Cross-Linked-Polymer-Supported *N*-{2′-[(Arylsulfonyl)amino][1,1′-binaphthalen]-2-yl}prolinamide as Organocatalyst for the Direct Aldol Intermolecular Reaction under Solvent-Free Conditions

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Dedicated to Prof. *Dieter Seebach* on the occation of his 75th birthday

A bottom-up strategy was used for the synthesis of cross-linked copolymers containing the organocatalyst *N*-{(1*R*)-2′-{[(4-ethylphenyl)sulfonyl]amino}[1,1′-binaphthalen]-2-yl}-D-prolinamide derived from **2** (*Scheme 1*). The polymer-bound catalyst **5b** containing 1% of divinylbenzene as cross-linker showed higher catalyst activity in the aldol reaction between cyclohexanone and 4-nitrobenzaldehyde than **5a** and **5c**. Remarkably, the reaction in the presence of **5b** was carried out under solvent-free, mild conditions, achieving up to 93% ee (*Table 1*). The polymer-bound catalyst **5b** was recovered by filtration and re-used up to seven times without detrimental effects on the achieved diastereo- and enantioselectivities (*Table 2*). The catalytic procedure with polymer **5b** was extended to the aldol reaction under solvent-free conditions of other ketones, including functionalized ones, and different aromatic aldehydes (*Table 3*). In some cases, the addition of a small amount of H_2O was required to give the best results (up to 95% ee). Under these reaction conditions, the cross-aldol reaction between aldehydes proceeded in moderate yield and diastereo- and enantioselectivity (*Scheme 2*).

Introduction. – The use of immobilized organocatalysts [1] to conduct enantioselective reactions enhances the greenness [2] of the processes due to the ease of separation and re-use of the catalysts. As organocatalytic reactions [3] are usually performed under mild reaction conditions, the catalyst is actually compatible with several immobilization strategies. However, this immobilization has been carried out generally by using polymeric supports [4], with the use of these materials complementing the inherent benefits of organocatalysis. Two different synthetic strategies have been applied to immobilize an organocatalyst in a polymer: the postmodification of a polymeric support and the bottom-up synthesis by copolymerization of several monomers, one of them containing the catalysts. The most used one is the first, which gives a polymer-supported organocatalyst that has been successfully applied in C–C bond-formation processes, such as *Michael* [5], *Morita–Baylis–Hillmann* [6], and aldol reactions [7], or to selectively form C–heteroatom [8] bonds. This type of immobilization makes sense when high-cost and sophisticated organocatalysts are anchored to the also expensive polymeric resins, with the insolubility of the system requiring the need of more complex technologies for their characterization than the homogeneous catalysts. Meanwhile, the bottom-up immobilization, where the polymeric catalyst is prepared by a copolymerization strategy of a catalyst-functionalized monomer with other mono-

mers and cross-linkers, is more cost-efficient and, therefore, scalable. Furthermore, the degree of incorporation of the active monomer to the polymeric matrix is controllable, and by changing the monomers, ratios, or structures, the chemical reactivity and physical properties, such as solubility, can be fine-tuned. Notwithstanding, this strategy has been less studied probably because it presents a greater synthetic challenge. Thus, methacrylate-polymer beads containing *trans*-4-hydroxy-L-proline and prolinamide have been synthesized following this protocol, and applied to the aldol reaction between cyclohexanone and aromatic aldehydes achieving up to 99% ee in H_2O as solvent [9][10]. For the same reaction in DMF/H_2O, polystyrene-based copolymers incorporating 4-hydroxyproline afforded similar results [11]. Also metacrylic betaines containing this catalyst have been prepared and tested as catalysts in the aldol reaction between 4-nitrobenzaldehyde and 2,2-dimethyl-1,3-dioxan-5-one in DMF as solvent, affording the expected product in 76% de and 88% ee [12]. The acrylic copolymerization has been applied also to diarylprolinol (for recent reviews on the use of this catalyst, see [13]) and to the *MacMillan* imidazolidinone [14], that were used as catalysts in a cascade reaction and *Diels–Alder* process, respectively, giving the corresponding products with good enantioselectivities [10]. With the same bottom-up strategy, diarylprolinol has been embedded into a chiral porous polymer which catalyzed the *Michael* addition of aldehydes to nitrostyrene with high selectivities [15].

On the other hand, we have recently immobilized an *N*-{(1*R*)-2′-{[(4-ethylphenyl)sulfonyl]amino}[1,1′-binaphthalen]-2-yl}-D-prolinamide derivative[1]) [16] into a polystyrene resin to give a supported prolinamide system **1** [17] (*Fig.*), which was used as catalyst for the intermolecular aldol reaction. Remarkably, this catalytic system was highly efficient under solvent-free conditions (for reviews, see [18]), increasing the efficiency and sustainability of the chemical process [19] since, for example, more than 80% of the mass of any pharmaceutical batch process [20] is due to the use of solvents. Therefore, we thought of interest the preparation of several copolymers containing the *N*-{(1*R*)-2′-{[(4-ethylphenyl)sulfonyl]amino}[1,1′-binaphthalen]-2-yl}-D-prolinamide framework by a styrene copolymerization strategy, which has been used to immobilize

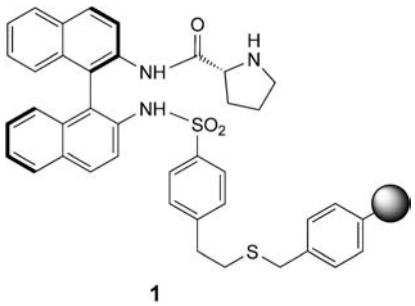

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Figure. *Polystyrene resin* **1** *containing an* N-*{(1*R*)-2′{[(4-ethylphenyl)sulfonyl]amino}[1,1′-binaphthalen]-2-yl}-*D*-prolinamide catalyst*

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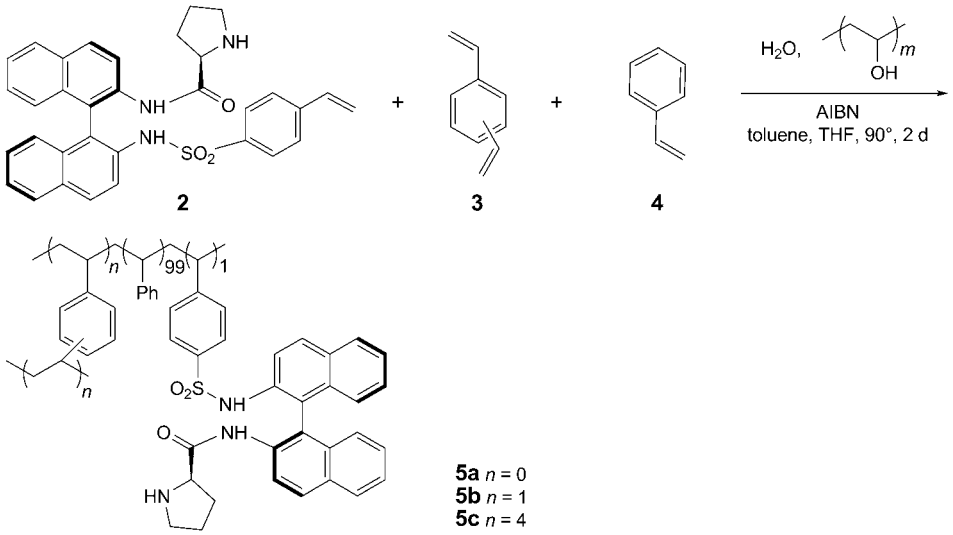
[1]) In [16], the general name of the immobilized derivative was *N*-sulfonyl-(R_a)-binam-D-prolinamide

typical chiral ligands (see, *e.g.*, [21]) and the organocatalyst *trans*-4-hydroxy-L-proline by two radical-controlled polymerization technologies [11]. After the synthesis of these new copolymers, we will study their performance in the aldol reaction under different reaction conditions including solvent-free conditions.

Results and Discussion. – To successfully incorporate the *N*-(2′-amino-[1,1′-binaphthalen]-2-yl)-D-prolinamide derivative into a polystyrene-based cross-linked polymer, the styrene derivative monomer **2** was synthesized from commercially available (1*R*)-[1,1′-binaphthalene]-2,2′-diamine and *N*-Boc-D-proline by the already described procedure [16]. Thus, the commercially available sodium 4-vinylbenzenesulfonate was transformed to the corresponding sulfonyl chloride, which was trapped with (1*R*)-[1,1′-binaphthalene]-2,2′-diamine (binam) to give a binam-derived sulfanamide derivative. This compound was further treated with the *in situ* generated *N*-Boc-D-Pro chloride followed by deprotection with CF_3COOH, affording the (binamsulfonyl)styrene derivative **2** in 46% overall yield.

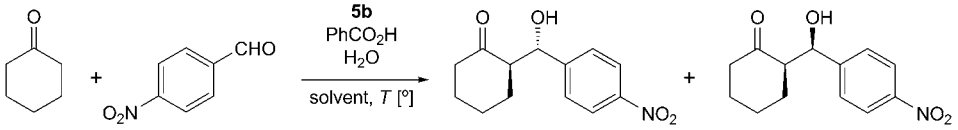
Once the synthesis of monomer **2** was achieved, its incorporation in the copolymer was carried out by copolymerization with styrene (**4**) and divinylbenzene (=diethenylbenzene; **3**), by means of a typical radical polymerization protocol in a suspension of polyvinyl alcohol (average relative molecular masses 85000–146000). In this manner, the three polymers **5a**–**5c** were prepared by changing only the amount of the added cross-linker divinylbenzene monomer **3** (*Scheme 1*). The polymers **5a**–**5c** have different swelling properties and were all isolated from the reaction media just by filtration, purified by successive washings with H_2O, MeOH, EtOH, and hexane, and finally dried *in vacuo*. The chemical yields were nearly quantitative, and the microanalysis of the S-atom showed *ca.* 80% of monomer incorporation, with a maximum of 86.7% for copolymer **5b**.

Scheme 1. *Copolymerization Process of Monomer* **2** *with Styrene* (**4**) *and Divinylbenzene* (**3**)



Then, the reactivity conditions were studied with polymer **5b** as catalyst (10 mol-%) in the reaction of cyclohexanone (**6a**) and 4-nitrobenzaldehyde (**7a**) as a model reaction (*Table 1*), analyzing the effect of solvent, additives such as H_2O and benzoic acid, ketone amount, and temperature. First, the effect of the solvents were explored at room temperature with 10 mol-% of **5b**; the conversions to **8aa** were low in most solvents used (*Table 1*, *Entries 1–6*), except for DMSO and H_2O (*Entries 1* and *6*), better conversion and diastereo- and enantioselectivities being achieved in H_2O. To our delight, when the solvent-free conditions were applied to this process, the reaction took place almost quantitatively, with only slightly reduced selectivities (*Entry 7*). Thus, under these solvent-free conditions, the other parameters of the reaction were optimized. As the addition of small portions of H_2O and organic acids generally increases the rate for the prolinamide-catalyzed aldol reaction [16][17], the effect of the addition of small amounts of H_2O and benzoic acid were evaluated (*Entries 8–12*). Both additives were compulsory for the achievement of high yields and enantiose-

Table 1. *Optimization of the Reaction Conditions for the Reaction of Cyclohexanone* (**6a**) *and 4-Nitrobenzaldehyde* (**7a**)[a])



6a **7a** '*anti*'-**8aa** '*syn*'-**8aa**

Entry	Solvent (0.15 ml)	**5b** [mol-%]	H_2O [equiv.]	$PhCO_2H$ [mol-%]	Time [d]	Conversion[b]) [%]	*'anti'*/*'syn'*[c])	ee[d]) [%]
1	DMSO	10	–	–	3	50	80 : 20	85
2	THF	10	–	–	3	< 20	87 : 13	88
3	AcOEt	10	–	–	3	< 20	75 : 25	87
4	H_2O/DMF	10	–	–	3	< 20	84 : 16	78
5	NMP	10	–	–	3	< 20	66 : 34	82
6	H_2O	10	–	–	3	66	84 : 16	91
7	–	10	–	–	2	100	81 : 19	82
8	–	10	20	–	2	100	85 : 15	89
9	–	10	20	2.5	1	100	89 : 11	93
10	–	10	–	2.5	1	100	86 : 14	88
11	–	10	10	2.5	1	100	89 : 11	90
12	–	10	20	5	1	100	80 : 20	88
13[e])	–	10	20	2.5	3	0	–	–
14[f])	–	10	20	2.5	1	95	87 : 13	92
15	–	20	20	2.5	1	100	82 : 18	85
16	–	5	20	2.5	1	73	90 : 10	90

[a]) General reaction conditions: 4-nitrobenzaldehyde (**7a**; 0.125 mmol), cyclohexanone (**6a**; 0.375 mmol), benzoic acid (2.5 mol-%), H_2O (20 equiv.), and catalyst **5b** (10 mol-%); at 25° in 0.15 ml of solvent; unless otherwise stated. [b]) Conversion based on the amount of the unreacted aldehyde **7a**. [c]) Determined by ^{1}H-NMR of the crude product. [d]) Determined by chiral-phase HPLC analysis for the *'anti'*-**8aa** isomer. [e]) The reaction was carried out at 0°. [f]) 2 equiv. of cyclohexanone (**6a**) with respect to **7a** were used.

lectivities, the best diastereo- and enantioselectivity for the *'anti'*-**8aa** product being obtained with 20 equiv. of H_2O and 2.5 mol-% of benzoic acid within the shorter reaction time of 1 day (*Entry 9*). The use of less H_2O or more benzoic acid led to a slight decrease of the diastereo- and enantioselectivities (*Entries 10–12*). In the presence of 20 equiv. of H_2O and 2.5 mol-% of benzoic acid, the decrease of the temperature from 25° to 0° led to the total suppression of the process (*Entry 13*). When the amount of **6a** was reduced to 2 equiv. at 25°, the reaction proceeded although with lower conversion (*Entry 14*). Finally, under the best reaction conditions, 20 equiv. of H_2O and 2.5 mol-% of benzoic acid at 25°, the effect of the catalyst loading was tested, revealing that 20 mol-% of catalyst led to reduced selectivities and that 5 mol-% of catalyst gave a lower conversion (*Entries 15* and *16*).

Having optimized the reaction conditions with polymer **5b**, the influence of the cross-linking within the polymer on the model reaction was explored. Thus, under solvent-free conditions, the linear polymer **5a** and the cross-linked polymer **5c**, which contains 4% of divinylbenzene in its structure were used as catalysts. While polymer **5a** (10 mol-%) was ineffective in the model reaction under solvent-free conditions, even in the presence of 20 equiv. of H_2O, the use of polymer **5c** (10 mol-%) gave similar results to those achieved with polymer **5b** albeit with lower conversion. For instance, the use of **5c** (10 mol-%) in the presence of 20 equiv. of H_2O and 2.5 mol-% of benzoic acid at room temperature, produced *'anti'*-**8aa** with 88% conversion after 2 d of reaction and 83:17 *'anti'*/*'syn'* ratio, and in 88% enantiomeric excess. These results were somewhat inferior to those achieved with polymer **5b** under the same reaction conditions (*Table 1*, *Entry 9*). Therefore, the best polymeric catalyst was **5b**, which contains only 1 mol-% of divinylbenzene in its structure, giving the appropriate balance between activity and solubility properties and making possible its recovery since the polymer is insoluble in apolar solvents.

The best catalyst and reaction conditions being identified, the possibility of the catalyst recovery was examined. Thus, on completion of the reaction, the catalyst was washed several times with hexane, dried under vacuum, and re-used in a next cycle under the same reaction conditions. The results of each cycle are summarized in *Table 2*, showing that catalyst **5b** is highly recyclable and re-usable at least for seven cycles, with only a marginal decrease of the yield being observed after the consecutive cycles.

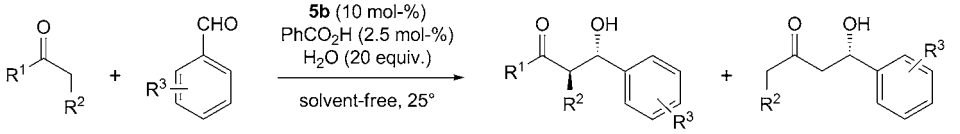
The optimized reaction conditions with catalyst **5b** were applied to the aldol reaction between various aromatic aldehydes **7** and several aliphatic ketones **6** (*Table 3*). The reaction of cyclohexanone (**6a**) with activated and nonactivated aromatic aldehydes proceeded in good yields, the diastereoselectivities being highly dependent on the aldehyde structure. While 4-cyanobenzaldehyde (=4-formylbenzonitrile; **7b**) gave modest results in terms of diastereo- and enantioselectivities (*Table 3*, *Entry 2*), 3- and 4-nitrobenzaldehyde led to high enantioselectivities (*Entries 1* and *3*). Better results in terms of enantioselectivities were achieved by changing the nucleophile to tetrahydro-2*H*-pyran-2-one achieving up to 95% ee in the presence of H_2O (*Entry 5*). Although the yield increased when the same reaction was carried out in the absence of H_2O, the diastereo- and enantioselectivity achieved under these reaction conditions were lower (*Entry 6*). As expected, changing the nucleophile to cyclopentanone (**6c**), the obtained major diastereoisomer was the *'syn'*-product but in a

Table 2. *Recycling Studies of Catalyst* **5b** *in the Reaction between Cyclohexanone* (**6a**) *and* 4-*Nitrobenzaldehyde* (**7a**)[a])

Cycle	Yield [%][b])	*'anti'*/*'syn'*[c])	ee [%][d])
1	88	89 : 11	93
2	90	87 : 13	90
3	88	87 : 13	92
4	87	84 : 16	93
5	85	86 : 16	91
6	80	85 : 15	91
7	77	86 : 16	92

[a]) Reaction conditions: 4-nitrobenzaldehyde (**7a**; 0.125 mmol), cyclohexanone (**6a**; 0.375 mmol), benzoic acid (2.5 mol-%), H_2O (20 equiv.), and catalyst **5b** (10 mol-%); at 25° under solvent-free conditions for 1 d. [b]) After purification by column chromatography. [c]) Determined by ^{1}H-NMR of the pure product. [d]) Determined by chiral-phase HPLC analysis.

Table 3. *Solvent-Free Intermolecular Aldol Reaction Catalyzed by* **5b**[a])



6 **7** *'anti'*-**8** **9**

Entry	R^1	R^2	R^3	Main product	Time [d]	Yield [%][b])	**8/9**	*'anti'*/*'syn'*[c])	ee [%][d])
1		$(CH_2)_4$	4-NO_2	*'anti'*-**8aa**	1	88	–	89 : 11	93
2		$(CH_2)_4$	4-CN	*'anti'*-**8ab**	3	75	–	67 : 33	66
3		$(CH_2)_4$	3-NO_2	*'anti'*-**8ac**	3	82	–	73 : 27	82
4		$(CH_2)_4$	H	*'anti'*-**8ad**	3	74	–	60 : 40	85
5		$(CH_2)_2OCH_2$	4-NO_2	*'anti'*-**8ba**	3	69	–	85 : 15	95
6[e])		$(CH_2)_2OCH_2$	4-NO_2	*'anti'*-**8ba**	3	77	–	83 : 17	85
7		$(CH_2)_3$	4-NO_2	*'syn'*-**8ca**	1	89	–	55 : 45	39 (93[f]))
8	Me	H	4-NO_2	**8da**	3	78	–	–	53
9[e])	Me	H	4-NO_2	**8da**	2	83	–	–	56
10	Me	Me	4-NO_2	**9ea**	5	25	32 : 68	n.d.	87
11[e])	Me	Me	4-NO_2	**9ea**	5	48	30 : 60	n.d.	72
12	Me	MeO	4-NO_2	*'anti'*-**8ea**	3	71	83 : 17	78 : 22	88
13[e])	Me	MeO	4-NO_2	*'anti'*-**8ea**	3	76	94 : 6	83 : 17	87

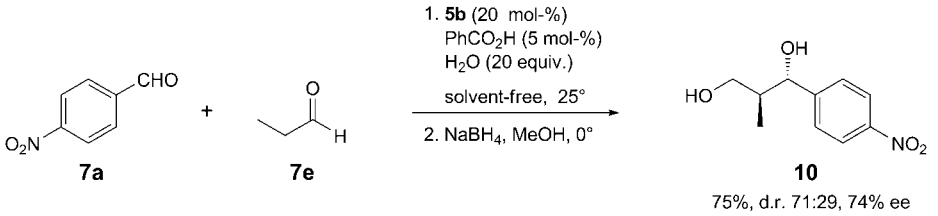
[a]) Reaction conditions: **6** (0.6 mmol), **7** (0.3 mmol), benzoic acid (5 mol-%), H_2O (12 equiv.) and catalyst **5b** (10 mol-%). [b]) Yield of the pure product after purification by column chromatography. [c]) Determined by ^{1}H-NMR of the crude product. [d]) Determined by chiral phase HPLC analysis of the major product. [e]) The reaction was carried out in the absence of H_2O. [f]) Enantiomer excess of the *'anti'*-isomer.

lower enantiomer excess. However, the enantiomer excess of the minor *'anti'*-**8ca** was as high as the one obtained with cyclohexanone (*cf. Entry 7 vs. Entry 1*). The use of linear ketones was also evaluated. Acetone (**6d**) gave the corresponding aldol product in low enantiomer excess independently of the presence or absence of H_2O (*Entries 8*

and *9*). With butan-2-one, mainly product **9ea** was obtained, the absence of H_2O providing a higher yield and the presence of H_2O leading to higher enantiomer excess (*Entries 11* and *10*). The use of α-functionalized ketones such as α-methoxyacetone (**6e**) gave mainly the *'anti'*-isomer *'anti'*-**8ea** as the major product with high regio-, diastereo- and enantioselectivities, slightly better results being achieved in the absence of H_2O (*Entries 12* and *13*).

Finally, the cross-aldol reaction between aldehydes were tested in the presence of polymer **5b** (*Scheme 2*). Higher catalyst loading (20 mol-%) and longer reaction times (7 d) were needed to afford product **10** with moderate diastereo- and enantioselectivity, after further reduction of the aldol product to the corresponding diol. Unfortunately, the use of polymer **5b** under various reaction conditions for the direct intramolecular aldol reaction of 1,5-diketones failed.

Scheme 2. *Cross-Aldol Reaction between Aldehydes Catalyzed by Copolymer* **5b**



Conclusions. – An easy and simple synthesis of polymers containing *N*-{(1*R*)-2′-{[(4-ethylphenyl)sulfonyl]amino}[1,1′-binaphthalen]-2-yl}-D-prolinamide by a bottom-up strategy was described. One of these polymers showed a good performance as catalyst in the aldol reaction between several ketones, including functionalized ones, and aromatic aldehydes under solvent-free conditions, the addition of a small amount of H_2O being required in most cases to achieve the best results. These reaction conditions were also extended to the cross-aldol reaction between aldehydes. The catalyst could be recovered after filtration and re-used up to seven times without detrimental effects on the achieved diastereo- and enantioselectivities.

Experimental Part

General. All reactions for the catalyst preparation were carried out under Ar. Dry DMF, dry toluene, dry CH_2Cl_2, dry THF, pyridine, Et_3N, and all other reagents were commercially available and used without further purification. Aldehydes were distilled prior to use. Anal. TLC: *Schleicher & Schüll F1400/LS* silica gel (SiO_2) plates; visualized under UV light (254 nm). Flash chromatography (FC): *Merck* SiO_2 *60* (0.063–0.2 mm). HPLC Analyses: *Agilent-1100* instrument equipped with a chiral column (detailed for each compound below); hexane/i-PrOH mixtures as mobile phase; at 25°; t_R in min. Optical rotations: *Perkin-Elmer-341* polarimeter. IR Spectra: *Nicolet-Impact-400D*; $\tilde{\nu}$ in cm^{-1} (only the structurally most important peaks are given). ^1H- and ^{13}C-NMR Spectra: *Bruker-AC-300* spectrometer; at 300 or 400 (^1H) and 75 MHz (^{13}C) and 25° in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz; unless otherwise stated. Elemental analyses were carried out by the Research Technical Services of the University of Alicante.

Catalyst Synthesis: General Procedure. To a soln. of sodium 4-vinylbenzenesulfonate (1.1 g, 5.3 mmol) in dry toluene (30 ml) were added $SOCl_2$ (2 ml, 27.6 mmol) and a few drops of dry DMF.

The resulting soln. was heated to 80° for 15 h, and all the volatiles were evaporated (0.1 Torr) to yield the corresponding sulfonyl chloride derivative. This compound was dissolved in dry CH_2Cl_2 (20 ml) under Ar and added to a soln. of (1*R*)-[1,1′-binaphthalene]-2,2′-diamine (1 g, 3.5 mmol) in dry CH_2Cl_2 (20 ml) and dry pyridine (3.5 ml, 43.44 mmol). The resulting mixture was stirred for 12 h at r.t., and then treated with 5% HCl soln. (3 × 15 ml). The org. layer was dried (Na_2SO_4), and concentraded (15 Torr) and the resulting crude product purified by FC (hexane/AcOEt); *N-[(1*R*)-2-amino-[1,1′-binaphthalene]-2-yl]-4-ethenylbenzenesulfonamide* (65%).

To a soln. of Boc-D-proline (0.215 g, 1.0 mmol) and Et_3N (0.14 ml, 1.0 mmol) in dry THF (7.5 ml) at 0° was dropwise added ethyl carbonochloridate (0.102 ml, 1.0 mmol). After stirring for 30 min at 0°, a soln. of *N*-[(1*R*)-2′-amino-[1,1′-binaphthalene]-2-yl]-4-ethenylbenzenesulfonamide (0.45 g, 1.0 mmol) in dry THF (7.5 ml) was added over 15 min. The ice-bath was removed, and the mixture was refluxed for 48 h. The solvents were evaporated (15 Torr), the resulting solid residue was dissolved in CH_2Cl_2 (7.5 ml), and CF_3COOH (2 ml) was added. The resulting mixture was stirred for 1 h, then 3M NaOH was added until pH 7 was reached, and the resulting soln. was washed with H_2O (3 × 7 ml). The org. layer was dried ($MgSO_4$) and concentrated (15 Torr) and the resulting crude product purified by FC (hexane/AcOEt): *(2*R*)-N-{(1*R*)-2′-{[(4-ethenylphenyl)sulfonyl]amino}[1,1′-binaphthalen]-2-yl}pyrrolidine-2-carboxamide* (**2**; 0.380 g, 70%) [16]. White solid. HPLC (*Chiralpak AD-H*, hexane/i-PrOH 80:20, 1.0 ml min^{-1}); t_R = 51.29, R_f 0.28 (AcOEt), M.p. 210–212° (AcOEt). $[\alpha]_D$ = +111.7 (*c* = 1.0, $CHCl_3$) (*ent*-**2** $[\alpha]_D$ = −16.9 (*c* = 1.0, $CHCl_3$)). IR (KBr): 3828, 3369, 3289, 3167, 2965, 2855, 1682, 1592, 1501, 1402, 1313, 1160. ^{1}H-NMR (400 MHz_3): 0.66 (*m*, 1 H); 1.17 (*m*, 2 H); 1.58 (*m*, 1 H); 1.73 (*m*, 1 H); 2.18 (*m*, 1 H); 3.27 (*dd*, *J* = 4.1, 9.6, 1 H); 5.42 (*d*, *J* = 10.8, 1 H); 5.48 (*d*, *J* = 17.6, 1 H); 6.67 (*dd*, *J* = 10.8, 17.6, 1 H); 6.84 (*d*, *J* = 8.4, 1 H); 6.92 (*d*, *J* = 8.4, 1 H); 7.17 (*m*, 2 H); 7.31 (*d*, *J* = 8.2, 2 H); 7.39 (*m*, 2 H); 7.50 (*d*, *J* = 8.6, 2 H); 7.86 (*d*, *J* = 8.2, 1 H); 7.93 (*d*, *J* = 8.2, 1 H); 8.00 (*d*, *J* = 9.0, 1 H); 8.06 (*d*, *J* = 9.2, 1 H); 8.21 (*d*, *J* = 9.2, 1 H); 8.83 (*d*, *J* = 9.0, 1 H); 9.26 (*s*, 1 H). ^{13}C-NMR: 25.2; 30.5; 46.0; 60.4; 116.8; 117.9; 119.1; 119.2; 120.6; 124.0; 125.1; 125.6; 126.4; 127.4; 127.45; 127.6; 127.7; 128.1; 128.6; 130.1; 130.5; 130.7; 131.1; 132.1; 133.5; 135.0; 138.0; 142.0; 173.4.

To a soln. of monomer **2** (0.282 g, 0.5 mmol) in toluene (6 ml) and THF (2 ml) at 25° under Ar were successively added styrene (**4**; 5.65 ml, 49.5 mmol), 2,2′-azobis[2-methylpropanenitrile (AIBN; 0.064 g, 0.4 mmol), and divinylbenzene (**3**; for amounts, see *Scheme 1*). This soln. was slowly added to an aq. soln. of polyvinyl alcohol at 0°, obtained in turn by heating polyvinyl alcohol (0.1 g) in H_2O (25 ml) at 40° for 30 min and final filtration. The resulting mixture was heated at 90° for 2 d. Polymers **5a**–**5c** were obtained easily after filtration, washing with portions of H_2O, MeOH, EtOH, and hexane, and final drying at 0.1 Torr during 24 h. Analyses, see *Table 4*.

Table 4. *Analyses of the Polymers* **5a**–**5c**

	S[a])[%]	Catalyst incorporated [%]	Catalyst load[b]) [mmol/g]
Calc. value	0.30	100.0%	0.092
Exper. Value (0% **3**; see **5a**)	0.22	73.3%	0.067
Exper. Value (1% **3**; see **5b**)	0.26	86.7%	0.080
Exper. Value (4% **3**; see **5c**)	0.25	83.3%	0.077

[a]) Percentage of sulfur determined by elemental analysis of **5a**–**5c**. [b]) Calculated from the percentage of sulfur found in the elemental analysis.

Aldehyde-Ketone Aldol Reaction Catalyzed by Polymer **5b**: *General Procedure*. To a mixture of the aromatic aldehyde **7** (0.125 mmol), catalyst **5b** (0.0125 mmol, 180 mg), and benzoic acid (0.003 mmol, 0.4 mg) at 25°, the corresponding ketone **6** (0.375 mmol) and H_2O (2.5 mmol, 50 µl) were added. The mixture was stirred until **7** was consumed (TLC monitoring). Then, the mixture was filtered and the filter washed with hexane (10–15 ml). The filtrate and washings were concentrated, and the residue was purified by FC (25–30 ml of hexanes/AcOEt): pure aldol products **8** and **9**.

*(2*R*)-2-[(1*S*)-Hydroxy(4-nitrophenyl)methyl]cyclohexanone* (*'anti'*-**8aa**) [22]: HPLC (*Chiralpak AD;* hexane/i-PrOH 90:10, 0.7 ml/min; 280 nm): *'anti':* t_R 36.232 (major) and 48.639 (minor); *'syn'*: t_R 28.446 (major) and 33.033 (minor). ^{1}H-NMR (300 MHz): 1.28–1.49 (*m*, 1 H); 1.52–1.73 (*m*, 3 H); 1.79–1.83 (*m*, 1 H); 2.06–2.14 (*m*, 1 H); 2.31–2.45 (*m*, 1 H); 2.45–2.55 (*m*, 1 H); 2.55–2.66 (*m*, 1 H); 4.12 (br. *s*, 1 H); 4.90 (*d*, *J* = 8.4, 1 H); 7.49 (*d*, *J* = 8.7, 2 H); 8.19 (*d*, *J* = 8.7, 2 H). ^{13}C-NMR: 24.6; 27.5; 30.6; 42.6; 57.1; 73.9; 123.5; 127.8; 147.4; 148.3; 214.6.

*(2*R*)-2-[(1*S*)-(4-Cyanophenyl)hydroxymethyl]cyclohexanone (=4-[(1*S*)-Hydroxy[(1*R*)-2-oxocyclohexyl]methyl}benzonitrile*; *'anti'*-**8ab**) [23]. HPLC (*Chiralpak AD*, hexane/i-PrOH 95:5, 1.0 ml/min; 230 nm): *'anti'*: t_R 44.854 (mayor), and 59.214 (minor); *'syn'*: t_R 29.828 (minor) and 38.261 (major). ^{1}H-NMR (300 MHz): 1.28–1.49 (*m*, 1 H); 1.52–1.84 (*m*, 4 H); 2.04–2.17 (*m*, 1 H); 2.30–2.47 (*m*, 1 H); 2.50–2.61 (*m*, 2 H); 4.07 (*s*, 1 H); 4.84 (*d*, *J* = 8.4, 1 H); 7.45 (*d*, *J* = 8.3, 2 H); 7.65 (*d*, *J* = 8.3, 2 H). ^{13}C-NMR: 24.6; 27.6; 30.6; 42.6; 57.0; 74.1; 11.6; 118.6; 127.7; 132.2; 146.3; 214.8.

*(2*R*)-2-[(1*S*)-Hydroxy(3-nitrophenyl)methyl]cyclohexanone* (*'anti'*-**8ac**) [24]: HPLC (*Chiralpak AD*, hexane/i-PrOH 95:05, 0.7 ml/min; 254 nm): *'anti'*: t_R 50.356 (minor) and 64.643 (major); *'syn'*: t_R 39.063 (minor) and 44.716 (major). ^{1}H-NMR (300 MHz): 1.37–1.43 (*m*, 1 H); 1.52–1.75 (*m*, 3 H); 1.79–1.87 (*m*, 1 H); 2.09–2.15 (*m*, 1 H); 2.33–2.41 (*m*, 1 H); 2.45–2.55 (*m*, 1 H); 2.56–2.68 (*m*, 1 H); 4.12 (*s*, 1 H); 4.89 (*d*, *J* = 8.4, 1 H); 7.51–7.55 (*m*, 1 H); 7.67 (*d*, *J* = 7.6, 1 H); 8.15–8.21 (*m*, 2 H). ^{13}C-NMR: 24.6; 27.6; 30.7; 42.6; 57.1; 74.0; 122.0; 122.8; 129.2; 133.1; 143.2; 148.2; 214.8.

*(2*R*)-2-[(1*S*)-Hydroxy(phenyl)methyl]cyclohexanone* (*'anti'*-**8ad**) [23]: HPLC (*Chiralcel OD-H*, hexane/i-PrOH 95:5, 0.5 ml/min; 210 nm): *'anti'*: t_R 23.507 (minor) and 31.015 (major); *'syn'*: t_R 18.107 (mayor) and 20.340 (minor). ^{1}H-NMR (300 MHz): 1.27–1.36 (*m*, 1 H); 1.50–1.80 (*m*, 4 H); 2.04–2.12 (*m*, 1 H); 2.30–2.42 (*m*, 1 H); 2.43–2.54 (*m*, 1 H); 2.58–2.67 (*m*, 1 H); 4.05 (br. *s*, 1 H); 4.78 (*d*, *J* = 8.9, 1 H); 7.29–7.37 (*m*, 5 H). ^{13}C-NMR: 24.7; 27.8; 30.8; 42.6; 57.4; 74.7; 127.0; 127.9; 128.3; 140.8; 215.5.

*(3*R*)-3-[(1*S*)-Hydroxy(4-nitrophenyl)methyl]tetrahydro-4*H*-pyran-4-one* (*'anti'*-**8ba**) [24]: HPLC (*Chiralpak AD-H*, hexane/i-PrOH 80:20, 1.0 ml/min; 280 nm): *'anti'*: t_R 19.021 (minor) and 22.454 (major); *'syn'*: t_R 13.727 (minor) and 15.700 (major). ^{1}H-NMR (300 MHz): 2.50–2.60 (*m*, 1 H); 2.63–2.73 (*m*, 1 H); 2.85–2.93 (*m*, 1 H); 3.46 (*dd*, *J* = 11.4, 9.6, 1 H); 3.73–3.81 (*m*, 2 H); 3.9 (*s*, 1 H); 4.16–4.27 (*m*, 1 H); 5.00 (*d*, *J* = 9.8, 1 H); 7.52 (*d*, *J* = 8.7, 2 H); 8.23 (*d*, *J* = 8.8, 1 H). ^{13}C-NMR: 42.7; 57.5; 68.2; 69.7; 71.2; 123.8; 127.4; 147.4; 147.7; 209.1.

*(2*R*)-2-[(1*S*)-Hydroxy(4-nitrophenyl)methyl]cyclopentanone* (*'syn'*-**8ca**) [22]: HPLC (*Chiralpak AD*, hexane/i-PrOH 97:03, 1.0 ml/min; 280 mm): *'anti'*: t_R 75.661 (minor) and 83.634 (major); *'syn'*: t_R 43.228 (minor) and 65.514 (major). ^{1}H-NMR (300 MHz): 1.72–1.75 (*m*, 2 H); 1.90–2.55 (*m*, 5 H); 2.95 (*s*, 1 H, *'syn'*); 4.77 (*s*, 1 H, *'anti'*); 4.84 (*d*, *J* = 9.1, 1 H, *'anti'*); 5.42 (*s*, 1 H, *'syn'*); 7.52 (*d*, *J* = 8.4, 2 H); 8.21 (*d*, *J* = 8.7, 2 H).^{13}C-NMR: *'syn'*: 20.2; 22.2; 38.8; 56.0; 70.3; 123.6; 126.3; 147.0; 150.2; 219.6; *'anti':* 20.2; 26.7; 38.5; 55.0; 74.3; 123.5; 127.3; 147.2; 148.5; 222.8.

*(4*S*)-4-Hydroxy-4-(4-nitrophenyl)butan-2-one* (**8da**) [22]: HPLC (*Chiralpak AS-H*, hexane/i-PrOH 85:15, 1.0 ml/min; 280 nm): t_R 25.755 (minor) and 34.741 (major). ^{1}H-NMR (300 MHz): 2.22 (*s*, 3 H); 2.86 (*d*, *J* = 1.8, 1 H); 2.88 (*s*, 1 H); 3.70 (*s*, 1 H); 5.27 (*dd*, *J* = 2.9, 3.3, 1 H); 7.54 (*d*, *J* = 8.8, 2 H); 8.21 (*d*, *J* = 8.8, 2 H). ^{13}C-NMR: 30.6; 51.4; 68.8; 123.7; 126.3; 147.3; 149.9; 208.2.

*(1*S*)-1-Hydroxy-1-(4-nitrophenyl)pentan-3-one* (**9ea**) [22]: HPLC (Chiralpak AS-H, hexane/i-PrOH 95:05, 1.0 ml/min; 280 mm): t_R 63.672 (minor) and 125.772 (major). ^{1}H-NMR (300 MHz): 1.09 (*t*, *J* = 7.3, 3 H); 2.48 (*q*, *J* = 7.3, 2 H); 2.82 (*m*, 2 H); 3.67 (*d*, *J* = 3.3, 1 H); 5.27 (*dt*, *J* = 3.5, 7.7, 1 H); 7.53 (*d*, *J* = 8.6, 2 H); 8.21 (*d*, *J* = 9.8, 2 H). ^{13}C-NMR: 7.4; 36.8; 50.2; 69.1; 123.7; 126.4; 147.3; 150.1; 211.4.

*(3*R*,4*R*)-4-Hydroxy-3-methoxy-4-(4-nitrophenyl)butan-2-one* (*'anti'*-**8ea**) [25]: HPLC (*Chiralcel OD-H*, hexane/i-PrOH 90:10, 0.7 ml/min; 280 mm): *'anti'*: t_R 17.047 (minor) and 18.578 (major); *'syn'*: t_R 21.181 (major) and 25.327 (minor). ^{1}H-NMR (300 MHz): 2.16 (*s*, 3 H); 3.32 (*s*, 3 H); 3.70 (*d*, *J* = 6.2, 1 H); 5.02 (*d*, *J* = 6.2, 1 H); 7.56 (*d*, *J* = 8.8, 2 H); 8.22 (*d*, *J* = 8.8, 2 H).^{13}C-NMR: 27.5; 59.6; 73.3; 89.6; 123.4; 127.7; 146.7; 147.7; 209.9.

Aldol Reaction between Aldehydes Catalyzed by **5b**: *General Procedure.* To a mixture of the aromatic aldehyde **7a** (0.125 mmol), catalyst **5b** (0.05 mmol, 360 mg), and benzoic acid (0.006 mmol, 0.8 mg) at 25°, propanal (**7e**; 0.625 mmol, 46 µl) and H_2O (2.5 mmol, 50 µl) were added. The mixture was stirred until **7a** was consumed (TLC monitoring). Then, the mixture was filtered and the filter washed with hexane (10–15 ml). The filtrate and washings were, concentrated, and the residue was diluted with

MeOH (1 ml). Then $NaBH_4$ (0.125 mmol, 5 mg) was added at 0°, and the mixture was stirred for 1 h. The resulting residue was purified by FC (hexanes/AcOEt 4:1): pure *(1S,2S)-2-methyl-1-(4-nitrophenyl)-propane-1,3-diol* (**10**) [23]: HPLC (*Chiralpak AD*, hexane/i-PrOH 96:04, 0.9 ml/min; 254 nm): t_R 72.965 (minor) and 74.885 (major). ^{1}H-NMR (300 MHz): 0.78 (*d*, *J* = 7.0, 3 H); 2.01–2.06 (*m*, 1 H); 2.74 (br. *s*, 1 H); 3.72–3.85 (*m*, 3 H); 4.72 (*d*, *J* = 7.8, 1 H, *'anti'*), 7.54 (*d*, *J* = 8.7, 2 H); 8.23 (*d*, *J* = 8.7, 2 H). ^{13}C-NMR: 13.6; 41.5; 67.4; 79.3; 123.6; 127.5; 147.4; 150.5.

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