (d, J(H, H) = 8.9 Hz, 2H; arom. H (BINOL)), 7.50

(dd, J(H, H) = 6.5, 1.7 Hz, 4H; arom. H), 7.57 (dd, J(H, H) = 8.8, 1.9 Hz, 2H; arom. H (BINOL)), 7.64 (dd, J(H, H) = 6.5, 1.8 Hz, 4H; arom. H), 8.02 (d, J(H, H) = 8.7 Hz, 2H; 2H (BINOL)), 8.10 (d, J(H, H) = 1.9 Hz, 2H; arom. H (BINOL)); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 110.79, 113.97, 118.30, 124.83, 126.16, 126.77, 126.97, 127.28, 127.37, 129.77, 131.77, 132.62, 136.38, 136.46, 136.66, 140.12, 152.89; IR ($CHCl_3$): $\tilde{\nu}$ = 3537 (s), 3008 (m), 1625 (w), 1599 (s), 1500 (m), 1473 (w), 1402 (w), 1384 (m), 1357 (m), 1289 (w), 1176 (m), 1151 (m), 1130 (w), 1042 (w), 1014 (w), 990 (w), 935 (w), 912 (m), 895 (w), 848 (m), 826 cm^{-1} (s); MS (FAB): m/z (%): 490.2 (100) $[M]^+$, 245.2 (11), 217.2 (5); elemental analysis calcd (%) for $C_{36}H_{26}O_2$ (490.59): C 88.14, H 5.34; found: C 87.46, H 5.38.

4-Styryl-benzyl alcohol (4):[31] Styrene boronic acid[29] (4.0 g, 27.1 mmol), 4-bromo benzyl alcohol (3.9 g, 20.8 mmol), Na_2CO_3 (2 M, 27.1 mL, 54.1 mmol) and [Pd(PPh_3)$_4$] (716 mg, 0.62 mmol) were heated under Ar at 70 °C for 20 h. After cooling to room temperature, the organic layer was separated and the aqueous layer was extracted with Et_2O (100 mL). After drying over $MgSO_4$, evaporation of the solvents and subsequent flash column chromatography (hexane/CH_2Cl_2/acetone 10:10:1 → hexane/acetone 4:1) afforded **4** (3.15 g, 72%) as a white powder. M.p. 156.0–157.0 °C; R_f (hexane/acetone 2:1): 0.35; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.83 (s, 1H; OH), 4.72 (s, 2H; OCH_2), 5.27 (dd, J(H, H) = 10.9, 0.9 Hz, 1H; vinyl H), 5.78 (dd, J(H, H) = 17.6, 0.9 Hz, 1H; vinyl H), 6.75 (dd, J(H, H) = 17.6, 10.9 Hz, 1H; C*H*CH_2), 7.41–7.60 (m, 8H; arom. H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 65.07, 113. 96, 126.67, 127.10, 127.14, 127.48, 136.36, 136.66, 139.94, 140.10, 140.14; IR ($CHCl_3$): $\tilde{\nu}$ = 3605 (m), 3415 (s), 3008 (s), 2877 (w), 1909 (w), 1827 (w), 1628 (m), 1499 (s), 1398 (m), 1259 (w), 1118 (w), 1044 (m), 1004 (s), 990 (s), 912 (s), 836 cm^{-1} (s); MS (EI): m/z (%): 210.1 (100) $[M]^+$, 193.1 (22), 181.1 (28), 179.1 (16), 178.0 (27), 165.0 (36.2), 152.0 (20), 139.0 (5), 128.0 (5), 115.0 (9), 104.1 (8), 89.0 (4), 77.0 (10), 63.0 (3); elemental analysis calcd (%) for $C_{15}H_{14}O$ (210.27): C 85.68, H 6.71; found: C 85.43, H 7.00.

4-Styryl-benzyl bromide (5): PBr_3 (0.63 mL, 6.8 mmol) was added slowly to a solution of alcohol **4** (0.95 g, 4.52 mmol) in Et_2O (80 mL) under ice-bath cooling. The resulting suspension was stirred at room temperature for 1 h, then further PBr_3 (0.63 mL, 6.8 mmol) was added at 0 °C. After stirring for 1 h the reaction was complete (TLC control); H_2O (100 mL) was added, and the layers were separated. After extraction of the aqueous layer with Et_2O (3 × 100 mL), the combined organic phases were washed with saturated $NaHCO_3$ (100 mL) and dried over $MgSO_4$. Evaporation of the solvents afforded **5** (1.20 g, 97%) as a white solid that was pure according to TLC and NMR analysis, and was used without further purification. A small amount thereof was subjected to flash column chromatography (hexane/CH_2Cl_2 4:1) for analytical data. M.p. 142.0–143.0 °C; R_f (hexane/CH_2Cl_2 1:1): 0.59; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 4.54 (s, 2H; CH_2Br), 5.28 (dd, J(H, H) = 10.9, 0.9 Hz, 1H; vinyl H), 5.79 (dd, J(H, H) = 17.6, 0.9 Hz, 1H; vinyl H), 6.75 (dd, J(H, H) = 17.6, 10.9 Hz, 1H; C*H*CH_2), 7.46–7.58 (m, 8H; arom. H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 33.36, 114.14, 126.70, 127.19, 127.34, 129.53, 136.31, 136.83, 136.92, 139.75, 140.88; IR ($CHCl_3$): $\tilde{\nu}$ = 3088 (w), 3008 (m), 1910 (w), 1701 (w), 1628 (m), 1610 (m), 1499 (s), 1398 (m), 1098 (w), 1005 (m), 999 (m), 912 (s), 832 cm^{-1} (s); MS (EI): m/z (%): 274.0 (5), 272.0 (5) $[M]^+$, 238.1 (6), 210.1 (8), 193.1 (100), 178.1 (10), 165.1 (13), 152.1 (5), 131.1 (9), 103.1 (5), 96.6 (3), 73.1 (18), 63.0 (3), 44.1 (5); elemental analysis calcd (%) for $C_{15}H_{13}Br$ (273.17): C 65.95, H 4.80; found: C 65.81, H 4.97.

3-(4-Vinylbenzyloxy)benzyl alcohol (6): A solution of 3-hydroxybenzyl alcohol (5.0 g, 40.2 mmol), *p*-vinyl-benzyl chloride (7.5 g, 44.3 mmol), and K_2CO_3 (5.6 g, 40.2 mmol) in CH_3CN (100 mL) was heated at 50 °C for 48 h. After cooling to room temperature, the salts were filtered off, and the solvent was evaporated under reduced pressure. H_2O (100 mL) and CH_2Cl_2 (100 mL) were added to the resulting residue; the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). Drying of the combined organic phases over $MgSO_4$ followed by evaporation of the solvent under reduced pressure afforded the crude product which was purified by flash column chromatography (hexane/ethyl acetate 3:1) to give **6** (8.9 g, 92%) as a white powder. M.p. 57.0–58.0 °C; R_f (hexane/ethyl acetate 3:1): 0.21; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 4.64 (d, J(H, H) = 4.7 Hz, 2H; CH_2OH), 5.05 (*s*, 2H; OCH_2), 5.25 (dd, J(H, H) = 10.9, 0.8 Hz, 1H; vinyl H), 5.75 (dd, J(H, H) = 17.6, 0.9 Hz, 1H; vinyl H), 6.71 (dd, J(H, H) = 17.6, 10.9 Hz, 1H; C*H*CH_2), 6.88–7.24 (m, 4H; arom. H); 7.37–7.43 (m, 4H; arom. H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 65.22, 69.71, 113.27, 114.10, 114.13, 119.39, 126.42, 127.67, 129.65, 136.44, 136.51, 137.34, 142.60, 159.03; IR ($CHCl_3$): $\tilde{\nu}$ = 3604 (m), 3428 (w), 3008 (m), 2930 (w), 2875 (m), 1585 (s), 1514 (s), 1488 (s), 1448 (s), 1407 (m), 1378 (m), 1262 (s), 1154 (s), 1016 (m), 992 (m), 913 (m), 857 (w), 830 cm^{-1} (m); MS (EI): m/z (%): 240.2 (8.7) $[M]^+$, 118.2 (11), 117.2 (100), 115.1 (11), 91.1 (5); elemental analysis calcd (%) for $C_{16}H_{16}O_2$ (240.30): C 79.97, H 6.71; found: C 79.97, H 6.88.

3-(4-Vinylbenzyloxy)benzyl bromide (7): According to GP I, CBr_4 (4.3 g, 12.5 mmol) and PPh_3 (3.3 g, 12.5 mmol) were added to a solution of alcohol **6** (2.0 g, 8.3 mmol) in THF (80 mL) at 0 °C. After stirring at this temperature for 1 h and at RT for 16 h, workup and flash column chromatography (hexane/ethyl acetate 3:1) afforded **7** (2.1 g, 83%) as a white solid. M.p. 66.0–67.0 °C; R_f (hexane/acetone 3:1): 0.46; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 4.45 (s, 2H; CH_2Br), 5.04 (s, 2H; OCH_2), 5.25 (dd, J(H, H) = 10.9, 0.9 Hz, 1H; vinyl H), 5.75 (dd, J(H, H) = 17.6, 0.9 Hz, 1H; vinyl H), 6.74 (dd, J(H, H) = 17.6, 10.9 Hz, 1H; C*H*CH_2), 6.88–7.26 (m, 4H; arom. H), 7.37–7.44 (m, 4H; arom. H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 33.43, 69.80, 114.16, 114.97, 115.48, 121.59, 126.44, 127.71, 129.85, 136.25, 13641, 137.42, 139.20, 158.94; IR ($CHCl_3$): $\tilde{\nu}$ = 3008 (m), 1599 (m), 1586 (m), 1514 (m), 1488 (s), 1445 (m), 1407 (w), 1378 (w), 1295 (m), 1264 (s), 1158 (s), 1017 (m), 991 (m), 914 (m), 830 cm^{-1} (m); MS (EI): m/z (%): 303.9 (1), 302.0 (1) $[M]^+$, 224.0 (1), 223.0 (6), 117.0 (100), 116.0 (3), 115.0 (9), 91.1 (4), 78.0 (2); elemental analysis calcd (%) for $C_{16}H_{15}OBr$ (303.20): C 63.38, H 4.99; found: C 63.46, H 4.85.

3,5-Di(4-vinylbenzyloxy)benzoic acid methyl ester (8):[33–35] 18-crown-6 (11.7 g, 45 mmol), K_2CO_3 (65.2 g, 494.1 mmol) and 4-vinyl-benzyl chloride (80 g, 471.8 mmol) were added to a solution of 3,5-dihydroxy benzoic acid methyl ester (37.8 g, 224.6 mmol) in acetone (900 mL). The mixture was stirred at 70 °C for 48 h. After cooling to room temperature, the insoluble salts were filtered off and most of the solvent of the filtrate was evaporated under vacuum. Et_2O (900 mL) and H_2O (500 mL) were added, and the organic layer was separated. The aqueous layer was extracted with Et_2O (2 × 500 mL), the combined organic layers were dried over $MgSO_4$, and the solvents were removed under vacuum. The resulting solid was redissolved in acetone and, after careful addition of hexane, **8** (76.9 g, 85.5%) precipitated as a white solid. M.p. 74.0–74.5 °C; R_f (acetone/hexane 1:2): 0.29; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.90 (s, 3H; OCH_3), 5.05 (s, 4H; 2OCH_2), 5.26 (dd, J(H, H) = 11.1, 0.9 Hz, 2H; vinyl H), 5.76 (dd, J(H, H) = 17.6, 0.9 Hz, 2H; vinyl H), 6.72 (dd, J(H, H) = 17.6, 10.4 Hz, 2H; 2C*H*CH_2), 6.78 (t, J(H, H) = 2.3 Hz, 1H; arom. H), 7.28 (d, J(H, H) = 2.3 Hz, 2H; arom. H), 7.33–7.47 (m, 8H; arom. H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 52.3, 70.0, 107.3, 108.4, 114.2, 126.4, 127.8, 132.0, 136.0, 136.4, 137.5, 159.7, 166.7; IR ($CHCl_3$): $\tilde{\nu}$ = 3691 (w), 3008 (w), 1714 (s), 1597 (s), 1514 (w), 1446 (m), 1375 (m), 1296 (s), 1158 (s), 1107 (w), 1054 (m), 990 (w), 914 (w), 829 cm^{-1} (w); MS (EI): m/z (%): 400 (1.2) $[M]^+$, 369 (1), 283 (2), 234 (2), 233 (12), 118 (10), 117 (100), 116 (3), 115 (12), 91 (9), 69 (3), 28 (5); elemental analysis calcd (%) for $C_{26}H_{24}O_4$ (400.47): C 77.98, H 6.04; found: C 77.78, H 6.16.

3,5-Di(4-vinylbenzyloxy)benzyl alcohol (9): A solution of **8** (46.9 g, 0.12 mol) in THF (250 mL) was added slowly to a suspension of $LiAlH_4$ (10.0 g, 0.27 mol) in THF (250 mL). The reaction mixture was heated at 70 °C for 4 h and stirred at room temperature for 12 h. After hydrolysis with H_2O (10 mL), 15% NaOH (10 mL), and H_2O (30 mL), the resulting gray solid was filtered off and washed with Et_2O. The filtrate was washed with H_2O (500 mL), and the aqueous layer was extracted with Et_2O (3 × 500 mL). After removal of the solvents under reduced pressure, **9** (38.7 g, 89%) was obtained as a colorless oil, which solidified upon standing. M.p. 60.8–61.2 °C; R_f (hexane/acetone 2:1): 0.23; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.74–1.81 (m, 1H; OH), 4.60 (*d*, J(H, H) = 4.8 Hz, 2H; CH_2OH), 5.00 (s, 4H; 2OCH_2), 5.25 (dd, J(H, H) = 10.9, 0.8 Hz, 2H; vinyl H), 5.75 (dd, J(H, H) = 17.6, 0.9 Hz, 2H; vinyl H), 6.52 (t, J(H, H) = 2.3 Hz, 1H; arom. H), 6.60 (d, J(H, H) = 2.3, 2H; arom. H), 6.71 (dd, J(H, H) = 17.6, 10.4 Hz, 2H; 2C*H*CH_2), 7.33–7.43 (m, 8H; arom. H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 65.2, 69.8, 101.3, 105.7, 114.1, 126.0, 126.4, 127.7, 128.6, 132.7, 136.3, 136.4, 137.4, 143.4, 160.1; IR ($CHCl_3$): $\tilde{\nu}$ = 3410 (w), 3008 (m), 1710 (s), 1596 (s), 1451 (m), 1371 (m), 1293 (w), 1156 (s), 1053 (m), 1017 (m), 914 (w), 832 cm^{-1} (m); MS (EI): m/z (%): 372 (3.0) $[M]^+$, 278 (1), 234 (2), 233 (8), 152 (2), 151 (14), 119 (1), 118 (11), 117 (100), 116 (4), 115 (12), 91 (8), 78 (1), 77 (2), 65 (1); elemental analysis calcd (%) for $C_{25}H_{24}O_3$ (372.46): C 80.62, H 6.49; found: C 80.48, H 6.56.

3,5-Di(4-vinylbenzyloxy)benzyl bromide (10): According to GP I, CBr_4 (35.3 g, 106.5 mmol) and PPh_3 (27.9 g, 106.5 mmol) were added to a

0947-6539/00/0620-3700 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 20

solution of **9** (26.4 g, 71.0 mmol) in THF (160 mL). Workup and flash column chromatography (hexane/CH_2Cl_2 2:1) afforded **10** (17.5 g, 57 %) as a white powder. M.p. 82.5 – 83.5 °C; R_f (hexane/acetone 9:1): 0.53; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 4.39 (s, 2H; CH_2Br), 5.00 (s, 4H; 2CH_2O), 5.25 (dd, J(H, H) = 10.9, 0.8 Hz, 2H; vinyl H), 5.75 (dd, J(H, H) = 17.6, 0.9 Hz, 2H; vinyl H), 6.52 (t, J(H, H) = 2.2 Hz, 1H; arom. H), 6.62 (d, J(H, H) = 2.2 Hz, 2H; arom. H), 6.71 (dd, J(H, H) = 17.6, 10.4 Hz, 2H; 2$CH$$CH_2$), 7.34 – 7.42 (m, 8H; arom. H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 33.54, 69.92, 102.22, 108.21, 114.17, 126.54, 127.7, 136.3, 136.42, 137.4, 139.79, 160.03; IR ($CHCl_3$): $\tilde{\nu}$ = 3008 (w), 2870 (w), 1595 (s), 1513 (w), 1459 (m), 1407 (w), 1373 (m), 1160 (s), 1056 (m), 990 (m), 914 (m), 832 cm^{-1} (m); MS (EI): m/z (%): 436.2 (0.15) $[M]^+$, 355.3 (0.4), 233.1 (6), 149.0 (2), 117.0 (100), 85.9 (33), 83.9 (55), 48.9 (21); elemental analysis calcd (%) for $C_{25}H_{23}O_2Br$ (435.36): C 68.97, H 5.32; found: C 69.00, H 5.24.

3,5-Di[3,5-di(4-vinylbenzyloxy)benzyloxy]benzyl alcohol (11): A solution of bromide **10** (15.0 g, 34.5 mmol), 3,5-dihydroxybenzyl alcohol (2.2 g, 15.7 mmol), 18-crown-6 (0.82 g, 3.1 mmol), and K_2CO_3 (4.77 g, 34.5 mmol) in acetone (100 mL) was heated at 70 °C for 48 h. After cooling to room temperature, CH_2Cl_2 (200 mL) and H_2O (200 mL) were added to the resulting suspension, the layers were separated and the organic layer was dried over $MgSO_4$. Evaporation of the solvents afforded a brown oil as crude product, which was dissolved in toluene (40 mL). Upon slow addition of hexane (20 mL), compound **11** (10.92 g, 82 %) precipitated from the solution as a white solid. M.p. 66.0 – 67.0 °C; R_f (hexane/acetone 1:1): 0.51; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.59 (t, J(H, H) = 6.1 Hz, 1H; OH), 4.61 (d, J(H, H) = 5.4 Hz, 2H; CH_2OH), 4.97 (s, 4H; 2OCH_2), 5.01 (s, 8H; 4OCH_2), 5.25 (dd, J(H, H) = 10.9, 0.7 Hz, 4H; vinyl H), 5.75 (dd, J(H, H) = 17.6, 0.8 Hz, 4H; vinyl H), 6.51 (t, J(H, H) = 1.7 Hz, 1H; arom. H), 6.54 (t, J(H, H) = 1.8 Hz, 2H; arom. H), 6.58 (d, J(H, H) = 2.2 Hz, 2H; arom. H), 6.66 (d, J(H, H) = 2.2 Hz, 4H; arom. H), 6.71 (dd, J(H, H) = 17.6, 10.4 Hz, 4H; 4$CH$$CH_2$), 7.35 – 7.41 (m, 16H; arom. H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 62.71, 69.90, 69.97, 101.38, 101.65, 105.81, 106.38, 114.13, 126.44, 127.76, 136.34, 136.47, 137.39, 139.34, 143.44, 160.10, 160.15; IR ($CHCl_3$): $\tilde{\nu}$ = 3614 (w), 3008 (m), 1596 (s), 1514 (w), 1450 (m), 1407 (w), 1373 (m), 1295 (s), 1157 (s), 1050 (m), 1017 (w), 990 (m), 914 (m), 833 cm^{-1} (m); MALDI-TOF-MS (2,5-DHB): 871.7 $[M+Na]^+$; elemental analysis calcd (%) for $C_{57}H_{52}O_7$ (849.0): calcd: C 80.64, H 6.17; found: C 80.38, H 6.41.

3,5-Di[3,5-di(4-vinylbenzyloxy)benzyloxy]benzyl bromide (12): According to GP I, CBr_4 (8.1 g, 24.4 mmol) and PPh_3 (6.4 g, 24.4 mmol) were added to a solution of alcohol **11** (10.32 g, 12.2 mmol) in THF (70 mL) at 0 °C. After stirring at 0 °C for 1 h and at room temperature for 48 h and working up, the crude product was purified by flash column chromatography (hexane/CH_2Cl_2 1:1 → CH_2Cl_2) to give **12** (7.0 g, 63 %) as a white solid. M.p. 86.5 – 88.5 °C; R_f (CH_2Cl_2/hexane 2:1): 0.66; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 4.38 (s, 2H; CH_2Br), 4.94 (s, 4H; 2OCH_2), 5.01 (s, 8H; 4OCH_2), 5.24 (dd, J(H, H) = 10.9, 0.8 Hz, 4H; vinyl H), 5.74 (dd, J(H, H) = 17.6, 0.8 Hz, 4H; vinyl H), 6.50 (t, J(H, H) = 2.2 Hz, 1H; arom. H), 6.55 (t, J(H, H) = 2.2 Hz, 2H; arom. H), 6.60 (d, J(H, H) = 2.2 Hz, 2H; arom. H), 6.64 (d, J(H, H) = 2.2 Hz, 4H; arom. H), 6.71 (d, J(H, H) = 17.6 Hz, 10.4 Hz, 4H; 4$CH$$CH_2$), 7.34 – 7.41 (m, 16H; arom. H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 33.58, 69.88, 70.02, 101.71, 102.23, 106.41, 108.24, 114.11, 126.43, 127.73, 136.31, 136.45, 137.37, 139.09, 139.77, 159.96, 160.14; IR ($CHCl_3$): $\tilde{\nu}$ = 3008 (m), 1596 (s), 1514 (w), 1449 (m), 1407 (w), 1372 (m), 1295 (s), 1157 (s), 1048 (m), 990 (m), 914 (m), 832 cm^{-1} (m); MALDI-TOF-MS (2,5-DHB): 933.9 $[M+Na]^+$; elemental analysis calcd (%) for $C_{57}H_{51}O_6Br$ (911.9): C 75.07, H 5.64; found: C 75.26, H 5.75.

Compound 13: According to GP II, NaH (252 mg, 10.5 mmol) was added slowly to a solution of **2** (2.65 g, 4.2 mmol) in DMF (20 mL) at 0 °C. After stirring at room temperature for 5 min, the green suspension was recooled to 0 °C with an ice-bath and a solution of **5** (2.52 g, 9.24 mmol) in DMF (20 mL) was added. After stirring at room temperature for 1 h, H_2O (100 mL) was added and the reaction was worked up to give an orange oil as crude product, which was purified by flash ccolumn chromatography (hexane/CH_2Cl_2 2:1) to give **13** (1.82 g, 43 %) as a colorless foam. R_f (hexane/CH_2Cl_2 1:1): 0.54; $[\alpha]_D^{20}$ = +13.1 (c = 0.98 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.73 (d, J(H, H) = 7.5 Hz, 18H; 6CH_3), 0.81 (d, J(H, H) = 7.5 Hz, 18H; 6CH_3), 1.00 (m, 6H; 6CH(CH_3)$_2$), 5.17 (d, J(H, H) = 11.7 Hz, 2H; 2OCHH), 5.21 (d, J(H, H) = 11.7 Hz, 2H; 2OCHH), 5.27 (dd, J(H, H) = 10.9, 0.8 Hz, 2H; vinyl H), 5.78 (dd, J(H, H) = 17.6, 0.9 Hz, 2H; vinyl H), 6.75 (dd, J(H, H) = 17.6, 10.9 Hz, 2H; 2$CH$$CH_2$), 6.96 (dd, J(H, H) = 9.2, 2.6 Hz, 2H; arom. H (BINOL)), 7.15 – 7.17 (m, 4H; arom. H (BINOL)); 7.23 (d, J(H, H) = 2.6, 2H; arom. H (BINOL)); 7.47 – 7.62 (m, 16H; arom. H), 7.66 (d, J(H, H) = 8.7, 2H; arom. H (BINOL); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 12.77, 17.75, 17.83, 69.79, 107.35, 113.94, 118.66, 120.63, 121.76, 126.66, 127.12, 127.20, 127.62, 128.07, 129.69, 130.21, 136.33, 136.39, 136.67, 140.21, 140.35, 149.90, 154.84; IR ($CHCl_3$): $\tilde{\nu}$ = 3006 (w), 2946 (s), 2866 (s), 1626 (w), 1595 (s), 1500 (s), 1463 (w), 1379 (m), 1351 (s), 1282 (m), 1170 (m), 1125 (m), 1080 (m), 1012 (s), 965 (w), 914 (w), 883 (m), 847 cm^{-1} (m); MALDI-TOF MS (2,5-DHB): 1015.8 $[M]^+$; elemental analysis calcd (%) for $C_{68}H_{78}O_4Si_2$ (1015.52): C 80.43 H 7.74; found: C 80.25, H 7.70.

Compound 14a: According to GP II, NaH (162 mg, 4.1 mmol) was added to a solution of **2** (1.00 g, 1.62 mmol) in DMF (20 mL) at 0 °C. After stirring at room temperature for 5 min and recooling to 0 °C, a solution of **7** (986 mg, 3.3 mmol) in DMF (20 min) was added, and the reaction mixture was stirred at room temperature for 1 h. Workup and subsequent purification of the crude product by flash column chromatography afforded **14a** (810 mg, 46 %) as a colorless foam. R_f (hexane/acetone 2:1): 0.54; $[\alpha]_D^{20}$ = −12.0 (c = 1.00 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.71 (d, J(H, H) = 7.5 Hz, 18H; 6CH_3), 0.78 (d, J(H, H) = 7.5 Hz, 18H; 6CH_3), 1.00 (m, 6H; 6CH(CH_3)$_2$), 5.05 (s, 4H; 2OCH_2), 5.10 (d, J(H, H) = 11.8 Hz, 2H; 2OCHH), 5.13 (d, J(H, H) = 11.8 Hz, 2H; 2OCHH), 5.25 (dd, J(H, H) = 10.9, 0.9 Hz, 2H; vinyl H), 5.74 (dd, J(H, H) = 17.6, 0.9 Hz, 2H; vinyl H), 6.72 (dd, J(H, H) = 17.6, 10.9 Hz, 2H; 2$CH$$CH_2$), 6.90 – 6.94 (m, 2H; arom. H), 6.93 (dd, J(H, H) = 9.2, 2.5 Hz, 2H; arom. H (BINOL)), 7.04 – 7.11 (m, 6H; arom. H), 7.14 (d, J(H, H) = 9.2 Hz, 2H; arom. H (BINOL)), 7.16 (d, J(H, H) = 8.8 Hz, 2H; arom. H (BINOL)), 7.19 (d, J(H, H) = 2.5 Hz, 2H; arom. H (BINOL)), 7.29 (dd, J(H, H) = 7.9, 7.8 Hz, 2H; arom. H), 7.39 (d, J(H, H) = 8.3 Hz, 4H; arom. H), 7.41 (d, J(H, H) = 8.3 Hz, 4H; arom. H), 7.64 (d, J(H, H) = 8.8 Hz, 2H; arom. H (BINOL)); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 12.78, 17.74, 17.82, 69.77, 69.90, 107.37, 113.90, 114.06, 114.32, 118.65, 120.00, 120.62, 121.76, 126.42, 127.14, 127.60, 127.72, 129.61, 129.70, 130.22, 136.46, 136.56, 137.33, 138.93, 149.90, 154.82, 159.02; IR ($CHCl_3$): $\tilde{\nu}$ = 3008 (w), 2945 (m), 2866 (m), 1594 (s), 1499 (w), 1463 (w), 1408 (w), 1378 (m), 1350 (s), 1252 (s), 1156 (m), 1124 (m), 1081 (w), 1014 (s), 965 (w), 913 (w), 883 (m), 847 (w), 823 cm^{-1} (w); MS (FAB): m/z (%): 1075.4 (100) $[M]^+$, 1074.4 (72), 9583 (5), 915 (4), 852 (7), 586 (5), 223 (13), 157 (5), 117 (92), 115 (29), 101 (7); elemental analysis calcd (%) for $C_{70}H_{82}O_6Si_2$ (1075.57): C 78.17, H 7.68; found: C 78.11, H 7.71.

Compound 14b: According to GP III, a solution of **14a** (370 mg, 0.34 mmol) in THF (30 mL) was treated with TBAF · 3H_2O (227 mg, 0.72 mmol) at 0 °C. Workup and flash column chromatography (hexane/CH_2Cl_2 3:1) gave **14b** (261 mg) as a colorless foam in quantitative yield. R_f (hexane/acetone 1:1): 0.52; $[\alpha]_D^{20}$ = +55.7 (c = 1.00 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 4.89 (s, 2H; 2OH), 5.05 (s, 4H; 2OCH_2), 5.12 (s, 4H; 2OCH_2), 5.25 (dd, J(H, H) = 10.9, 0.9 Hz, 2H; vinyl H), 5.74 (dd, J(H, H) = 17.6, 0.9 Hz, 2H; vinyl H), 6.72 (dd, J(H, H) = 17.6, 10.9 Hz, 2H; 2$CH$$CH_2$), 6.91 – 6.93 (m, 2H; arom. H), 7.04 – 7.09 (m, 8H; arom. H), 7.26 – 7.40 (m, 14H; arom. H), 7.81 (d, J(H, H) = 8.9 Hz, 2H; arom. H (BINOL)); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 69.77, 70.00, 108.38, 111.28, 113.94, 114.10, 114.32, 118.18, 119.95, 120.17, 125.87, 126.42, 127.41, 128.70, 129.72, 130.06, 130.34, 136.43, 137.36, 138.56, 151.08, 155.52, 159.05; IR ($CHCl_3$): $\tilde{\nu}$ = 3533 (m), 3008 (w), 2872 (w), 1599 (s), 1513 (m), 1490 (m), 1450 (w), 1371 (m), 1263 (m), 1157 (m), 1120 (m), 1016 (m), 991 (w), 960 (w), 913 (w), 851 (m), 827 cm^{-1} (m); MS (FAB): m/z (%): 762.4 (100) $[M]^+$, 646 (6), 317 (5), 223 (27), 117 (76); elemental analysis calcd (%) for $C_{52}H_{42}O_6$ (762.89): C 81.87, H 5.55; found: C 81.87, H 5.52.

Compound 15a: According to GP II, NaH (158 mg, 3.9 mmol) was added to a solution of **2** (1.00 g, 1.58 mmol) in DMF (10 mL) under ice-bath cooling. After stirring at room temperature for 5 min, the green suspension was recooled to 0 °C and a solution of **10** (1.38 g, 3.17 mmol) in DMF (10 mL) was added. After stirring at room temperature for 1 h, workup, and purification of the crude product by flash column chromatography (hexane/CH_2Cl_2 1:1), **15a** (1.06 g, 50 %) was obtained as a colorless foam. R_f (hexane/acetone 2:1): 0.51; $[\alpha]_D^{20}$ = −11.2. (c = 1.10 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.72 (d, J(H, H) = 7.5 Hz, 18H; 6CH_3), 0.79 (d, J(H, H) = 7.5 Hz, 18H; 6CH_3), 0.99 (m, J(H, H) = 7.5 Hz, 6H; 6CH(CH_3)$_2$), 5.02 (s, 8H; 4OCH_2), 5.05 (d, J(H, H) = 9.1 Hz, 2H; 2OCHH), 5.08 (d, J(H, H) = 9.1 Hz, 2H; 2OCHH), 5.25 (dd, J(H, H) = 10.9, 0.9 Hz, 4H; vinyl H), 5.74 (dd, J(H, H) = 17.6, 0.9 Hz, 4H; vinyl H),

6.54 (t, J(H, H) = 2.3 Hz, 2H; arom. H), 6.67–6.74 (m, 8H; arom. H + 4C*H*CH_2), 6.94 (dd, J(H, H) = 9.2, 2.5 Hz, 2H; arom. H (BINOL)), 7.14 (d, J(H, H) = 9.2 Hz, 2H; arom. H (BINOL)), 7.15 (d, J(H, H) = 8.8 Hz, 2H; arom. H (BINOL)), 7.17 (d, J(H, H) = 2.5 Hz, 2H; arom. H (BINOL)), 7.36 (d, J(H, H) = 8.2, 8H; arom. H), 7.41 (d, J(H, H) = 8.2 Hz, 8H; arom. H), 7.63 (d, J(H, H) = 8.8 Hz, 2H; arom. H (BINOL)); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.76, 17.73, 17.81, 69.85, 69.94, 101.52, 106.43, 107.35, 114.08, 118.63, 120.61, 121.74, 126.41, 127.16, 127.59, 127.75, 129.67, 130.21, 136.36, 136.44, 137.34, 139.73, 149.89, 154.76, 160.09; IR ($CHCl_3$): $\tilde{\nu}$ = 3008 (m), 2944 (m), 2866 (m), 1595 (s), 1500 (w), 1462 (w), 1407 (w), 1376 (m), 1350 (m), 1286 (w), 1248 (m), 1156 (s), 1125 (w), 1064 (w), 1015 (m), 965 (w), 914 (w), 883 (w), 831 cm^{-1} (m); MS (FAB): m/z (%): 1339.4 (100) $[M]^+$, 116.9 (31); MALDI-TOF-MS (2,5-DHB): 1362.7 $[M+Na]^+$, 1339.7 $[M]^+$; elemental analysis calcd (%) for $C_{88}H_{98}O_8Si_2$ (1339.89): C 78.88, H 7.37; found: C 79.03, H 7.62.

Compound *ent*-15a: Compound *ent*-**15a** was synthesized according to the procedure described for **15a**. The specific rotation of *ent*-**15a** was $[\alpha]_D^{20}$ = +12.6 (c = 0.38 in $CHCl_3$).

Compound 15b: TBAF · 3H_2O (335 mg, 1.06 mmol) was added to a solution of **15a** (570 mg, 0.43 mmol) in THF (60 mL) under ice-bath cooling, according to GP III. Workup and subsequent purification by flash column chromatography (CH_2Cl_2/acetone 10:1) afforded pure **15b** (413 mg, 95%) as a colorless foam. R_f (CH_2Cl_2/acetone 10:1): 0.50; $[\alpha]_D^{20}$ = +41.0 (c = 1.03 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 4.89 (s, 2H; 2OH), 5.02 (s, 8H; 4OCH_2), 5.09 (s, 4H; 2OCH_2), 5.24 (dd, J(H, H) = 10.9, 0.9 Hz, 4H; vinyl H), 5.74 (dd, J(H, H) = 17.6, 0.9 Hz, 4H; vinyl H), 6.55 (t, J(H, H) = 2.3 Hz, 2H; arom. H), 6.68–6.73 (m, 8H; arom. H + 4C*H*CH_2), 7.03–7.08 (m, 4H; arom. H), 7.33–7.41 (m, 18H; arom. H), 7.25 (s, 2H; arom. H), 7.81 (d, J(H, H) = 8.9 Hz, 2H; arom. H (BINOL)); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 69.89, 70.07, 101.64, 106.44, 108.45, 11.25, 114.13, 118.19, 120.18, 125.87, 126.43, 127.74, 128.71, 130.12, 130.34, 136.30, 136.43, 137.39, 139.38, 151.10, 155.47, 160.16; IR ($CHCl_3$): $\tilde{\nu}$ = 3534 (m), 3007 (w), 2931 (w), 1598 (s), 1513 (m), 1456 (m), 1407 (w), 1371 (s), 1293 (w), 1158 (s), 1120 (w), 1064 (w), 1016 (w), 990 (w), 960 (w), 913 (m), 851 (m), 831 cm^{-1} (m); MS (FAB): m/z (%): 1026.0 (74) $[M]^+$, 910 (9), 672 (6); MALDI-TOF-MS (HABA): 1050.4 $[M+Na]^+$, 1027.1 $[M]^+$; elemental analysis calcd (%) for $C_{70}H_{58}O_8$ (1027.20): C 81.85, H 5.69; found: C 81.89, H 5.72.

Compound 16a: According to GP II, NaH (110 mg, 2.7 mmol) was added to a solution of **2** (0.69 g, 1.1 mmol) in DMF (30 mL) at 0 °C. After stirring at room temperature for 5 min, the solution was cooled to 0 °C again, and a solution of **12** (2.00 g, 2.2 mmol) in DMF (30 mL) was added. After stirring at room temperature for 1 h and working up, purification of the crude product by flash column chromatography (hexane/CH_2Cl_2 1:1) yielded **16a** (1.05 g, 42%) as a colorless foam. R_f (hexane/acetone 1:1): 0.64; $[\alpha]_D^{20}$ = −7.1 (c = 1.00 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.71 (d, J(H, H) = 7.5 Hz, 18H; 6CH_3), 0.78 (d, J(H, H) = 7.5 Hz, 18H; 6CH_3), 1.00 (d, J(H, H) = 7.5 Hz, 6H; 6C*H*$(CH_3)_2$), 4.96 (s, 8H; 4OCH_2), 4.99 (s, 16H; 8OCH_2), 5.03 (d, J(H, H) = 11.9 Hz, 2H; 2OC*H*H), 5.07 (d, J(H, H) = 11.9 Hz, 2H; 2OC*H*H), 5.25 (dd, J(H, H) = 10.9, 0.9 Hz, 8H; vinyl H), 5.74 (dd, J(H, H) = 17.6, 0.9 Hz, 8H; vinyl H), 6.53 (t, J(H, H) = 2.2 Hz, 6H; arom. H), 6.55 (d, J(H, H) = 2.2 Hz, 20H; arom. H + 8C*H*CH_2), 6.93 (dd, J(H, H) = 9.2, 2.5 Hz, 2H; arom. H (BINOL)), 7.13 (d, J(H, H) = 9.2 Hz, 2H; arom. H (BINOL)), 7.15 (d, J(H, H) = 8.8 Hz, 2H; arom. H (BINOL)), 7.18 (d, J(H, H) = 2.5 Hz, 2H; arom. H (BINOL)), 7.34 (d, J(H, H) = 8.2 Hz, 16H; arom. H), 7.38 (d, J(H, H) = 8.2 Hz, 16H; arom. H), 7.64 (d, J(H, H) = 8.8 Hz, 2H; arom. H (BINOL)); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 12.77, 17.74, 17.82, 69.85, 39.99, 101.66, 106.41, 106.50, 107.37, 114.07, 118.60, 120.62, 121.75, 126.41, 127.17, 127.60, 127.73, 129.69, 130.23, 136.32, 136.45, 137.34, 139.30, 139.70, 149.91, 154.81, 160.06, 160.11; IR ($CHCl_3$): $\tilde{\nu}$ = 3052 (w), 3008 (m), 2945 (m), 2867 (m), 1595 (s), 1513 (w), 1450 (m), 1407 (w), 1375 (m), 1348 (m), 1294 (m), 1156 (s), 1057 (m), 1016 (m), 914 (w), 882 (w), 831 cm^{-1} (m); MALDI-TOF-MS (DHB): 2334.1 $[M+K]^+$, 2317.0 $[M+Na]^+$, 2294.1 $[M+1]^+$; elemental analysis calcd (%) for $C_{152}H_{154}O_{16}Si_2$ (2293.01): calcd: C 79.62, H 6.77; found: C 79.72, H 6.83.

Compound 16b: According to GP III, a solution of **16a** (343 mg, 0.15 mmol) in THF (10 mL) was treated with TBAF · 3H_2O (94 mg, 0.30 mmol). Work-up and purification of the crude product by flash column chromatography (hexane/CH_2Cl_2 2:1) afforded **16b** (250 mg, 84%) as a colorless foam. R_f (hexane/acetone 1:1) 0.55; $[\alpha]_D^{20}$ = +22.0 (c = 0.70 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 4.92 (s, 2H; 2OH), 4.96 (s, 8H; 4OCH_2), 4.99 (s, 16H; 8OCH_2), 5.07 (s, 4H; 2OCH_2), 5.24 (dd, J(H, H) = 10.9, 0.9 Hz, 8H; vinyl H), 5.74 (dd, J(H, H) = 17.6, 0.9 Hz, 8H; vinyl H), 6.52–6.54 (m, 6H; arom. H), 6.64–6.73 (m, 20H; arom. H + 8C*H*CH_2), 7.04 (m, 4H; arom. H), 7.31–7.38 (m, 36H; arom. H + arom. H (BINOL)), 7.81 (d, J(H, H) = 8.9 Hz, 2H; arom. H (BINOL)); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 69.85, 69.99, 101.62, 106.37, 106.42, 108.41, 111.29, 114.11, 118.22, 120.13, 125.89, 126.42, 127.74, 127.82, 128.71, 130.10, 130.32, 136.28, 136.43, 137.35, 139.23, 139.36, 151.10, 155.46 160.11; IR ($CHCl_3$): $\tilde{\nu}$ = 3528 (w), 3005 (w), 1595 (s), 1513 (m), 1456 (m), 1405 (w), 1369 (m), 1292 (m), 1267 (w), 1154 (s), 1118 (m), 1056 (m), 1015 (m), 990 (m), 913 (m), 851 (w), 826 cm^{-1} (m); MALDI-TOF-MS (DHB): 2003.6 $[M+Na]^+$; elemental analysis calcd (%) for $C_{134}H_{114}O_{16}$ (1980.33): C 81.27, H 5.80; found: C 81.18, H 6.02.

Compound 17a: Compound **17a** was prepared according to the following procedure for *ent*-**17a** given below. The specific rotation of **17a** was $[\alpha]_D^{20}$ = −179.9 (c = 1.02 in $CHCl_3$).

Compound *ent*-17a:[19j] A mixture of (*S*)-3,3′-diiodo-2,2′-di(methoxymethyl)-1,1′-binaphthalen[38] (4.70 g, 7.5 mmol), 4-styrene boronic acid[29] (2.77 g, 18.8 mmol), $[Pd(PPh_3)_4]$ (0.52 g, 0.45 mmol) and K_2CO_3 (1M, 38 mL, 37.6 mmol) in THF (100 mL) was heated at 70 °C for 20 h. After cooling to room temperature, Et_2O (100 mL) was added, and the phases were separated. The organic layers were dried over $MgSO_4$, and the solvents were evaporated under reduced pressure. The residue was redissolved in a minimum of Et_2O (50 mL). After the Pd-salts had precipitated, the mixture was filtered over Celite, and the filtrate was concentrated in vacuo to yield the crude product as a yellowish foam. Flash column chromatography (hexane/Et_2O 10:1) afforded *ent*-**17a** (2.70 g, 62%) as a colorless foam. R_f (hexane/ethyl acetate 5:1): 0.29; $[\alpha]_D^{20}$ = +206.4 (c = 1.01 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 2.35 (s, 6H; 2CH_3), 4.38 (d, J(H, H) = 5.8 Hz, 2H; OC*H*H), 4.43 (d, J(H, H) = 5.8 Hz, 2H; OC*H*H), 5.29 (dd, J(H, H) = 10.9, 0.8 Hz, 2H; vinyl H), 5.82 (dd, J(H, H) = 17.6, 0.9 Hz, 2H; vinyl H), 6.78 (dd, J(H, H) = 17.6, 10.9 Hz, 2H; 2C*H*CH_2), 7.28–7.44 (m, 6H; arom. H (BINOL)), 7.51 (dd, J(H, H) = 6.5, 1.5 Hz, 4H; arom. H), 7.74 (dd, J(H, H) = 6.5, 1.8 Hz, 4H; arom. H), 7.88 (d, J(H, H) = 8.3 Hz, 2H; arom. H (BINOL)), 7.95 (s, 2H; arom. H (BINOL)); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 55.91, 98.55, 113.00, 125.21, 126.23, 126.35, 126.45, 126.58, 127.88, 129.76, 130.44, 130.87, 133.64, 135.03, 136.55, 136.59, 138.54, 151.31; IR ($CHCl_3$): $\tilde{\nu}$ = 3008 (s), 1628 (w), 1512 (m), 1448 (w), 1430 (w), 1391 (m), 1353 (w), 1156 (s), 1079 (m), 1018 (w), 998 (s), 971 (s), 914 (s), 846 cm^{-1} (s); MS (FAB): m/z (%): 591.5 (5), 579.5 (9), 578.5 (7) $[M]^+$, 548.5 (6), 547.4 (10), 531.4 (9), 518.4 (8), 517.4 (17), 516.4 (35), 515.4 (100), 505.4 (27), 503.4 (74), 502.4 (88), 501.3 (43), 489.3 (17), 488.3 (16), 487.3 (25), 486.4 (15), 485.3 (24), 475.3 (27), 474.3 (54), 473.3 (49), 472.3 (26), 459.3 (13), 457.3 (17), 445.3 (10), 415.3 (12), 341.2 (14), 339.2 (13), 326.2 (14), 313.1 (13); elemental analysis calcd (%) for $C_{40}H_{34}O_4$ (578.70): C 83.02, H 5.92; found: C 83.15, H 6.12.

Compound 17b: Compound **17b** was prepared according to the procedure for *ent*-**17b** given below. The specific rotation of **17b** was $[\alpha]_D^{20}$ = −21.7 (c = 0.52 in $CHCl_3$).

Compound *ent*-17b: Under ice-bath cooling, HCl (concd, 20 drops) was slowly added to a solution of *ent*-**17a** (180 mg, 0.31 mmol) in THF (10 mL) and MeOH (10 mL). After stirring at room temperature for 2 h, further HCl (concd, 20 drops) was added whereupon the reaction proceeded to completion (tlc control). After cooling to 0 °C, H_2O (20 mL) was added, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). Drying of the combined organic layers over $MgSO_4$ and evaporation of the solvents gave the crude product, which was purified by flash column chromatography (hexane/acetone 15:1) to yield *ent*-**17b** (120 mg, 80%) as a white foam. R_f (hexane/CH_2Cl_2 1:2): 0.52; $[\alpha]_D^{20}$ = +20.0 (c = 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 5.29 (dd, J(H, H) = 10.9, 0.8 Hz, 2H; vinyl H), 5.35 (s, 1H; OH), 5.35 (s, 1H; OH), 5.82 (dd, J(H, H) = 17.6, 0.9 Hz, 2H; vinyl H), 6.78 (dd, J(H, H) = 17.6, 10.9 Hz, 2H; 2C*H*CH_2), 7.21–7.41 (m, 6H; arom. H (BINOL)), 7.53 (dd, J(H, H) = 6.6, 1.6 Hz, 4H; arom. H), 7.71 (dd, J(H, H) = 6.5, 1.8 Hz, 4H; arom. H), 7.92 (d, J(H, H) = 8.0 Hz, 2H; arom. H (BINOL)), 8.03 (s, 2H; arom. H (BINOL)); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 112.34, 114.25, 124.27, 124.39, 126.31, 127.41, 128.48, 129.49, 129.78, 130.32, 131.29, 132.95, 136.47, 136.93, 137.06, 150.20; IR ($CHCl_3$): $\tilde{\nu}$ = 3520 (s), 3056 (w), 3008 (m), 1704 (w), 1628 (m), 1598 (m), 1512 (m), 1439 (m), 1401 (m), 1360 (m), 1319 (w), 1294 (w), 1171 (m), 1148 (m), 1129 (m), 1018 (w), 910 (s),

0947-6539/00/0620-3702 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 20

847 cm^{-1} (s); MS (FAB): *m*/*z* (%): 492.2 (23), 491.2 (74), 490.2 (100) $[M]^+$, 489.2 (11), 245.1 (11), 147.1 (14), 137.1 (9), 136.0 (10), 133.0 (9), 109.0 (12), 106.9 (10); elemental analysis calcd (%) for $C_{36}H_{26}O_2$ (490.59): C 88.14, H 5.34; found: C 88.05, H 5.37.

Addition of Et_2Zn to PhCHO mediated by Ti-BINOLates[39, 40] in homogeneous solution. General procedure IV (GP IV):[41, 42] Detailed example for the catalysis with **15b**. $Ti(OiPr)_4$ (65 μL, 0.21 mmol, 1.2 equiv) was added to a solution of **15b** (37 mg, 0.036 mmol, 0.2 equiv) in toluene (1.8 mL) at room temperature, whereupon the solution immediately became orange. After stirring at room temperature for 30 min, PhCHO (18 μL, 0.18 mmol, 1.0 equiv) was added. After cooling the solution to $-20\,^{\circ}C$ and addition of Et_2Zn (2 M, 0.27 mL, 0.54 mmol, 3.0 equiv), the reaction mixture was stirred at this temperature for 2 h. To monitor the conversion and enantioselectivity of the reaction, small samples were taken from the reaction mixture at intervals. Et_2O and HCl (1 N) were added to the samples, and the organic layer was analyzed by CGC [β-CD; heating rate $110\,^{\circ}C/1.5\,^{\circ}C\,min^{-1}$; pressure: 1.3 bar H_2; t_R (PhCHO) ca. 2.8 min, t_R ((*R*)-1-phenyl-1-propanol) ca. 9.9 min, t_R ((*S*)-1-phenyl-1-propanol) ca. 10.3 min]: (*R*)/(*S*)-1-phenyl-1-propanol: 6.3:93.7, conversion: 88% after 2 h.

Suspension copolymerization of BINOL cross-linkers 3a, 13, and 14a–17a with styrene and subsequent deprotection: **Polymers p-3 and p-13–p-17. General procedure V (GP V)**:[15–17, 44] Detailed example for the preparation of BINOL/styrene-copolymer p-*ent*-**15**. In a three-necked flask, equipped with a condenser and an overhead stirrer, a warm solution of poly(vinyl alcohol) (120 mg, degree of polymerization 100 000, 86–89% hydrolyzed) in H_2O (11 mL), which was prepared by violent stirring at 40–50 °C and filtering off of the insoluble parts, was added to a solution of *ent*-**15a** (746 mg, 0.557 mmol), styrene (3.77 g, 36.21 mmol, 65 equiv), and AIBN (75 mg) in THF (3.0 mL) and benzene (4.7 mL). After stirring at room temperature for 5 min to homogenize the emulsion, the temperature was slowly raised to 75–80 °C and stirred at this temperature for 14 h. The suspension was filtered through a glass filter (G2) and the resulting polymer beads were washed with hot H_2O (500 mL), MeOH/H_2O (200 mL), MeOH (200 mL), THF (200 mL), MeOH (200 mL), and pentane (200 mL). The beads were then collected and dried under high vacuum for several hours to give polymer p-*ent*-**15** (4.29 g, 95%, theoretical loading: 0.123 mmol g^{-1}). The beads were sieved through a sieve (mesh width: 1000, 800, 630, 500, 400, 250, 160, 100) to give fractions of uniform size. IR (KBr): $\tilde{\nu}$ = 3445 (m), 3080 (w), 3058 (w), 3024 (m), 2921 (s), 2850 (m), 1942 (m), 1869 (m), 1801 (m), 1597 (s), 1541 (w), 1492 (s), 1451 (s), 1348 (s), 1224 (m), 1153 (s), 1067 (s), 1028 (s), 964 (w), 906 (m), 882 (w), 842 (w), 802 (w), 756 (s), 697 (s), 538 cm^{-1} (s); elemental analysis calcd (%) for $C_{88}H_{98}O_8Si_2 \cdot 65\,C_8H_8$ (8109.74): C 90.05, H 7.68; found: C 88.49, H 7.73.

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.

The protecting groups were cleaved from the polymers in the following ways:

Deprotection of polymers containing TIPS-protected BINOL cross-linkers to give polymers p-3 and p-13–p-16. General procedure VI (GP VI): Detailed example for the deprotection of TIPS-protected p-*ent*-**15** with a loading of 0.123 mmol g^{-1}. A suspension of beads of TIPS-protected polymer p-*ent*-**15** (1.78 g, 0.22 mmol) in THF (10 mL) was treated with a solution of $TBAF \cdot 3H_2O$ (152 mg, 0.48 mmol, 2.2 equiv) in THF (2 mL), whereupon the beads immediately turned yellow. After stirring for 14 h at room temperature, the beads were filtered through a glass filter (G2) and washed with THF/H_2O 10:1 (10 × 25 mL), THF/HOAc 300:1 (10 × 25 mL; the beads lost their yellow color during this washing step), THF/H_2O (10 × 25 mL), THF (10 × 25 mL), MeOH (2 × 25 mL), and pentane (1 × 25 mL), and subsequently dried under high vacuum to afford deprotected p-*ent*-**15** (1.65 g, 97%) with a new theoretical loading of 0.128 mmol g^{-1}.

Deprotection of polymers containing MOM-protected BINOL cross-linker 17a to give polymers p-17. General procedure VII (GP VII): Detailed example for the deprotection of MOM-protected p-**17** with a loading of 0.136 mmol g^{-1}. The polymer beads (805 mg, 0.11 mmol) were suspended in THF (16 mL) and HCl (6 M, 5 mL, 30 mmol) was added. After heating at 70 °C for 1 h, HCl (concd, 30 drops) was added, and the mixture was heated at 70 °C for a further 6 h. The beads were filtered through a glass filter and extensively washed with THF/H_2O 10:1 (5 × 25 mL), THF (5 × 25 mL), MeOH (2 × 25 mL), and pentane (2 × 25 mL) and dried under high vacuum to give deprotected p-**17** (738 mg, 93%) as colorless beads with a new theoretical loading of 0.138 mmol g^{-1}.

Addition of Et_2Zn to PhCHO mediated by polymer-bound Ti-BINOLates. General procedure VIII (GP VIII):[15–17] Detailed example for the catalysis with polymer p-*ent*-**15** with a loading of 0.128 mmol g^{-1}. Beads of polymer p-*ent*-**15** (1.62 g, 0.21 mmol, 0.2 equiv) were suspended in toluene (10 mL) and stirred for 15 min at room temperature. After removal of toluene under high vacuum (in order to remove traces of water in the polymer), the dry beads were resuspended in toluene (10 mL). After addition of $Ti(OiPr)_4$ (157 μL, 0.52 mmol, 0.5 equiv), whereupon the beads immediately turned orange, the suspension was stirred at room temperature for 14 h. $Ti(OiPr)_4$ (314 μL, 1.04 mmol, 1.0 equiv), and PhCHO (107 μL, 1.04 mmol, 1.0 equiv) were added; the solution was cooled to $-20\,^{\circ}C$, and Et_2Zn (2 M, 1.56 mL, 3.12 mmol, 3.0 equiv) was added. After 4.5 h, the reaction solution was drawn off with a syringe under Ar and the polymer beads were washed with toluene (5 × 10 mL). HCl (1 N, 50 mL) was added to the combined organic fractions, the organic phase was separated, and the aqueous layer was extracted with Et_2O (2 × 50 mL). Drying of the combined organic phases over $MgSO_4$ and evaporation of the solvents afforded 1-phenyl-1-propanol (ca. 67 mg, 48%). The enantioselectivity and conversion of the reaction were determined by CGC analysis [β-CD; heating rate $110\,^{\circ}C/1.5\,^{\circ}C\,min^{-1}$; pressure: 1.3 bar H_2; t_R (PhCHO) ca. 2.8 min, t_R ((*R*)-1-phenyl-1-propanol) ca. 9.9 min, t_R ((*S*)-1-phenyl-1-propanol) ca. 10.3 min] of the crude reaction product: (*R*)/(*S*)-1-phenyl-1-propanol: 92.8:7.2, conversion: 99% after 4.5 h. For multiple use of the catalyst, the washed beads were resuspended in toluene (10 mL), then $Ti(OiPr)_4$ (314 μL, 1.04 mmol, 1.0 equiv) and PhCHO (107 μL, 1.04 mmol, 1.0 equiv) were added, followed by Et_2Zn (2 M, 1.56 mL, 3.12 mmol, 3.0 equiv) at $-20\,^{\circ}C$. After stirring at $-20\,^{\circ}C$ for several hours, a small sample of the reaction mixture was diluted with Et_2O, several drops of HCl (1 N) were added, and the enantioselectivity and conversion determined by CGC analysis of the organic layer.

1,3-Dipolar cycloadditions of diphenyl nitrone with vinyl ethers[48] using polymers p-17. General Procedure IX (GP IX): Detailed example for the catalysis of the addition of *tert*-butyl vinyl ether to diphenyl nitrone with p-**17** with a loading of 0.215 mmol g^{-1}. Beads of p-**17** (456 mg, 0.098 mmol, 0.2 equiv) were suspended in toluene (4 mL) and stirred for 30 min at room temperature. The solvent was then removed under high vacuum (eliminating traces of water in the polymer). The dry beads were resuspended in toluene (4 mL), and $AlMe_3$ (50 μL, 0.098 mmol, 2 M in heptane, 0.2 equiv) was added whereupon the beads turned yellow and evolution of CH_4 was visible. After stirring at room temperature for 3 h, a solution of diphenyl nitrone (97 mg, 0.49 mmol, 1.0 equiv) in toluene (1 mL) was added, followed by the addition of freshly distilled *tert*-butyl vinyl ether (0.32 mL, 2.5 mmol, 5 equiv). The reaction mixture was stirred for 12 h, the solvent was then removed by syringe, and the beads washed with toluene (3 × 10 mL). The combined extracts were concentrated under vacuum to give a yellow oil (135 mg) as crude product. ^1H NMR analysis[48] showed a conversion of >95% (no nitrone visible) and an *exo*/*endo* selectivity of >95:5 (only *exo*-cycloadduct visible). Flash column chromatography (hexane/Et_2O 20:1) afforded pure *exo*-cycloadduct (114 mg, 78%) as a white solid. HPLC analysis of the *exo*-cycloadduct (Daicel Chiralcel OD, hexane/*i*PrOH 99.5:0.5, flow rate 0.7 mL min^{-1}, t_R (minor): ca. 9.8 min, t_R (major): ca. 14.3 min) gave an enantioselectivity of 4.4:95.6.

Addition of TMSCN to pivalaldehyde[49] mediated by polymer-bound Ti-BINOLate p-*ent*-15. General Procedure X (GP X): Detailed example for the catalysis with polymer p-*ent*-**15** with a loading of 0.128 mmol g^{-1}. Beads of polymer p-*ent*-**15** (495 mg, 0.064 mmol, 0.2 equiv) were suspended in toluene (10 mL) and stirred for 15 min at room temperature. After removal of toluene under high vacuum (in order to remove traces of water in the polymer), the dry beads were resuspended in CH_2Cl_2 (3 mL), and $Ti(OiPr)_4$ (19 μL, 0.064 mmol, 0.2 equiv) was added. After stirring at room temperature for 3 h, the reaction suspension was cooled to 0 °C and TMSCN (99 μL, 0.794 mmol, 2.5 equiv) was added, followed by pivalaldehyde (35 μL, 0.318 mmol, 1.0 equiv) after a further 30 min at this temperature. After stirring at 0 °C for 16 h, the reaction solution was drawn off with a syringe under Ar, and the beads were washed with CH_2Cl_2 (5 × 5 mL). The combined organic phases were concentrated under vacuum to a total volume of about 5 mL and HCl (4 N, 10 mL) and MeOH (5 mL) were added. After vigorous stirring at room temperature for 4 h, the organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (2 ×

10 mL). Drying of the combined organic layers over $MgSO_4$ and evaporation of the solvent afforded the cyanohydrine 2-hydroxy-3,3-dimethylbutanenitrile (18 mg, 50 %) as a slightly orange oil. The enantioselectivity of the reaction was determined by CGC analysis [β-CD; heating 100 °C/isothermal; pressure: 1.0 bar H_2; t_R (pivalaldehyde) ca. 5.1 min, t_R (*S*)-2-hydroxy-3,3-dimethylbutanenitrile ca. 20.3 min, t_R (*R*)-2-hydroxy-3,3-dimethylbutanenitrile ca. 21.3 min] of the crude reaction product: (*R*)/(*S*)-2-hydroxy-3,3-dimethylbutanenitrile: 71.7:28.3. The conversion, determined by CGC analysis of a sample taken from the reaction solution prior to hydrolysis, was quantitative. For multiple use of the catalyst, the beads were resuspended in CH_2Cl_2 (3 mL) and TMSCN and pivalaldehyde were added, as described above. Workup of the reaction solution and analysis of the crude product were performed as described.

Acknowledgements

We are grateful for financial support by the Swiss National Science Foundation (project no. 2027-048157 and 20-50674.97). The following companies provided chemicals: Hüls AG, Troisdorf (titanates), Witco AG (Et_2Zn). The continued generous financial support from Novartis AG (Basel) is gratefully acknowledged.

[1] J. Seyden-Penne, *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, Wiley, New York, **1995**.
[2] R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**.
[3] H.-U. Blaser, *Chem. Rev.* **1992**, *92*, 935 – 952.
[4] 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.
[5] P. Hodge in *Innovatives and Perspectives in Solid Phase and Combinatorial Libraries* (Ed.: R. Epton), Mayflower Scientific, Kingswinford, **1990**, pp. 273 – 292.
[6] S. Itsuno in *Polymeric Materials Encyclopedia; Synthesis, Properties and Applications*, *Vol. 10* (Ed.: J. C. Salamone), CRC, Boca Raton, **1996**, pp. 8078 – 8087.
[7] S. J. Shuttleworth, S. M. Allin, P. K. Sharma, *Synthesis* **1997**, 1217 – 1239.
[8] 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.
[9] L. Pu, *Tetrahedron: Asymmetry* **1998**, *9*, 1457 – 1477.
[10] P. Hodge, *Chem. Soc. Rev.* **1997**, *26*, 417 – 424.
[11] D. C. Sherrington, *Chem. Commun.* **1998**, 2275 – 2286.
[12] A. Guyot in *Synthesis and Separations using Functional Polymers* (Eds.: D. C. Sherrington, P. Hodge), Wiley, Chichester, **1988**, pp. 1 – 42.
[13] P. Hodge, D. C. Sherrington in *Synthesis and Separations using Functional Polymers* (Eds.: D. C. Sherrington, P. Hodge), Wiley, Chichester, **1988**, pp. 469 – 478.
[14] 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 cited therein.
[15] 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.
[16] P. B. Rheiner, H. Sellner, D. Seebach, *Helv. Chim. Acta* **1997**, *80*, 2027 – 2032.
[17] H. Sellner, D. Seebach, *Angew. Chem.* **1999**, *111*, 2039 – 2041; *Angew. Chem. Int. Ed.* **1999**, *38*, 1918 – 1920.
[18] a) C. Rosini, L. Franzini, A. Raffaelli, P. Salvadori, *Synthesis* **1992**, 503 – 517; b) O. Reiser, *Nachr. Chem. Tech. Lab.* **1996**, *44*, 380 – 388; c) R. Zimmer, J. Suhrbier, *J. Prakt. Chem.* **1997**, 758 – 762; d) L. Pu, *Chem. Rev.* **1998**, *98*, 2405 – 2494.
[19] a) Q.-S. Hu, D. Vitharana, G.-Y. Liu, V. Jain, M. W. Wagaman, L. Zhang, T. R. Lee, L. Pu, *Macromolecules* **1996**, *29*, 1082 – 1084; b) Q.-S. Hu, D. Vitharana, G. Liu, V. Jain, L. Pu, *Macromolecules* **1996**, *29*, 5075 – 5082; c) L. Ma, Q.-S. Hu, K. Y. Musick, D. Vitharana, C. Wu, C. M. S. Kwan, L. Pu, *Macromolecules* **1996**, *29*, 5083 – 5090; d) Q.-S. Hu, D. Vitharana, X.-F. Zheng, C. Wu, C. M. S. Kwan, L. Pu, *J. Org. Chem.* **1996**, *61*, 8370 – 8377; e) H. Cheng, L. Ma, Q.-S. Hu, X.-F. Zheng, J, Anderson, L. Pu, *Tetrahedron: Asymmetry* **1996**, *7*, 3083 – 3086; f) L. Ma, Q.-S. Hu, L. Pu, *Tetrahedron: Asymmetry* **1996**, *7*, 3103 – 3106; g) L. Ma, Q.-S. Hu, D. Vitharana, C. Wu, C. M. S. Kwan, L. Pu, *Macromolecules* **1997**, *30*, 204 – 218; h) W.-S. Kuang, Q.-S. Hu, X.-F. Zheng, J, Anderson, L. Pu, *J. Am. Chem. Soc.* **1997**, *119*, 4313 – 4314; i) Q.-S. Hu, W.-S. Huang, D. Vitharana, X.-F. Zheng, L. Pu, *J. Am. Chem. Soc.* **1997**, *119*, 12 454—12 464; j) Q.-S. Hu, W.-S. Huang, L. Pu, *J. Org. Chem.* **1998**, *63*, 1364 – 1365; k) W.-S. Huang, Q.-S. Hu, L. Pu, *J. Org. Chem.* **1998**, *63*, 2798 – 2799; l) L. Ma, L. Pu, *Macromol. Chem. Phys.* **1998**, *199*, 2395 – 2401; m) K. T. Musick, Q.-S. Hu, L. Pu, *Macromolecules* **1998**, *31*, 2933 – 2942; n) W.-S. Huang, L. Pu, *J. Org. Chem.* **1999**, *64*, 4222 – 4223; o) K. B. Simonsen, K. A. Jørgensen, Q.-S. Hu, L. Pu, *Chem. Commun.* **1999**, 811 – 812; p) M. Johannsen, K. A. Jørgensen, X.-F. Zheng, Q.-S. Hu, L. Pu, *J. Org. Chem.* **1999**, *64*, 299 – 301; q) H.-B. Yu, X.-F.Zheng, Z.-M. Lin, Q.-S. Hu, W.-S. Huang, L. Pu, *J. Org. Chem.* **1999**, *64*, 8149 – 8155; H. Cheng, L. Pu, *Macromol. Chem. Phys.* **1999**, *200*, 1274 – 1283; r) L. Pu, *Chem. Eur. J.* **1999**, *5*, 2227 – 2232.
[20] A. Mandoli, D. P. Pini, S. Orlandi, F. Mazzini, P. Salvadori, *Tetrahedron: Asymmetry* **1998**, *9*, 1479 – 1482.
[21] a) K. Nozaki, Y. Itoi, F. Shibahara, E. Shirakawa, T. Ohta, H. Takaya, T. Hiyama, *J. Am. Chem. Soc.* **1998**, *120*, 4051 – 4052; b) K. Nozaki, F. Shibahara, Y. Itoi, E. Shirakawa, T. Ohta, H. Takaya, T. Hiyama, *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1911 – 1918.
[22] D. J. Bayston, J. L. Fraser, M. R. Ashton, A. D. Baxter, M. E. C. Polywka, E. Moses, *J. Org. Chem.* **1998**, *63*, 3137 – 3140.
[23] Q.-H. Fan, C.-H. Yeung, W.-H. Hu, A. S. C. Chan, *J. Am. Chem. Soc.* **1999**, *121*, 7407 – 7408.
[24] S. Yamago, M. Furukawa, A. Azuma, J. Yoshida, *Tetrahedron Lett.* **1998**, *39*, 3783 – 3786.
[25] J. Cuntze, L. Owens, V. Alcazar, P. Seiler, F. Diederich, *Helv. Chim. Acta* **1995**, *78*, 367 – 390.
[26] P. Castro, F. Diederich, *Tetrahedron Lett.* **1991**, *32*, 6277 – 6280.
[27] H. C. Brown, R. L. Sharp, *J. Am. Chem. Soc.* **1966**, *88*, 5851 – 5854.
[28] This compound was extremely sensitive to both air and light, and was therefore directly employed in subsequent coupling steps without prior storage.
[29] J. Braun, H. Normant, *Bull. Soc. Chim. Fr.* **1966**, *8*, 2557 – 2564.
[30] Special precautions had to be taken to avoid undesired polymerization of the styryl-substituted compounds during synthesis and workup. Only sufficiently dilute solutions were heated; crude products were purified immediately by flash-column chromatography; purified compounds were stored in a refrigerator, with exclusion of light.
[31] N. Miyaura, T. Yanagi, A. Suzuki, *Synth. Commun.* **1981**, *11*, 513 – 519.
[32] We also tried to synthesize a *para*-substituted spacer molecule by etherification of 4-hydroxy-benzyl alcohol and 4-vinyl-benzyl chloride, followed by Appel reaction. However, the resulting benzyl bromide could not be isolated due to hydrolysis during workup.
[33] C. J. Hawker, J. M. J. Fréchet, *J. Am. Chem. Soc.* **1990**, *112*, 7638 – 7647.
[34] P. B. Rheiner, Ph.D. Dissertation No. 12773, ETH Zürich, **1998**.
[35] P. B. Rheiner, D. Seebach, *Chem. Eur. J.* **1999**, *5*, 3221 – 3236.
[36] Change of the reaction conditions by using K_2CO_3 as base and acetone as solvent did not suppress silyl migration and gave the coupling products in comparable yields after heating for 72 h at 50 – 60 °C. In order to reduce the risk of racemization of BINOL during the several days of coupling conditions at elevated temperatures, we decided to perform the coupling step under the conditions described above (NaH, DMF, RT).
[37] Cross-linker **13** could not be successfully deprotected. The reaction product of the deprotection reaction was insoluble in every solvent tested, so that no characterization was possible.
[38] P. J. Cox, W. Wang, V. Snieckus, *Tetrahedron Lett.* **1992**, *33*, 2253 – 2256.
[39] D. Seebach, A. K. Beck, S. Roggo, A. Wonnacott, *Chem. Ber.* **1985**, *118*, 3673 – 3682.
[40] D. Seebach, A. K. Beck, R. Imwinkelried, S. Roggo, A. Wonnacott, *Helv. Chim. Acta* **1987**, *70*, 954 – 974.
[41] D Seebach, A. K. Beck, B. Schmidt, Y. M. Wang, *Tetrahedron* **1994**, *50*, 4363 – 4384.

  0947-6539/00/0620-3704 $ 17.50+.50/0

[42] M. Mori, T. Nakai, *Tetrahedron Lett.* **1997**, *38*, 6233–6236.
[43] A similar observation was made by Yoshida et al. (ref. [24]) by using dendritically substituted BINOLs (with Fréchet branches without peripheral styryl groups up to the third generation) in the Ti-BINOLate-mediated addition of allyl stannane to PhCHO.
[44] S. Itsuno, Y. Sakurai, K. Ito, T. Maruyama, S. Nakahama, J. M. J. Fréchet, *J. Org. Chem.* **1990**, *55*, 304–310.
[45] For example, immobilization of nonprotected BINOL **15b**, following the described procedure, afforded polymer beads, which after loading with titanate, gave racemic 1-phenyl-1-propanol in the addition of Et_2Zn to PhCHO; most probably the BINOL moiety had racemized during the copolymerization process.
[46] Especially in the case of the deprotection of the TIPS groups with tetrabutyl ammonium fluoride (TBAF), extensive washing of the beads with THF/H_2O was necessary to remove fluoride and tetrabutyl ammonium salts. Washing of the polymer beads with water only was not sufficient as the polymer beads do not swell in water. The beads were therefore treated with THF, a solvent in which they swell very well, and some H_2O was added. In this way, the salts could be completely removed from the beads.
[47] The same trend was also observed during our work on polymer-bound cross-linking TADDOLs (ref. [17]).
[48] K. B. Simonsen, P. Bayon, R. G. Hazell, K. V. Gothelf, K. A. Jørgensen, *J. Am. Chem. Soc.* **1999**, *121*, 3845–3853.
[49] M. Mori, H. Imma, T. Nakai, *Tetrahedron Lett.* **1997**, *38*, 6229–6232.
[50] The selectivity in the 17th run was lower than in the 16th run, although the catalyst had been treated with titanate in between the two runs. This might be due to the fact that an excess of titanante was used for recharging of the beads; even after extensive washing, some $Ti(OiPr)_4$ might still have been present within the polymer beads, giving rise to formation of racemic cyanohydrine.
[51] **Note added in proof**: After submission of this paper, a publication appeared in which grafting of a BINOL to Merrifield resin through a 3,3′-dicarboxylic acid amide was described: X.-W. Yang, J.-H. Sheng, C.-S. Da, H.-S. Wang, W. Su, R. Wang, A. S. C. Chan, *J. Org. Chem.* **2000**, *65*, 295–296.

Received: January 21, 2000 [F2249]

  0947-6539/00/0620-3705 $ 17.50+.50/0