Nickel(II)-Catalyzed Highly Enantioselective Hydrophosphinination of Methacrylonitrile

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Chiral phosphines, as ligands in transition metal complexes, efficiently create asymmetric catalysts for enantioselective transformations.1 However, chiral phosphines are expensive, and their syntheses frequently require a resolution or are limited to the use of starting materials derived from enantiopure natural products. An alternative synthetic strategy might involve the enantioselective transition-metal-catalyzed addition of a P–H bond to a C=C double bond (eq 1).2

Although hydrophosphinations have proven valuable for the synthesis of achiral or chiral phosphines (when involving stereospecific reactions),3–7 methodologies for enantioselective P–H additions are limited. Among the few asymmetric catalysts, Pt0 (MeDuponh) complexes catalyze hydrophosphinations of Michael acceptors via P–H bond oxidative addition and olefin insertion, but unfortunately the reaction’s enantioselectivity is low.8 Additionally, lanthanide-catalyzed intramolecular hydrophosphinations give chiral cyclic phosphines with good diastereometric ratios.9 Interestingly, the mechanisms of lanthanide-catalyzed hydrophosphinations and hydroaminations appear to be closely related.10

We have recently described enantioselective intermolecular hydrorearrangements of vinyl nitriles that are catalyzed by the dicationic nickel complex [Ni(Pigiphos)(THF)](ClO4 )2 ([1]ClO4 ) containing the C1-symmetric trisphosphine Pigiphos (Scheme 1; the (R)-(S)-enantiotomer of Pigiphos was used exclusively).11,12

Preliminary studies suggested that coordination of the vinyl nitrile to the dicationic NiII center activates its C=C bond toward 1,4-addition of the amine. On the basis of this proposal, we speculated that [1](ClO4 )2 might also catalyze hydrophosphinations. Herein, we report a new method for the preparation of a series of enantioenriched (2-cyanopropyl)phosphines and present results that implicate 1,4-conjugate addition for P–C bond formation.

Initially, we attempted the nickel-catalyzed addition of Cy2PH (2a) to methacrylonitrile under conditions similar to those developed for our hydrorearrangements (5 mol % [1](ClO4 )2 in THF).12 After 1 h, the 31P(1H) NMR spectrum of the reaction mixture displayed a new singlet at −8.12 ppm. Unfortunately, the reaction did not proceed to completion under these conditions even after extended reaction times (<2 weeks). However, under optimized conditions (methacrylonitrile as solvent and 10 mol % [1](ClO4 )2), the reaction is complete after ca. 5 h at room temperature. Three multiplets (2.18, 1.48, and 1.44 ppm, 1 H each) in the 1H NMR spectrum of the product indicated the formation of the anti-Markovnikov addition product Cy2PCH2CHMeCN (3b). The ee (65%) was determined by coordination of 3a to an enantiopure chiral Pd complex.8,13

We then surveyed the reaction of a few primary and secondary phosphines with methacrylonitrile in the presence of [1](ClO4 )2 at room temperature. Ph2PH (2b, 10 equiv) forms Ph2PCH2CHMeCN (3b) quantitatively, but with low ee (14%). Mes2PH does not react (only starting material is detected by 1H and 31P[1H] NMR spectroscopy) after 2 weeks at room temperature, and the primary phosphines CyPH2 and (1-MeCy)PH2 do not give isolable hydrophosphination products. The best results are obtained for the reaction of methacrylonitrile and Bu3PH (2c, 98 equiv) to form Bu3PCH2CHMeCN (3c, 65% ee).

Noting that the bulky dialkylphosphines gave more promising results, we focused on the effects of the counterion, solvent, and temperature in the Ni-catalyzed reaction of Bu3PH and methacrylonitrile (Table 1). The enantioselectivities follow the trend F3CCH2OH < thf ≈ methacrylonitrile < acetonitrile, and the use of [1](BF4 )2 gives lower enantioselectivities than observed with [1](ClO4 )2 at room temperature (Table 1, entries 1–5). However, addition of i-Pr2PH or (1-adamantyl)2PH to a −78 °C acetonitrile solution of [1](BF4 )2 and methacrylonitrile affords 3e in 84% ee (entry 6). The highest enantioselectivity is obtained from [1](ClO4 )2 in acetonitrile at −25 °C (entry 7, 89% ee). The catalyst is highly active under these conditions, giving 600 turnovers after 48 h and 900 turnovers after 1 week (0.1 mol % catalyst). Hydrophosphinations with Pr2PH or (1-adamantyl)2PH to give 3d (49 turnovers, 24 h, 69% ee) or 3e (100 turnovers, 96 h, 94% ee) are also optimal in acetonitrile at −25 °C (Table 2).14 Although the Pigiphos ligand is sterically demanding, conversion and enantioselectivity of the hydrophosphination are apparently enhanced by bulky, nucleophilic phosphate substrates.

This suggests a pathway involving coordination of methacrylonitrile to the nickel center followed by nucleophilic attack of the secondary phosphate. To investigate this possibility, methacrylonitrile...
trile (1–10 equiv) was added to a mixture of Pigiphos and \([\text{Ni-(H}_2\text{O)}_6]\)(ClO_4)_2 in THF-\(d_8\) to form \([\text{Ni}(\text{Pigiphos})(\text{NCMeCCH}_3)]-(\text{ClO}_4)_2\) and \([5](\text{ClO}_4)_2\). The \(3^1\)P chemical shifts and coupling constants for \([5](\text{ClO}_4)_2\) and the acetonitrile complex \([\text{Ni}(\text{Pigiphos})(\text{NCCH}_3)]-(\text{ClO}_4)_2\) are similar, suggesting that in solution the methacrylonitrile is coordinated to Ni via the nitrile nitrogen.\(^{15,16}\) This bonding mode is maintained in the solid state, as evidenced by the X-ray crystal structure illustrated in Figure 1. In the dication \([5]^2+\), the nickel atom is bonded to its ligands in a distorted square planar geometry,\(^7\) in which the nickel dication and nitrogen atom of the nitrile are displaced 0.33 and 1.15 Å, respectively, from a plane defined by the three phosphorus atoms. Notably, the two axial faces of the complex are distinguished by this displacement, and the methacrylonitrile ligand is sterically contained within a chiral environment created by the \(\text{Ph}_2\text{P}\) phenyl groups.\(^1\)

Reaction of \([5]^2+\) and \(\text{R}_2\text{PH} (\text{R} = \text{Cy}, \text{Ph}, \text{‘Bu}; 1–2\text{ equiv})\) in THF-\(d_8\) gives \(\text{R}_2\text{PCH}_2\text{CHMeCN}\). Furthermore, yields and enantioselectivities of hydrophosphination products from \([1](\text{ClO}_4)_2\) and \([5](\text{ClO}_4)_2\) as catalysts are indistinguishable. These results suggest that the dication \([5]^2+\) is an intermediate in the catalytic cycle (Scheme 2). Note that in this mechanism, \(\text{P–C}\) bond formation produces a phosphonium ion and an axially chiral azazaenyll ligand coordinated to the chiral \([\text{Ni}(\text{Pigiphos})]^2+\) fragment (i.e., two diastereoisomers of type A). Stereospecific proton transfer from the pendant phosphonium to the \(\text{N} = \text{C} = \text{CRR}^2\) carbon of each diastereoisomer generates the \(\sigma\)-stereogenic center. Compound \([5](\text{ClO}_4)_2\) is also an intermediate in the \([1](\text{ClO}_4)_2\)-catalyzed asymmetric hydromination.\(^{12}\) Accordingly, there are similar solvent and counterion effects in the hydromination and hydrophosphination reactions. Additionally, the absolute configuration of the major enantiomer of hydromination and hydrophosphination, respectively, demonstrates that the sense of chiral induction is the same in both reactions.\(^{15,17}\)

These similarities suggest that \([\text{Ni}(\text{Pigiphos})(\text{L})]^2+\) complexes may be able to catalyze the asymmetric addition of other \(\text{E}–\text{H}\) nucleophiles to vinyl nitriles for the synthesis of highly enantioenriched organic compounds containing main group elements. Along these lines, we are currently working to further develop the synthetic utility of this class of asymmetric transformation.

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Supporting Information Available: Experimental section including X-ray crystallographic data for \((\text{ClO}_4)_2\) and for the complexes used in the determinations of absolute configurations (PDF, CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

17. (a) See Supporting Information. (b) Absolute configurations were determined by X-ray crystallographic analysis of adducts derived from 3 and an enantiopure PhP complex of known absolute configuration. Note that the sense of chiral induction is the same in both reactions, although the descriptor of the absolute configuration of the major enantiomers changes from \(\text{S}\) (hydroamination) to \(\text{R}\) (hydrophosphination) due to different priority sequences of the substituents at the respective stereogenic center.

(Right)