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Internal Alkene Hydroaminations Catalyzed by Zirconium(IV) Complexes and Asymmetric Alkene Hydroaminations Catalyzed by Yttrium(III) Complexes

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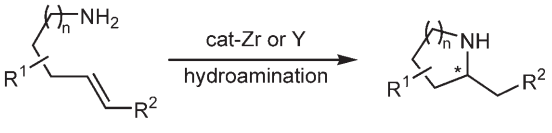
This paper is dedicated to Professor Eun Lee on the occasion of his 60th birthday.

Abstract: The thiophosphinic amide **2** was prepared in 68% yield by the reaction of 2,2-dimethyl-1,3-propanediamine with diisopropylchlorophosphine followed by the addition of sulfur. Attachment of the proligand **2** to zirconium was achieved by direct metalation with $Zr(NMe_2)_4$ in benzene-d_6 or toluene-d_8 to afford complex **3** *via* elimination of dimethylamine. The neutral Zr(IV) complex **3** has been shown to be an effective precatalyst for intramolecular alkene hydroaminations that provide cyclic amines in good to excellent yields. A variety of chiral ligands (**20**, **22**, **24**, and **25**–**30**) were prepared for asymmetric internal alkene hydroaminations. Metalation of chiral ligands to yttrium was accomplished with $Y[N(TMS)_2]_3$ in benzene-d_6 or toluene-d_8 to give complexes. Treatment of **7** with 5 mol% of **33** in benzene-d_6 (25 °C, 18 h) or toluene-d_8 (25 °C, 15 h) afforded 2,4,4-trimethylpyrrolidine **14** in 95% yield (61% *ee*).

Keywords: asymmetric hydroamination; catalysis; cyclization; yttrium; zirconium

Introduction

The catalyzed intramolecular hydroamination of alkenes constitutes a powerful method for the synthesis of nitrogen heterocycles.[1] A variety of novel non-metallocene complexes[2] of group 3 metals as catalysts for this reaction has recently been added to the group 3 metallocene catalysts developed by Marks and co-workers.[3] Although there are many reviews that describe both the intra- and intermolecular hydroamination of alkynes[4a–d] and allenes[4e,f] catalyzed by various complexes of the group 4 metals, there have been only very few reports of intramolecular alkene hydroaminations mediated by complexes of metals belonging to this group. Recently, we communicated Zr-catalyzed intramolecular alkene hydroaminations,[5] and Schafer and Hultzsch found that Ti-$(NMe_2)_4$[6] and cationic species[7] of the group 4 metals were efficient for alkene hydroaminations. Also, Livinghouse has previously reported that chelating bis-(thiophosphinic amidate), "NPS", complexes of the group 3 metal (yttrium) are potent catalysts for intramolecular alkene hydroamination.[2i] In this paper, we show that the neutral Zr(IV) bis(thiophosphinic amidate) complex is an efficient precatalyst for the cyclization of representative primary aminoalkenes. Also, the chiral Y(III) bis(thiophosphinic amidate) complexes obtained from chiral ligands (**20**, **22**, **24**, and **25**–**30**) and $Y[N(TMS)_2]_3$ were evaluated for the catalytic asymmetric intramolecular hydroamination of alkenes (Scheme 1).



R^1 = Me, Me_2
R^2 = H, Ph
n = 1, 2

Scheme 1.

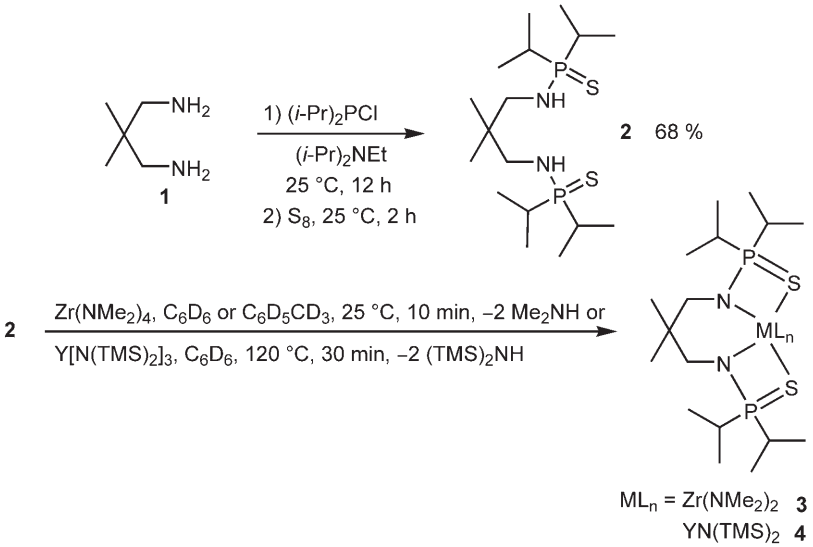
Results and Discussion

Preparation of Ligand, Precatalyst, and Aminoalkenes

The thiophosphinic amide **2** used in this study was prepared in 68% yield by the reaction of 2,2-dimethyl-1,3-propanediamine with diisopropylchlorophosphine (2.0 equivs.) followed by the addition of sulfur (2.1 equivs.) (Scheme 2). Attachment of the proligand **2** to zirconium was quantitatively achieved by direct metalation with 1 equiv. of $Zr(NMe_2)_4$ in benzene-d_6 or toluene-d_8 (25 °C, 10 min) to afford complex **3** *via* dimethylamine elimination. The ^1H, ^{13}C, and ^{31}P NMR spectra of **3** are consistent with a monomeric species possessing an octahedral structure in which both dimethylamino ligands are axial. The NMe_2 resonance (500 MHz) appears as a sharp singlet at $\delta = 3.11$ and the linker CH_2 as a doublet ($\delta = 2.69$, $J = 10$ Hz). The signal for the CH adjacent to P appears as a well defined octet centered at $\delta = 2.00$ ($J = 7$ Hz), with the diastereomeric isopropyl methyls appearing as a set of doublets between $\delta = 1.16$ and 1.10 ($J = 7$ Hz). The ^{31}P NMR spectrum of **3** reveals a singlet at $\delta = 75.10$. The thermal stability of **3** was demonstrated by heating at 150 °C for 19 h, whereupon no alteration of the NMR spectra was detected. Precatalyst **4** was obtained from the reaction of **2** with $Y[N(TMS)_2]_3$ in benzene-d_6 (120 °C, 30 min) *via* elimination of bis(trimethylsilyl)amine.

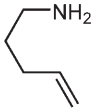
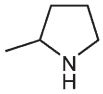
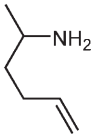
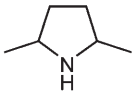
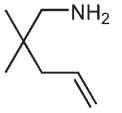
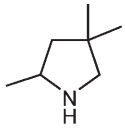
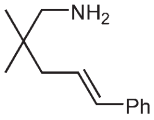
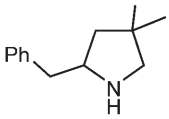
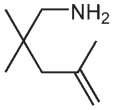
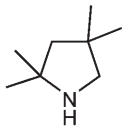
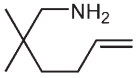
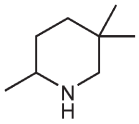
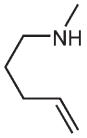
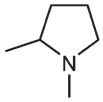
Intramolecular Hydroaminations of Aminoalkenes Catalyzed by Zirconium(IV) Complexes

The internal hydroamination of 2,2-dimethyl-4-penten-1-amine (**7**) was selected for initial examination as it was expected that cyclization of this substrate would be facilitated by the *gem*-dimethyl effect.[8] Addition of **7** to **3** (5 mol%), followed by heating at 100 °C for 105 h, then afforded the pyrrolidine **14** in 97% yield by NMR. Alternatively, cyclization of **7** at 120 °C (benzene-d_6) and 150 °C (toluene-d_8) provided **14** in 94% (12 h) and 98% (2.5 h) yield, respectively. Closely-related reaction conditions were subsequently utilized for the cyclization of a series of representative primary amines **5**, **6**, **8**, **9**, and **10**, albeit unsuccessfully for the secondary amine **11**. A compilation of reaction times and yields observed for the cyclization of aminoalkenes **5**–**11** in the presence of the Zr(IV)·NPS chelate **3** appears in Table 1. Significantly, cyclization of **6**, **7**, and **8** on a preparative (3.0 mmol) scale in toluene, followed by separation of the products from the catalyst by vacuum transfer and protonation (HCl-MeOH), furnished **13**, **14**, and **15** as their hydrochloride salts in 88, 90, and 85% isolated yields, respectively. Several of the trends that emerge from the previous examples are worthy of comment. The occurrence of the *gem*-dimethyl effect is helpful but not a prerequisite for successful cyclization, as 4-penten-1-amine (**5**) and 5-hexen-2-amine (**6**) partake in the reaction. Accordingly, **5** was smoothly converted to **12** in 91% yield by NMR in the presence of **3** (10 mol%) in 10 h at 150 °C. By way of comparison, cyclization of **5** using $Zr(NMe_2)_4$ as the precatalyst (10 mol%, 150 °C, toluene-d_8) gave **12** (91%) but required 28 h. Therefore, the Zr(IV)·NPS complex **3** shows higher activity as a precatalyst than $Zr(NMe_2)_4$. In addition, the styrenyl substrate **8**, containing an internal alkene, underwent cyclization at 150 °C to provide **15** in 93% yield after 120 h. In this instance, the reaction time could be shortened to 39 h when 10 mol% of the precatalyst was employed. A similar result was observed in the case of the 1,1-disubstitut-



Scheme 2. Preparation of the ligand and precatalyst.

Table 1. Intramolecular hydroaminations of aminoalkenes.[a]

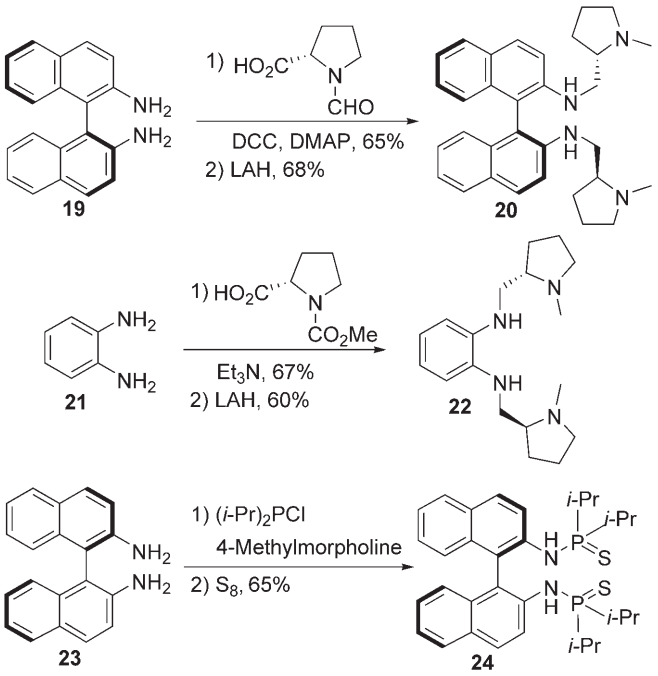
Entry	Aminoalkenes		Temp [°C]	Time [h]	Product		Yield [%][b]
1		**5**	120[c]	41		**12**	89
2			150[c]	10			91
3		**6**	120	172		**13**	98[d]
4			150	22			96 (88)[d,e]
5			60	1			95[f,g]
6		**7**	120	12		**14**	94 (90)[e]
7			150	2.5			98
8		**8**	150	120		**15**	93
9			150[c]	39			91 (85)[e]
10		**9**	150	104		**16**	92
11			150[c]	45			94
12		**10**	120	9		**17**	99
13			150	1			99
14		**11**	150	18		**18**	0

[a] Reactions performed in the presence of 5 mol% Zr·NPS in benzene-d_6 (120 °C) and toluene-d_8 (150 °C), respectively.
[b] NMR yields based on *p*-xylene as the internal standard.
[c] 10 mol% catalyst was used.
[d] *cis*/*trans* = 1.0/1.3.
[e] Isolated yield of HCl salts after 3.0 mmol scale reaction.
[f] *cis*/*trans* = 1.0/7.0.
[g] 5 mol% Y·NPS (**4**) was used as a catalyst.

ed aminoalkene **9**. That this substrate undergoes cyclization to give the product derived from exocyclic addition to the alkene is consistent with the mechanism shown in below in Scheme 6. It is also of significance that the secondary aminoalkene **11** is resistant to cyclization. This stands in sharp contrast to the results of Scott and Hultzsch who have reported that secondary, but not primary, aminoalkenes participate in internal hydroamination catalyzed by cationic Zr(IV) complexes.[7a]

Asymmetric Internal Alkene Hydroaminations Catalyzed by Yttrium

A variety of chiral ligands (**20**, **22**, **24**, and **25–30**) was selected for asymmetric internal alkene hydroaminations. Treatment of (*S*)-1,1′-binaphthyl-2,2′-diamine (**19**) with *N*-formyl-(*S*)-proline in the presence of DCC and a catalytic amount of DMAP followed by reduction with LAH produced **20** in 44% yield (Scheme 3). Subjecting 1,2-diaminobenzene to *N*-methoxycarbonyl-(*S*)-proline with triethylamine followed by reduction with LAH gave **22** in 40% yield. The chiral NPS ligand **24** having an (*R*)-binaphthyldiamine

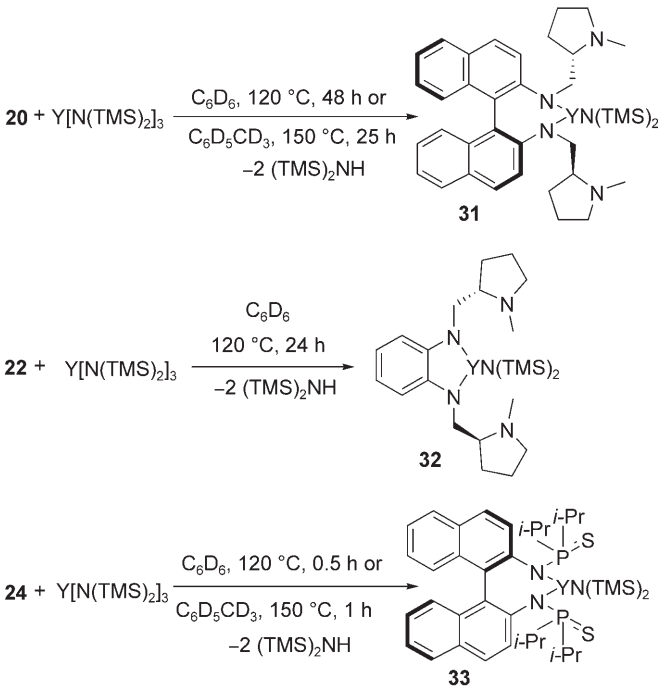


Scheme 3. Preparation of the chiral ligands.

skeleton as a backbone was obtained in 65% yield by the reaction of (*R*)-1,1′-binaphthyl-2,2′-diamine (**23**) with diisopropylchlorophosphine (2.0 equivs.) followed by the addition of 2.1 equivs. of sulfur. The other ligands (**25**–**30**) were prepared in a method analogous to **20**, **22**, and **24** (Figure 1).

Attachment of the proligand **20** to yttrium was quantitatively achieved by direct metalation with 1 equiv. of $Y[N(TMS)_2]_3$ in benzene-d_6 (120 °C, 48 h) or toluene-d_8 (150 °C, 25 h) to afford complex **31** *via* bis(trimethylsilyl)amine elimination (Scheme 4). Precatalysts **32** and **33** were prepared *in situ* in a fashion analogous to **31** using J. Young NMR tubes. Also, attachment of the proligands **25**–**30** to yttrium was carried out in a similar method as for the preparation of **31**, **32**, and **33**.

Reaction of 2,2-dimethyl-4-penten-1-amine (**7**) with 5 mol% **31** in toluene-d_8 (60 °C, 5.5 h) produced **14** in 95% yield (2% *ee*) (entry 1, Table 2). Enantiomeric excess was determined by NMR interpretation of **34**



Scheme 4. Preparation of the precatalyst.

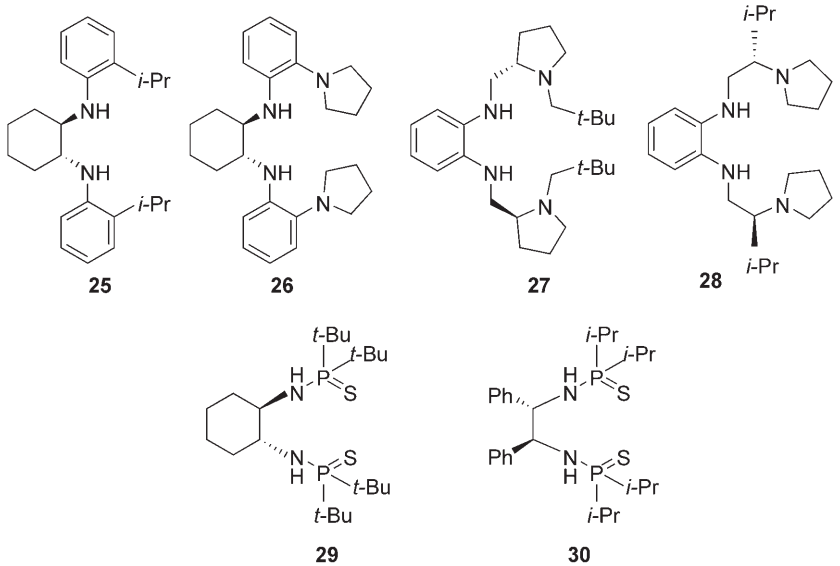
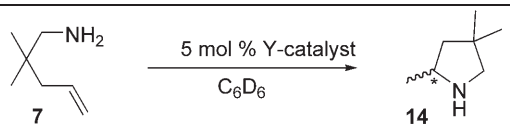


Figure 1. A variety of chiral ligands used for asymmetric hydroamination.

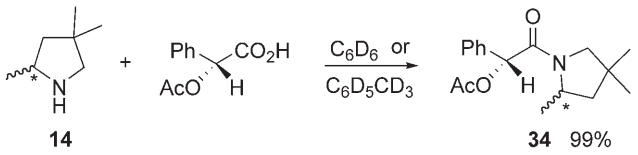
Table 2. Catalytic asymmetric hydroamination of **7**.[a]



7 14

Entry	Proligands	Temp [°C]	Time [h]	Yield [%][b]
1	**20**	60	5.5	95 (2)[c]
2	**22**	25	22	95 (56)
3	**22**	10	7[d]	95 (66)
4	**24**	25	18	95 (61)
5	**24**	25	15	95 (61)[c]
6	**25**	25	3	95 (0)
7	**26**	25	57	95 (17)
8	**27**	25	12[d]	95 (5)
9	**28**	25	34	95 (10)
10	**29**	25	5[d]	95 (13)
11	**30**	25	4	95 (22)

[a] Reactions performed in the presence of 5 mol% yttrium catalyst in benzene-d_6 (120°C) or toluene-d_8 (150°C), respectively.
[b] NMR yields based on *p*-xylene as the internal standard. Numbers in parenthesis indicated enantiomeric excess.
[c] $C_6D_5CD_3$ was used as a solvent.
[d] Days.



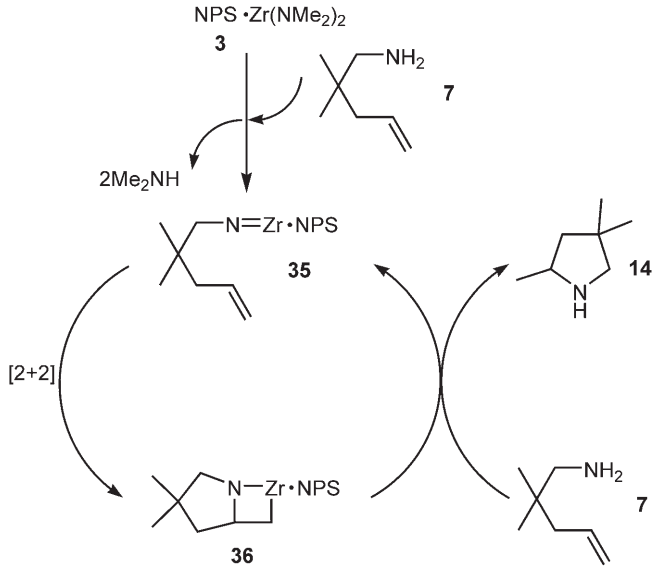
14 **34** 99%

Scheme 5. Asymmetric hydroaminations.

obtained from the reaction of **14** with *R*-(−)-*O*-acetylmandelic acid (Scheme 5).[9] The use of 5 mol% **32** as a precatalyst afforded **14** in 95% yield (56% *ee*, entry 2). Also, treatment of **7** with 5 mol% **33** in benzene-d_6 (25°C, 18 h, entry 4) or toluene-d_8 (25°C, 15 h, entry 5) afforded **14** in 95% yield (61% *ee*). Use of the yttrium catalyst derived from 1,2-diamine ligand (**25**) gave a racemic mixture (entry 6). Although a variety of catalysts obtained from the reaction of tetra(amine) ligands (**26–28**) and NPS ligands (**29–30**) with $Y[N(TMS)_2]_3$ produced the hydroamination product **14** in quantitative yields (entries 7–11), the enantiomeric excess of **14** was low (5–22% *ee*).

Mechanism

The dynamics of hydroamination involving precatalyst **3** can be conveniently monitored by ^{31}P NMR. Addition of **7** to a benzene-d_6 solution of **3** (5 mol%) results in the immediate disappearance of the phosphorus resonance at $\delta = 75.10$ with concomitant appearance of a new signal at $\delta = 78.12$. That this is accompanied by the production of 2 equivs. of Me_2NH (^1H NMR) is strongly indicative of quantitative exchange of the amido ligands at zirconium, resulting in the incorporation of two aminoalkene substrates. Significantly, cyclization of **7** at 120°C over 12 h results in 92% conversion to **14** with no change to the ^{31}P NMR resonance at $\delta = 78.12$, thus providing evidence that the zirconium catalyst is robust under the reaction conditions. In addition, at no time during this reaction did the ^{31}P NMR resonance associated with the free proligand **2** at $\delta = 89.54$ ppm appear. A probable mechanistic pathway for the intramolecular hydroamination of **7**, involving the putative Zr(IV) imido complex **35**[10] and azazirconacyclobutane **36** based on these observations, is depicted in Scheme 6.



Scheme 6.

Conclusions

We have prepared the thiophosphinic amide **2** in 68% yield by the reaction of 2,2-dimethyl-1,3-propanediamine with diisopropylchlorophosphine followed by the addition of sulfur. Attachment of the proligand **2** to zirconium was achieved by direct metalation with $Zr(NMe_2)_4$ in benzene-d_6 or toluene-d_8 to afford complex **3** *via* elimination of dimethylamine. The neutral Zr(IV)·NPS complex **3** is a competent precatalyst for intramolecular alkene hydroaminations involving primary amines that provide cyclic amines in good to excellent yields. Although the catalytic activity of **3** is lower than that exhibited by a related Y(III)·NPS chelate, the results presented here are among the first

examples of internal alkene hydroamination catalyzed by a neutral complex of a group 4 metal.[6] A variety of chiral ligands (**20**, **22**, **24**, and **25**–**30**) were prepared for asymmetric internal alkene hydroaminations. Metalation of chiral ligands to yttrium was accomplished with $Y[N(TMS)_2]_3$ in benzene-d_6 or toluene-d_8 to give complexes. Treatment of **7** with 5 mol% **33** in benzene-d_6 (25 °C, 18 h) or toluene-d_8 (25 °C, 15 h) to afford 2,4,4-trimethylpyrrolidine **14** in 95% yield (61% *ee*). These results should immediately provide more opportunities for the elucidation of efficient and selective new catalytic C–N bond forming reactions by way of neutral catalyst development. Extention of this study is now under investigation in this laboratory.

Experimental Section

General Remarks

Melting points were obtained using a Mel-Temp II apparatus equipped with a digital thermometer and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer model 1600 FT-IR. Infrared spectra of solids were obtained by standard KBr pellet procedures. ^{1}H NMR spectra were recorded on a Bruker AVANCE DPX-300 (300 MHz) or AVANCE DPX-500 (500 MHz) spectrometer. J. Young NMR tubes were purchased from Aldrich or J. Young Ltd. Chemical shifts were reported in ppm from tetramethylsilane with the residual protic solvent resonance as the internal standard (chloroform: 7.27, benzene: 7.16, toluene: 7.09). ^{13}C NMR spectra were recorded on a Bruker AVANCE DPX-300 (300 MHz) or AVANCE DPX-500 (500 MHz) spectrometer with complete decoupling. Chemical shifts were reported in ppm from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: 77.23). Analytical thin layer chromatography was performed on Polygram® SIL G/UV_{254} 1.25 mm silica gel plates with a fluorescent indicator. Flash chromatography was performed on Merck silica gel 60. Solvents for extraction and flash chromatography were reagent grade. All experiments were carried out under an argon atmosphere. Organozirconium and organoyttrium complexes were manipulated under an argon atmosphere in a glove box. Benzene-d_6 and toluene-d_8 were distilled from Na and aminoalkenes were distilled from CaH_2 under an argon atmosphere and stored at −30 °C in a glove box. J. Young NMR tubes, purchased from Aldrich or J. Young Ltd, were used under refluxing conditions (bath temperature, 120 °C or 150 °C) with a safety shield. 4-Penten-1-amine (**5**),[11] 1-methyl-4-penten-1amine (**6**),[12] 2,2-dimethyl-4-penten-1-amine (**7**),[11] 2,2-dimethyl-5-phenyl-4-penten-1-amine (**8**),[13] 2,2,4-trimethyl-4-penten-1-amine (**9**),[11] 2,2-dimethyl-5-hexen-1-amine (**10**),[11] and *N*-methyl-4-penten-1-amine (**11**)[14] were prepared according to reported procedures.

Synthesis of *N,N′*-Bis(*P,P*-diisopropylthiophosphinyl)-2,2-dimethyl-1,3-propanediamine (2)

To a solution of 2,2-dimethylpropane-1,3-diamine (255.0 mg, 2.5 mmol) and *N,N*-diisopropylethylamine (1.96 mL, 11.3 mmol) in dichloromethane (5 mL) was added dropwise chlorodiisopropylphosphine (0.8 mL, 5.0 mmol) dissolved in dichloromethane (3 mL) with stirring at 0 °C. The reaction mixture was allowed to warm to 25 °C and then stirred overnight. Sulfur (170.0 mg, 5.3 mmol) was added in small portions to the resulting mixture. The reaction mixture was stirred for 2 h at room temperature and then it was concentrated under vacuum. The residue was purified by column chromatography on silica gel to give **2** using 20% ethyl acetate in *n*-hexane for elution; yield: 710.0 mg (72%). Recrystallization from methylcyclohexane gave pure **2** as a white solid; yield: 670.0 mg (68%); mp 143–144 °C; ^{1}H NMR (500 MHz, C_6D_6, 25 °C): $\delta = 2.95$ (t, $J = 8.0$ Hz, 4H, CH_2), 2.67 (q, $J = 8.0$ Hz, 2H, N*H*), 2.10 (septet, $J = 7.0$ Hz, 4H, C*H*), 1.11 (d, $J = 7.0$ Hz, 6H, $CHCH_3$), 1.07 (t, $J = 5.75$ Hz, 12H, $CHCH_3$), 1.03 (d, $J = 7.0$ Hz, 6H, $CHCH_3$), 0.82 (s, 6H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, C_6D_6, 25 °C): $\delta = 47.4$, 31.1, 30.6, 24.1, 17.0, 17.0; ^{31}P NMR (121 MHz, C_6D_6, 25 °C): $\delta = 89.54$; IR (KBr): $\nu = 3324.3$, 3207.0, 2974.0, 1446.5, 1073.8, 829.8, 708.4 cm^{-1}; HR-MS (EI): $m/z = 398.2097$, exact mass calcd. for $[C_{17}H_{40}N_2P_2S_2]^+$: 398.2108.

Zr(IV) Bis(thiophosphinic amidate) Complex (3)

In an argon-filled glove box, $Zr(NMe_2)_4$ (20 μL, 0.02 mmol, 1.0 M solution in benzene-d_6 or toluene-d_8) and *N,N′*-bis(*P,P*-diisopropylthiophosphinyl)-2,2-dimethyl-1,3-propanediamine (7.97 mg, 0.02 mmol) in benzene-d_6 (0.4 mL) or toluened_8 (0.4 mL) were introduced sequentially into a J. Young NMR tube. The reaction mixture was stirred at 25 °C for 10 min until ligand attachment was judged completed by the disappearance of the $Zr(NMe_2)_4$ resonance in the ^{1}H NMR spectrum with concomitant production of Me_2NH. ^{1}H NMR (500 MHz, C_6D_6, 25 °C): $\delta = 3.11$ {s, 12H, Zr[N-$(CH_3)_2]_2$}, 2.69 (d, $J = 10.0$ Hz, 4H, CH_2), 1.99 (septet, $J = 7.25$ Hz, 4H, C*H*), 1.16 (d, $J = 7.0$ Hz, 6H, $CHCH_3$), 1.13 (dd, $J = 7.0$ Hz, $J = 1.5$ Hz, 12H, $CHCH_3$), 1.09 (d, $J = 7.0$ Hz, 6H, $CHCH_3$), 0.89 [s, 6H, $C(CH_3)_2$]; ^{13}C NMR (125 MHz, C_6D_6, 25 °C): $\delta = 57.9$, 44.1, 29.1, 28.7, 26.4, 17.7, 16.7; ^{31}P NMR (121 MHz, C_6D_6, 25 °C): $\delta = 75.10$; anal. calcd. (%) for $C_{21}H_{50}N_4P_2S_2Zr$: C 43.79, H 8.75, N 9.73; found: C 43.74, H 8.73, N 9.69.

Typical Procedure for Intramolecular Hydroaminations of Aminoalkenes using NPS·Zr(NMe$_2$)$_2$ Complexes

In an argon-filled glove box, $Zr(NMe_2)_4$ (20 μL, 0.02 mmol, 1.0 M solution in benzene-d_6 or toluene-d_8) and *N,N′*-bis(*P,P*-diisopropylthiophosphinyl)-2,2-dimethyl-1,3-propanediamine (7.97 mg, 0.02 mmol) in benzene-d_6 (0.4 mL) or toluene-d_8 (0.4 mL) were introduced sequentially into a J. Young NMR tube. The reaction mixture was stirred at 25 °C for 10 min until ligand attachment was judged completed by the disappearance of the $Zr(NMe_2)_4$ resonance in the ^{1}H NMR spectrum with concomitant production of Me_2NH. The appropriate aminoalkene (0.40 mmol) and *p*-xylene (10.0 μL, 0.08 mmol) were added to the resulting solution

and then, the reaction mixture was subsequently heated at 120 °C or 150 °C in an oil bath to achieve hydroamination.

(*S*)-(−)-*N,N′*-Bis-(1-methylpyrrolidin-2-ylmethyl)-6,7-dihydro-1,1′-binaphthalenyl-2,2′-diamine (20)

(*S*)-(−)-1,1′-Binaphthyl-2,2′-diamine (100.0 mg, 0.35 mmol), 1-formylpyrrolidine-2-carboxylic acid (which was obtained from *N*-formylation of L-proline) (100.0 mg, 0.7 mmol), DCC (160.0 mg, 0.77 mmol), and DMAP (8.6 mg, 0.07 mmol) in dichloromethane (4.5 mL) were stirred for 4 h at room temperature. The reaction mixture was washed with 15% HCl and $NaHCO_3$, then extracted with CH_2Cl_2 (10 mL). The solution was dried with anhydrous $MgSO_4$, filtered, and purified by column chromatography (EtOH/CH_2Cl_2 = 1/30) to afford the amide product; yield: 121.0 mg (65%).

The amide compound (660.0 mg, 1.23 mmol) was reduced by addition to $LiAlH_4$ (280.0 mg, 7.4 mmol) in THF (8 mL) and then heating the resulting mixture at 70 °C for 4 h. The reaction mixture was cooled to 0 °C and carefully quenched *via* sequential addition of H_2O (0.5 mL), 15% aqueous NaOH (0.5 mL) and H_2O (0.5 mL). The mixture was stirred at room temperature for 2 h, and extracted with Et_2O. The solution was dried with anhydrous $MgSO_4$. After filtration, the solvent was evaporated under vacuum. The residue was purified by column chromatography (EtOH/CH_2Cl_2 = 1/7) to afford **20**; yield: 400.0 mg (68%); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.84 (d, J = 9.0 Hz, 2H, Ar*H*), 7.74 (d, J = 7.5 Hz, 2H, Ar*H*), 7.20 (d, J = 9.0 Hz, 2H, Ar*H*), 7.13 (qd, J = 8.0 Hz, J = 2.0 Hz, 4H, Ar*H*), 6.98 (d, J = 8.0 Hz, 2H, Ar*H*), 3.90 (bs, 2H, N*H*), 3.35 (d, J = 12.0 Hz, 2H, NHCH*H*), 2.98 (dd, J = 12.0 Hz, J = 7.0 Hz, 2H, NHCH*H*), 2.78 (t, J = 6.75, 2H, CH_2CHN), 2.24–2.20 (m, 2H, MeNC*H*H), 2.19 (s, 6H, NCH_3), 2.02 (q, J = 8.5 Hz, 2H, MeNC*H*H), 1.54 (m, 2H, C*H*HCH$_2$), 1.38 (m, 2H, C*H*HCH$_2$), 1.22 (m, 4H, CH_2CH_2); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 144.7, 133.9, 129.4, 128.0, 127.5, 126.5, 123.9, 121.6, 114.0, 112.0, 64.6, 57.3, 47.0, 40.7, 29.2, 22.4; IR (KBr): ν = 3389.7, 3050.3, 2941.8, 2839.6, 2776.7, 1616.0, 1595.3, 1511.6, 1424.6, 1343.9, 1211.3, 807.5, 743.9 cm^{-1}; HR-MS (EI): m/z = 478.3093, exact mass calcd. for $[C_{32}H_{38}N_4]^+$: 478.3096.

N,N′-Bis[(2*S*)-1-methylpyrrolidin-2-ylmethyl]-1,2-phenylenediamine (22)

To a solution of 1,2-phenylenediamine (300.0 mg, 2.77 mmol) and triethylamine (0.97 mL, 6.92 mmol) in dichloromethane (10 mL) at 0 °C was added dropwise (2*S*)-pyrrolidine-1,2-dicarboxylic acid 1-methyl ester (1.0 g, 5.82 mmol). The reaction mixture was stirred at room temperature overnight. The mixture was diluted with dichloromethane (20 mL), then washed with H_2O (10 mL), 1.0 N HCl (5 mL) and saturated $NaHCO_3$ (5 mL). The solution was dried with anhydrous $MgSO_4$, filtered, and concentrated under vacuum to afford the amide compound; yield: 722.0 mg (67%).

The amide compound (2.5 g, 6.40 mmol) was reduced by addition to $LiAlH_4$ (971.2 mg, 25.6 mmol) in THF (35 mL) at room temperature and then heating the resulting mixture at reflux overnight. The reaction mixture was cooled to 0 °C and carefully quenched *via* sequential addition of H_2O (0.5 mL), 15% aqueous NaOH (0.5 mL) and H_2O (0.5 mL). The mixture was stirred at room temperature for 2 h, and anhydrous $MgSO_4$ was added. After filteration, the solvent was evaporated under vacuum. The residue was purified by preparative TLC coated by neutral alumina (ethyl acetate for elution) to afford **22**; yield: 1.14 g (60%); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.73 (m, 2H, Ar*H*), 6.06 (m, 2H, Ar*H*), 3.94 (bs, 2H, N*H*), 3.07 (m, 6H, NCH_2, NC*H*), 2.53 (m, 2H, NCH*H*), 2.35–2.2 (m, 2H, NC*HH*), 2.31 (s, 6H, CH_3), 1.98–1.83 (m, 8H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 137.82, 118.37, 110.40, 64.18, 57.73, 45.28, 40.47, 29.05, 23.32. IR (KBr): ν = 3325.8, 2938.5, 2842.4, 2789.1, 1600.2, 1522.8, 1438.1, 727.3 cm^{-1}; HR-MS (EI): m/z = 302.2475, exact mass calcd. for $[C_{18}H_{30}N_4]^+$: 302.2470.

(1*R*,2*R*)-*N,N′*-Bis(2-isopropylphenyl)-1,2-cyclohexanediamine (25)

A round-bottom flask with magnetic stir bar was charged with $Pd(OAc)_2$ (20.2 mg, 8.76×10^{-5} mmol), *rac*-BINAP (111.0 mg, 1.75×10^{-4} mmol), and *t*-BuOK (521.0 mg, 5.25 mmol), then evacuated and backfilled with argon. After addition of toluene (12 mL), the mixture was stirred at room temperature for 20 min, followed by addition of (1*R*,2*R*)-(−)-diaminocyclohexane (200.0 mg, 1.75 mmol) and 1-bromo-2-isopropylbenzene (732.0 mg, 3.68 mmol) sequentially. The reaction mixture was then heated at 100 °C for 4 days. The reaction mixture was purified by column chromatography on silica to afford **25**; yield: 438.0 mg (82%). The value of the enantiomeric excess (99% *ee*) was determined based on the enantiomeric purity of (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine purchased from Aldrich. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.07 (m, 4H, Ar*H*), 6.70 (m ,4H, Ar*H*), 3.84 (bs, 2H, N*H*), 3.30 (m, 2H, NC*H*), 2.66 (septet, J = 6,9 Hz, 2H, C*H*), 2.34 (m, 2H, CH_2), 1.74 (m, 2H, CH_2), 1.40 (m, 2H, CH_2), 1.21 (m, 2H, CH_2) 1.13 (d, J = 6.9 Hz, 3H, CH_3), 1.08 (d, J = 6.9 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 144.3, 133.2, 126.6, 125.3, 117.4, 111.1, 57.7, 32.6, 27.0, 24.6, 22.4, 22.3; HR-MS (EI): m/z = 350.2717, exact mass calcd. for $[C_{24}H_{34}N_2]^+$: 350.2721.

(1*R*,2*R*)-*N,N′*-Bis(2-pyrrolidine-1-ylphenyl)-1,2-cyclohexanediamine (26)

A solution of *N,N′*-bis(2-amiophenyl)cyclohexane-1,2-diamine (200.0 mg, 0.67 mmol), 1,3-dibromopropane (161 μL, 1.34 mmol) and *N,N′*-diisopropylethylamine (560 μL, 3.2 mmol) in toluene (3 mL) was heated at 110 °C. When the reaction was completed, the reaction mixture was diluted with ethyl acetate (10 mL), washed with water (2×2 mL), and dried over $MgSO_4$. After filtration, the solvent was evaporated under vacuum. The residue was purified by column chromatography on silica (5% ethyl acetate in *n*-hexane for elution). An undesired volatile substance, which was not separable by column chromatography, was removed by evaporation using a Schlenk vacuum line at 60 °C/0.05 torr; yield of **26**: 160.0 mg (59%). The value of the enantiomeric excess (99% *ee*) was determinded based on the enantiomeric purity of (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine purchased from Aldrich. ^{1}H NMR (250 MHz, benzene-

d_6, 25 °C): $\delta = 7.03$ (m, 4H, Ar*H*), 6.74 (m ,4H, Ar*H*), 4.88 (bs, 2H, N*H*), 3.18 (m, 2H, NC*H*), 2.80 (m, 8H, NCH_2), 2.21 (m, 2H, CH_2), 1.48 (m, 10H, CH_2), 1.15 (m, 4H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 144.8$, 137.7, 124.6, 119.2, 116.9, 110.5, 57.7, 51.4, 32.9, 24.8, 24.2; IR (KBr): $\nu =$ 3324.1, 2929.4, 2811.3, 1596.3, 1505.9, 736.2 cm^{-1}, HR-MS (EI): $m/z = 404.2950$, exact mass calcd. for $[C_{26}H_{36}N_4]^+$: 404.2939.

N,N′-Bis[(2*S*)-1-(2,2-dimethylpropionyl)pyrrolidine-2-ylmethyl]-1,2-phenylenediamine (27)

To a solution of L-proline (1.0 g, 8.68 mmol) and triethylamine (2.4 mL, 17.4 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added dropwise trimethylacetyl chloride (2.1 mL, 17.4 mmol), followed by stirring at room temperature for 15 min. After the addition of 1,2-phenylenediamine (470.0 mg, 4.34 mmol) and 4-dimethylaminopyridine (5.0 mg, 0.05 mmol), the reaction mixture was allowed to attain room temperature and stirred overnight. The reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with 10% HCl, saturated $NaHCO_3$ and dried over $MgSO_4$. After filtration, the solvent was evaporated under vacuum. The residue was purified by column chromatography on silica gel (80% ethyl acetate in *n*-hexane for elution) to provide *N,N′*-bis[(2*S*)-1-(2,2-dimethylpropionyl) pyrrolidine-2-ylacetyl]-1,2-phenylenediamine; yield: 822.0 mg (40%); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): $\delta = 8.76$ (bs, 2H, N*H*), 7.52 (m, 2H, Ar*H*), 7.07 (m, 2H, Ar*H*), 4.70 (t, $J = 5.8$ Hz, 2H, NC*H*), 3.71 (m, 4H, NCH_2), 2.1–2.0 (m, 6H, CH_2), 1.90 (m, 2H, CH_2), 1.20 (s, 18H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 177.3$, 172.0, 130.3, 125.6, 125.1, 62.6, 48.6, 38.9, 27.4, 27.1, 26.1; IR (KBr): $\nu = 3245.8$, 2971.7, 1703.3, 1605.2, 1539.0, 1410.6, 1172.3, 755.2 cm^{-1}, HR-MS (EI): $m/z =$ 470.2900, exact mass calcd. for $[C_{26}H_{38}N_4O_4]^+$: 470.2893.

This compound (800.0 mg, 1.7 mmol) was reduced by addition to $LiAlH_4$ (0.5 g, 13.6 mmol) in THF (30 mL), at room temperature and then heating the resulting mixture at reflux overnight. The reaction mixture was cooled to 0 °C and carefully quenched *via* sequential addition of H_2O (0.5 mL), 15% aqueous NaOH (0.5 mL) and H_2O (1 mL). The mixture was stirred at room temperature for 2 h and anhydrous $MgSO_4$ (1.0 g) was added. After filtration, the solvent was evaporated under vacuum. The residue was purified by preparative TLC coated by silica gel (10% methanol in CH_2Cl_2 for elution) to afford **27**; yield: 270.0 mg (19%). The value of enantiomeric excess (>95%) was determined by a ^{1}H NMR technique using (*S*)-(+)- and (*R*)-(−)-*O*-acetylmandelic acid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta =$ 6.70 (m, 2H, Ar*H*), 6.55 (m, 2H, Ar*H*), 4.17 (bs, 2H, N*H*), 3.30 (m, 2H, NC*H*H), 3.01 (s, 4H, NCH_2), 2.80 (m, 2H, NCH*H*), 2.42, (d, NC*H*H), 2.30 (q, 2H, NC*H*), 2.14 (d, NCH*H*), 2.0–1.7 (m, 8H, CH_2), 0.82 (s, 18H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 138.1$, 117.9, 109.6, 68.4, 65.1, 58.2, 44.9, 32.45, 28.6, 27.8, 24.9; IR (KBr): $\nu =$ 3305.8, 2950.3, 2808.4, 1603.1, 1519.1, 1435.1, 1259.4, 1109.2, 731.9 cm^{-1}; HR-MS (EI): $m/z = 414.3724$, exact mass calcd. for $[C_{26}H_{46}N_4]^+$: 414.3722.

N,N′-Bis[(2S)-2-isopropyl-2-pyrrolidinylethyl]-1,2-phenylenediamine (28)

To a solution of 1,2-phenylenediamine (540.0 mg, 5.02 mmol) and (2*S*)-2-(2,5-dioxopyrrolidin-1-yl)-3-methylbutyric acid (2.0 g, 10.0 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added dropwise DCC (2.07 g, 10.0 mmol) in CH_2Cl_2 (5 mL). The mixture was allowed to attain room temperature with stirring for overnight. The resulting solid was filtered off, washed with 5% HCl and saturated $NaHCO_3$ solution sequentially. The organic phase was dried with anhydrous $MgSO_4$, filtered, and evaporated under vacuum. The crude material was subjected to column chromatography on silica gel (ethyl acetate for elution) to give *N,N′*-bis[(2*S*)-2-(2,5-dioxopyrrolidin-1-yl)-2-isopropylacetyl]-1,2-phenylenediamine; yield: 250.0 mg (10%); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 8.75$ (bs, 2H, N*H*), 7.55 (dd, $J = 5.5$ Hz, $J = 3.5$ Hz, 2H, Ar*H*), 7.16 (dd, $J = 5.5$ Hz, $J = 3.5$ Hz, 2H, Ar*H*), 4.38 (d, $J = 11.0$ Hz, 2H, NC*H*), 2.81–2.74 (m, 2H, C*H*), 2.78 (s, 8H, CH_2) 1.12 (d, $J = 7.0$ Hz, 6H, CH_3), 0.84 (d, $J = 7.0$ Hz, 6H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 177.6$, 167.2, 129.6, 126.3, 63.0, 28.1, 26.8, 25.5, 20.1, 19.4; IR (KBr): $\nu = 3292.6$, 2966.7, 1704.4, 1538.0, 1389.3, 1102.1, 755.7 cm^{-1}; HR-MS (EI): $m/z = 470.2180$, exact mass calcd. for $[C_{24}H_{30}N_4O_6]^+$: 470.2165.

This compound (200.0 mg, 0.42 mmol) was reduced by addition to $LiAlH_4$ (130.0 mg, 3.4 mmol) in THF (20 mL) at room temperature and then, heating the resulting mixture at reflux overnight. The reaction mixture was cooled to 0 °C and carefully quenched with H_2O (0.5 mL), 15% aqueous NaOH (0.5 mL), and H_2O (1 mL). The mixture was stirred at room temperature for 2 h and anhydrous $MgSO_4$ (1.0 g) was added. After filtration, the solvent was evaporated under vacuum. The residue was purified by preparative TLC on silica gel (10% ethyl acetate in *n*-hexane for elution) to afford **28**; yield: 20.0 mg (12%). The value of the enantiomeric excess (>95%) was determined by ^{1}H NMR technique using (*S*)-(+)- and (*R*)-(−)-*O*-acetylmandelic acid. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 7.04$ (dd, $J =$ 5.5 Hz, $J = 3.5$ Hz, 2H, Ar*H*), 6.70 (dd, $J = 5.5$ Hz, $J = 3.5$ Hz, Ar*H*), 4.22 (bs, 2H, N*H*), 3.05 (m, 4H, NCH_2), 2.37 (m, 8H, NCH_2), 2.13 (app q, 2H, NC*H*), 1.91 (octet, 2H, C*H*), 1.55 (s, 8H, CH_2), 1.12 (d, $J = 5.0$ Hz, 6H, CH_3), 0.92 (d, $J =$ 5.0 Hz, 6H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta =$ 138.0, 118.6, 109.8, 66.81, 50.9, 42.2, 30.2, 23.6, 21.0, 18.3; HR-MS (EI): $m/z = 386.3398$, exact mass calcd. for $[C_{24}H_{42}N_4]^+$: 386.3409.

(1*R*,2*R*)-*N,N′*-Bis(*P,P*-di-*tert*-butylthiophosphinyl)-cyclohexanediamine (29)

To a solution of (1*R*,2*R*)-1,2-diaminocyclohexane (570.0 mg, 5.0 mmol) and 4-methylmorpholine (1.3 mL, 12 mmol) in toluene (25 mL) was added dropwise chlorodi-*tert*-butylphosphine (2.16 g, 12.0 mol) dissolved in toluene (25 mL) with stirring at 0 °C. The reaction mixture was allowed to attain room temperature and stirred overnight. The resulting white precipitate was rapidly filtered with care being taken to minimize exposure to air and the filter cake was leached with dry toluene (2 × 3 mL). Sulfur (0.337 g, 10.5 mmol) was the added in portions (exothermic) to the resulting mixture. The reaction mixture was heated to 80 °C with stirring for 30 min under argon. After cooling to room temperature, the

mixture was concentrated under vacuum. The residue was purified by column chromatography on silica gel (20% ethyl acetate in *n*-hexene) to afford **29** as a white solid; yield: 1.59 g (68%); mp 157–158 °C. The product was recrystallized from methylcyclohexane. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 3.52$ (bs, 2H, NH), 2.24 (d, 2H, NCH), 1.85 (m, 4H, CH_2), 1.45 (m, 4H, CH_2), 1.29 (s, 36H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 52.9$, 40.5 (d, $J_{C,P} = 40.5$), 39.0 (d, $J_{C,P} = 53.62$), 30.6, 27.6, 27.4, 21.1; ^{31}P NMR (121 MHz, $CDCl_3$, 25 °C): $\delta = 96.02$; IR (KBr): $\nu = 3413.0$, 3246.1, 2932.0, 1474.2, 671.2 cm^{-1}; HR-MS (EI): $m/z = 466.2724$, exact mass calcd. for $[C_{22}H_{48}N_2P_2S_2]^+$: 466.2734.

(1*R*,2*R*)-*N*,*N*′-Bis(*P*,*P*-diisopropylthiophosphinyl)-1,2-diphenylethylenediamine (30)

This compound was prepared in a method analogous to **24** utilizing (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine (100.0 mg, 4.57×10^{-4} mol), chlorodiisopropylphosphine (145 μL, 9.14×10^{-4} mol), and 4-methylmorpholine (120 μL, 1.1 mmol) in toluene (3 mL), followed by the addition of sulfur (15.0 mg, 4.8×10^{-4} mol) to give **30** which was purified by column chromatography on silica gel (CH_2Cl_2 for elution); yield: 73.0 mg (31%); mp 153–154 °C. The value of the enantiomeric excess (99% *ee*) was determined based on the enantiomeric purity of (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine purchased from Aldrich. ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): $\delta = 7.09$ (m, 6H, ArH), 6.87 (m, 4H, ArH), 4.44 (m, 2H, NCH), 4.05 (bs, 2H, NH), 2.40 (septet, $J =$ 7.2 Hz, CH), 1.81 (septet, $J = 7.2$ Hz, 2H, CH), 1.40 (d, $J =$ 7.2 Hz, 6H, CH_3), 1.27 (d, $J = 7.2$ Hz, 6H, CH_3), 0.91 (d, $J =$ 7.2 Hz, 6H, CH_3), 0.90 (d, $J = 7.2$ Hz, 3H, CH_3), 0.81 (d, $J =$ 7.2 Hz, 6H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta =$ 141.6, 128.1, 127.8, 127.0, 61.2, 31.6 ($J_{C,P} = 63$ Hz), 29.3 ($J_{C,P} = 61$ Hz), 17.3, 17.2, 16.8, 16.5; ^{31}P NMR (250 MHz, $CDCl_3$, 25 °C): $\delta = 91.86$; IR (KBr): $\nu = 3321.9$, 2963.2, 2670.9, 1456.1, 1066.0, 700.1 cm^{-1}. HR-MS (EI): $m/z =$ 509.2334, exact mass calcd. for $[C_{26}H_{42}N_2P_2S_2 + H]^+$: 509.2342.

2,4,4-Trimethylpyrrolidine (14)

2,2-Dimethyl-4-penten-1-amine (36.0 mg, 0.32 mmol) and *p*-xylene (10.0 μL, 0.08 mmol) were added to the Y-complexes (**33**) *via* microsyringe and the reaction mixture was subsequently heated at 25 °C for 18 h in an oil bath until hydroamination was judged complete by disappearance of the vinylic resonances in the ^{1}H NMR. ^{1}H NMR (500 MHz, C_6D_6, 25 °C): $\delta = 3.10$ (m, 1H, NCH), 2.64 (m, 1H, NCHH), 2.49 (m, 1H, NCHH), 1.48 (dd, $J = 12.3$ Hz, $J = 6.9$ Hz, 1H, CHH), 1.24 (bs, 1H, NH), 1.05 (d, $J = 6.3$ Hz, 3H, CH_3), 0.98 (s, 3H, CH_3), 0.96 (s, 3H, CH_3).

Preparative Scale Synthesis of 2,4,4-Trimethylpyrrolidine·HCl

In an argon-filled glove box, $Zr(NMe_2)_4$ (150 μL, 0.15 mmol, 1.0 M solution in benzene-d_6), *N*,*N*′-bis(*P*,*P*-diisopropylthiophosphinyl)-2,2-dimethyl-1,3-propanediamine (59.79 mg, 0.15 mmol) and toluene (3 mL) were introduced into a 10-mL Schlenk flask equipped with a magnetic stirring bar. The flask was sealed and the homogeneous reaction mixture was stirred at 25 °C for 10 min to effect ligand attachment. To the resulting solution was added 2,2-dimethyl-4-penten-1-amine (339.6 mg, 3.0 mmol). The reaction mixture was then heated to 150 °C in an oil bath with stirring for 3 h to complete hydroamination. The product amine and solvent were subsequently separated from the catalyst by vacuum transfer and the resultant mixture was cautiously added at 0 °C to a solution of HCl in MeOH (9 mL) that was prepared by the methanolysis of acetyl chloride (0.6 mL). Removal of the solvents under vacuum provided the HCl salt of 2,4,4-trimethylpyrrolidine; yield: 405.0 mg (90%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 10.0$ (br s, 1H, $NH_2^+Cl^-$), 9.56 (br s, 1H, $NH_2^+Cl^-$), 3.86 (m, 1H, $CH_2CHNH_2^+Cl^-$), 3.13 (m, 1H, $CH_2NH_2^+Cl^-$), 3.02 (m, 1H, $CH_2NH_2^+Cl^-$), 1.95 (dd, $J =$ 12.9 Hz, $J = 6.5$ Hz, 1H, CH_2CHCH_3), 1.58 (dd, $J = 12.9$ Hz, $J = 11.5$ Hz, 1H, CH_2CHCH_3), 1.55 (d, $J = 6.5$ Hz, 3H, $CHCH_3$), 1.23 [s, 3H, $C(CH_3)_2$], 1.19 [s, 3H, $C(CH_3)_2$]; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 56.6$, 55.6, 47.3, 39.1, 27.5, 18.5; anal. calcd. (%) for $C_7H_{16}ClN$: C 56.18, H 10.78, N 9.36; found: C 56.01, H 10.66, N 9.33.

Acetic Acid 2-Oxo-1-phenyl-2-(2,4,4-trimethylpyrrolidin-1-yl)ethyl Ester (34)

The product amines (**14**) and solvent (benzene-d_6 or toluene-d_8) were separated from the catalyst by vacuum transfer and *R*-(−)-*O*-acetylmandelic acid (0.07 g, 0.35 mmol) was added to the resulting mixture. The reaction mixture was stirred at 25 °C for 30 min. Removal of solvents under vacuum provided **28**; yield: 87.5 mg (99%, 61% *ee*); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) (major isomer): $\delta = 7.55$ (d, $J = 6.5$ Hz, 2H, ArH), 7.35–7.29 (m, 3H, ArH), 5.83 (s, 1H, CHOAc), 3.52 (m, 1H, NCH), 2.89 (d, $J = 11.5$ Hz, 1H, NCHH), 2.75 (q, $J = 11.5$ Hz, 1H, NCHH), 2.16 (s, 1H, CH_3CO), 1.71–1.65 (m, 1H, $CHCH_2$), 1.31 (td, $J = 13.0$ Hz, $J = 2.0$ Hz, 1H, $CHCH_2$), 1.19 (d, $J = 6.5$ Hz, 3H, $NHCH_3$), 1.08 (s, 1H, CH_3), 0.99 (s, 1H, CH_3); (minor isomer): $\delta =$ 7.55 (d, $J = 6.5$ Hz, 2H, ArH), 7.35–7.29 (m, 3H, ArH), 5.83 (s, 1H, CHOAc), 3.40 (m, 1H, NCH), 2.89 (d, $J = 11.5$ Hz, 1H, NCHH), 2.75 (q, $J = 11.5$ Hz, 1H, NCHH), 2.16 (s, 1H, CH_3CO), 1.71–1.65 (m, 1H, $CHCH_2$), 1.31 (td, $J = 13.0$ Hz, $J = 2.0$ Hz, 1H, $CHCH_2$),), 1.26 (d, $J = 6.5$ Hz, 3H, $NHCH_3$), 1.00 (s, 1H, CH_3), 0.97 (s, 1H, CH_3).

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