Dendrimers Containing Chiral Ferrocenyl Diphosphine Ligands for Asymmetric Catalysis

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The preparation and characterization of dendrimers containing transition-metal-complex fragments has received considerable attention in recent years,[1] and the aspect of chirality in dendritic architectures[2] has been recognized as a multifaceted problem most recently.[3] However, the application of chiral organometallic dendrimers in asymmetric catalysis is a field still very much in its infancy.[4] Because of the proven efficacy of chiral ferrocenyl ligands in a number of asymmetric catalytic reactions,[5] we set up a study aimed at incorporating such ligands into dendritic structures. Thus, well-defined, high-molecular multicenter catalysts offer a potential solution to the notorious problem of catalyst recovery, by virtue of, e.g., nanofiltration or precipitation. We report herein the preparation of dendritic ligands containing up to eight ferrocenyl diphosphines, as well as first selected applications in hydrogenation reactions.

One of us has previously developed the synthesis of the Josiphos derivative (*R*)-(*S*)-**1** as a precursor for the immobilization of such ferrocenyl ligand on a variety of supports.[6] In the present work (*R*)-(*S*)-**1** was chosen as starting material because it fulfills two important criteria. First, the necessary functional group, a primary amine, is well suited for the construction of dendritic structures using amide connectivities, and is placed at a remote position from the phosphine fragments. This minimizes the steric interactions that could alter the delicate conformational properties of the chelate ring of the catalyst. Second, the chain length of the tether appears to be sufficient to ensure conformational flexibility at the periphery of the dendrimer.

Thus, a slight excess of (*R*)-(*S*)-**1** cleanly reacts with benzene-1,3,5-tricarboxylic acid trichloride (**2**)[7] and adamantane-1,3,5,7-tetracarboxylic acid tetrachloride (**3**),[8] affording the first generation dendrimers **4** and **5**, respectively, in good yields after chromatographic purification.[9] With a view to preparing dendrimers of the second generation, intermediate **7** was obtained, after deprotection, from the reaction of (*R*)-(*S*)-**1** with 5-(*tert*-butyldimethylsiloxy)isophthaloyl dichloride (**6**),[10] in 92% yield (Scheme 1). Hence, macromolecules **8** and **9** (Chart 1), containing six and eight ferrocenyl units, respectively, were prepared in excellent yields when building block **7** was reacted with the acid chlorides **2** and **3**. For the efficient formation of the ester connections the addition of catalytic amounts of 4-(pyrrolidino)pyridine was necessary.[9]

All new multiple ferrocenyl ligands display relatively simple NMR characteristics and are monodisperse.[9] As one would expect, in the ^{31}P NMR spectra of compounds **4**, **5**, **7**, **8**, and **9** only one pair of doublets is observed, with the typical long range $^4J_{PP}$ coupling constant of ca. 34 to 37 Hz. This indicates the equivalence of the ferrocenyl units. The larger dendrimers **8** and **9** show broad signals in the ^{1}H NMR 300 MHz spectra at room temperature, possibly indicating slow conformational equilibria in the sterically rather crowded inner core of the dendrimers. However, well-resolved spectra for these two compounds are obtained when corresponding DMSO-d_6 solutions are measured at 80 and 120 °C, respectively. The new high-molecular-weight compounds were also characterized by MALDI-TOF mass spectrometry.[11] Molecular peaks at *m*/*z* values in very good agreement with the calculated ones, as well as in-source fragmentation[11c] patterns very similar to those of the "monomeric"

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Scheme 1

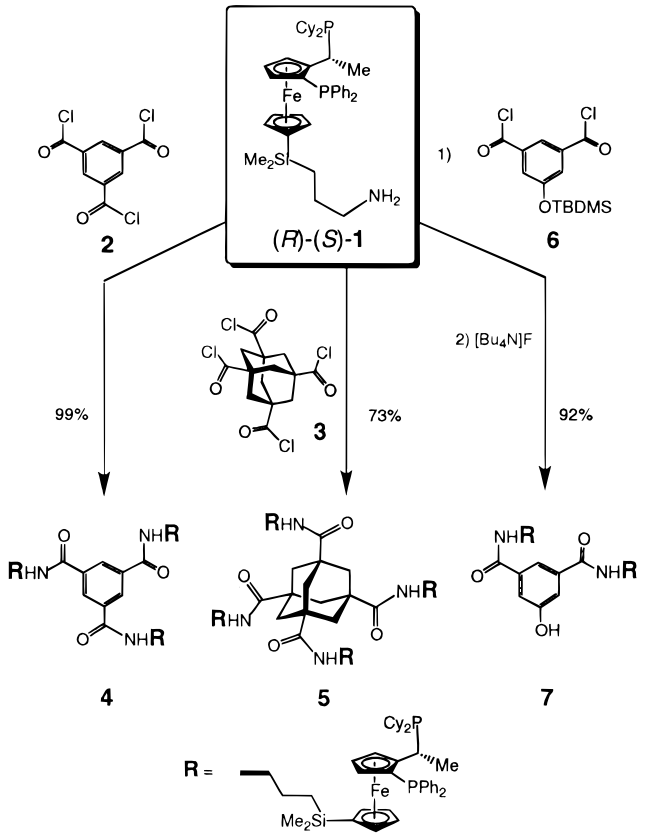
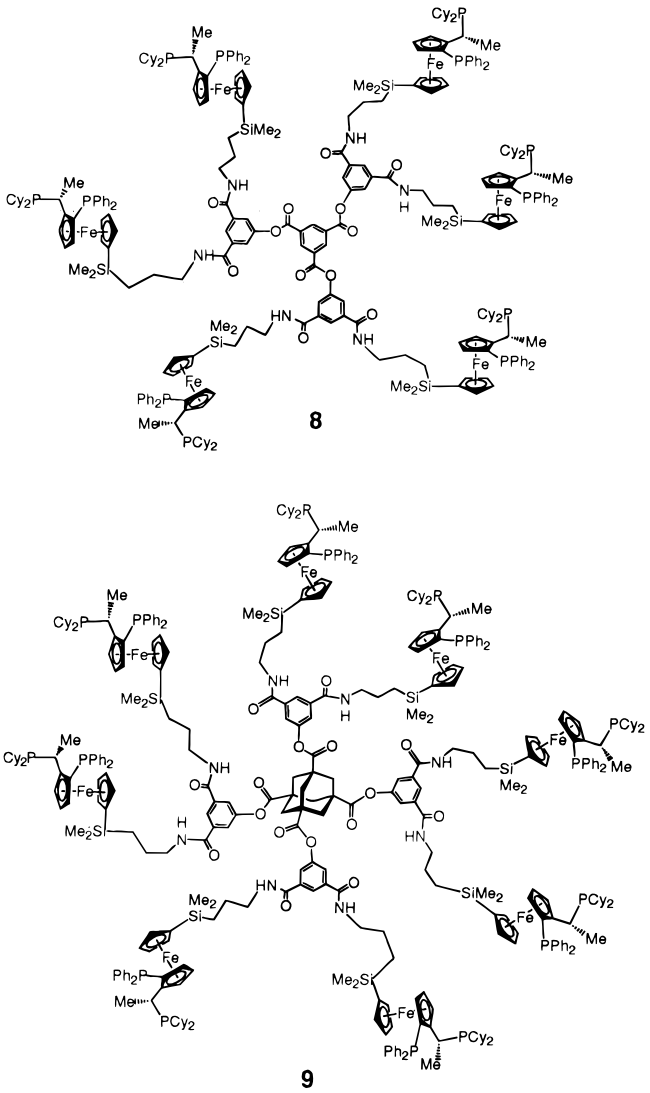


Chart 1



counterpart Josiphos under EI conditions, were observed (MALDI TOF spectra of **8** and **9** are provided as Supporting Information).[12]

To gain insight as to the behavior of the new dendritic ligands in catalytic reactions, the simple Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate in MeOH was chosen as a standard reaction for comparing their performances. In situ catalyst preparation was attained by mixing the ligand (1 equiv/number of ferrocenyl units) with 1 equiv of $[Rh(COD)_2]BF_4$ in CH_2Cl_2 and stirring for 15 min under Ar. The orange solid obtained after evaporation of the solvent was used as a catalyst precursor. ^{31}P NMR spectra of these materials showed a single AMX spin system, as expected when all ferrocenyl sites are bonded to Rh.[9] Hydrogenation experiments performed with 1 mol % Rh under 1 bar of hydrogen pressure[12] gave very similar results. In all cases hydrogen take-up ceased after ca. 20 min, and substrate was no longer detectable. The enantioselectivities afforded by the dendritic catalysts (98.6% ee for **4**, 98.7% ee for **5**, 98.1% ee for **8**, and 98.0% ee for **9**) are only slightly lower than that obtained with the corresponding mononuclear Josiphos catalyst (99.0% ee). However, a weak trend to lower enantioselectivities seems to parallel the increasing size of the dendritic ligands. In conclusion, we presented a straightforward and high-yield synthesis of the first multiple site nanoscopic ligand system (the estimated molecule size is ca. 3 nm across for **8** and **9**[13]) suited for applications in highly enantioselective hydrogenation reactions. Preliminary experiments indicate that these materials are completely retained by a commercial nanofiltration membrane.[14] This is a fundamental prerequisite for the use of our dendritic catalysts in a membrane reactor, currently being pursued. Moreover, studies with larger dendrimers (third generation), as well as applications to other catalytic reactions, are presently being carried out to better evaluate the influence of the dendrimer backbone, combined with the effect due to the high local catalyst concentration, on stereoselectivity. Finally, we are performimg a synthetic approach aimed at introducing the ligand fragment attached to the stereogenic center *after* assembling the dendrimer. Results on these lines will be reported in due course.

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Supporting Information Available: Procedures for the preparation and characterization details for **1**, **4**, **5**, **7**, **8**, and **9**, including systematic compound names according to the cascade nomenclature proposed by Newkome et al.[1a] (11 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(14) A Millipore, Centricon-3 membrane with pore size of 3 kD was used for experiments with MeOH solutions of catalysts derived from dendrimers **8** and **9**.