5730 *J. Org. Chem.* **1999,** *64,* 5730−5731

Communications

Synthesis of Catalytically Active Polymers by Means of ROMP: An Effective Approach toward Polymeric Homogeneously Soluble Catalysts

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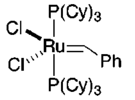
Received March 29, 1999

Polymeric reagents and catalysts have widely been used in organic synthesis.[1] In large-scale industrial processes the application of polymer-supported catalysts is also desirable because it can lead to durable catalytic activity or allow easy catalyst separation.[1,2] A common strategy for the preparation of such catalysts involves the attachment of a previously identified catalytically active subunit to a preformed polymeric support. For the development of chiral catalysts to be used in the synthesis of optically active products, this protocol is particularly difficult because the systematic optimization of reactivity and enantioselectivity is hindered due to the fact that the catalytically active subunits are more or less randomly distributed along an irregular polymer chain. Recently, another synthetic concept was nicely examplified by Pu and co-workers,[3] who introduced a new type of polymeric catalysts having a rigid, highly organized binaphthyl-based chiral backbone. These polymers are prepared by multiple palladium-catalyzed Suzuki couplings of appropriately substituted arenes, and they have successfully been applied in Mukaiyama aldol reactions,[3] diethylzinc additions to aldehydes,[4] and hetero-Diels−Alder reactions.[5] Here, we present an alternative approach for the generation of polymeric multivalent chiral catalysts, which is based on ring opening metathesis polymerization (ROMP)[6] of strained bicyclic olefins. A successful application of this method that leads to homogeneously soluble catalysts is demonstrated.

Encouraged by the results of Kiessling et al.,[7,8] who used Grubbs's commercially available ROMP catalyst **1**[9] for the synthesis of complex carbohydrate-substituted polymers, we envisaged functionalized bicyclic monomers **2** and **3** as appropriate starting materials. This approach has the advantage of being highly modular and thus allows a flexible process optimization by combining independently selected bicyclic frameworks, linkers, and catalytically active subunits. Furthermore, the polymer structure could easily be modified by random copolymerization or systematic block-copolymerization with other olefins[10] and by introduction of backbone chirality, respectively.[11]



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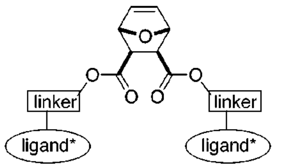

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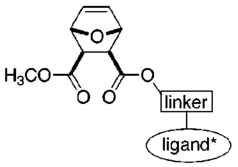

3

ligand* = catalytically active chiral subunit

On the basis of our previous work with **4a**,[12] a chiral hydroxylpyridinyl fragment was selected as the catalytically active subunit. A two-carbon linker was attached to known pyridine (*R*)-**4b**[13] to give (*R*)-**5** in 83% yield. Bicyclic olefin **7** was then obtained by coupling of 2 equiv of (*R*)-**5** with *exo*-7-oxanorbornene anhydride (**6**) under Mukaiyama esterification conditions.[14] This route provides rapid access to monomers bearing two identical homochiral hydroxylpyridinyl residues. Preparation of the unsymmetrical bicyclic monomer **9** was achieved by reacting monomethyl ester **8**[15] with 1 equiv of pyridinyl diol (*R*)-**5**. Standard DCC coupling gave **9**, bearing only a single hydroxylpyridinyl unit, in 94% yield.

ROMP of **7** and **9**, respectively, was accomplished by treatment of their dichloromethane solutions with Grubbs's

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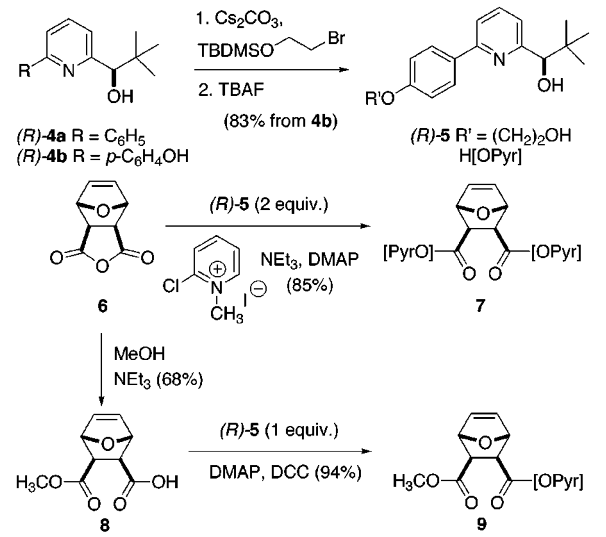
10.1021/jo990533u CCC: $18.00

Table 1. Reaction of Benzaldehyde (10) and Diethylzinc Catalyzed by Various Pyridinyl Alcohols

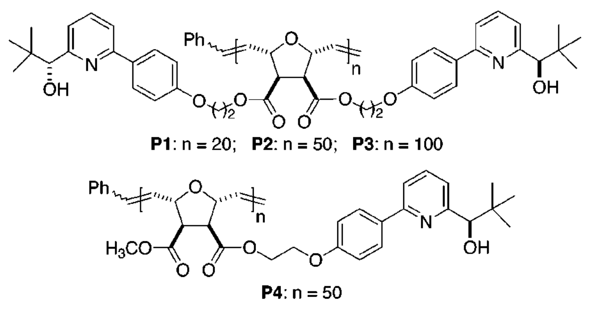
$$\underset{\mathbf{10}}{\mathrm{PhCHO}} + \mathrm{ZnEt_2} \xrightarrow[\text{2. work-up}]{\text{1. catalyst}} \underset{\mathbf{11}}{\mathrm{PhC^{*}H(OH)Et}}$$

pyridinyl alcohol/polymer	M_w/M_n	amount of pyridinyl alcohol (mg/μmol[a])	time (h)	yield of **11** (%)	ee of **11** (%)[d]
4a	–	15.0/62.1	4[b]	91	87
5	–	15.0/49.8	24[c]	86	83
7	–	16.8/44.6	24[b]	72	79
9	–	38.1/79.1	24[c]	89	80
P1	1.2	22.6/60.2	48[b]	88	73
P2	1.4	23.1/61.5	48[b]	83	73
P3	1.7	48.7/130.0	48[b]	77	73
P4	1.1	35.3/73.0	48[c]	78	71

[a] With respect to catalytically active subunits. [b] Reaction was performed at 0 °C. [c] Reaction was performed at room temperature. [d] Determined by HPLC using a chiral stationary phase.



catalyst **1**, affording the corresponding polymers in good to excellent yields (up to 99%). These results convincingly demonstrate the tolerance of the ruthenium catalyst toward the various functional groups in **7** or **9**.[8] The polymeric products were analyzed by ^{1}H NMR spectroscopy (cf. Supporting Information) and by gel permeation chromatography. By comparison of the elution volume of the polymers relative to polystyrene standards, it was estimated that for polymerizations with 2 mol % of **1**, the molecular masses of polymers **P2** and **P4** derived from **7** and **9**, respectively, were about 3 × 10^4 g/mol. Polymers of this size can be easily recovered through ultrafiltration techniques and might find application in continuously operating flow reactors.[16] Varying the monomer-to-catalyst ratio from 50 to 20 and 100 (to give polymers **P1** and **P3**, respectively) allowed the modification of the molecular weight of the polymer (for details cf. Supporting Information).



Next, the catalytic activity of each polymer was evaluated. To allow a comparison with known systems, the well-established addition of diethylzinc to benzaldehyde (**10**) was used as a test reaction.[17,18] All catalyses proceeded under homogeneous conditions in toluene using 5 mol % of catalyst and an excess of diethylzinc (1.5 equiv). The most significant results are summarized in Table 1.

All polymers showed catalytic activity, and optically active 1-phenylpropanol (**11**) was obtained in good yield (Table 1). Compared to the low-molecular weight pyridinyl alcohols **4a**, **5**, **7**, and **9**, the catalytic activity of the polymers **P1**–**P4** is somewhat decreased. Thus, for achieving high aldehyde conversion, longer reaction times were required. Fortunately, we noticed that the enantioselectivity in the product formation was only slightly reduced even though we were using functionalized polymers with a high density of potentially catalytically active sites.[19] For example, catalysis with polymer **P1** gave **11** with 73% ee whereas its monomeric counterpart afforded the same product with 79% ee. As expected from our previous results,[12] (*R*)-configured pyridinyl alcohols gave (*R*)-**11** as the major enantiomer. Variation of the polymer chain length did not influence the enantioselectivity. Thus, with all three polymers (**P1**–**P3**) derived from **7**, 1-phenylpropanol was formed with 73% ee.

In conclusion, we have demonstrated that the ROMP reaction can be used for the synthesis of chiral homogeneous polymeric catalysts which found first application in enantioselective diethylzinc additions to benzaldehyde.

Acknowledgment. This work was supported by Katalyseverbund NRW, Deutsche Forschungsgemeinschaft (DFG; Graduiertenkolleg), Volkswagenstiftung, and Fonds der Chemischen Industrie. We are grateful to Witco and Degussa-Hüls for the generous donation of chemicals.

Supporting Information Available: Detailed experimental procedures, characterization of all new compounds, and the analyses of chiral alcohols **4b** and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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