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Supported Chiral Amino Alcohols and Diols Functionalized with Aluminium and Titanium as Catalysts of Diels-Alder Reaction.

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Abstract. Several chiral amino alcohols are supported on chloromethylated polystyrene-divinylbenzene and treated with $AlEtCl_2$. The supported catalysts are far more active than the corresponding homogeneous which is explained by site isolation. The catalyst derived from (S)-prolinol leads to a 14% e.e. Tartaric acid supported on polystyrene-divinylbenzene by means of two ester linkages is treated with aluminium and titanium derivatives. The aluminium catalyst yields a 13% e.e. and the titanium one can be recovered and reused. The different behaviour of homogeneous and heterogeneous systems is discussed.

Interest in the development of new heterogeneous and supported catalysts which are able to promote organic reactions has increased over the last few years. This interest has frequently been justified on the basis of their easier use in large scale applications. In fact merely the possibility of separating them by filtration is an important advantage from a practical point of view.

The number of heterogeneous and supported systems that leads to results comparable with, or even better than the related homogeneous catalysts in organic reactions, has noticeably increased:[1] However, the situation is not the same if chiral catalysts are considered.[2] This fact is particularly true in the case of acid catalysts and a clear example is the Diels-Alder reaction. There are a lot of chiral homogeneous Lewis acids which promote Diels-Alder reactions of particular dienophiles with high enantioselectivity.[3] There are also a lot of heterogeneous catalysts that efficiently promote Diels-Alder reactions of non-chiral[4,5] and chiral[5,6] dienophiles. However, the number of papers dealing with the use of chiral heterogeneous Lewis acids is scarce. Recently Itsuno and co-workers have used chiral oxazoborolidinones supported on organic polymers to promote reactions of 2-bromoacrolein and methacrolein with cyclopentadiene,[7] and these authors have shown that the enantioselectivity strongly depends on the method used to support the chiral catalyst and decreases noticeably when going from co-polymerization to grafting. Also recently we have described the use of menthoxyaluminium derivatives, supported on silica gel and alumina, as catalysts in the reaction of cyclopentadiene with methacrolein.[8] In both cases the chiral heterogeneous catalysts are designed on the basis of chiral Lewis acids previously described as efficient catalysts under homogeneous conditions. The results obtained noticeably change when going from homogeneous to heterogeneous phase or from one support to another, which clearly shows that homogeneous catalysis cannot be easily extrapolated to supported phase and, as a consequence, further studies comparing both kinds of catalysts are necessary. These studies may help to understand the behaviour of heterogeneous catalysts and to design more efficient systems.

In this paper we are presenting the results obtained using several chiral aminoalcohols and diols, supported on organic polymers, as catalysts of model Diels-Alder reactions. The results are compared with related homogeneous catalysts.

RESULTS AND DISCUSSION

Chiral aminoalcohols are easily grafted to solid supports and they have been frequently used to induce asymmetry under heterogeneous conditions.[9] Furthermore, chiral alcohols bearing another oxygen in the adjacent carbon, namely 1,2-diols and α-hydroxyethers, have been used by Kagan and co-workers to obtain chiral aluminium Lewis acids able to promote enantioselective Diels-Alder reactions of methacrolein with cyclopentadiene.[10] In this case it has been proposed that the second oxygen coordinates to the aluminium atom of the alcoholate which increases the rigidity of chiral Lewis acids. This coordination is also possible with aluminium α-aminoalcoholates (Figure 1).

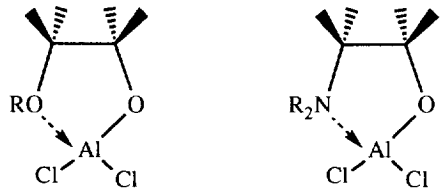
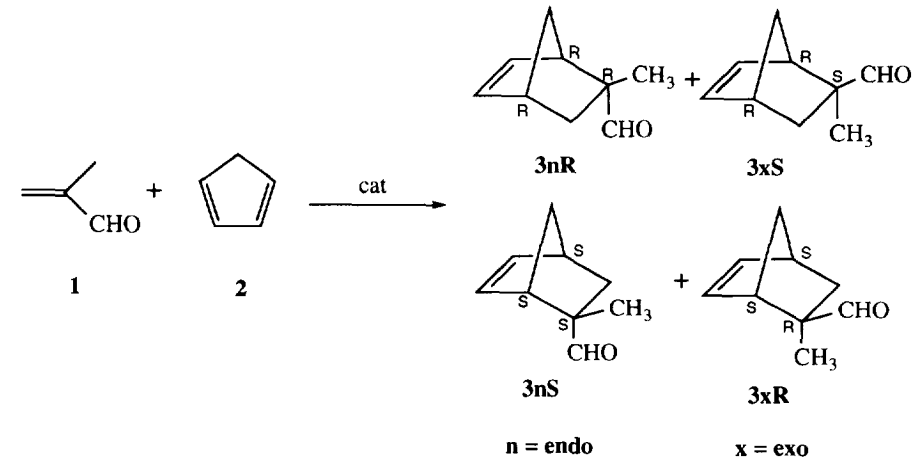
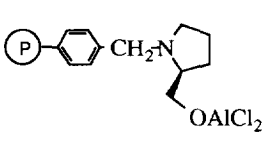


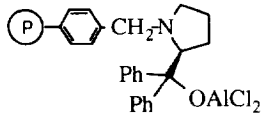
Figure 1

In view of previous works[9] (*1R,2S*)-ephedrine and (*S*)-prolinol were used as chiral auxiliaries. They were supported on crosslinked polystyrene by reaction with a chloromethylated resin under conditions that prevent quaternization. Best results were obtained when DMF was used as a solvent and $NaHCO_3$ as a base. Quantitative conversion of chloromethylated groups was observed and the excess of chiral aminoalcohol could be recovered from the mother liquors after filtering. The supported aminoalcohols were transformed in the corresponding Lewis acids by treatment with $AlEtCl_2$. In order to compare the performance of homogeneous and heterogeneous catalysts we obtained the corresponding *N*-benzylalcohols which were treated with $AlEtCl_2$ to obtain the homogeneous catalysts. The catalytic activity of these catalysts was compared for the reaction of methacrolein (**1**) with cyclopentadiene (**2**) (Scheme 1). The results obtained are gathered in Table 1. As it can be seen, supported catalysts are far more active than the corresponding homogeneous derivatives, which is particularly noticeable in the (*S*)-prolinol derivative (**P1**). Two different factors could account for these results; it could be thought that the low activity is connected with the coordination of the aluminium to the nitrogen which would make more difficult the coordination of the dienophile. However this problem should also be present in the supported compound. When we tested a β-aminoalcohol, namely (*R*)-3-pyrrolidinol where this coordination does not seem to be possible, again the supported catalyst (**P4**) was much more efficient. A plausible explanation could be related to the formation of oligomers in the homogeneous phase (Figure 2) which is restricted in the supported catalyst as these oligomers are less active than the monomeric species. Although site isolation in gels is generally only partial, its effect is an increase in the catalytic activity.[11]

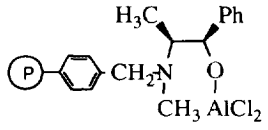




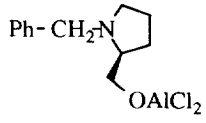
P1 (0.74 meq Al g^{-1})



P2 (0.76 meq Al g^{-1})



P3 (0.63 meq Al g^{-1})



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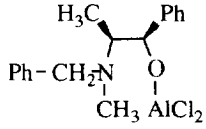

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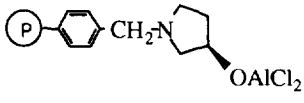
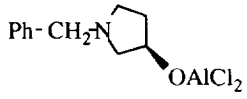


P4 (0.60 meq Al g^{-1})



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Scheme 1

Endo/exo selectivity is in general less influenced by changes in the nature of the catalyst. In view of this, a minor influence of site isolation on this selectivity should be expected which in fact only changes slightly when going from homogeneous to heterogeneous phase.

With regard to the asymmetric induction, the supported (*S*)-prolinol-aluminium catalyst (**P1**) leads to a 14% ee, but this cannot be compared with results in solution because of the very low activity of homogeneous analogue.

Table 1. Results Obtained in the Reaction of Methacrolein (**1**) with Cyclopentadiene (**2**), Catalyzed by Homogeneous and Supported Aminoalcohol-Aluminium Lewis Acids, in Methylene Chloride at -25°C.[a]

Entry	Catalyst	t (min)	% conv.[b]	exo/endo[b]	% e.e.[c]
1	---	1320	< 1	---	---
2	$AlEtCl_2$	15	98	7.5	---
3	**P1**	15	98	11.2	14[d]
4	**P2**	105	70	9.2	7[d]
5	**4**	240	1	---	---
6	**P3**	60	95	9.1	0
7	**5**	300	95	11.3	0
8	**P4**	30	97	11.5	0
9	**6**	1140	96	14.4	25[e]

a. Molar ratio Al:**1**:**2**=1:4:6. b. Determined by gas chromatography. c. Determined by ^{1}H-NMR in the presence of Eu(hfc)$_3$. d. **3xR** is the major adduct. e. **3xS** is the major adduct.

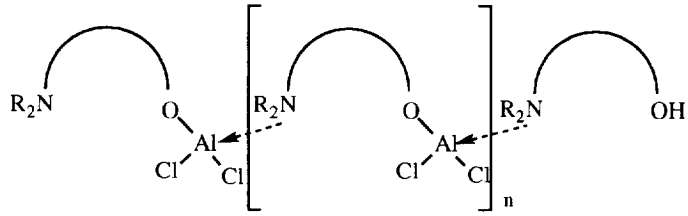


Figure 2

It is difficult to account for the direction of the enantioselectivity in such complex systems where the support can modify the conformational preferences of the reactive intermediates. It has been shown[12] that, in spite of the relative stability of the *s-cis* and *s-trans* forms of the dienophile-Lewis acid complexes, the Diels-Alder reactions of α,β-unsaturated aldehydes occurs through the *s-cis* form, so we have only considered these conformers in our discussion. The major cycloadduct is **3xS** which comes from the attack of the diene on the Re face of the dienophile. To account for this result it must be considered that part of the reaction takes place through the intermediate complex **A** (Figure 3), where the prolinol ring shields the Si face of the dienophile. It is important to note that this intermediate maximizes the steric interaction between the dienophile and the chiral auxiliary and, in principle, it should be less stable than **B**, where this interaction is minimized. It may be speculated that the position of this equilibrium is modified by the interaction of the dienophile with the polymeric backbone, which is probably more important in **B**. In order to verify this hypothesis we tried to increase the steric hindrance of the conformer **A** by using the α,α-diphenyl-(*S*)-prolinol as the chiral auxiliary (**P2**). The results obtained (Table 1) show a reduction of the asymmetric induction, which can be accounted for by taking into account that in conformer **B** both faces of the double bond are less shielded and, in any case, the possible small differences in shielding would favour the attack on the Si-face of the dienophile.

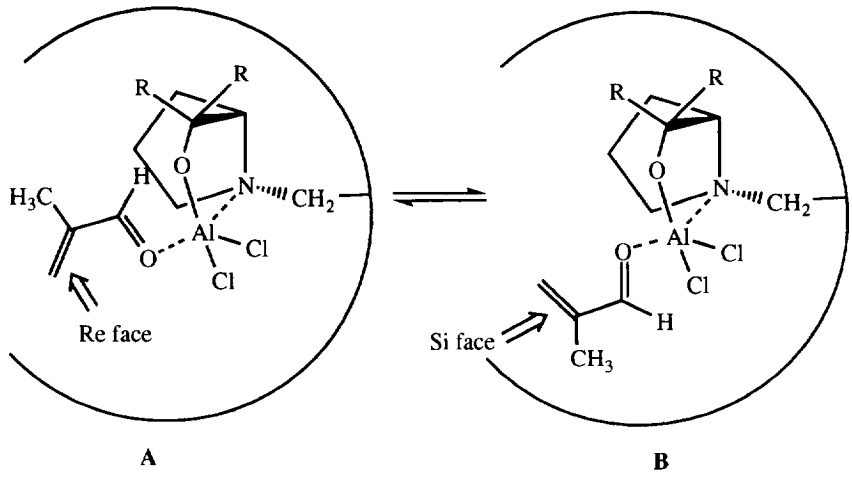
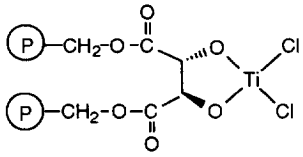


Figure 3. Models for the reactive intermediates methacroleine-**P1**.

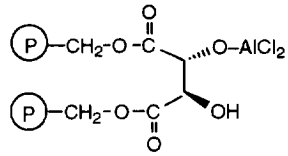
The reaction catalyzed by (*R*)-3-pyrrolidinol-aluminium dichloride (**6**) takes place with a 25% ee, but the enantioselectivity disappears in the supported catalyst (**P4**).

In these cases the advantages of supported catalysts, related to a higher catalytic activity partly due to site isolation, are clear. In view of this we considered it interesting to test a catalyst whose catalytic activity is high in solution, such as in the case of the tartrate-aluminium catalysts described by Kagan and co-workers.[10]

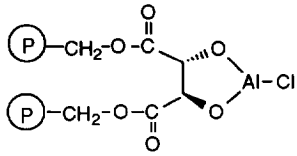
(*2R,3R*)-Tartaric acid was supported on polystyrene-divinylbenzene[13] and functionalized by treatment with $AlEtCl_2$ and $TiCl_4$. The functionalization degree (determined by nitrogen analysis of the bis-3,5-dinitrobenzoate[14]) obtained by supporting the tartaric acid indicates the structures proposed in Figure 4 where both ester groups are linked to the polymeric backbone.



P5 (0.32 mmol Ti g^{-1})



P6 (0.23 mmol Al g^{-1})



P7 (0.32 mmol Al g^{-1})

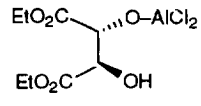


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Figure 4

The catalytic activity of these Lewis acids was tested in the reaction of methacrolein (**1**) with cyclopentadiene (**2**) and the results obtained are gathered in Table 2. In this case the homogeneous catalyst is more active, particularly at low temperatures. In fact, the reactions promoted by the supported Lewis acids are very slow at low temperatures, which must be due to diffusional limitations. In fact the double binding of tartrate will produce a highly crosslinked network with the potentially active sites on the crosslinks and diffusion to these sites will be hindered. *Endo/exo* selectivity seems to be more dependent on the temperature than on the nature of the catalyst. Both the homogeneous and supported aluminium catalysts lead to a low asymmetric induction, but the direction of the enantioselectivity is reversed. This result may be due to a change in the structure of the ester groups, ethyl in the homogeneous system and a polymeric backbone in the supported one. Finally the titanium catalyst (**P5**), not the aluminium ones, can be recovered and reused keeping a reasonable catalytic activity (Figure 5). This fact may be related to the hydrophobic character of the polymer which hinders the access of water and makes the hydrolysis of the titanium-chlorine bonds more difficult. It is more difficult to explain why aluminium catalyst cannot be recovered. Probably the lack of a chelate structure changes the arrangement of the polymer in the surrounding of the active centre and reduces the hydrophobicity. Furthermore, the catalyst **P6** can be transformed in **P7** and this supported Lewis acid, obtained with $AlEt_2Cl$, is less active (Figure 4 and Table 2).

Table 2. Results Obtained in the Reaction of Methacrolein (**1**) with Cyclopentadiene (**2**) Catalyzed by Homogeneous and Supported Lewis Acids Derived from Tartaric Acid.

Entry	Catalyst	T (°C)	t (min)	% conv[a]	exo/endo[a]	% e.e.[b]
1	---	25	1440	7	---	---
2	**7**[c]	-78	1200	80	24	18
3	**P6**[d]	25	30	93	8.8	3
4	**P6**[d]	-35	2880	74	10.5	13
5	**P5**[e]	25	30	86	6.5	0
6	**P5**[f]	25	30	60	6.4	0
7	**P5**	-35	1440	96	9.3	3
8	**P7**[g]	25	1440	43	8.1	0

a. Determined by gas chromatography. b. Determined by ^{1}H-NMR in the presence of Eu(hfc)$_3$. c. Ref. 10, **3xS** is the major adduct. d. Molar ratio Al:**1**:**2**=0.13:1:1.5, **3xR** is the major adduct. e. Molar ratio Ti:**1**:**2**=0.19:1:1.5. f. Catalyst recovered by filtration and reused. g. Molar ratio Al:**1**:**2**=0.22:1:1.5.

It can be concluded that supporting a homogeneous catalyst on an organic polymer strongly modifies its performance. Whereas the *endo/exo* selectivity is not strongly modified the reaction rate is, which is related to a pair of particular characteristics of the heterogeneous system, namely the site isolation and the diffusional restriction at low temperatures. Supported and homogeneous catalysts may have very different conformational dispositions in the surrounding of the active centre which must strongly influence the asymmetric induction obtained with chiral catalysts. Finally, the hydrophobic character of the polymeric backbone may protect the active centre from hydrolysis and may make possible the recovery and reuse of the catalysts.

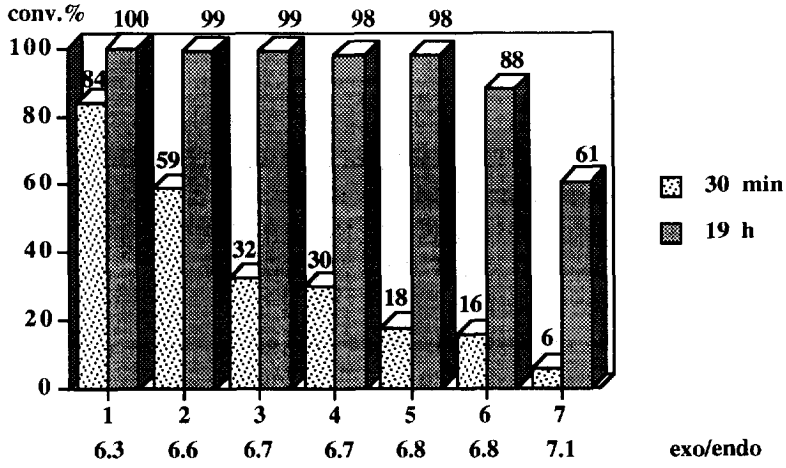

Figure 5

EXPERIMENTAL

1. Preparation of supported (S)-prolinol.

A suspension of chloromethylated polystyrene (1% crosslinked, 1 meq Cl g^{-1}, DF=0.11, $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_9H_9Cl)_{0.11}]$) (1 g, 1 meq Cl) and (*S*)-prolinol (303 mg, 3 mmol) in 100 ml of dry DMF was heated at 80°C for 4 days. After this time the polymer was separated by filtration and thoroughly washed with DMF, CH_2Cl_2 and acetone and dried under vacuum at 50°C overnight.

IR (KBr): 3450 cm^{-1} (OH), peak absent at 1265 cm^{-1} (C-Cl).

Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{14}H_{19}NO)_{0.11}]$: N, 1.32. Found: N, 1.12. The nitrogen content corresponds to 0.8 meq prolinol g^{-1} (DF=0.094, 86% conversion).

2. Preparation of supported α,α-diphenyl-(S)-prolinol.

Under argon, a suspension of chloromethylated polystyrene (1% crosslinked, 1 meq Cl g^{-1}, DF=0.11, $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_9H_9Cl)_{0.11}]$) (1 g, 1 meq Cl), (*S*)-proline methyl ester hydrochloride (500 mg, 3 mmol) and $NaHCO_3$ (510 mg) in 70 ml of dry DMF was stirred over 4 days at 60°C. The polymer was separated by filtration and thoroughly washed with DMF, methanol/water (1:2), methanol/water (2:1), methanol, CH_2Cl_2 and acetone. Under argon 1 g of this polymer suspended in 80 ml of dry THF was mixed at room temperature with phenylmagnesium chloride (7 ml of a 2.0 M solution in THF), then the mixture was heated at 80°C for 7 h. The polymer was separated by filtration,washed with 1 N HCl, THF, methanol and acetone and dried under vacuum during 3 days.

IR (KBr): 3450 cm^{-1} (OH), peak absent at 1265 cm^{-1} (C-Cl).

Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{26}H_{27}NO)_{0.11}]$: N, 1.15. Found: N, 1.15. The nitrogen content corresponds to 0.82 meq prolinol g^{-1} (DF=0.11, 100% conversion).

3. Preparation of supported (1R,2S)-ephedrine.

A suspension of chloromethylated polystyrene (1% crosslinked, 1 meq Cl g^{-1}, DF=0.11, $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_9H_9Cl)_{0.11}]$) (1 g, 1 meq Cl), (*1R,2S*)-ephedrine hydrochloride (1 g, 5 mmol) and Na_2CO_3 (1 g) in 93 ml of dry DMF was heated over 4 days at 80°C. The polymer was separated by filtration and thoroughly washed with DMF, CH_2Cl_2 and acetone and dried under vacuum overnight.

IR (KBr): 3450 cm^{-1} (OH), peak absent at 1265 cm^{-1} (C-Cl).

Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{19}H_{23}NO)_{0.11}]$: N, 1.24. Found: N, 0.93. The nitrogen content corresponds to 0.66 meq ephedrine g^{-1} (DF=0.080, 73% conversion).

4. Preparation of supported (R)-3-pyrrolidinol.

A suspension of chloromethylated polystyrene (1% crosslinked, 1 meq Cl g^{-1}, DF=0.11, $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_9H_9Cl)_{0.11}]$) (1 g, 1 meq Cl), (*R*)-3-pyrrolidinol hydrochloride (494 mg, 4 mmol) and $NaHCO_3$ (680 mg) in 150 ml of dry DMF was heated over 3 days at 80°C. The polymer was separated by filtration and thoroughly washed with DMF, CH_2Cl_2 and acetone and dried under vacuum overnight.

IR (KBr): 3450 cm^{-1} (OH), peak absent at 1265 cm^{-1} (C-Cl).

Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{13}H_{16}NO)_{0.11}]$: N, 1.34. Found: N, 0.92. The nitrogen content corresponds to 0.65 meq pyrrolidinol g^{-1} (DF=0.075, 68% conversion).

5. Preparation of supported (2R,3R)-tartaric acid.

A suspension of chloromethylated polystyrene (1% crosslinked, 1 meq Cl g^{-1}, DF=0.11, $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_9H_9Cl)_{0.11}]$) (1 g, 1 meq Cl), (*2R,3R*)-tartaric acid (100 mg, 0.67 mmol) and NEt_3 (10 ml) in 100 ml of xylenes was heated under reflux for 3 days. The polymer was separated by filtration and thoroughly washed with DMF, 1,4-dioxane, CH_2Cl_2 and acetone and dried under vacuum overnight.

IR (KBr): 1750 cm^{-1} (C=O), peak absent at 1265 cm^{-1} (C-Cl).

For analytical purposes the 3,5-dinitrobenzoate was prepared.[14] Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{18}H_{13}N_2O_8)_{0.11}]$: N, 2.29. Found: N, 1.84. The nitrogen content corresponds to 0.33 meq tartrate g^{-1} (DF=0.075, 68% conversion).

6. Preparation of the catalysts.

Under argon 1 g of polymer is shaken with the Lewis acid (1 mL of $AlEtCl_2$ 1 M in hexanes for **P1-P4**; 0.26 mL of $TiCl_4$ 1M in CH_2Cl_2 and 0.26 mmol of $Ti(O^iPr)_4$ for **P5**; 0.5 mL of $AlEtCl_2$ 1M in hexanes for **P6**; 0.5 mL of $AlEt_2Cl$ 1 M in hexanes for **P7**) at -20°C for 20 min and then 1 h at room temperature in dry methylene chloride. The catalyst was filtered, thoroughly washed with CH_2Cl_2 and kept in dry CH_2Cl_2 under argon atmosphere. The metal contents were determined by plasma emision spectroscopy.

7. Diels-Alder reactions with supported catalysts.

Polymer supported catalysts were suspended in dry CH_2Cl_2 in a Schlenk tube under argon atmosphere at the corresponding temperature (Tables 1 and 2) and freshly distilled methacrolein (**1**) (the amount in relation to the amounts of catalysts are given in Tables 1 and 2) was added. The mixture was shaken for 15 min and freshly distilled cyclopentadiene (**2**) (a 1.5 fold excess over methacrolein) was added. The suspension was shaken and periodically monitored by gas chromatography (FID from Hewlett-Packard 5890 II, cross-linked methyl silicone column 25m x 0.2mm x 0.33μm, helium as carrier gas: 17 psi, injector temperature 230°C, detector temperature 250°C, oven temperature programm: 40°C (3 min) - 25°C/min - 100°C (10 min), retention times: methacrolein (**1**) 2.7 min, *exo* cycloadducts (**3x**) 10.8 min, *endo* cycloadducts (**3n**) 11.5 min). After completion the polymer was filtered, washed with dry methylene chloride and kept under argon atmosphere to be reused. The solvent and the

non-reacted methacrolein were evaporated under reduced pressure and the cycloadducts were separated and purified by means of column chromatography on silica gel using methylene chloride/n-hexane = 1:1. The enantiomeric composition was analyzed in the major *exo* cycloadduct using $Eu(hfc)_3$/**3x** molar ratio 0.2. The signal at higher chemical shift corresponds to **3xS**.

8. Diels-Alder reactions with the homogeneous catalysts.

The *N*-benzyl aminoalcohol in dry methylene chloride and under argon was treated with 1 mol equivalent of $AlEtCl_2$ at -25°C. Then freshly distilled methacrolein (**1**) (4 mol equivalent) was added and the mixture stirred for 20 min. After this time freshly distilled cyclopentadiene (**2**) (6 mol equivalent) was added and the solution stirred. The reaction was monitored by gas chromatography. After the corresponding time the reaction was quenched by the addition of $Na_2CO_3.10H_2O$, the solution was filtered and then analyzed as described above.

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REFERENCES

1. (a) *Solid Supports and Catalysts in Organic Synthesis*; Smith, K. Ed.; Ellis Horwood: Chichester, 1992. (b) *Syntheses and Separations using Functional Polymers*, Sherrington, D.C.; Hodge, P.Eds.; John Wiley & Sons Inc.: New York, 1988.
2. Blaser, H.U.; Pugin, B. In *Chiral Reactions in Heterogeneous Catalysis*; Jannes, G.; Dubois, J. Eds., Plenum Press: New York, 1995.
3. (a) Tamioka, K. *Synthesis* **1990**, 541. (b) Narasaka, K. *Synthesis* **1991**, 1. (c) Kagan, H.B.; Riant, O. *Chem. Rev.* **1992**, 92, 1007. (d) Wallbaum, S.; Martens, J. *Tetrahedron: Asymmetry* **1992**, 3, 1475 . (e) Pindur, U.; Lutz, G.; Otto, C.*Chem. Rev.* **1993**, 93, 742. (f) Oh, T.; Reilly, M. *Org. Prep. Proced. Int.* **1994**, 26, 129. (g) Waldmann, H. *Synthesis* **1994**, 535.
4. (a) Cativiela, C.; García, J.I.; Mayoral, J.A.; Pires, E.; Brown, R. *Tetrahedron* **1995**, 51, 9217. (b) Cativiela, C.; Fraile, J.M.; García, J.I.; Mayoral, J.A.; Pires, E.; Royo, A.J.; Figueras, F.; de Ménorval, L.C. *Tetrahedron* **1993**, 49, 4073. (c) Luis, S.V.; Burguete, M.I.; Ramírez, N.; Mayoral, J.A.; Cativiela, C.; Royo, A.J. *React. Polym.* **1992**, 18, 237. (d) Cativiela, C.; Fraile, J.M.; García, J.I.; Mayoral, J.A.; Figueras, F.; de Ménorval, L.C.; Alonso, P.J. *J. Catal.* **1992**, 137, 394 and references cited therein.
5. (a) Cativiela, C.; García, J.I.; Mayoral, J.A.; Pires, E.; Royo, A.J.; Figueras, F. *Appl. Catal. A* **1995**, 131, 159. (b) Cativiela, C.; García, J.I.; Mayoral, J.A.; Pires, E.; Royo, A.J.; Figueras, F. *Tetrahedron* **1995**, 51, 1295. (c) Cativiela, C.; Fraile, J.M.; García, J.I.; Mayoral, J.A.; Pires, E.; Figueras, F.; de Ménorval, L.C. *Tetrahedron* **1992**, 48, 6467. (d) Cativiela, C.; Figueras, F.; Fraile, J.M.; García, J.I.; Mayoral, J.A.; de Ménorval, L.C.; Pires, E. *Appl. Catal. A* **1993**, 101, 253.
6. (a) Cativiela, C.; Fraile, J.M.; García, J.I.; Mayoral, J.A.; Pires, E.; Figueras, F. *J. Mol. Catal.* **1994**, 89, 159. (b) Cativiela, C.; Fraile, J.M.; García, J.I.; Mayoral, J.A.; Campelo, J.M.; Luna, D.; Marinas, J.M. *Tetrahedron: Asymmetry* **1993**, 4, 2507. (c) Cativiela, C.; Figueras, F.; García, J.I.; Mayoral, J.A.; Pires, E.; Royo, A.J. *Tetrahedron: Asymmetry* **1993**, 4, 621. (d) Cativiela, C.; Figueras, F.; Fraile, J.M.;

García, J.I.; Mayoral, J.A. *Tetrahedron: Asymmetry* **1993**, 4, 223. (e) Kabalka, G.W.; Pagni, R.M.; Bains, S.; Hondrogiannis, G.; Plesco, M.; Kurt, R.; Cox, D.; Green, J. *Tetrahedron: Asymmetry* **1991**, 2, 1283.

7. (a) Itsuno, S.; Kamahori, K.; Watanabe, W.; Koizumi, F.; Ito, H. *Tetrahedron: Asymmetry* **1994**, 5, 523. (b) Kamahori, K.; Tado, S.; Ito, K.; Itsuno, S. *Tetrahedron: Asymmetry* **1995**, 6, 2547.
8. Cativiela, C.; García, J.I.; Mayoral, J.A.; Pires, E.; Royo, A.J. *An. Quim.* **1994**, 90, 467.
9. See for instance: (a) Itsuno, S.; Ito, K.; Hirao, A.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2887. (b) Itsuno, S.; Nakano, M.; Ito, K.; Hirao, A.; Owa, M.; Kanda, S.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2615. (c) Fréchet, J.M.J.; Bald, E.; Lecavalier, P. *J. Org. Chem.* **1986**, 51, 3462. (d) Itsuno, S.; Fréchet, J.M.J. *J. Org. Chem.* **1987**, 52, 4140. (e) Itsuno, S.; Sakurai, V.; Ito, K.; Hirao, A.; Nakahama, S. *Bull. Chem. Soc. Jpn.* **1987**, 60, 395. (f) Soai, K.; Niwa, S.; Watanabe, M. *J. Org. Chem.* **1988**, 53, 927. (g) Itsuno, S.; Sakurai, Y.; Ito, K.; Maruyama, T.; Nakahama, S.; Fréchet, J.M.J. *J. Org. Chem.* **1990**, 55, 304.
10. Rebiere, F.; Riant, O.; Kagan, H.B. *Tetrahedron: Asymmetry* **1990**, 1, 199.
11. Ford, W.T. Site isolation organic synthesis in polystyrene networks. In *Polymeric reagents and catalysts;* Ford, W.T. Ed.; ACS Symposium Series, 308. ACS: Washington, 1986.
12. Gung, B.W.; Yanik, M.M. *J. Org. Chem.* **1996**, 61, 947.
13. (a) Altava, B.; Burguete, M.I.; Luis, S.V.; Mayoral, J.A. *Tetrahedron* **1994**, 50, 7535. (b) Farrall, M.J.; Alexis, M.; Trecarten, M. *Nouv. J. Chim.* **1983**, 7, 449.
14. Darling, G.D.; Fréchet, J.M.J. *J. Org. Chem.* **1986**, 51, 2270.

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