Polymer-Grafted Ti−TADDOL Complexes. Preparation and Use as Catalysts in Diels−Alder Reactions

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Different strategies have been evaluated for the preparation of polymers functionalized with chiral fragments containing the α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanol (TADDOL) structure. Best results are obtained when TADDOL derivatives containing OH phenolic groups (**17** and **18**) are prepared in solution and then selectively anchored to chloromethylated polymers by reaction in THF containing NaH and small amounts of 18C6 and NBu_4I. Resins **19** having the desired functionality have been prepared in this way. The procedure allows the efficient introduction of this functional group in PS-DVB polymers with different loading and cross-linking degrees, as well as on SMOP resins. These functionalized resins have been used to prepare Ti−TADDOL-supported complexes which have been tested as catalysts in the reaction of cyclopentadiene with 3-crotonoyl-1,3-oxazolidin-2-one. Although all the polymers obtained efficiently catalyze the reaction, only the one prepared from α,α,α′,α′-tetra-3,5-dimethylphenyl-1,3-dioxolane-4,5-dimethanol induces asymmetry.

Introduction

Since the pioneering work of Merrifield on the solid phase synthesis of peptides,[1] solid phase methodology has been successfully applied to a number of different areas. Besides the solid phase synthesis of biologically important oligomers such as peptides,[1−6] polynucleotides,[7] oligosaccharides,[8] and other important organic compounds,[9−11] solid phase techniques have been used for the development of chromatographic enantioseparations,[12] polymer-supported reagents and catalysts,[3,5,13,14] study of reaction mechanisms,[15,16] etc. More recently, progress in the field of combinatorial chemistry has produced a renewed interest in the use of solid phase methodologies and a need for additional research in this area of work.[17]

α,α,α′,α′-Tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLS) having the general structure **1** have been widely studied as chiral ligands for the preparation of homogeneous enantioselective catalysts.[18−21]

In general, they seem to have the advantages associated with ligands having a C_2 or pseudo-C_2 symmetry.[22]

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Chart 1

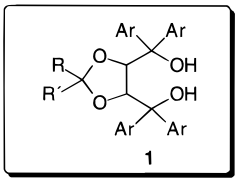
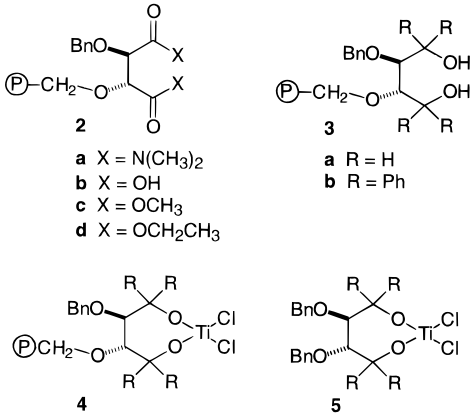


Chart 2



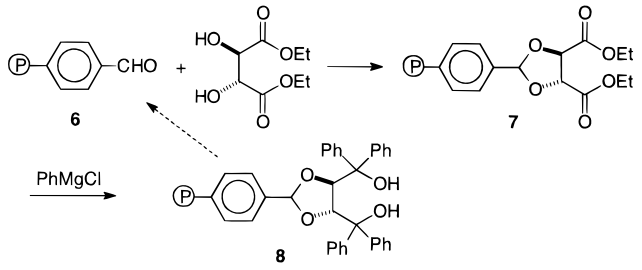
On the other hand, the presence in **1** of the four aromatic rings at the α positions as well as the dioxolane ring, and the chelating behavior of those compounds for transition metal cations allow for the existence of a well defined steric environment in the catalytic site which can favor asymmetric induction. Additionally, a high degree of structural modification through changes in the nature of R, R′, and Ar groups can be achieved. Moreover, TADDOLs can be easily prepared from simple tartaric acid derivatives in both enantiomeric forms. According to this, different TADDOL derivatives have been used as ligands for the preparation of transition metal catalysts. In particular, Ti catalysts have been shown to produce very interesting results in the catalysis of different processes such as Diels−Alder reactions, dialkyl zinc addition to carbonyl groups, etc.

Several advantages are generally associated with polymer-supported catalysts. The easy separation of the catalyst from the reaction mixture is probably considered the most important feature for these systems. However, the increased stability of some polymer-bound catalysts, their ease of recovery, their reusability, and their potential utility for continuous processes must also be considered.[2−4,13,14]

Recently, we have prepared different PS-DVB polymers functionalized with chiral groups derived from tartaric acid, having the structures **2** and **3**.[23]

Preliminary results obtained with Ti catalysts **4** prepared from polymeric diols **3a** and **3b**, as well as with their soluble analogue **5**, have shown that the Ti species which are formed act as efficient catalysts for the Diels−Alder reaction between 3-crotonoyl- or 3-acryloyl-1,3-oxazolidin-2-one and cyclopentadiene. However, no asymmetric induction was observed for both the soluble and the insoluble catalysts. A lower degree of asymmetric induction has only been obtained by a supported aluminum catalyst derived from a polymeric tartrate ester.[24]

Scheme 1



In this sense, the presence of the dioxolane ring in structure **1** seems to play an important role, so that the preparation of functionalized polymers containing such a structure represents an interesting target. Very recently, Seebach and co-workers have published reports dealing with the preparation and the use as catalysts of several polymer-supported TADDOL derivatives obtained by grafting and copolymerization.[25] In the meantime we have synthetized several TADDOL derivatives grafted on polymeric resins and have tested their Ti-complexes as catalysts in the reaction of cyclopentadiene with 3-crotonoyl-1,3-oxazolidin-2-one. The appearance of the above-mentioned paper together with the differences observed using the grafted catalysts prompted us to publish our results.

Results and Discussion

Preparation of the Supported TADDOL Derivatives. According to the general methodology developed by Kagan and Stille to prepare polymer-bound chiral phosphines, derived from tartaric acid,[26] our first attempts to obtain polymers containing the α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanols were based on the synthetic procedure shown in Scheme 1.

Reaction of polymeric aldehyde **6**, prepared from a Merrifield's resin of 1 mmol Cl/g and 1% cross-linking as described by Fréchet,[8a] with (*R*,*R*)-diethyl tartrate in benzene or toluene containing a catalytic amount of *p*-toluenesulfonic acid (PTSA), quantitatively afforded ketal **7**. Complete disappearance of the aldehyde carbonyl group at 1701 cm^{-1} and the presence of the novel C=O ester band at 1745 cm^{-1} were observed for the resulting resin. Reaction of **7** with an excess of phenyl magnesium chloride produced a polymer **8** which apparently had the desired functionality as shown by the complete absence of the C=O ester bands. However, the resulting resin was contaminated by the presence of magnesium salts deposited in the inside of the polymeric beads. Attempts to eliminate these salts resulted in the hydrolysis of the ketal group giving place to the recovering of the starting polymeric aldehyde **6**.

A second strategy was then assayed by trying to produce a transacetalization reaction between com-

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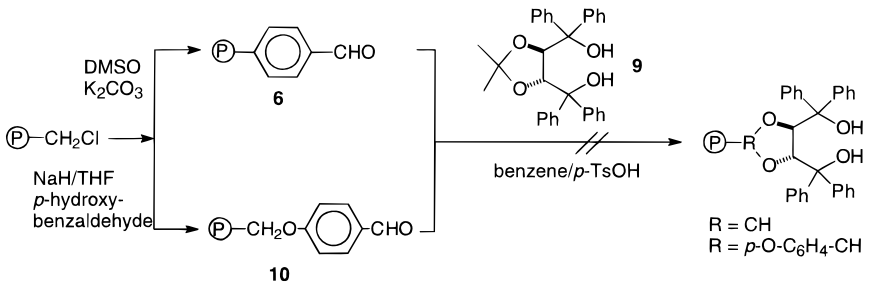
Scheme 2



mercial TADDOL **9** and polymers **6** and **10** which contain aldehyde groups (Scheme 2).

Resin-bound aldehyde **10** (1 mmol/g, 1% cross-linking DF = 0.11) was obtained by reaction of a chloromethylated polymer with *p*-hydroxybenzaldehyde.[11b] Transacetalization reactions have been recently found to be very useful for the preparation of TADDOL analogues (TARTROLs) containing a 1,4-dioxane ring instead of the dioxolane ring.[27] However, this strategy was also unsuccessful in our hands. After refluxing the corresponding resin with **9** for 48 h, in the presence of PTSA, a complete disappearance of the C=O group was observed, but no incorporation of the ketal functionality was detected. Thus, for instance, the treatment of the resulting resins under hydrolytic conditions, which should produce the loss of the ketal moiety, did not allow us to observe the regeneration of the original C=O group. In this sense, the main process accounting for the consumption of the aldehyde group should be, most likely, a Friedel−Crafts type reaction giving place to a highly cross-linked polymer.[28] In good agreement with this hypothesis, gel-phase ^{13}C NMR analysis,[29,30] which showed the expected features for the starting resins **6** and **10,** could not be carried out efficiently in the resulting polymers, indicating a decreased mobility of the polymeric chains.

In view of the former results, a different approach was considered. The general strategy was to prepare TADDOL derivatives having additional functional groups which could allow their anchoring to an appropriately functionalized polymer. Such derivatives could be obtained starting from hydroxybenzaldehyde **11** as summarized in Scheme 3.

Reaction of *m*- and *p*-hydroxybenzaldehyde (**11** and **12**) with a mixture of (*R*,*R*)-dimethyl tartrate and $HC(OMe)_3$ afforded ketals **14** and **15** in good yields. Ketal **15** derived from *p*-hydroxybenzaldehyde was very sensitive to hydrolysis and was more difficult to handle than ketal **14**. Accordingly, the synthetic scheme was only completed for the *meta* derivative. The treatment of **14** with a large enough excess of the appropriate arylmagnesium chloride or bromide afforded, after the usual workup, the expected TADDOL derivatives **17a**−**d**. The results obtained are summarized in Table 1. Ketal **16** prepared from *p*-hydroxyacetophenone was also more stable to hydrolysis than **15**, and the reaction of **16** with ArMgX

Scheme 3

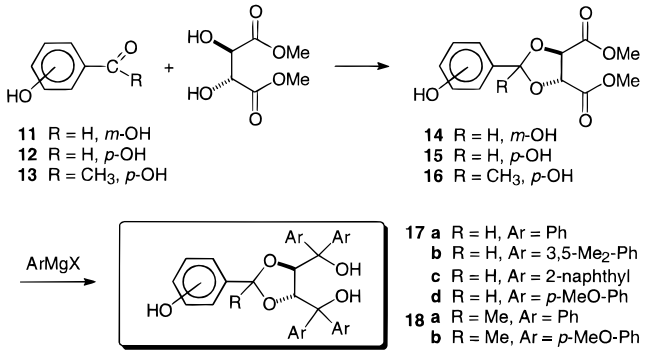


Table 1. Results Obtained In the preparation Of TADDOLs 17 and 18

compound	OH position	R	Ar	yield (%)[a]
17a	*m*-	H	Ph	33
17b	*m*-	H	3,5-Me_2-Ph	32
17c	*m*-	H	2-naphthyl	26
17d	*m*-	H	4-MeO-Ph	44
18a	*p*-	CH_3	Ph	15
18b	*p*-	CH_3	4-MeO-Ph	35

[a] Yields after chromatographic purification and/or crystallization.

species gave the expected TADDOLs **18**. In general TADDOLs **17** and **18** were more stable than the starting ketals **14**−**16**.

TADDOLs **17** and **18** displayed the expected spectroscopic features, similar to those described for other TADDOL derivatives. However, compound **17b** containing four 3,5-dimethylphenyl groups in the α and α′ positions seems to present a particular behavior. At room temperature its ^1H NMR displays a large number of broad signals that partially coalesce upon heating. Thus, for instance, at 60 °C three broadened signals were observed for the three protons of the dioxolane ring at 4.66, 5.44, and 5.65 ppm instead of the very broad multiplet observed between 4.4 and 6.0 at lower temperatures. A similar situation was also observed for the ^{13}C NMR spectra. Molecular mechanics calculations using the Macromodel V3.5 package revealed the existence of two families of conformers for TADDOLs **17a**−**d**.[31] The structure of the minimum energy conformers of each family found for **17b** are shown in Figure 1. As can be seen, one of the conformers, which is ca. 1 kcal/mol more stable than the other, is characterized by the presence of two parallel aromatic rings and the existence of two hydrogen bonds between one OH group and the oxygens of the dioxolane ring. The NMR data suggest that the presence of the methyl groups on the aromatic moieties

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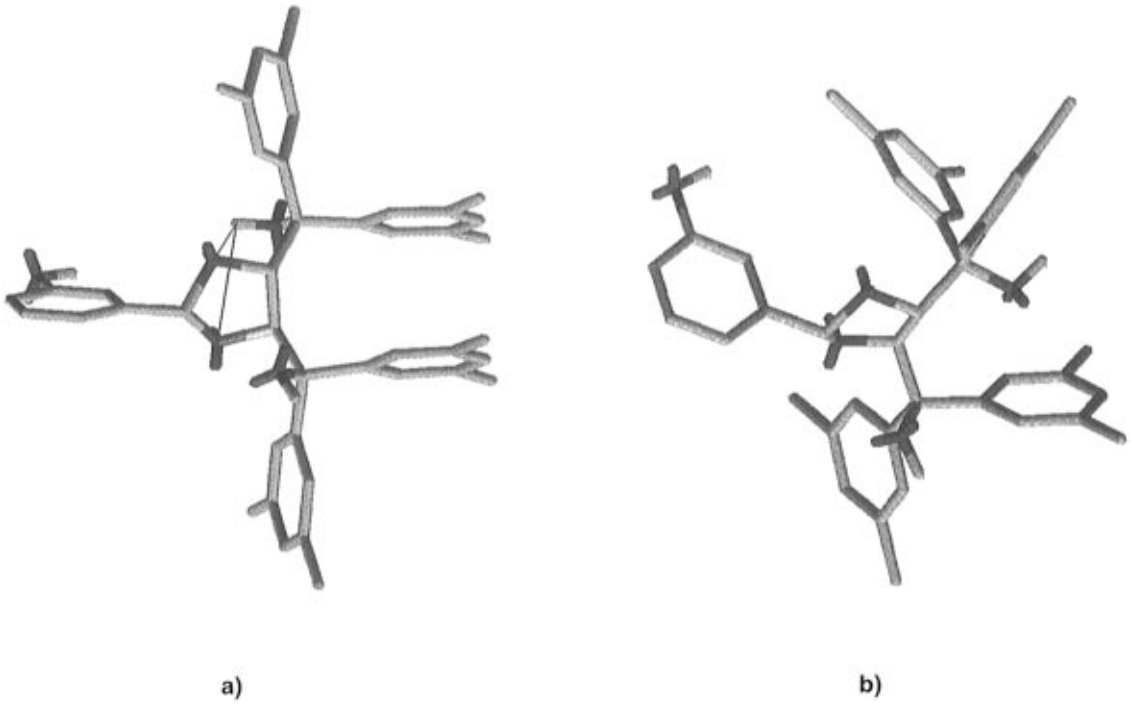
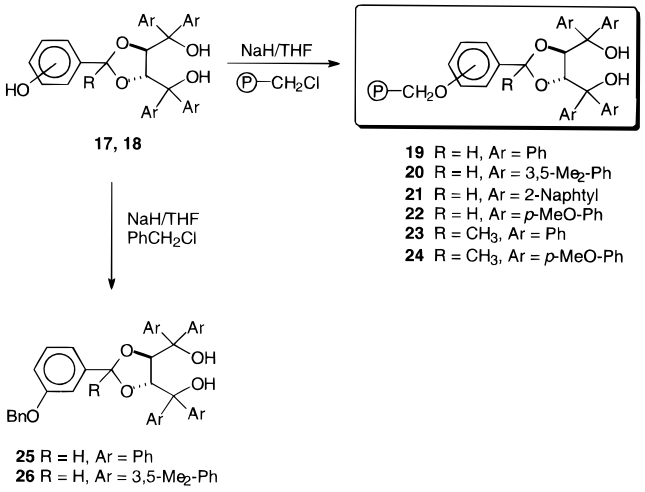


Figure 1. First and third minimum energy conformers calculated for compound **17b**.

Scheme 4



prevents fast interconversion between the different conformers for compound **17b**, the interconversion being easier for the other TADDOLs. This is important as it has been shown that conformational factors can be essential in order to understand the behavior of catalysts prepared from TADDOL derivatives.[18e,20,21c]

The preparation of polymer-supported TADDOLs was easily accomplished starting from compounds **17** and **18** (Scheme 4). The reaction of a chloromethylated resin with the corresponding TADDOL in THF using NaH as a base allowed quantitative and selective anchoring of the chiral fragment through the OH phenolic group to give polymers **19**−**24** (see Table 2).

The FT-IR analysis of the resulting resins showed the absence of the C−Cl band at 1265 cm^{-1} and the presence of a distinct OH band at 3345−3465 cm^{-1}. The FT-Raman analysis also allowed us to check that disappearance of the C−Cl band was complete. Gel phase ^{13}C NMR spectroscopy could also be applied to those functionalized polymers. In addition to the polymeric backbone bands, these resins showed the absence of the CH_2Cl peak at 46 ppm, the presence of the PS-CH_2O peak at ca. 70 ppm, the expected signals for the dioxolane ring at ca. 80−81 ppm and 105 ppm, the $C(Ph)_2OH$ signal at 78 ppm, and additional peaks in the aromatic region and sharp signals corresponding to substituents present in the α,α′ aromatic groups of the TADDOL fragment (see Figure 2). Polymers **23** and **24** present a distinctive peak at 55 ppm for the methyl group at the 2-position of the dioxolane ring.

As can be seen in Table 2 the anchoring reaction works well for the different phenolic TADDOL derivatives (**17** and **18**) prepared. Entries 1−5 also show how this reaction can also be applied to the functionalization of resins of different characteristics. The binding of TADDOL **17a** to PS-DVB polymers having different degrees of functionalization and cross-linking was quantitatively obtained. Results were also positive when a SMOP-3 resin, a polyethylene polymer containing polyvinylbenzyl chloride chains, was used (see entry 5).[32] When PS-DVB resins with a high content of chloromethyl groups were used (see, for instance, entries 3 and 4), gel phase ^{13}C NMR spectra could not be obtained, but this does not seem to be related with the presence of undesired side reactions. A more detailed analysis of the starting materials revealed that cross-linking degrees of these resins were much higher than the nominal ones corresponding to the percentage of DVB introduced in the polymerization process, precluding the possibility of obtaining ^{13}C NMR spectra. The increase of cross-linking as a side reaction on the chloromethylation of PS-DVB polymers in particular for commercial materials with high loading levels, is well documented.[29] The IR spectra showed the presence of bands in the 810 cm^{-1} region which suggest important changes in the structure of the polymeric chains. A clear confirmation of this hypothesis was obtained using the FT-Raman spectroscopy which is very sensitive to the nature of the polymeric back-

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Table 2. Results Obtained in the Preparation of Polymer-Supported TADDOL Derivatives 19−24

		starting resin[a]							
entry	starting TADDOL	loading, (mmol Cl/g)	% DVB	final polymer	R	Ar	loading, mmol/g	DF[b]	conv (%)
1	**17a**	1	1	**19a**	H	Ph	0.69	0.11	100
2	**17a**	1	2	**19b**	H	Ph	0.67	0.11	100
3	**17a**	1.6	1	**19c**	H	Ph	0.89	0.18	100
4	**17a**	2.1	2	**19d**	H	Ph	1.02	0.24	100
5	**17a**	3	SMOP-3	**19e**	H	Ph	1.2	1	100
6	**17b**	1	1	**20**	H	3,5-Me_2-Ph	0.65	0.11	100
7	**17c**	1	1	**21**	H	2-naphthyl	0.62	0.11	100
8	**17d**	1	1	**22**	H	4-MeO-Ph	0.59	0.11	100
9	**18a**	1	1	**23**	Me	Ph	0.67	0.11	100
10	**18b**	1	1	**24**	Me	4-MeO-Ph	0.62	0.11	100

[a] PS-DVB were used except where indicated. [b] The DF of a polystyrene resin is a measure of the proportion of aromatic styrene rings carrying the desired functional group. Thus, DF = 0.11 means that 11% of the styrene units have been fuctionalized.

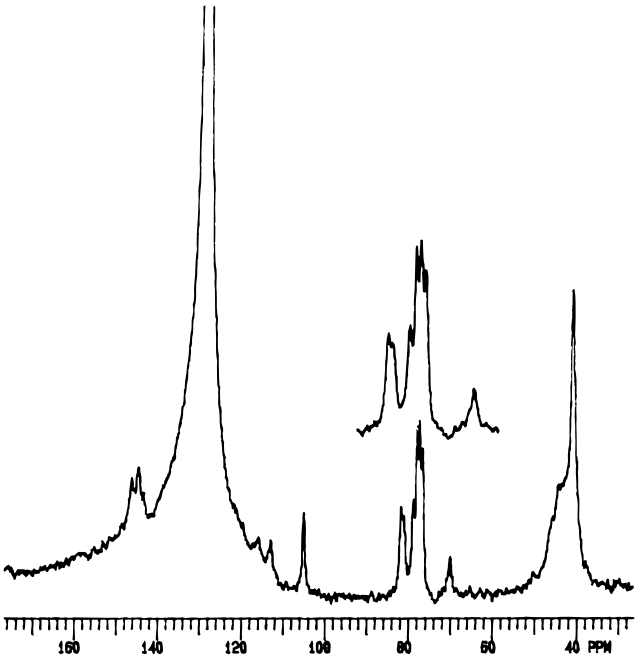


Figure 2. ^{13}C gel phase NMR spectra for polymer **20**. Resin swollen in $CDCl_3$ in a 5 mm tube at 25 °C. Acquisition time 1 s, pulse 70°, number of transients 50000, line broadening 15.0 Hz.

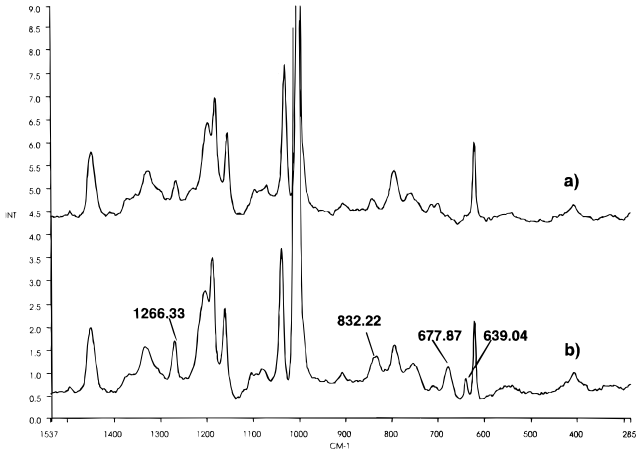


Figure 3. FT-Raman spectra for chloromethylated resins containing (a) 1 mmol Cl/g (nominal DVB content 1%) and (b) 2.1 mmol Cl/g (nominal DVB content 2%).

bone.[33] As can be seen in Figure 3 the resin containing a loading degree of 2.1 mmol Cl/g (used for the experiment of entry 4) shows very important changes relative to similar resins of lower functionalization degrees.

Application of the Supported Titanium Complexes as Catalysts in Diels−Alder Reactions. There are few reports dealing with the use of polymer-supported chiral Lewis acids to promote enantioselective Diels−Alder cycloadditions.[24,25,34] In spite of the excellent results obtained in the reactions of 1,3-dienes with 3-acryloyl- and 3-crotonoyl-1,3-oxazolidin-2-ones catalyzed by Ti−TADDOL complexes, only Seebach and co-workers have recently described the use of related polymer-supported species.[25]

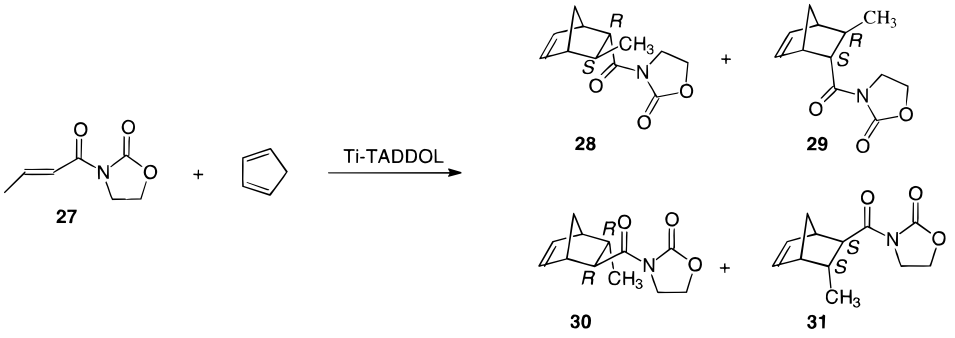
The polymer-supported TADDOL derivatives **19**−**24** together with a pair of homogeneous analogous (**25**, **26**) were transformed into the corresponding chiral complexes by treatment with $Ti(OCHMe_2)_2Cl_2$, and these complexes were tested as catalysts in the reaction of cyclopentadiene with 3-crotonoyl-1,3-oxazolidin-2-one (**27**) (Scheme 5). The reactions were monitored by GC, the heterogeneous catalyst was separated by filtration and thoroughly washed. The solvent was eliminated under reduced pressure, and the final yield and endo/exo selectivity were determined by ^1H NMR. The endo cycloadducts were separated by column chromatography, and the ee was determined by ^1H NMR in the presence of $Eu(hfc)_3$, integrating the signals corresponding to the vinyl protons (Figure 4). The absolute configuration of the major cycloadduct was determined by polarimetric measurement of the mixture of endo cycloadducts **28**, **29**.

The results obtained (Table 3) show that all these solids promote the reaction studied, even with an excess of diene much lower than commonly used. As could be expected, an increase of the steric crowding in the surroundings of the titanium atoms reduces the catalytic activity, as shown by the 2-naphthyl and 3,5-dimethylphenyl derivatives (entries 7 and 9). This catalytic behavior is in contrast with the results recently described by Seebach and co-workers.[25] These authors have shown that a closely related Ti−TADDOL complex bound to Merrifield resins **32** does not promote the same cycloaddition even using a 20-fold excess of cyclopentadiene. The grafting to the polymer through different spacers, as well as the different temperatures used (0 and 25 °C), can hardly justify the differences experimentally observed. The method used to incorporate the titanium, toluene at

(33) For an application of FT-Raman to the study of the Merrifield peptide synthesis see, for instance: Due Larsen, B.; Christensen, D. H.; Holm, A.; Zillmer, R.; Faurskov Nielsen, O. *J. Am. Chem. Soc.* **1993**, *115*, 6247−6253.

(34) (a) Itsuno, S.; Watanabe, H.; Koizumi, T.; Ito, K. *React. Polym.* **1995**, *24*, 219. (b) Kamahori, H.; Tada, S.; Ito, K.; Itsuno, S. *Tetrahedron: Asymm.* **1995**, *6*, 2547−2555.

Scheme 5



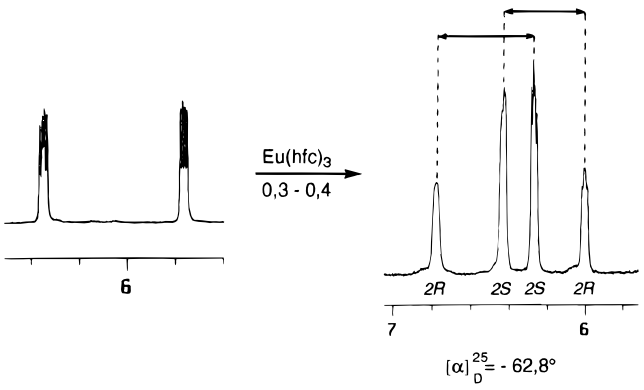


Figure 4. ^{1}H-NMR of the vinyl protons of the endo cycloadducts **28** and **29** in the presence of 0.3 equiv of Eu(hfc)$_3$.

rt in the work of Seebach and co-workers, and reflux in carbon tetrachloride in this work, can be more important, as it can determine the amount of supported Ti−TADDOL complexes and, as a consequence, the catalytic activity of the polymer. Moreover, our results show that the catalytic activity depends on the nature of the polymer more than on the loading of chlorine or titanium. So, for instance, the yield of the titanium incorporation on the SMOP-3 resin is very low (38%) and in spite of the low content of titanium this polymer displays a noticeable catalytic activity (entry 5). In this respect it has to be noted that only low degrees of conversion have been reported by Seebach in the preparation of **32**, and thus, additional functional groups are present in the polymer which can affect the catalytic efficiency of the final resins.

Supporting the Lewis acids does not have a great influence on the endo/exo ratio but reduces the enantioselectivity. In most of cases the reactions promoted by the supported catalysts are not enantioselective, independently of the nature of the resin used to graft the TADDOL. This result indicates that the support has an important influence on the steric course of the reaction. Only the catalyst obtained from the supported α,α,α′,α′-tetrakis(3,5-dimethylphenyl) derivative **20** yields a 25% ee of the *2R*,*3S*-cycloadduct (**28**). With the related homogeneous TADDOL **26** a similar 38% ee of the same enantiomer is obtained, which seems to indicate that the nature of the chiral auxiliary may allow reduction of the influence of the support on the steric course of the reaction. To the best of our knowledge this is the highest asymmetric induction obtained in a Diels−Alder reaction, using as catalyst a polymer-supported Lewis acid prepared by grafting the chiral auxiliary on a preformed resin. The results obtained indicate that, as it happens in solution, the asymmetric induction depends on the structure of the supported TADDOL.

Conclusions

A practical approach for the introduction of TADDOL fragments on polymeric supports involves the initial preparation of TADDOL derivatives containing OH phenolic groups. Different TADDOL derivatives of this class (**17** and **18**) can be easily obtained starting from *m*-hydroxybenzaldehyde or *p*-hydroxyacetophenone. Selective alkylation of the OH phenolic groups with chloromethylated resins allowed the obtention of the desired functionalized polymers **19**−**24**. Resins containing variable degrees of functionalization and cross-linking can be prepared in this way. Under the conditions used, the bulky nature of the groups to be introduced do not preclude the easy approach to the reactive sites, and conversion is essentially quantitative.

The corresponding Ti-complexes, easily obtained by treatment with Ti(OCHMe$_2$)$_2$Cl$_2$, efficiently catalyze the reaction of cyclopentadiene with 3-crotonoyl-1,3-oxazolidin-2-one. The asymmetric induction is noticeably reduced in comparison with similar homogeneous species and only the catalyst obtained from the α,α,α′,α′-tetrakis-(3,5-dimethylphenyl) derivative leads to a 25% ee.

Experimental Section

General. All reactions were carried out under an argon atmosphere. Resins were always vacuum dried to constant weight after each reaction. FT-IR spectra (cm^{-1}) were obtained from KBr pellets. ^{1}H and ^{13}C NMR spectra (ppm, δ) were obtained at 200 and 50.1 MHz using $CDCl_3$ as the solvent (gel phase spectra for polymers).

Polymeric Aldehyde 10. NaH (0.128 g, 4.1 mmol) and *p*-hydroxybenzaldehyde (0.5 mg, 4.1 mmol) were suspended in THF (15 mL). The mixture was stirred at rt for 15 min, and then the chloromethylated resin (1 mmol Cl/g, 1% DVB) (0.135 g, 0,135 mmol) ((C$_{10}$H$_8$)$_{0.01}$ (C$_8$H$_8$)$_{0.88}$ (C$_9$H$_9$Cl)$_{0.11}$) was added as well as a small amount of 18C6 and Bu$_4$NI. The resulting suspension was refluxed for 24 h, and the polymer was filtered, washed with THF (3×), THF/H$_2$O (2:1) (3×), THF/H$_2$O (1:1) (3×), MeOH (3×), and CH_2Cl_2 (3×) to give polymer **10**. IR: peak absent at 1265 cm^{-1}; peak present at 1691 cm^{-1}.

For analytical purposes, the polymer **10** (100 mg), KOH (40 mg), and NH$_2$OH·HCl (27 mg) were suspended in EtOH (20 mL). The mixture was kept at reflux for 48 h, and the resulting resin was filtered and washed with EtOH (3×), dioxane (3×), dioxane/MeOH (1:1) (3×), dioxane/MeOH (1:2) (3×), MeOH (3×), and CH_2Cl_2 (3×). IR: peak absent at 1691 cm^{-1}; peak present at 3550 cm^{-1}. Anal. Calcd for (C$_{10}$H$_8$)$_{0.01}$ (C$_8$H$_8$)$_{0.88}$ (C$_{16}$H$_{14}$0$_2$N)$_{0.11}$: C, 88.6; H, 7.20; N, 1.28. Found: C, 88.03; H,7.05; N, 1.25.

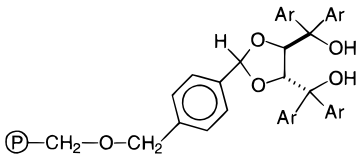
Polymeric Ketal 7. The resin **6** (200 mg, 1 mmol/g, 1% DVB, 0.2 mmol) was suspended in toluene (100 mL) and (*R*,*R*)-diethyl tartrate (165 mg, 0.8 mmol), and a small amount of PTSA was added. The mixture was refluxed and the water formed was continuously distilled in a Dean-Stark system. When the reaction was complete, the polymer was filtered and

Table 3. Results Obtained in the Reaction of Cyclopentadiene with 3-Crotonoyl-1,3-oxazolidin-2-one, Catalyzed by Ti−TADDOL Complexes at Room Temperature Using a 2.5 Fold Excess of Diene

entry	catalyst precursor	mmol Ti/g[a]	Ti/dienophile	time (h)	% conv[b]	endo/exo[c]	% ee[d]
1	**19a**	0.46	0.10	168	32	84:16	0
2	**19b**	0.52	0.12	7	62		
				22	86	80:20	0
3	**19c**	0.80	0.13	7	48		
				22	72		
				48	99	83:17	0
4	**19d**	0.68	0.10	7	60		
				22	84	83:17	0
5	**19e**	0.43	0.05	8	75		
				23	93	79:21	0
6	**25**[e]	–	0.11	24	100	82:18	33 (*2S*,*3R*)
7	**20**	0.59	0.14	48[f]	95	71:29	25 (*2R*,*3S*)
8	**26**[e]	–	0.11	24	100	71:29	38 (*2R*,*3S*)
9	**21**	0.58	0.14	48[f]	85	75:25	0
10	**22**	0.67	0.16	48[f]	80	76:24	0
11	**23**	0.62	0.13	8	70		
				23	90	86:14	0
12	**24**	0.72	0.18	8	56		
				23	88	85:15	0

[a] Determined by plasma emission spectroscopy. [b] Determined by gas chromatography. [c] Determined by ^{1}H-NMR. [d] Determined by ^{1}H-NMR in the presence of Eu(hfc)$_3$. [e] At 0 °C with a 12:1 molar ratio diene:dienophile. [f] After 24 h an additional 2.5 fold excess of diene is added.

Chart 3



32

washed with toluene (3×), MeOH (3×), and Cl_2H_2 (3×). IR: peak absent at 1701 cm^{-1}; peaks present at 1745, 1212, 1178 cm^{-1}.

Attempted Preparation of Polymeric Ketal 8. Polymer **7** (200 mg, 0.89 mmol/g, 0.18 mmol) was suspended in dry THF (25 mL), and PhMgCl (1 mL, 2.2 mmol) was added. The mixture was refluxed for 24 h, and then water (10 mL), 15% NaOH (5 mL), and water (10 mL) were successively added. The resin was filtered, washed with 3 M HCl (3×), 6 M HCl in H_2O/MeOH (1:1) (3×), H_2O/MeOH (1:2) (3×), MeOH (3×), CH_2Cl_2 (3×), and acetone (3×) to give a polymer whose IR showed no peaks in the 1690−1750 cm^{-1} region. Plasma analysis revealed the presence of Mg salts. Additional washings with different HCl/dioxane mixtures were carried out to obtain a polymer containing no Mg residues. The IR spectrum of the final polymer showed the presence of a band at 1701 cm^{-1} characteristic of the functional group present in resin **6**.

Attempted Transacetalization of TADDOL 9 with Polymer-Bound Aldehyde 10. Polymer **10** (6 g, 1 mmol/g, 1% DVB, 6 mmol) was suspended in benzene (***caution***) (250 mL), and TADDOL **9** (6 g, 0.13 mmol) and a small amount of PTSA were added. The mixture was heated with stirring, under reflux, and the azeotropes formed were continuously distilled in a Dean-Stark system. After 30 min the reaction mixture was cooled, and the polymer was filtered and washed with benzene (***caution***) (3×), MeOH (3×), and CH_2Cl_2 (3×). IR: peaks absent at 1691 and 3500−3400 cm^{-1}. Repeated treatment with HCl/dioxane mixtures, as described before, did not allowed us to recover the starting resin **10**.

2-(*m*-Hydroxyphenyl)-4(*R*),5(*R*)-bis(methoxycarbonyl)-1,3-dioxolane (14). HC(OMe)$_3$ (2.6 mL, 0.02 mol) was added at 0 °C to a solution of *m*-hydroxybenzaldehyde (2.48 g, 0.02 mol) in dry benzene (***caution***) (30 mL) containing a small amount of PTSA. The mixture was stirred for 30 min, and then (*R*,*R*)-dimethyl tartrate (3.3 g, 0.02 mol) was added. Distillation of the benzene/methanol azeotrope was then carried out at 60 °C, and, after cooling, Et_3N was added to neutralize the acid. The solvent was vacuum evaporated to give 5.6 g of a reddish oil. The crude product was purified by column chromatography (SiO_2) using hexanes/EtOAc mixtures (1:0, 10:1, 10:3, 10:5) as the eluent to give a yellowish solid (3.94 g, 70%). $[\alpha]^{25}_D$: −20.8 (*c* 0.026, THF). Mp 65 °C. IR 3440, 1743, 1237, 1181, 1109. ^{1}H NMR 3.8 (s, 3 H), 3.85 (s, 3 H), 4.8−5.0 (two doublets, 2 H), 6.05 (s, 1 H), 6.8−6.9 (dd, 1 H), 7.0−7.4 (m, 3 H). ^{13}C NMR 53.2, 53.3, 77.0, 77.1, 106.4, 114.0, 117.3, 119.2, 129.6, 136.7, 156.3, 170.4, 172.1. MS (EI, *m*/*z*) 281 ($M^+ - 1$). Anal. Calcd for $C_{13}H_{14}O_7$: C, 55.3; H, 5.0. Found: C, 55.6; H, 5.1.

2-(*p*-Hydroxyphenyl)-2-methyl-4(*R*),5(*R*)-bis(methoxycarbonyl)-1,3-dioxolane (16). Prepared as described for **14**, starting from *p*-hydroxyacetophenone (5 g, 0.07 mol). Purification of the crude product was carried out by column chromatography (SiO_2) using hexanes/EtOAc mixtures (100:0, 90:20, 90:40) as the eluent to obtain the pure product as a clear oil (5.5 g, 50%). $[\alpha]^{25}_D$: 5.4 (*c* 0.023, THF). IR 3439, 1743, 1253, 1171, 1093. ^{1}H NMR 1.7 (s, 3 H), 3.5 (s, 3 H), 3.8 (s, 3 H), 4.8 (d, 1 H), 4.9 (d, 1 H), 6.74 (d, 2 H), 7.32 (d, 2 H). ^{13}C NMR 28.1, 52.6, 53.1, 76.3, 77.1, 113.4, 114.9, 127.1, 133.1, 156.3, 169.9, 170.0, MS (EI, *m*/*z*) 295 ($M^+ - 1$). Anal. Calcd for $C_{14}H_{16}O_7$:C, 56.8; H, 5.4. Found: C, 56.6; H, 5.6.

General Procedure for the Preparation of α,α,α′,α′-Tetraaryl-1,3-dioxolane-4(*R*),5(*R*)-dimethanols (TADDOLs) 17 and 18. Synthesis of 17a. A 2 M solution of PhMgCl (40 mL, 84 mmol) was carefully added to ketal **14** (1.9 g, 6.7 mmol) in dry THF (35 mL). When addition was complete, the mixture was refluxed for 16 h. After cooling, a saturated solution of NH_4Cl was added to obtain a complete solubilization of the salts formed. The resulting solution was extracted with EtOAc, and the organic phase was dried (anhyd $MgSO_4$) and vacuum evaporated. The oil obtained was crystallized in CH_2Cl_2 to give dioxolane **17a** as a white solid (1.2 g, 34%). Mp 135 −140 °C, $[\alpha]^{25}_D$: +7.4 (*c* 0.004, THF). IR 3600−3300, 1279, 1175, 1100, 1049, 1032. ^{1}H NMR 4.88 (d, 1 H), 4.89 (s, 1 H), 4.98 (d, 1 H), 6.5−7.6 (m, 24 H). ^{13}C NMR 78.6, 78.7, 80.9, 81.6, 104.7, 113.5, 116.5, 119.0, 126.9−129.6 (several peaks) 129.8, 134.7, 143.0, 144.1, 145.9, 155.6. MS (EI, *m*/*z*) 530 (M^+). Anal. Calcd for $C_{35}H_{30}O_5$: C, 79.2, H, 5.7. Found: C, 78.8; H, 5.8.

TADDOL 17b. Prepared from ketal **14** (1.5 g, 5.3 mmol) and (3,5-dimethylphenyl)magnesium bromide (70 mmol), obtained from 3,5-dimethylbromobenzene (14.7 g, 70 mmol) and Mg (1.5 g, 70 mmol). The crude product was purified by column chromatography (SiO_2) using hexanes/EtOAc mixtures (100:0, 89:0, 80:20, 60:40) as the eluent. Yield: 1.2 g, 35%. Mp 145−158 °C. $[\alpha]^{25}_D$: +129 (*c* 0.008, THF). IR 3385, 1380, 1280, 1178, 1103. ^{1}H NMR (50 °C) 2.22 (s), 2.27 (s), 2.28 (s), 2.32 (s) (24 H), 4.66 (s, 1 H), 5.44 (s, 1 H), 5.65 (s, 1 H), 6.72−7.78 (m, 16 H). ^{13}C NMR (50 °C) 20.8, 22.2, 78.7, 82.2, 104.5,

112.9, 116.9, 118.7, 124−141 (19 peaks), 155.6. MS (FAB, *m/z*) 643 ($M^+ + 1$), 642 (M^+). Anal. Calcd for $C_{43}H_{46}O_5$: C, 80.3; H, 7.2. Found: C, 79.9; H, 7.5.

TADDOL 17c. Prepared from ketal **14** (1.5 g, 5.3 mmol) and 2-naphthylmagnesium bromide (70 mmol), obtained from 2-bromonaphthalene (14.3 g, 70 mmol) and Mg (1.5 g, 70 mmol). Purified by column chromatography as for **17b**. Yield: 1.8 g, 25%. Mp 165−173 °C. $[\alpha]^{25}_D$: +137 (*c* 0.006, THF), IR 3391, 1178, 1122, 1103. ^{1}H NMR 3.4 (s, 1 H), 4.6 (s, 1 H), 5.6 (d, 1 H), 5.8 (d, 1 H), 5.9 (s, 1 H) 6.5−8.5 (m, 33 H). ^{13}C NMR 79.4, 80.4, 81.4, 81.6, 105.6, 113.2, 116.5, 118.6, 124.6, 124.8, 125.0, 125.1, 126−129 (13 peaks), 129.8, 132−133 (6 peaks), 139.2, 140.6, 141.4, 141.7, 141.9, 142.2, 156.2. MS (EI, *m/z*) 730 (M^+). Anal. Calcd for $C_{51}H_{38}O_5$ $2H_2O$: C, 79.9, H, 5.5. Found: C, 80.2; H, 5.7.

TADDOL 17d. Prepared from ketal **14** (13 g, 4.6 mmol) and (*p*-methoxyphenyl)magnesium bromide (70 mmol), obtained from 1-bromo-4-methoxybenzene (13.4 g, 70 mmol) and Mg (1.5 g, 70 mmol). Purified by column chromatography as for **17b**. Yield: 1.3 g, 44%. Mp 113−118 °C. $[\alpha]^{25}_D$: +25 (*c* 0.012, THF). IR 3538, 3383, 1177, 1098. ^{1}H NMR 2.35 (s, 1 H), 3.24 (s, 1 H), 3.74 (s, 3 H), 3.77 (s, 3 H), 3.79 (s, 3 H), 3.81 (s, 3 H), 4.96 (s, 1 H), 5.07 (d, 1 H), 5.21 (d, 1 H), 5.29 (s, 1 H), 6.5-7.5 (m, 20 H). ^{13}C NMR 55.2, 55.3, 78.1, 78.6, 81.1, 82.0, 104.7, 113.1, 113.3, 113.5, 113.8, 116.5, 118.8, 128.2, 128.4, 129.3, 129.5, 129.6, 135.9, 136.6, 136.6, 138.2, 138.9, 156.0, 158.4, 158.5, 158.8. MS (EI, *m/z*) 650 (M^+). Anal. Calcd for $C_{39}H_{38}O_9$: C, 72.0; H, 5.9. Found: C, 71.5; H, 6.1.

TADDOL 18a. Prepared from ketal **16** (5.5 g, 19 mmol) and PhMgBr (0.56 mol) obtained from bromobenzene (29.4 mL, 0.56 mol) and Mg (13.5 g, 0.56 mol). Purified by column chromatography (SiO_2) with hexanes/EtOAc (80:20) as the eluent to give **18a** as a white solid. Yield: 1.55 g, 15%. Mp 110−115 °C. $[\alpha]^{25}_D$: +53.67 (*c* 0.0086, THF). IR 3550, 3316, 1241, 1169, 1043. ^{1}H NMR 1.33 (s, 3 H), 2.40 (s, 1 H), 2.64 (s, 1 H), 5.12 (d, 1 H), 5.18 (d, 1 H), 5.48 (s, 1 H), 6.7 (d, 2 H), 7.0−7.6 (m, 22 H). ^{13}C NMR 30.1, 78.5, 79.2, 81.7, 83.3, 111.5, 115.3, 126−128 (several peaks), 137.3, 143.2, 143.5, 145.1, 145.2, 155.5. MS (EI, *m/z*) 544 (M^+). Anal. Calcd for $C_{36}H_{32}O_5.H_2O$: C, 76.9; H, 5.9. Found: C, 76, 6; H, 6.0.

TADDOL 18b. Prepared from ketal **16** (3.55 g, 12 mmol) and (*p*-methoxyphenyl)magnesium bromide (0.1 mol) prepared from 1-bromo-4-methoxybenzene (12.5 mL, 0.1 mol) and Mg (2.5 g, 0.1 mol). Purified by column chromatography (SiO_2) with mixtures hexanes/EtOAc (100:0, 100:10, 100:20) as the eluent, to give **18b** as a white solid. Yield: 2.8 g, 35%. Mp 122.5 °C. $[\alpha]^{25}_D$: +55.37 (*c* 0.0051, THF). IR 3355, 1251, 1177, 1034. ^{1}H NMR 1.41 (s, 3 H), 2.75 (s, 1 H), 2.87 (s, 1 H), 3.71 (s, 3 H), 3.76 (s, 6 H), 3.83 (s, 3 H), 5.04 (broad, 2 H), 5.7 (s, 1 H), 6.5−7.5 (m, 20 H). ^{13}C NMR 30.2, 55.1, 78.2, 78.6, 81.9, 83.2, 111.2, 112.9, 113.4, 115.2, 126.4, 127.7, 128.2, 128.6, 129.4, 136.4, 137.3, 137.5, 155.5, 158.2, 158.3, 158.3, 158.6. MS (EI, *m/z*) 664 (M^+). Anal. Calcd for $C_{40}H_{40}O_9 \cdot H_2O$: C,-70.4; H, 6.2. Found: C, 69.9; H, 6.0.

General Procedure for the Preparation of Polymer-Supported TADDOLs 19−24. Obtention of 19. A mixture of TADDOL **17a** (0.314 g, 0.6 mmol), NaH (24 mg, 0.6 mmol), $INBu_4$ (23 mg, 0.06 mmol), and a small amount of 18C6 in dry THF (30 mL) were stirred at rt for 30 min. After that period, a chloromethylated resin (1 mmol Cl/g, 1% DVB, 200 mg, 0.2 mmol) $(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_9H_9Cl)_{0.11}$ was added, and the suspension was refluxed for 48 h. The polymer was filtered and washed with THF (3×), THF/H_2O (1:1) (3×), THF/MeOH (3×), MeOH (3×), CH_2Cl_2 (3×), and acetone (3×) to give resin **19** containing 0.69 mmol of functional group/g (DF = 0.11, 100% conversion). IR 3557, 1179, 1155, 1108, 1029, 1017. ^{13}C NMR (gel phase) 40.7, 69.9, 78.5, 80.8, 81.4, 104.8, 112.7, 115.6, 125−130, 143.0, 144.3. Anal. Calcd for $(C_{10}H_{10})_{0.01}$-$(C_8H_8)_{0.88}(C_{44}H_{38}O_5)_{0.11}$: C, 88.0; H, 7.0. Found: C, 87.9; H, 7.1.

General Procedure for the Preparation of TADDOLs 25 and 26. Obtention of 25. A mixture of TADDOL **17a** (1.5 g, 2.8 mmol), NaH (112 mg, 2.8 mmol), $INBu_4$ (103 mg, 0.28 mmol), and a small amount of 18C6 in dry THF (30 mL) were stirred at rt for 30 min. After that period, benzyl bromide (0.34 mL, 2.8 mmol) was added, and the reaction was refluxed for 24 h. After cooling, a saturated solution of NH_4Cl was added until neutralization. The resulting solution was extracted with EtOAc, and the organic phase was dried (anhyd $MgSO_4$) and vacuum evaporated. The crude product was purified by column chromatography (SiO_2) using hexanes/EtOAc (10/1) as the eluent. Yield: 400 mg, 29%. Mp 80−85 °C. $[\alpha]^{25}_D$: +35 (*c* 0.011, THF). IR 3560, 1608, 1497, 1174, 1026. ^{1}H NMR 4.95 (s, 2 H), 5.23 (d, 1 H), 5.41 (d, 1 H), 5.17 (s, 1 H), 6.8−7.7 (m, 29 H). ^{13}C NMR 70.1, 78.7, 78.8, 81.0, 81.8, 104.9, 113.1, 116.1, 119.5, 127.0, 127.2, 127.3, 127.5, 127.7, 127.8, 128.1, 128.3, 128.4, 128.7, 129.6, 137.0, 138.8, 143.2, 144.4, 144.5, 146.2, 158.9. Anal. Calcd for $C_{42}H_{36}O_5.H_2O$: C,79.0; H, 6.0. Found: C, 78.7; H, 5.9.

TADDOL 26. Prepared from TADDOL **17b** (300 mg, 0.45 mmol). Yield: 250 mg, 78%. Mp 103 °C. $[\alpha]^{25}_D$: +75 (*c* 0.006, THF). IR 3564, 1613, 1496, 1455, 1380, 1265, 1179, 1028, 814. ^{1}H NMR (50 °C) 2.22 (s), 2.26 (s), 2.27 (s), 2.32 (s) (24 H), 4.97 (s, 2 H), 5.42 (s, 1 H), 5.65 (s, 1H), 6.5−8.0 (m, 21 H). ^{13}C NMR (50 °C) 20.8, 22.1, 79.8, 82.2, 112.9, 115.6, 118.9, 128−137 (several overlapped peaks), 158.7. Anal. Calcd for $C_{35}H_{30}O_5$: C,82.0; H, 7.1. Found: C, 81.8; H, 7.4.

General Procedure for the Preparation of Polymer Supported Ti−TADDOL Complexes. A solution of $TiCl_4$ (1 mL of a 1 M solution in toluene) and 1 mmol of $Ti(OCHMe_2)_4$ in 10 mL of dry toluene was stirred at −30°C for 30 min and then at rt for 20 min. After this time the solution was diluted with 10 mL of dry CCl_4 and added to a suspension of the corresponding polymer (**19**−**24**) in dry CCl_4 (16 mL g^{-1} of polymer). The amount of polymer depends on the degree of functionalization and it is calculated to have 2 mmol of TADDOL. The resulting mixture was heated under reflux for 24 h, and after this time the polymer was separated by filtration and thoroughly washed with dry toluene. The loading of titanium was determined by plasma emission spectroscopy.

General Procedure for Diels−Alder Reactions Using Homogeneous Catalysts. A solution of $TiCl_4$ (1 mL of a solution 1 M in toluene) and 1 mmol of $Ti(OCHMe_2)_4$ in 6 mL of dry toluene was stirred at −30°C for 30 min and then at rt for 20 min. After this time a solution of 1 mmol of the corresponding TADDOL (**25**, **26**) in 20 mL of dry toluene, and 3.56 g of molecular sieves (4 Å) were added and stirring was maintained for additional 60 min at 0°C. After this time a solution of 3-crotonoyl-1,3-oxazolidin-2-one (1.395 g, 9 mmol) in 30 mL of dry toluene, and freshly distilled cyclopentadiene (7.92 g, 120 mmol) were added. The mixture was stirred for 24 h. Then 200 mL of 1 N HCl were added, and the mixture was stirred for 15 min. The organic phase was filtered through Celite, and the Celite was washed with 200 mL of 1 N HCl and 200 mL of Et_2O. The organic phase was separated and dried over anhyd Na_2SO_4. The conversion was determined by GC (FID, cross-linked methyl silicone column 25 m × 0.2 mm × 0.33 μm, helium as carrier gas 18 psi, oven temperature program 190°C (1 min), 5°C/min to 200°C (10 min), t_R: **27** 3.6 min, **28**−**31** 7.7 min). The solvent was eliminated under reduced pressure, and the conversion and endo/exo selectivity were determined by ^{1}H NMR integrating the signals corresponding to the methyl group (exo cycloadducts **30** + **31** 0.83 ppm, endo cycloadducts **28** + **29** 1.10 ppm, 3-crotonoyl-1,3-oxazolidin-2-one 1.94 ppm). The endo cycloadducts were purified by column chromatography on silica gel using *n*-hexane:EtOAc (2:1) as an eluent and the spectral data agree with the previously described.[19b] The enantiomeric excess of the endo cycloadducts was determined by ^{1}H NMR in the presence of $Eu(hfc)_3$ (L/S molar ratio 0.3). Under these conditions the signals corresponding to the vinyl protons of the cycloadducts are split (Figure 4). The ee was confirmed by polarimetry, and the mixture of endo cycloadducts coming from the reaction promoted by the complex Ti−TADDOL **25** (Table 3, entry 5) gave $[\alpha]^{25}_D = -62.8$ (*c* 3.36, CCl_4), which, taking into account the specific rotation of the pure enantiomer,[19b] corresponds to a 33% ee of the *2S,3R*-cycloadduct **28**. This determination allowed us to assign the signals in the ^{1}H NMR spectrum to the corresponding enantiomers (Figure 4).

General Procedure for Diels−Alder Reactions with Polymeric Catalysts. A solution of 3-crotonoyl-1,3-oxazolidin-2-one (155 mg, 1 mmol) in 2 mL of dry toluene was added over the corresponding amount of polymeric catalyst (Table 3), and then freshly distilled cyclopentadiene (165 mg, 2.5 mmol) was added. The mixture was shaken, and the reaction was monitored by GC. In some cases additional cyclopentadiene (165 mg, 2.5 mmol) was added after 24 h of reaction. After the corresponding time (Table 3) the catalyst was separated by filtration and thoroughly washed with toluene. The results of the reaction were determined as described above.

Molecular Mechanics Calculations. The torsional Monte Carlo method exploited by the BATCHMIN V3.5 molecular mechanics program, as a part of the MACROMODEL package, was used for the conformational searches of compounds **17** and **18**. Calculations were carried out with the MM2* force field, used as implemented in Macromodel without modification of any of the parameters. For initial calculations, solvent was not considered. When the GB/SA solvation treatment[35] was considered for chloroform, results were very similar in terms of the geometries obtained. Structures were minimized using the conjugate gradient minimization with the Polak−Ribiere first derivative method, and the convergence criterion was a value of 0.05 kJ mol^{-1} $Å^{-1}$ for the root-mean-square of the gradient. All structures were characterized as true minima. For each conformational search, 1000 structures were generated to yield, in general, a high number of unique conformers. The energy interval was selected from 20 to 50 kJ mol^{-1}. Most conformers found could be grouped in two structural families as illustrated for compound **17b** in Figure 1. Conformational searches were carried out in duplicate, in most cases, starting from different geometries, a good convergence of results being obtained.

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