might arise from thermal populations of ground- and excited-state manifolds. Complex **1** provides the first example of such behavior in a Mn(III/IV) model complex.

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Supplementary Material Available: Tables of fractional atomic coordinates, thermal parameters, bond distances, and bond angles for all atoms (Tables 1-4), P-band EPR spectrum of **1** at 20 K (Figure 3), and complete numbering scheme for **1** (Figure 4) (16 pages); table of observed and calculated structure factors (Table 5) (28 pages). Ordering information is given on any current masthead page.

Tailored Ligands for Asymmetric Catalysis: The Hydrocyanation of Vinylarenes

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Despite the enormous progress made in enantioselective synthesis during the last decade, the development of asymmetric, metal-catalyzed carbon-carbon bond forming reactions remains a challenging area of research.[1] In this communication we report our initial findings on the asymmetric Markovnikov addition of HCN to vinylarenes in the presence of Ni(0) complexes of 1,2-diol phosphinites derived from readily available sugars.[2] The enantioselectivity of this reaction has been optimized by steric and electronic tuning of an easily modified ligand system (Figure 1), and ee's (enantiomeric excesses) up to 85% have been achieved. Vinylarenes constitute an important class of substrates for this reaction because the resulting 2-aryl-2-propionitriles are potential precursors for a variety of commercially important non-steroidal antiinflammatory agents.[3,4] Historically, the only significant asymmetric inductions observed for this important carbon-carbon bond forming reaction[5] have been limited to norbornene derivatives,[6] and the highest selectivity reported thus far is 40% ee for a low-yielding hydrocyanation of norbornene at 120 °C.[6b,c]

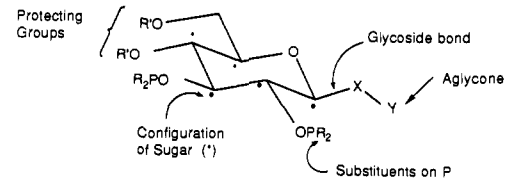
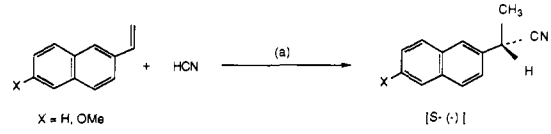


Figure 1. Tunable sites on a diol phosphinite ligand system.

Because of the current commercial importance of the well-known antiinflammatory drug naproxen, we chose 6-methoxy-2-vinylnaphthalene (MVN) and 2-vinylnaphthalene (2-VN) as prototypical substrates for our initial studies. Addition of HCN to these substrates, carried out according to the protocol in the equation below, gave the corresponding 2-naphthalene-2-propionitriles with unprecedented enantioselectivity.[7] In sharp contrast to the well-known Pt-catalyzed carbonylation of vinylarenes,[8] no trace of the linear product was detected under these conditions.[8,9]



(a) 0.001 to 0.05 equiv [Ni]:L* to Ni ; 1.3 - 2.0; rt
[Ni] = $Ni(COD)_2$; L* = 1,2-diolphosphinite

Initial screening of a variety of 1,2- and 1,3-diol phosphinites prepared from readily available mono- and disaccharides[10a] indicated the overwhelming importance of the gluco configuration of the sugar backbone and the juxtaposition of a β-aryl *O*-glycoside (X-Y = *O*-aryl in Figure 1) for high enantioselectivity. While the steric and electronic manipulations of the aglycone (Y in Figure 1) yielded a modest, yet discernible, improvement on the

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(7) In a typical scouting reaction, a solution of $Ni(COD)_2$ (0.009 g, 0.033 mmol) in about 1 mL of benzene was added to a solution of the chiral ligand (0.042 mmol) in about 1 mL of benzene under an N_2 atmosphere, stirred for 30 min, and added to the vinylarene (0.65 mmol). The reaction mixture was brought to the specified temperature, and HCN (0.600 mL, 0.22 M in toluene, 0.13 mmol) was added by syringe or autopipet. The reaction mixture was analyzed by GC and HPLC after about 3-4 h of stirring. Yields typically ranged from 5 to 100%. ee's were determined (on a sample filtered through silica gel; ether/hexane) by HPLC using either a Daicel Chiralcel OJ or OB column: 5% *i*-PrOH/hexane, 1 mL/min, 40 °C. For MVN the faster eluting enantiomer was determined to be the *S* isomer by comparison to an enriched sample prepared from (*S*)-naproxen via dehydration of the amide. In preparative runs with the best catalysts (entries 4a,b), up to 2.5 equiv of HCN and 0.1-1.0 mol % of Ni was used in appropriate solvents and the product (>85 % yield) was isolated by column chromatography. Optically pure (*S*)-(-)-6-methoxy-2-naphthalene-2-propionitrile (mp 99-100 °C; >99 % ee; $[\alpha]^{25}_D = -28.4°$, *c* 1, $CHCl_3$) may be prepared by two recrystallizations of enriched (75-85% ee) nitrile using ether/hexanes as the solvent system. (See supplementary material for details.)

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(10) (a) These include phosphinites from galactose, fructofuranose, lactose, and trehalose. The importance of the sugar backbone is evident from the low ee's observed upon using bis[3-(trifluoromethyl)phenyl]phosphinite from *R*-binaphthol and (*S,S*)-1,2-*trans*-cyclohexanediol (32 and 7% ee respectively for 6-methoxy-2-vinylnaphthalene). For a more complete list, see supplementary material. (b) See supplementary material.

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Table I. Electronic and Solvent Effects on Hydrocyanation Selectivity[a]

entry	R	selectivity (ee, %) 2-VN	MVN	solvent
1	Ph	46	40 (29)	benzene (THF)
2	3,5-$(CH_3)_2C_6H_3$	25	16	benzene
3	3,5-$(F)_2C_6H_3$	75	77	hexane
4a	3,5-$(CF_3)_2C_6H_3$	74	78	benzene[b]
4b	3,5-$(CF_3)_2C_6H_3$		85	hexane or C_6F_6[c]

[a] See Figure 1 for X, Y, and R; XY = OPh. 4,6-Hydroxyls were protected as the benzylidene acetal, R'-R' = PhCH. See footnote 7 for reaction protocol and analytical procedures. [b] 0.001 equiv of catalyst yielding 769 turnovers with 2.5 equiv of HCN in toluene. [c] 100% conversion (85% ee) for MVN with 2.5 equiv of HCN in C_6F_6.

selectivity of the reaction,[10b] substituents on the ligating phosphorus had a more pronounced effect. Several examples of these ligands derived from β-phenyl glucoside and their respective selectivities are shown in Table I. From this study, we found that *electron-withdrawing substituents on phosphorus-linked aryl groups dramatically enhance the enantioselectivity*. Such electronic effects of ligands on the enantioselectivity are rare, and as in the well-documented case of Mn(III)-mediated epoxidation reactions,[11] these may play an important role in the design of new catalysts. The highest enantioselectivities are obtained in nonpolar solvents ($C_6F_6 \approx$ hexane > benzene > THF), while increasing the reaction temperature decreases the enantioselectivity. Other factors such as the extent of reaction, Ni to substrate ratio, and ligand to Ni ratio[12] do not affect the observed enantioselectivity.

Remarkably, the highly enantioselective 3,5-$(CF_3)_2C_6H_3$ catalyst derivative also exhibits very high activity in the hydrocyanation of MVN. Catalytic activities as high as 552 turnover numbers/h (769 total) have been measured at 25 °C for the hydrocyanation of MVN using 0.13 mol % of this ligand and 0.1 mol % of Ni. By comparison, at 25 °C this catalyst is an order of magnitude more active than the commonly used NiP(*p*-$OC_6H_4CH_3)_4$ catalyst.[4,5] Using this catalyst, the naproxen precursor (*S*)-(−)-6-methoxy-2-naphthalene-2-propionitrile has been prepared in an optically pure form for the first time by recrystallization of the resulting product.[7]

Even though the enantioselectivity of our system has been optimized only for the naproxen precursor, we briefly investigated the selectivity in a number of other vinylarenes in the presence of the diphenylphosphinite ligand (R = Ph; XY = OPh) and the corresponding bis[bis(trifluoromethyl)phenyl]phosphinite derivative (R = 3,5-$(CF_3)_2C_6H_3$; XY = OPh). Listed below are the respective ee's for these ligands under our standard conditions: 4-isobutylstyrene, 10 and 50; 4-phenyl-3-fluorostyrene, 10 and 55; acenaphthylene, 0 and 59; 1-vinylnaphthalene, 63 and 68. In each case, the overall yield and the enantioselectivity with the electron-deficient phosphinite systems are unprecedented, and the unmistakable electronic effect on the ee has been confirmed.

Further studies on the asymmetric hydrocyanation reaction and applications of this ligand system in other reactions will be reported in due course.

Acknowledgment. We gratefully acknowledge the invaluable technical assistance of Mrs. M. S. Beattie, Ms. E. A. Duvall, and Ms. K. G. Messner.

Supplementary Material Available: Descriptions of typical experimental procedures for the synthesis of key ligands and hydrocyanation reactions (9 pages). Ordering information is given on any current masthead page.

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(12) Ligand to Ni ratios greater than 2 inhibit the hydrocyanation reaction.

Enantioselective Hydrogenation of the C=N Group: A Catalytic Asymmetric Reductive Amination Procedure

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In contrast to the high enantioselectivities observed in both catalytic olefin[1] and keto group[2] hydrogenations, only limited success has been achieved in the catalytic asymmetric hydrogenation of the C=N group in compounds such as imines.[3] We recently described[4] a new homochiral series of 1,2-bis(phospholano)benzenes (Me-, Et-, and *i*-Pr-DuPHOS) and now demonstrate a unique and general application of these ligands in the rhodium-catalyzed asymmetric hydrogenation of the C=N group of *N*-acylhydrazones **1** (Scheme I).

Hydrogenation of the *N*-benzoylhydrazone of acetophenone (**1a**: R = R'' = Ph; R' = Me) proceeded readily under mild conditions (20 °C, 0.1 mol % catalyst, 1 atm of H_2, 1 h) using [(COD)-Rh(DuPHOS)]$^+CF_3SO_3^-$ as catalyst precursors. Of the three DuPHOS ligands, Et-DuPHOS proved to be superior in terms of enantioselectivity, providing the product *N*-benzoylhydrazine **2a** in 88% ee. Analogous rhodium catalysts bearing chiral phenylphosphines such as BDPP, CHIRAPHOS, and BINAP hydrogenate hydrazone **1a** relatively slowly, and with low enantioselectivity (9% ee, 23% ee, and 20% ee, respectively). The carbonyl function of the hydrazones **1** appears to be the crucial structural feature required for these hydrogenations to proceed; no hydrogenation was observed with either the *N*-phenylimine or the *N*-phenylhydrazone of acetophenone under the mild conditions used for hydrazones **1**. Substrate chelation to the cationic rhodium center most likely occurs initially via the carbonyl oxygen and the nitrogen of the hydrazone moiety. Complexes containing *N*-acylhydrazones which chelate in this fashion have been structurally characterized.[5]

In the hydrogenation of a series of *N*-aroylhydrazones **1**, 2-propanol was the best solvent found with respect to enantiose-

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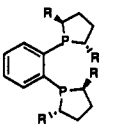

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