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Tunable Phosphoramidite Ligands for Asymmetric Hydrovinylation: Ligands par excellence for Generation of All-Carbon Quaternary Centers

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Abstract

1-Alkylstyrenes undergo efficient hydrovinylation (addition of ethylene) in the presence of a Ni-catalyst prepared from [(allyl)NiBr]₂, Na⁺ [BAr₄][−] (Ar = 3,5-bis-trifluoromethylphenyl), and a phosphoramidite ligand giving products in excellent yields and enantioselectivities. In many cases phosphoramidites derived from achiral 2,2'-biphenol are almost as good as ligands derived from the more expensive enantiopure 2,2'-binaphthols. The hydrovinylation products, which carry two versatile latent functionalities, an aryl and a vinyl group, are potentially useful for the synthesis of several important natural products containing benzylic all-carbon quaternary centers.

Keywords

alkenes; asymmetric catalysis; hydrovinylation; phosphoramidite ligands; nickel

Introduction

Catalytic asymmetric carbon-carbon bond forming reactions continue to attract great interest among synthetic chemists.¹ Among these, a subclass of reactions that depend on the *activation* and subsequent *stereoselective incorporation* of small molecules such as CO, CO₂, HCN, acetylene and ethylene into prochiral substrates, are among the most challenging.² Ideally, new reactions must accomplish the requisite transformations under nearly ambient conditions with high turnover frequencies, high regio- and stereoselectivities, all the while generating only little or no side products. Further, the newly installed functionality must be amenable to further transformations leading to valuable end products. Research in this area could lead to new breakthroughs in fundamental science, and under the most optimistic scenario, will add to our repertoire of methods for economically viable syntheses of valuable chemical intermediates.

In developing new metal-catalyzed reactions, the ligand is a major factor as efficiency (turnover frequency), selectivity, and catalytic stability are often dependent on the properties of the ligand. In the area of asymmetric catalysis, success often depends on the availability of enantiomerically pure ligands that are amenable to fine-tuning for optimum performance. Once the essential features of the catalytic system are identified, systematic modifications in the ligand scaffolding, especially, those affecting the steric and electronic environment around the chelating atoms, are often required to achieve acceptable levels of catalytic efficiency and selectivity. Such a strategy has been employed in the discovery of many new asymmetric

catalytic processes that involve the use of carbon feedstocks for selective C-C bond forming reactions.^{2,3} Phosphoramidites, originally introduced by Feringa^{4a,b} for the asymmetric Cu-catalyzed conjugate addition of dialkylzinc reagents to enones, are among the most versatile and tunable ligands for C-C and C-H bond-forming reactions.^{4c-i} Recently we⁵ and the Zhou group⁶ have described the use of phosphoramidite ligands derived from different sources for the asymmetric hydrovinylation reactions of 1-alkylvinylarenes leading to useful intermediates with all-carbon quaternary centers (Eq. 1).⁷ In this paper we disclose the full details of our efforts, including results of more recent studies aimed at exploring the scope and limitations of this reaction.

(1)

Asymmetric Hydrovinylation

Hydrovinylation,⁸ the addition of ethylene as a hydrogen and a vinyl group across an activated olefin (Eq. 1-2), has received much renewed attention⁹ since we disclosed new protocols for this prototypical heterodimerization reaction.¹⁰ During the past decade the scope of the reaction has also been considerably broadened.^{8c} Since ethylene is a cheap, abundantly available feedstock carbon source, and the vinyl group in the resulting product readily transformed into a variety of other common functionalities, this reaction has huge potential to be a scalable, environmentally benign method for the preparation of valuable chemical intermediates. Application of old (Figure 1, **5**,^{8a} **6**¹⁰) and new (**7**,^{11,7c} **8**,^{3g} **9**,⁷ **10**⁶) ligands have enabled successful asymmetric hydrovinylation of vinyl arenes, 1,3-dienes and strained bicyclic olefins such as norbornene. Asymmetric hydrovinylation of vinylarenes (Eq. 2) has been the most developed, and the resulting 3-arylbutenes (**4**) have been converted into a number of synthetically useful derivatives such as alcohols,^{3b,12} halides, aldehydes, carboxylic acids, and chiral 1-ethylarylamines.¹³

(2)

Ligand Tuning for the Generation of All-Carbon Quaternary Centers via Asymmetric Hydrovinylation

The search for new methods for stereoselective generation of all-carbon quaternary centers is a subject of considerable topical interest.¹⁴ Several important pharmaceutically relevant compounds, among them, analgesic (–)-eptazocine,^{15a,b} protein kinase C activator lyngbyatoxin and related structures like teleocidin B4,¹⁶ and cognitive enhancing agent (–)-

phenserine,¹⁷ contain an all-carbon quaternary center at the benzylic position. The viability of hydrovinylation of 1-alkylstyrene as a method for generating an all-carbon quaternary benzylic center was initially discovered during the scouting phase of our studies of hydrovinylation (Eq. 3, **11a** → **12a**), even though the conversions were only modest under the highly catalytic reaction conditions.^{3f}

We chose 1-ethylstyrene (**11b**, Eq. 3) as a prototypical substrate for the initial studies. A racemic sample of the expected product **12b** was conveniently prepared by carrying out the reaction under conditions described in Eq. 4, using [*o*-(benzyloxy)phenyl]diphenylphosphine (**13**)^{7c} as a ligand. This was followed by studies using **6–8**, a set of ligands we had used with varying degree of success in the asymmetric hydrovinylation of monosubstituted vinylarenes and 1,3-dienes. The results of these scouting experiments are listed in Table 1.

Catalysts derived from the MOP ligand (**6**, entry 2)¹⁰ and the phosphinite **8**^{3g} (entry 6) showed no reactivity while those derived from the phospholane ligand **7**, which gave very high ee's and turnover numbers in the hydrovinylation of a number of styrene derivatives,¹¹ and 1,3-dienes,^{7c} showed only moderate reactivity under similar conditions (entries 3–5). At this point we turned our attention to phosphoramidite ligands, starting with one of the 'original' Feringa ligands (**9**) derived from (*R*)-binaphthol and (*SS*)-*bis*- α -methylbenzyl amine.¹⁸ The results of these experiments on the asymmetric hydrovinylation of 1-ethylstyrene (**11b**) using the ligand **9** are shown in Table 2. In a typical experiment, the phosphoramidite ligand was treated with [(allyl)NiBr]₂ and Na⁺ [BARF][−] in CH₂Cl₂ and was subsequently placed under an ethylene atmosphere at −70 °C for a few minutes.¹⁹ The ethylene line was removed, and the styrene dissolved in CH₂Cl₂ was added while maintaining the reaction mixture at −70 °C. After all the starting material is consumed, the product was isolated after workup by simple filtration

through a silica column. Optimization of reaction conditions revealed that the enantioselectivity of the reaction depends critically on the temperature at which the reaction is carried out. As little as 10 °C difference can bring about a deterioration of the selectivity (entries 2, 3 and 4). We also noticed that the hydrovinylation reaction, even at -70 °C, is exothermic and careful control of the reaction conditions (<-70 °C) is essential for obtaining high enantioselectivities. Under these conditions, no isomerization [to (Z)- and (E)-1,2-dimethylstyrenes] or oligomerization of starting alkenes was detected, as judged by careful GC analysis and ¹H NMR spectroscopy. The surprisingly high yields and selectivities are highly reproducible and are independent of the catalyst loading (entries 5–7), indicating the total absence of non-selective reactions for this substrate. Entry 7 shows a reaction done on a 50 mmol scale using 0.02 equivalent of the Ni-catalyst.

Hydrovinylation of several 1-alkylstyrene derivatives were attempted under the optimal conditions and the results are tabulated in Table 3. While the 4-methyl substrate **14** gave excellent selectivity for the formation of the expected product (entry 1), the 4-chloro-derivative **15** gave up to 5% isomerization of the starting olefin to a mixture of Z- and E-1,2-disubstituted styrenes (entry 2). A similar minor side reaction was also observed for the substrate **17**. An isopropyl group at the 1-position of the styrene (**16**) retards the reaction (entry 4), and it is best accomplished at 24 °C with 10 mol% catalyst. Even though the yield of the reaction is only moderate, very high ee (~97%) was observed for the isolated product. The 2-naphthyl derivative **18** gave excellent yield (>98%) and selectivity (>98%) for the expected product. 2-(1-Naphthyl)butene (**19**) failed to undergo the reaction (entry 6) and (E)-1-phenyl-3-ethyl-1,3-butadiene (**20**) gave a nearly racemic product.

Asymmetric hydrovinylation of functionalized vinylarenes with and without a 1-substituent is a key reaction in a number of on-going total synthesis efforts in our group. Some limitations in the use of ligand **9** have been noted in the previous paragraph, and others have become apparent as our studies continued. This applies to asymmetric hydrovinylation of even simple vinylarenes where we had made the most progress. For example, 4-isobutylstyrene and 3-fluoro-4-phenylstyrene, precursors of ibuprofen and flurbiprofen gave only 90% and 86% ee using **9** as a ligand. In an attempt to improve the selectivity we decided to take advantage of the versatility of the phosphoramidite ligands, especially the ease with which the biaryl and the amine moieties can be modified.²¹ Figure 2 shows a selection of the modified phosphoramidites (**26–28**) that were found to be especially useful in early studies for the asymmetric hydrovinylation of simple vinyl arenes. We have since examined the scope of these ligands for the generation of all-carbon benzylic quaternary centers and the results are described in the following paragraphs.

One early application of the modified phosphoramidites has been in our approach to pyrrolidinoindolines like physostigmine and related compounds that carry a methyl-bearing quaternary center at the benzylic position.²² We reasoned that asymmetric hydrovinylation on a highly functionalized styrene of generic structure **29** would give **30**, from which it should be possible to reach the target molecule(s). Asymmetric hydrovinylation of these substrates would also test additional functional group compatibility of this demanding reaction.

In the event, a number of new styrene derivatives (**29a–29g**) were prepared by Stille coupling of a suitable tributylstannyl alkene and the appropriate aryl iodide partner.²³ Results of asymmetric hydrovinylation of these compounds using different phosphoramidite ligands, starting with **9** are shown in Table 4. As seen from entries 1, 2 and 3, *O*-TBS and N₃ substituents on the alkyl tether are detrimental to the reaction and no products are formed even when high catalyst loading (10 mol%) is used. Surprisingly, the *N*-phthalimido group is tolerated (entries 5–10) to give products **30d** and **30g** (Figure 3) from the respective precursors. But an ortho-substituent (e.g., **29e** and **29f**) prevents the reaction from taking place (entries 11 and 12).

Ligand **9** gave marginally better enantioselectivity in the asymmetric hydrovinylation of **29g** (entry 6, vs entry 9), compared to **26**, prepared from achiral 2,2'-biphenol and (*SS*)-*N,N*-bis- α -methylbenzylamine. But the latter was found to give a *quantitative yield* of the product (entry 9), especially under slightly elevated pressure. Ligand **27** gave 68% yield and 50% ee under comparable conditions. We had earlier found that ligand **28** gave low enantioselectivities in the hydrovinylation of even simpler substrates such as 1-ethylstyrene. In terms of the overall efficiency (10 mol% catalyst) and selectivity (best: 61% ee) of hydrovinylation, these highly functionalized molecules are among the worst substrates we have examined. Notice that the higher pressure of ethylene, in addition to having a decidedly beneficial effect on the overall yield of the reaction, also prevents isomerization of the starting alkene to **31** (entries 8 and 9).²⁵

The low turnover and enantioselectivity notwithstanding, one notable feature of these ligands is the small difference in the selectivities imparted by the more elaborate (and expensive) (*R*)-2,2'-binaphthol-derived phosphoramidite **9** and the simpler (and cheaper) 2,2'-biphenol-derived ligand **26**, and this may have practical consequences in terms of the cost of ligands.²⁴ Besides, the use of such ligands for the synthesis of racemic intermediates is not without some value since hydrovinylation represents a new method for the generation of quaternary centers.

Since the enantioselectivity in the asymmetric hydrovinylation of the alkene precursor **29g** was found to be unacceptable for the planned synthesis of pyrrolidinoindolines, we turned our attention to other substrates that could serve that role. One such class of compounds, more readily accessible compared to **29**, is represented by the 1-exomethylene tetralin derivatives (**32a–c**) shown in Figure 4. We reasoned that these alkenes would be sterically less demanding for the Ni-coordination in the hydrovinylation reaction, and, without the phthalimido group, would possibly be less Lewis basic, leading to larger turnovers in the catalyst. After hydrovinylation (to give **33**), the products would still carry either a relatively reactive benzylic position, or a functionalized aromatic carbon suitable for further elaboration into the desired compounds. For example, when X = CH₂, benzylic oxidation followed by some variation of the Beckmann or Schmidt rearrangement would place the N at the correct position.

Ni-Catalyzed asymmetric hydrovinylation of **32a–c** using ligands **9**, **26** and **27** were carried out under optimized reaction conditions (Eq. 5) and the results are shown in Table 5. Most gratifyingly, these substrates undergo efficient (<2 mol% catalyst) hydrovinylation at low temperature, giving excellent enantioselectivities (up to 99% ee) for the expected product. Apart from a minor isomerization of the double bond in the starting materials to give more stable internal alkenes (**34a** or **34b**), this is an exceptionally clean reaction to give the highly valued products. There is very little of this isomerization in the oxygenated substrate **32c**, but it undergoes a competitive dimerization (to give **35** in ~ 15% yield) in addition to the hydrovinylation product. Compounds like **33a** and **33b** have been used in the syntheses of analgesic (–)-eptazocine, narcotic (–)-aphanorphine and related compounds.^{15b,26,27} The minor detraction of the isomerization notwithstanding, the asymmetric hydrovinylation significantly shortens the synthesis of these compounds carrying a benzylic all-carbon quaternary center. For example, **33b** has been previously synthesized via stoichiometric oxazoline directed alkylation (12 steps, 35% overall yield, 99% ee)²⁶ or an enzyme-catalyzed desymmetrization of a chiral malonate (13 steps, 31% overall yield, 97% ee).²⁷ A closely related compound has been prepared by using asymmetric intramolecular Heck reaction (~10 steps, 37% overall yield, 93 % ee;) in a key step.^{15b} For comparison, asymmetric hydrovinylation yields the product **33b** in 80% yield and ~99% ee in 2 steps from 3-methoxytetralone! Attempts to convert these adducts into pyrrolidinoindolines, and intermediates for lyngbyatoxin and teleocidins, are currently underway. Incidentally, we also

found that the modified phosphoramidite ligands also give very high yields and selectivities in the asymmetric hydrovinylation of our model substrate, **11b** (entry 4).

(5)

We briefly examined the origin of asymmetric induction in the chroman (3,4-dihydro-2H-1-benzopyran) product **33c** using diastereomeric phosphoramidites. Upon examination of entry 3 in Table 5, it is clear that the chirality of the product is determined by the axial chirality of the biaryl moiety of the ligand, *not* by the chirality of the amine. Thus both ($R_aS_cS_c$)-ligand **9** and a diastereomer with ($R_aR_cR_c$) configuration gave the (R)-product in comparable ee's (94% and 89%). The ($S_aR_cR_c$)-ligand (ent-**9**) as expected gave the (S)-product. Since the phosphoramidite **26** (S_cS_c), a ligand derived from flexible biphenyl scaffolding, also gives the (R)-configuration in the product, it should be presumed that the chirality of the bis-amine (S_cS_c) induces R -configuration in the biphenyl unit, a behavior that was previously recorded by Alexakis and co-workers.²⁸ Further support in the present context comes from the solid state structure of a catalytically active Ni(allyl)(**26**)(Br) complex. These results will be reported in due course.

Conclusion

In this study, we report the details of a new catalytic method for the generation of all-carbon quaternary centers starting from relatively simple vinyl arene derivatives. Fine-tuning of the phosphoramidite ligands suggests that in the construction of these ligands, cheap 2,2'-biphenol can effectively replace the more expensive enantiopure 2,2'-binaphthols. Expansion of the scope of this reaction to dienes and strained bicyclic molecules, and applications in natural product synthesis will be reported in due course.

General methods

Reactions requiring air-sensitive manipulations were conducted under an inert atmosphere of nitrogen by using Schlenk techniques or a Vacuum Atmospheres glovebox. Methylene chloride was distilled from calcium hydride under nitrogen and stored over molecular sieves. Tetrahydrofuran was distilled under nitrogen from sodium/benzophenone ketyl. Unless specified other wise, vinylarenes were made via Wittig reaction of the corresponding aldehydes or ketones with methyl triphenylphosphonium bromide using *n*-BuLi/hexane in THF as a base to generate the ylide. Ligands^{4b,21b} **9**, ent-**9**, **26**, ent-**26**, **27** and **28**, Na^+ $[3,5-(\text{CF}_3)_2\text{C}_6\text{H}_3]_4\text{B}^-$ (NaBARF),^{20,29} and $[(\text{allyl})\text{NiBr}]_2$ ^{20,30} were prepared according to the literature. Ethylene (99.5%) was purchased from Matheson Inc., and passed through Drierite

before use. Analytical TLC was performed on E. Merck precoated (0.25 mm) silica gel 60 F254 plates. Flash column chromatography was carried out on silica gel 40 (Scientific Adsorbents Incorporated, Microns Flash). Enantiomeric excesses of chiral compounds **12b**, **21**, **22**, **23**, **25**, and **33a–33c** were determined by gas chromatographic analyses on chiral stationary phase, which were performed on a Hewlett-Packard 5890 equipped with Cyclodex B (25 m × 0.25 mm, 0.12 μm film thickness) capillary GC column purchased from Chrompack. Helium was used as the carrier gas. The enantiomeric excess of **24** was determined by ¹⁹F NMR using the corresponding Mosher ester of the alcohol derived from hydroboration of **24**. For determining the ee of **30g**, the free amine was liberated from the phthalimide, and was converted into the Mosher amide. ¹⁹F NMR analysis of the diastereomeric amides reveals the ee of the original HV product **30g**. Optical rotations were recorded on a Perkin-Elmer Model 241 polarimeter at the sodium D line in chloroform.

The following phosphoramidites were prepared using our recent modifications^{21b} of the previously reported methods.⁴

2,2'-biphenoyl-(*R,R*)-di(1-phenylethyl)aminoylphosphine (ent-26)

1,1'-Biphenyl-2,2'-dioxychlorophosphine (125 mg, 0.5 mmol) was reacted with (–)-bis[(*R*)-1-phenylethyl]amine (102 mg, 0.454 mmol) in THF to afford **ent-26**.

Yield: 94%; *R_f* = 0.49 (pentane-CH₂Cl₂, 3:1).

¹H NMR (400 MHz, CDCl₃): δ = 7.48–7.44 (m, 2H), 7.36–7.31 (m, 2H), 7.30–7.27 (m, 2H), 7.20–7.19 (m, 2H), 7.14–7.09 (m, 10H), 4.61–4.56 (m, 2H), 1.72 (d, *J* = 7.20 Hz, 6H).

¹³C NMR (100 MHz, CDCl₃): δ = 151.9, 151.0, 142.9, 131.2, 129.8, 129.0, 127.9, 126.6, 124.3 (d, *J* = 256.0 Hz), 122.2 (d, *J* = 192.0 Hz), 52.6, 22.1.

³¹P NMR (101 MHz, CDCl₃): δ = 146.4; lit.²⁸ 147.0

HRMS-ESI: *m/z* [M + Na]⁺ calcd for C₂₈H₂₆NO₂P + Na: 462.1593; found: 462.1591.

(*R*)-2,2'-binaphthoyl-benzyl-(*S*)-[1-(1-naphthylethyl)]aminoylphosphine (27)

The coupling of (*R*)-(–)-1,1'-binaphthyl-2,2'-dioxychlorophosphine (175 mg, 0.5 mmol) with *N*-benzyl-*N*-(*S*)-[1-(1-naphthylethyl)]amine (119 mg, 0.45 mmol) gave **27**.

Yield: 90%; *R_f* = 0.48 (pentane-CH₂Cl₂, 2:1).

¹H NMR (400 MHz, CDCl₃): δ = 7.94 (d, *J* = 8.8 Hz, 1H), 7.86–7.84 (m, 3H), 7.82 (d, *J* = 8.8 Hz, 1H), 7.8 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 7.2 Hz, 1H), 7.54 (d, *J* = 8.8 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 2H), 7.43–7.37 (m, 2H), 7.33–7.28 (m, 3H), 7.25–7.16 (m, 7H), 6.96 (d, *J* = 8.8 Hz, 1H), 5.40–5.33 (m, 1H), 3.95–3.36 (dAB quartet, *v_A* = 4.21, *v_B* = 3.11, *J_{AB}* = 15.3 Hz, *J_{H-P}* = 2.1 Hz, 2H), 1.69 (d, *J* = 6.8 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ = 150.1, 150.0, 149.5, 139.3, 136.52, 136.46, 133.9, 123.8, 132.5, 131.5, 131.4, 130.5, 130.2, 129.9, 128.8, 128.7, 128.4, 128.3, 128.1, 128.0, 127.02, 126.96, 126.9, 126.0, 125.6, 125.4, 125.3, 124.9, 124.8, 124.4, 124.1, 124.0, 123.8, 122.3, 122.2, 121.7, 52.0, 47.2, 21.7.

³¹P NMR (101 MHz, CDCl₃): δ = 145.5.

HRMS-ESI: *m/z* [M + Na]⁺ calcd for C₃₉H₃₀NO₂P + Na: 598.1906; found: 598.1907.

A typical Procedure for Asymmetric Hydrovinylation. Synthesis of (*R*)-3-Methyl-3-phenylpentene (**12b**)¹⁹

The pre-catalyst was prepared as follows *in a glove-box*: A 100-mL, pear-shaped Schlenk flask with one side-arm fitted with a rubber septum and equipped with a magnetic stirring bar was evacuated, flame-dried, and purged with argon. The flask was charged with anhydrous dichloromethane (50 mL) and was transferred into a glove-box. To the flask was quickly added [di(μ -bromo)bis(η -allyl)nickel(II) (180 mg, 0.50 mmol, 0.01 equiv), (*R*)-2,2'-binaphthoyl- (*S,S*)- di(1- phenylethyl)aminoylphosphine (**9**, 539 mg, 1.00 mmol, 0.02 equiv) and NaBARF (886 mg, 1.00 mmol, 0.02 equiv) in the order mentioned. The resulting suspension was stirred at ambient temperature for 2 h to afford a dark-brown solution containing a small amount of fine particles (NaBr). A 1-L, three-necked, round-bottomed flask equipped with a rubber septum, a Teflon-taped flow-controlled argon inlet, a thermometer, and a magnetic stir bar was flame-dried and purged with argon. The flask is then charged with 150 mL of anhydrous dichloromethane. The catalyst solution prepared above, now removed from the dry-box, was introduced to the vessel *via* cannula. The flask containing the catalyst solution was further rinsed with 10 mL of dichloromethane, and this solution was also transferred to the reaction mixture. Upon completion of pre-catalyst transfer, the system closed at the flow-controlled stopcock and then was cooled to $-70\text{ }^{\circ}\text{C}$ in a dryice/acetone bath, creating a small vacuum. A strong flow of dry ethylene was introduced through a needle through the serum stopper to relieve the vacuum and then was adjusted to maintain a pressure of 1 atm by releasing excess gas through an oil bubbler. The introduction of the ethylene caused the internal temperature to rise. Within ca. 5 min, the internal temperature increased by $5\text{ }^{\circ}\text{C}$ and the ethylene line was removed. The solution was cooled back to $-70\text{ }^{\circ}\text{C}$ with vigorous stirring. A solution of 2-phenyl-1-butene (**11b**) (6.60 g, 50.0 mmol) in 30 mL of dry dichloromethane was introduced as a weak stream into the solution of precatalyst over a two-minute period *via* syringe followed by a 10 mL rinse with dichloromethane. Ethylene was introduced again through a needle, first as a strong flow and then regulated to maintain a pressure of 1 atm. Under an ethylene atmosphere, the internal temperature of the reaction mixture was then maintained between $-65\text{ }^{\circ}\text{C}$ and $-70\text{ }^{\circ}\text{C}$ for a period of 4 h. At the end of this period the ethylene line was removed and the reaction mixture was slowly poured into an Erlenmeyer flask containing 500 mL of pentane and was combined with a 50-mL pentane rinse of the reaction vessel. After warming to ambient temperature, the resulting, cloudy solution was filtered through a plug of silica gel (Merck, grade 9385, mesh 230–400, $60\text{ }\text{\AA}$, $4\text{ cm} \times 5\text{ cm}$, ($d \times h$)), which was eluted with 100 mL of pentane. The combined eluates were concentrated by rotary evaporation ($20\text{ }^{\circ}\text{C}$, 20 mmHg) to afford 7.99 g (99.7%) of (*R*)-3-methyl-3- phenylpentene (97.6% ee) as clear liquid.

$[\alpha]_{\text{D}}^{22} = -22.3$ (c 1.05, CHCl_3), lit.³¹ $[\alpha]_{\text{D}}^{20} = -12.5$ (c 0.8, CHCl_3 , 92% ee). IR (neat): 3083, 3058, 2966, 2877, 1636, 1600, 1493, 1446, 1030, 913, 760, 700 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ = 7.33–7.27 (m 4H), 7.19–7.15 (m, 1H), 6.02 (dd, J = 17.6, 10.8 Hz, 1H), 5.10 (dd, J = 10.8, 1.2 Hz, 1H), 5.03 (dd, J = 17.6, 1.2 Hz, 1H), 1.88–1.70 (ABX₃, ν_{A} = 1.83, ν_{B} = 1.75, J_{AB} = 13.8 Hz, J_{AX} = 7.4 Hz, J_{BX} = 7.4 Hz, 2H), 1.34 (s, 3H), 0.76 (t, J = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3): δ = 147.4, 146.9, 128.0, 126.7, 125.7, 111.7, 44.5, 33.4, 24.4, 8.9.

HRMS-ESI: m/z [$\text{M}]^+$ calcd for $\text{C}_{12}\text{H}_{16}$: 160.1252; found: 160.1257.

GC: HP methylsilicone column, $25\text{ m} \times 0.25\text{ mm}$ conditions: 5 min at $100\text{ }^{\circ}\text{C}$, $5\text{ }^{\circ}\text{C}/\text{min}$, 5 min at $200\text{ }^{\circ}\text{C}$, retention time (min): 10.61. GC (chiral stationary phase, Cyclodex- β) 40 min at $70\text{ }^{\circ}\text{C}$, $5\text{ }^{\circ}\text{C}/\text{min}$, 10 min at $90\text{ }^{\circ}\text{C}$, retention time (min): 53.90 (*R*), 55.65 (*S*).

Other compounds in the Tables 3, 4 and 5 were prepared by appropriate modifications in the amount of catalyst, reaction temperature and reaction time as indicated therein.

(R)-3-Methyl-3-(4'-methylphenyl)-1-propene (21)

^1H NMR (500 MHz, CDCl_3): δ = 7.21 (d, J = 7.5 Hz, 2H), 7.11 (d, J = 7.5 Hz, 2H), 6.01 (dd, J = 17.5, 11.0 Hz, 1H), 5.09 (d, J = 11.0 Hz, 1H), 5.03 (d, J = 17.5 Hz, 1H), 2.32 (s, 3H), 1.90-1.70 (m, 2H), 1.34 (s, 3H), 0.77 (t, J = 6.5 Hz, 3H).

^{13}C NMR (125.7 MHz, CDCl_3): δ = 147.2, 144.6, 135.2, 128.9, 126.7, 111.7, 44.3, 33.5, 24.5, 21.0, 9.1

HRMS (LCT electrospray): $([\text{M}+\text{Na}]^+)$, m/z calcd for $\text{C}_{13}\text{H}_{18}\text{Na}$ 197.1306; found 197.1302.)

Enantiomeric excess: 90%; GC conditions: 85 °C isothermal, retention time: 53.69 min, 55.96 min; $[\alpha]_{\text{D}}^{20}$ = -22.1 (c 1.28, CHCl_3).

3-Methyl-3-(4'-chlorophenyl)-1-propene (22)

^1H NMR (500 MHz, CDCl_3): δ = 7.35-7.20 (m, 4H), 6.00 (dd, J = 17.5, 11.0 Hz, 1H), 5.14 (d, J = 11.0 Hz, 1H), 5.05 (d, J = 17.5 Hz, 1H), 1.90-1.70 (m, 2H), 1.36 (s, 3H), 0.78 (t, J = 7.5 Hz, 3H);

^{13}C NMR (125.7 MHz, CDCl_3) δ = 146.6, 146.1, 131.6, 128.4, 128.2, 112.4, 44.5, 33.6, 24.6, 9.0.

Enantiomeric excess: 90%; GC conditions: 105°C isothermal, retention time: 57.68 min, 62.15 min; $[\alpha]_{\text{D}}^{20}$ = -21.5 (c 1.25, CHCl_3).

3,4-Dimethyl-3-phenyl-1-propene (23)

^1H NMR (500 MHz, CDCl_3): δ = 7.40-7.25 (m, 3H), 7.25-7.10 (m, 2H), 6.19 (dd, J = 17.5, 11.0 Hz, 1H), 5.19 (d, J = 11.0 Hz, 1H), 5.06 (d, J = 17.5 Hz, 1H), 2.25-2.15 (m, 1H), 1.35 (s, 3H), 0.86 (d, J = 7.0 Hz, 3H), 0.78 (d, J = 7 Hz, 3H)

^{13}C NMR (125.7 MHz, CDCl_3): δ = 148.4, 144.9, 128.1, 126.8, 125.7, 113.3, 47.6, 36.3, 20.7, 18.3, 17.9.

Enantiomeric excess: 97%; GC conditions: 60 min at 70°C, 0.5°C/min, 60 min at 90°C, retention time: 101.39 min, 102.99 min.

3-Methyl-3-phenyl-1-octene (24)

^1H NMR (500 MHz, CDCl_3): δ = 7.40-7.28 (m, 4H), 7.25-7.15 (m, 1H), 6.05 (dd, J = 17.5, 10.5 Hz, 1H), 5.10 (d, J = 10.5 Hz, 1H), 5.04 (d, J = 17.5 Hz, 1H), 1.85-1.65 (m, 2H), 1.37 (s, 3H), 1.35-1.10 (m, 6H); 0.88 (t, J = 7.5 Hz, 3H).

^{13}C NMR (125.7 MHz, CDCl_3): δ = 147.9, 147.4, 128.2, 126.7, 125.8, 111.7, 44.4, 41.3, 32.7, 25.1, 24.3, 22.7, 14.2. HRMS (LCT electrospray): m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{22}\text{Na}$ 225.1619; found 225.1618.

Enantiomeric excess: 50~55% by Mosher method, ^{15}F NMR (376.5 MHz, CDCl_3) δ = -71.30 (diastereomer 1), and -71.31 (diastereomer 2); ^{13}C NMR (125.7 MHz, CDCl_3) δ 24.10 (diastereomer 1), 24.04 (diastereomer 2). $[\alpha]_{\text{D}}^{20}$ = -6.9 (c 1.06, CHCl_3).

(R)-3-Methyl-3-(2-naphthyl)-1-propene (25)

^1H NMR (500 MHz, CDCl_3): δ = 7.85-7.75 (m, 3H), 7.73 (s, 1H), 7.50-7.40 (m, 3H), 6.12 (dd, J = 17.5, 11 Hz, 1H), 5.16 (d, J = 11.0 Hz, 1H), 5.09 (d, J = 11.0 Hz, 1H), 2.00-1.90 (m, 1H), 1.90-1.80 (m, 1H), 1.46 (s, 3H), 0.80 (t, J = 7.5 Hz, 3H).

^{13}C NMR (125.7 MHz, CDCl_3): δ = 147.0, 145.0, 133.5, 132.0, 128.1, 127.6, 127.5, 126.0, 125.9, 125.5, 125.0, 112.2, 44.9, 33.4, 24.5, 9.1. HRMS (LCT electrospray): m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{18}\text{Na}$ 233.1306; found 233.1310.

Enantiomeric excess: 93%, GC conditions: 120 °C isothermal, retention time: 130.79 min, 132.86 min; $[\alpha]_{\text{D}}^{20}$ = -22.9 (c 1.43, CHCl_3).

General Procedure for the Synthesis of Alkenes (29a-f) via Stille Coupling

A flask was charged with the aryl iodide (100 mol%, 1 ~ 5 mmol scale), vinyltin (120 mol%), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (5 mol%), K_2CO_3 (100 mol%), Et_4NCl (100 mol%), and deoxygenated DMF (5 mL), and the resulting mixture was stirred at 110 °C overnight. After the reaction was completed, the mixture was cooled to rt, and then was filtered through Celite to remove solid impurities. After the solution was diluted with water, the crude product was extracted with EtOAc, dried over MgSO_4 , and purified by column chromatography.

Synthesis of *tert*-butyl(3-(3-methoxyphenyl)but-3-enyloxy)dimethylsilane (29a)

Following the general procedure, the desired product was obtained with 70 % isolated yield as colorless oil.

^1H NMR (400 MHz, CDCl_3): δ = 7.31-7.27 (t, 1H, J = 7.8 Hz, Ar), 7.09-7.02 (m, 2H, Ar), 6.89-6.86 (m, 1H, Ar), 5.40 (s, 1H, $\text{R}=\text{CH}_2$), 5.17 (s, 1H, $\text{R}=\text{CH}_2$), 3.85 (s, 3H, ArOMe), 3.80-3.77 (t, 2H, J = 7.2 Hz, RCH_2OTBS), 2.81-2.78 (m, 2H, $\text{RCH}_2\text{CH}_2\text{OTBS}$), 0.98 (s, 9H, *t*-Bu), 0.09 (s, 6H, $\text{Si}(\textit{t}\text{-Bu})\text{Me}_2$).

^{13}C NMR (100 MHz, CDCl_3): δ = 159.8, 145.4, 142.8, 129.4, 118.8, 114.2, 112.9, 112.2, 62.6, 55.3, 39.1, 26.1, 18.5, -5.2.

Synthesis of *tert*-butyl 2-(4-(*tert*-butyldimethylsilyloxy) but-1-en-2-yl)-4-methoxy-phenyl(methyl)carbamate (29b)

Following the general procedure, the desired product was obtained with 56 % isolated yield as pale yellow solid.

^1H NMR (400 MHz, CDCl_3): δ = 6.95-6.93 (d, 1H, J = 7.6 Hz, Ar), 6.75-6.69 (m, 2H, Ar), 5.15 (s, 1H, vinyl), 5.02 (s, 1H, vinyl), 3.78 (s, 3H), 3.60-3.55 (m, 2H), 3.03 (s, 3H), 2.52-2.50 (m, 2H), 1.32 (s, 9H), 0.84 (s, 9H), -0.02 (s, 6H).

^{13}C NMR (100 MHz, CDCl_3): δ = 157.9, 155.3, 129.3, 114.9, 113.1, 79.7, 61.6, 55.4, 39.4, 28.3, 27.8, 26.8, 25.9, 18.2, -4.5.

Synthesis of 1-[(4-azidobut-1-en-2-yl)]-3-methoxy-benzene (29c)

To a stirred solution of OTBS compound **29a** (50 mg, 0.017 mmol) in EtOH (2 mL) was added 1 N HCl (0.1 mL) and the resulting solution was stirred at rt for 1 h. After the deprotection was completed, the mixture was diluted with water (3 mL) and the product was extracted

CH₂Cl₂ (3 × 3 mL). Combined organic layers were dried over MgSO₄, and then filtered and evaporated. The crude alcohol was dissolved in CH₂Cl₂ (3 mL) and Et₃N (59 µL, 0.042 mmol) and methanesulfonyl chloride (16 µL, 0.021 mmol) were added in succession at 0 °C. The resulting mixture was stirred at rt for 2 h after which the solvent was evaporated. The residue was dissolved in DMF (2 mL) and NaN₃ (23 mg, 0.034 mmol) was added. The mixture was heated to 60 °C for 12 h. The solution was diluted with water (5 mL), and the product was extracted with EtOAc (3 × 5 mL). The crude product **29c** was purified by preparative TLC (28 mg, 82%, colorless oil).

¹H NMR (400 MHz, CDCl₃): δ = 7.33-7.29 (t, 1H, *J* = 8.0 Hz, Ar), 7.03-6.98 (m, 2H, Ar), 6.90-6.88 (dd, 1H, *J* = 4.0, 2.4 Hz, Ar), 5.44 (s, 1H, R=CH₂), 5.22 (s, 1H, R=CH₂), 3.86 (s, 3H, ArOMe), 3.42-3.38 (t, 3H, *J* = 7.2 Hz, RCH₂N₃), 2.85-2.81 (t, 2H, *J* = 7.0 Hz, RCH₂CH₂N₃).

¹³C NMR (100 MHz, CDCl₃): δ = 159.9, 144.8, 141.8, 129.6, 118.7, 115.1, 113.1, 112.3, 55.4, 49.9, 35.2.

Synthesis of 2-(3-(3-methoxyphenyl)but-3-enyl)isoindoline-1,3-dione (**29d**)

Following the general Stille procedure, the desired product was obtained in 63 % isolated yield as pale yellow oil.

IR cm⁻¹ (neat): 3072, 2941, 2835, 1770, 1712, 1598, 1576, 1488, 1466, 1434, 1394, 1359, 1328, 1287, 1231, 1187, 1120, 1087, 1047, 1001.

¹H NMR (400 MHz, CDCl₃): δ = 7.80-7.78 (dd, 2H, *J* = 3.0, 2.4 Hz, Ar), 7.69-7.66 (dd, 2H, *J* = 3.0, 2.4 Hz, Ar), 7.22-7.18 (t, 1H, *J* = 8.0 Hz, Ar), 7.04-7.02 (d, 1H, *J* = 7.6 Hz, Ar), 6.99 (s, 1H, Ar), 6.75-6.73 (dd, 1H, *J* = 8.0, 2.4 Hz, Ar), 5.37 (s, 1H, R=CH₂), 5.16 (s, 1H, R=CH₂), 3.85-3.79 (m, 5H, ArOMe and RCH₂NPhth), 2.91-2.88 (t, 2H, *J* = 7.2 Hz, RCH₂CH₂NPhth).

¹³C NMR (100 MHz, CDCl₃): δ = 168.1, 159.6, 144.9, 141.6, 133.8, 132.1, 129.3, 123.0, 118.6, 114.7, 113.1, 111.7, 55.2, 37.5, 34.0.

HRMS: (M+H)⁺ calcd. for C₁₉H₁₈NO₃ 308.1287; found 308.1272.

Synthesis of 2-(3-(5-methoxy-2-nitrophenyl)but-3-enyl)isoindoline-1,3-dione (**29e**)

Following the general procedure, the desired product was obtained, and was purified by column chromatography using 25% EtOAc in hexane. (rf 0.5 in 50% EtOAc/hexanes). The product was isolated yield in 39% yield as colorless oil.

IR cm⁻¹ (neat): 3085, 2943, 2848, 1770, 1722, 1601, 1574, 1514, 1393, 1337, 1249, 1187, 1097, 1065, 1027.

¹H NMR (400 MHz, CDCl₃): δ = 8.01-7.99 (d, 1H, *J* = 9.2 Hz, Ar), 7.81-7.79 (m, 2H, Ar), 7.70-7.66 (m, 2H, Ar), 6.86-6.80 (m, 2H, Ar), 5.16 (s, 1H, R=CH₂), 4.99 (s, 1H, R=CH₂), 3.89 (s, 3H, ArOMe), 3.80-3.77 (t, 2H, *J* = 7.0 Hz, RCH₂NPhth), 2.80-2.76 (t, 2H, *J* = 6.8 Hz, RCH₂CH₂NPhth).

¹³C NMR (125.7 MHz, CDCl₃): δ = 168.4, 163.2, 144.9, 140.7, 134.3, 131.9, 127.5, 126.2, 123.4, 118.2, 116.6, 116.3, 113.7, 56.2, 37.0, 35.2.

HRMS: (M+H)⁺ calcd for C₁₉H₁₇N₂O₅ 353.1137; found 353.1120.

2-(3-(2-bromo-5-methoxyphenyl)but-3-enyl)isoindoline-1,3-dione (29f)

Following the general procedure, the desired product was obtained with 40% isolated yield as colorless oil.

¹H NMR (400 MHz, CDCl₃): δ = 7.79-7.77 (m, 2H, Ar), 7.68-7.65 (m, 2H, Ar), 7.35-7.33 (d, 1H, *J* = 8.8 Hz, Ar), 6.63-6.60 (dd, *J* = 8.8, 3.2 Hz, 1 H, Ar), 6.81-6.80 (d, 1H, *J* = 2.8 Hz, Ar), 5.21 (s, 1H, R=CH₂), 5.00 (s, 1H, R=CH₂), 3.76-3.73 (m, 5H, ArOMe and RCH₂NPhth), 2.85-2.82 (t, 2H, *J* = 7.0 Hz, RCH₂CH₂NPhth).

¹³C NMR (100 MHz, CDCl₃): δ = 168.3, 158.8, 146.6, 143.7, 134.0, 133.5, 132.2, 123.3, 117.8, 116.2, 114.9, 112.3, 55.6, 36.9, 34.9.

Synthesis of 2-(3-(3-(benzyloxy)phenyl)but-3-enyl)isoindoline-1,3-dione (29g)

Following the general procedure, the desired product was obtained and was further purified by column chromatography using 10 % EtOAc in hexane (rf 0.3 in 15% EtOAc/hexane; isolated yield 63 %, pale yellow oil).

IR cm⁻¹ (neat): 3062, 3031, 2945, 2869, 1771, 1713, 1597, 1574, 1488.2, 1435, 1395, 1360, 1288, 1224, 1121, 1087, 1026, 1001.

¹H NMR (400 MHz, CDCl₃): δ = 7.79-7.77 (dd, 2H, *J* = 5.4, 3.2 Hz, Ar), 7.67-7.65 (dd, 2H, *J* = 5.4, 3.2 Hz, Ar), 7.45-7.31 (m, 5H, Ar), 7.20-7.18 (t, 1H, *J* = 8.0 Hz, Ar), 7.05-7.01 (m, 2H, Ar), 6.81-6.78 (m, 1H, Ar), 5.33 (s, 1H, R=CH₂), 5.12 (s, 1H, R=CH₂), 5.06 (s, 2H, ROCH₂Ph), 3.83-3.79 (t, 3H, *J* = 7.4 Hz, RCH₂NPhth), 2.88-2.85 (t, 2H, *J* = 7.2 Hz, RCH₂CH₂NPhth).

¹³C NMR (125.7 MHz, CDCl₃): δ = 168.2, 158.8, 144.8, 141.6, 137.1, 133.8, 132.1, 129.4, 128.6, 128.0, 127.6, 123.2, 118.9, 114.9, 114.0, 112.7, 70.0, 37.4, 34.0.

HRMS: (M+H)⁺ calcd for C₂₅H₂₂NO₃ 384.1600; found 384.1583.

General Procedure of Asymmetric Hydrovinylation of Substares 29a–29g

In a N₂-charged drybox, a two-necked Schlenk tube was charged with [allyl-NiBr]₂ (1 mol%), ligand (2 mol%), and NaBARF (2 mol%), and the mixture was dissolved in dry CH₂Cl₂ (5~7 mL/mmol of olefin). This precatalyst was stirred at rt for 10 min, and then taken out of the drybox. After ethylene line was connected to the reaction vessel, the line was evacuated 3 times to remove oxygen in a line, and then ethylene was introduced to the vessel. Into the activated catalyst, starting olefin in dry CH₂Cl₂ (1~2 mL/mmol of olefin) was added, and the resulting mixture was stirred at ambient temperature under the atmospheric pressure of ethylene. After the reaction, the solvent was evaporated, and the crude product was purified by column chromatography.

Synthesis of (R)-2-(3-(3-methoxyphenyl)-3-methylpent-4-enyl)isoindoline-1,3-dione (30d) [entry 7, Table 4]

Following the general procedure using allylNi(26)BARF (10 mol%) at 35 °C for 12 h, the desired product was obtained (81%, isolated yield, pale yellow oil).

IR cm^{-1} (neat) : 3072, 2930, 2837, 1772, 1707, 1601, 1484, 1396, 1366, 1284, 1249, 1173, 1049.

^1H NMR (400 MHz, CDCl_3): δ = 7.74-7.72 (m, 2H, Ar), 7.67-7.63 (m, 2H, Ar), 7.15-7.11 (t, 1H, J = 8.0 Hz, Ar), 6.92-6.87 (m, 2H, Ar), 6.59-6.56 (dd, 1H, J = 8.0, 2.4 Hz, Ar), 6.09-6.02 (dd, 1H, J = 11.2, 6.0 Hz, $\text{RCH}=\text{CH}_2$), 5.15 (s, 1H, $\text{RCH}=\text{CH}_2$), 5.12-5.10 (d, 1H, J = 8.0 Hz, $\text{RCH}=\text{CH}_2$), 3.76 (s, 3H, OMe), 3.64-3.60 (t, 2H, J = 8.0 Hz, RCH_2NPhth), 2.24-2.18 (m, 1H, $\text{RCH}_2\text{CH}_2\text{NPhth}$), 2.10-2.05 (m, 1H, $\text{RCH}_2\text{CH}_2\text{NPhth}$), 1.46 (s, 3H, RCH_3).

^{13}C NMR (100 MHz, CDCl_3): δ = 168.4, 159.6, 147.9, 145.9, 133.9, 132.4, 129.4, 123.2, 119.1, 112.9, 112.7, 111.2, 55.3, 43.5, 38.6, 34.8, 25.2.

Synthesis of (*R*)-2-(3-(3-(benzyloxy)phenyl)-3-methylpent-4-enyl)isoindoline-1,3-dione (30g) [entry 8, Table 4]

Following the general procedure using allylNi(**26**)BARF (10 mol%) under 35 °C for 48 h, the desired product was obtained (76%, isolated yield, pale yellow oil).

IR cm^{-1} (neat) : 3084, 3025, 2942, 2872, 1772, 1707, 1601, 1437, 1390, 1360, 1243, 1084, 1026.

^1H NMR (400 MHz, CDCl_3): δ = 7.76-7.74 (m, 2H, Ar), 7.66-7.63 (m, 2H, Ar), 7.44-7.30 (m, 5H, Ar), 7.16-7.12 (t, 1H, J = 8.0 Hz, Ar), 6.96-6.92 (m, 2H, Ar), 6.67-6.65 (m, 1H, Ar), 6.08-6.01 (dd, 1H, J = 10.8, 6.0 Hz, $\text{RCH}=\text{CH}_2$), 5.15 (s, 1H, $\text{RCH}=\text{CH}_2$), 5.12-5.10 (d, 1H, J = 8.0 Hz, $\text{RCH}=\text{CH}_2$), 5.01 (s, 2H, ROCH_2Ph), 3.63-3.59 (t, 2H, J = 8.0 Hz, RCH_2NPhth), 2.25-2.18 (m, 1H, $\text{RCH}_2\text{CH}_2\text{NPhth}$), 2.13-2.04 (m, 1H, $\text{RCH}_2\text{CH}_2\text{NPhth}$), 1.46 (s, 3H, RCH_3).

^{13}C NMR (100 MHz, CDCl_3): δ = 168.4, 158.9, 148.1, 145.8, 137.4, 133.9, 132.4, 129.4, 128.7, 128.4, 128.1, 127.8, 126.6, 123.2, 119.3, 113.9, 112.7, 112.2, 70.1, 43.5, 38.6, 34.8, 25.2, 21.3.

HRMS: $(\text{M}+\text{H})^+$ calcd for $\text{C}_{27}\text{H}_{26}\text{NO}_3$ 412.1913; found 412.1916.

$[\alpha]_{\text{D}}^{22} = +1.87$ (c 1.03, CHCl_3 , 53% ee)

Isomerized product

^1H NMR (400 MHz, CDCl_3): δ = 7.90 - 7.69 (m, 4H, phthalimidyl), 7.49 - 7.29 (m, 5H, Ar), 7.19 (t, J = 6.4 Hz, 1H, Ar), 7.05 - 6.85 (m, 2H, Ar), 6.84 - 6.79 (m, 1H, Ar), 5.85 (t, J = 7.0 Hz, 1H, Ar(CH_3) $\text{C}=\text{CHCH}_2\text{N-phth}$), 5.03 (s, 2H, OCH_2Ph), 4.50 (d, 7.5 Hz, 2H, Ar(CH_3) $\text{C}=\text{CHCH}_2\text{N-phth}$, E), 4.22 (d, J = 6.5 Hz, 2H, Ar(CH_3) $\text{C}=\text{CHCH}_2\text{N-phth}$, Z), 2.23 (s, 3H, Ar(CH_3) $\text{C}=\text{CHCH}_2\text{N-phth}$, E), 2.01 (s, 3H, Ar(CH_3) $\text{C}=\text{CHCH}_2\text{N-phth}$, Z); The configuration of the major product was established by nOe studies.

^{13}C NMR (100 MHz, CDCl_3): δ = 168.4, 144.5, 139.4, 137.3, 134.1, 132.5, 129.6, 128.1, 127.8, 123.4, 121.6, 119.1, 113.7, 113.1, 70.2, 36.5, 16.4.

HRMS ($\text{M}+\text{Na}^+$): calcd for $\text{C}_{25}\text{H}_{21}\text{NNaO}_3$ 406.1419; found 406.1400.

Synthesis of (*R*)-2-(3-(3-(Benzyloxy)phenyl)-3-methylpent-4-enyl)isoindoline-1,3-dione (30g**) Under Elevated Pressure of Ethylene (entry 9, Table 4)**

In N₂-charged drybox, 10 mol% of allylNi(**26**)BARF precatalyst in CH₂Cl₂ (1.5 mL) was prepared, and then the solution was added to a Fisher-Porter tube. After 10 min of stirring at rt, starting material **29g** (20 mg, 0.0487 mmol) in CH₂Cl₂ (1.5 mL) was added to the precatalyst solution. The tube was tightly closed, and then taken out from a drybox. After the tube was connected to an ethylene line, the line was evacuated 3 times, and then ethylene gas was introduced to the tube, and pressurized to 17 psi. During the reaction, internal pressure decreased, so the system was recharged for 3 times. After 30 min of stirring, the solution was concentrated. The crude product was purified by preparative TLC to get ~20 mg (> 95%) of the product **30g** identified in the previous experiment.

Determination of Enantiomeric Excess of **30g by Mosher's Method**

The phthalimide protecting group in hydrovinylation product **30g** was removed by refluxing this material (15 mg, mmol) with hydrazine hydrate (500 mol%), and ethanol (3 mL) for 12 h. The crude amine was purified by acid-base work-up, and subsequent extraction with CH₂Cl₂. A solution of the amine in CH₂Cl₂ (2 mL) was treated with triethyl amine (300 mol %), followed by MTPA-Cl (110 mol%). The %ee was determined by the integration of ¹⁹F NMR peaks in the diastereomers [¹⁹F NMR δ (C₆D₆): Mosher amides from the racemic product: 68.61, and 68.57]. Diastereomeric ratio using ligand **26** was 1.0 : 3.5 corresponding to an ee of ~ 55% in the asymmetric catalyzed reaction. For both reactions done under 1 atmosphere of ethylene at 35 °C for 48 h (entry 8, in Table 4), and under 17 psi of ethylene at 25 °C for 0.5 h (entry 9, in Table 4), the selectivity was approximately same, within experimental error. The enantioselectivities for reactions using other ligands were estimated the same way.

Ligand **9** (entry 6, in Table 4): ratio of diastereomers, 1.0 : 4.1 (~ 61% ee)

Ligand **27** (entry 10, in Table 4): ratio of diastereomers, 1.0 : 3.0 (~ 50% ee)

(R)-1-Methyl-1-vinyltetrahydronaphthalene (33a)

Yield: 71% contaminated with ~28% 1-methyl-3,4- dihydronaphthalene (**34a**).

¹H NMR (400 MHz, CDCl₃): δ = 7.21-7.13 (m, 4H), 6.01 (dd, J = 17.60 Hz, 10.40 Hz, 1H), 5.10 (dd, J = 10.40, 1.20 Hz, 1H), 4.89 (dd, J = 17.60, 1.20 Hz, 1H), 1.90-1.83 (m, 3H), 2.84 (d, J = 7.60 Hz, 2 H), 1.76-1.71 (m, 1H), 1.46 (s, 3H).

¹³C NMR (100 MHz, CDCl₃): δ = 148.8, 142.3, 135.8, 129.1, 128.5, 125.7, 125.6, 112.0, 40.9, 37.6, 34.1, 28.3, 22.4.

HRMS-ESI: m/z [M]⁺ calcd for C₁₃H₁₆: 172.1247; found: 172.1245.

GC (HP methylsilicone) conditions: 5 min at 100°C, 5°C/min, 5 min at 200°C, retention time (min): 13.10.

Enantiomeric Excess: >99%; GC (Cyclodex- β) conditions: 75 min. at 90°C, retention time (min): 62.85 (*S*) and 63.69 (*R*). [α]_D 20 = -35.4 (*c* 1.15 CHCl₃).

Isomerized product, 4-methyl-1,2- dihydronaphthalene (34a)

¹H NMR (400 MHz, CDCl₃): δ = 7.23-7.17 (m, 2 H), 7.15-7.10 (m, 2 H), 5.85-5.83 (m, 1 H), 2.75 (t, J = 8.0 Hz, 2 H), 2.26-2.20 (m, 2 H), 2.04 (dd, J_1 = 3.2 Hz, J_2 = 1.6 Hz, 3 H).

¹³C NMR (125.7 MHz, CDCl₃): δ = 136.3, 135.9, 132.3, 127.3, 126.7, 126.3, 125.4, 122.8, 28.3, 23.2, 19.3.

Synthesis of (R)-7-methoxy-1-methyl-1-vinyl- 1,2,3,4-tetrahydronaphthalene 33b (entry 2, Table 5)

Following the general procedure, using 4 mol% of allylNi(**9**)BARF as the catalyst, 7-methoxy-1- methylene-1,2,3,4-tetrahydronaphthalene (**32b**, 0.30 g, 1.72 mmol) was converted into the title compound in a reaction run for 6 h at -70 °C. The product, purified by column chromatography (0.30 g, > 99%) was obtained as a mixture of the hydrovinylation product **33b** (82%, > 99% ee by chiral GC), isomerized starting material **34b** (15%), and unconverted starting material **32b** (3%). The ratios of these compounds were determined by integration of the diagnostic peaks in the ¹H NMR spectrum.

IR cm⁻¹ (neat): 2958, 2829, 1722, 1637, 1606, 1580, 1488, 1443, 1368.2, 1322, 1223, 1190 1121, 1064.

¹H NMR (500 MHz, CDCl₃): δ = 7.01-6.96 (m, 2H, Ar), 6.68-6.65 (m, 1H, Ar), 5.95-5.88 (dd, 1H, J = 17.2, 10.4 Hz, RCH=CH₂), 5.85 (br s, 1H, isomerized product's vinyl-H), 5.02-4.99 (dd, 1H, J = 10.4, 1.2 Hz, RCH=CH₂), 4.87-4.82 (dd, 1H, J = 17.6, 1.2 Hz, RCH=CH₂), 3.75 (s, 3H, ROMe), 2.71-2.68 (t, 2H, J = 6.2 Hz, ArCH₂R), 1.85-1.73 (m, 4H, ArCH₂CH₂CH₂R and ArCH₂CH₂CH₂R), 1.36 (s, 3H, q-CCH₃)

¹³C NMR (125.7 MHz, CDCl₃): δ = 157.7, 148.8, 143.7, 130.0, 129.0, 113.8, 112.2, 111.9, 55.4, 41.4, 37.7, 29.6, 28.4, 19.6.

Enantiomeric Excess: 99%; GC conditions 120 °C isothermal with cyclodex- β column, retention times - *R*-isomer 56.09 min, *S*-isomer (obtained by *ent*-**9**) 57.10 min.; [α]_D 22 = -14.5 (*c* 0.142, CHCl₃), lit.²⁶ [α]_D 20 = -21.1 (*c* 3.8, CHCl₃).

Synthesis of (*R*)-4-methyl-4-vinylchroman 33c (entry 3, Table 5)

Following the general procedure using 10 mol% of allylNi(**9**)BARF and **32c** (0.2 g, 1.37 mmol) at 35 °C for 12 h, the desired product **33c** (0.167 g, 70%) was obtained as a pale yellow oil after purification. In addition to the expected product, a head-to-tail dimer **35** was also obtained.

IR cm^{-1} (neat): 2959, 2830, 1722, 1637, 1605, 1579, 1487, 1443, 1368, 1321, 1223, 1190, 1121, 1064. ^1H NMR (400 MHz, CDCl_3): δ = 7.15-7.07 (m, 2H, Ar), 6.88-6.84 (m, 1H, Ar), 6.81-6.79 (dd, 1H, J = 8.2, 1.2 Hz, Ar), 5.92-5.87 (dd, 1H, J = 17.5, 10.5 Hz, $\text{RCH}=\text{CH}_2$), 5.12-5.10 (dd, 1H, J = 10.5, 1.5 Hz, $\text{RCH}=\text{CH}_2$), 4.87-4.82 (dd, 1H, J = 12.2, 1.2 Hz, $\text{RCH}=\text{CH}_2$), 4.18-4.13 (m, 2H, $\text{ROCH}_2\text{R}'$), 1.89-1.86 (m, 2H, $\text{ROCH}_2\text{CH}_2\text{R}'$), 1.43 (s, 3H, RCH_3).

^{13}C NMR (100 MHz, CDCl_3): δ = 154.3, 147.5, 128.9, 127.9, 127.7, 120.4, 117.1, 114.2, 62.9, 37.9, 36.1, 27.9

Enantiomeric Excess: 94%; GC conditions (Cyclodex β column, isothermal 100 °C)- retention times: *S*-isomer (obtained from ligand *ent*-**9**): 47.03 min; *R*-isomer: 48.76 min.

Dimer (35) from HV of 32c

Isolated yields of dimer **35** from HV using ligand **9** and **26** were ~ 15% (a pale yellow oil).

IR cm^{-1} (neat): 3058, 2927, 2856, 1725, 1590, 1578, 1487, 1450, 1347, 1266, 1221, 1165, 1090.

^1H NMR (400 MHz, CDCl_3): δ = 7.16-7.02 (m, 4H, Ar), 6.84-6.76 (m, 4H, Ar), 5.42-5.40 (t, 1H, J = 3.8 Hz, vinyl), 4.63-4.62 (d, 2H, J = 3.6 Hz), 4.21-4.18 (m, 1H, $\text{ROCH}_2\text{CH}_2\text{R}'$), 4.14-4.11 (m, 1H, $\text{ROCH}_2\text{CH}_2\text{R}'$), 2.89-2.86 (d, 1H, J = 14.0 Hz, $\text{RCH}_2\text{CR}'$), 2.71-2.67 (d, 1H, J = 14.0 Hz, $\text{RCH}_2\text{CR}'$), 2.00-1.97 (m, 1H, $\text{ROCH}_2\text{CH}_2\text{R}'$), 1.75-1.69 (m, 1H, $\text{ROCH}_2\text{CH}_2\text{R}'$), 1.29 (s, 3H, RCH_3). The assignments were further confirmed by COSY and NOESY experiments.

^{13}C NMR (100 MHz, CDCl_3): δ = 154.1, 128.9, 127.7, 127.5, 124.1, 122.8, 121.2, 120.5, 117.2, 116.4, 65.3, 63.0, 42.4, 34.9, 34.5, 29.7.

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Figure 1.
Assorted Ligands for Asymmetric Hydrovinylation

Figure 2.
Selected Phosphoramidite Ligands

Figure 3.
1-Alkylstyrene Precursors for Pyrrolidinoindolines

Figure 4.
Vinylarenes and their HV Products as Precursors for Pyrrolidinoindoline

Figure 5.
Exo-methylene Precursors for Pyrrolidinoindolines

Table 1

Hydrovinylation of 1-Ethylstyrene (Ligand Scouting)

entry	ligand (mol%)	temp (°C)	time (h)	conv. (%)	ee%, conf. ^b
1.	13/5	25	48	74	racemic
2.	6/5	– ^a	– ^a	low	–
3.	7/5	–10	16	67	27 (<i>R</i>)
4.	7/5	0	19	76	27 (<i>R</i>)
5.	7/5	25	22	72	25 (<i>R</i>)
6.	8/5	– ^a	– ^a	low	–

^a Various.

^b Determined by GC analysis on cyclodex-B column. Configuration assigned by GC retention times of known compound.²⁰

Table 2
Asymmetric Hydrovinylation of 1-Ethylstyrene Using Ligand **9**

entry	ligand (mol%)	temp (°C)	time (h)	conv. (%)	ee%, conf. ^a
1	9/5	-10	21	>99	79 (<i>R</i>)
2	9/5	-30	17	>99	77 (<i>R</i>)
3	9/5	-55	19	>99	88 (<i>R</i>)
4	9/5	-70	17	>99	93 (<i>R</i>)
5	9/5	-70	4	>99	96 (<i>R</i>)
6	9/1	-70	4	>99	95 (<i>R</i>)
7	9/2	-70–-65	4	99.7	97.6 (<i>R</i>) ^b

^a Determined by GC analysis on cyclodex-B column, for authentic product see ref. 20.

^b Reaction done on 50 mmol scale.

product	T (°C)/t (h)	yield	ee (%) ^b
-60/12	>90	90

21

product	T (°C)/t (h)	yield	ee (%) ^b
22	-70/11	>90 ^c	90

product	T (°C)/t (h)	yield	ee (%) ^b
23	24/20	60 ^e	>95

product	T (°C)/t (h)	yield	ee (%) ^b
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-70.8

93^c

>50^f

product	T (°C)/t (h)	yield	ee (%) ^b
-70/14	>98	93
25	-70/14	0	--

product	T (°C)/t (h)	yield	ee (%) ^b
--	-70/14	0	--

Table 4

Asymmetric Hydrovinylation of 1-(2-Y-ethyl)Styrene (Y= OTBS, N₃, NPHT) Derivatives Using Phosphoramidite Ligands

entry	styrene	ligand, conditions, ethylene pres.	yield (%)	ee (%) ^a
1.	29a	10 mol% (9), 12 h at rt, 1 atm	0	--
2.	29a	10 mol% (9), 35°C, 12 h, 1 atm	0	--
3.	29b	10 mol% (9), rt, 12 h, 1 atm	0	--
4.	29c	5 mol% (9), rt, 12 h, 1 atm	< 5	--
5.	29d	10 mol% (9), 35°C, 12 h, 1 atm	47	--
6.	29g	10 mol% (9), 35°C, 48 h, 1 atm	69^b	61
7.	29d	10 mol% (26), 35°C, 12 h, 1 atm	81 ^b	--
8.	29g	10 mol% (26), 35°C, 48 h, 1 atm	76 ^b	53 ^d
9.	29g	10 mol% (26), 25°C, 0.5 h, 17 psi^c	>95	55
10.	29g	10 mol% (27), 35°C, 12 h, 1 atm	68 ^b	50
11.	29e	10 mol% (26), 25°C, 0.5 h, 17 psi ^c	0	--
12.	29f	10 mol% (26), 25°C, 0.5 h, 17 psi ^c	0	--

^a Determined by ¹⁹F NMR of *N*-MTPA derivative of the hydrovinylation product.

^b Isomerization of the double bond (~15% to **31**) observed.

^c Carried out in a Fischer-Porter tube.

^d Analyzed as a γ -lactam after oxidative degradation of the alkene and cyclization.

Table 5
Asymmetric Hydrovinylation of Exomethylene Compounds^a

entry	substrate	product	Ligand(s)			
			9		26	
			yield	%ee ^b	yield	%ee ^b
1.	32a	33a	71 ^c	99	68 ^c	>95
2.	32b	33b	82 ^c	99	--	--
3.	32c	33c	70 ^d	94 ^e	66 ^c	84
4.	11b	12b	>97	>97	95	92
					92	94

^a See Eq. 5 and experimental section for details.

^b Determined by GC, (*R*) isomer of products. Configurations assigned by comparison of [α]_D 25 to an authentic sample.²⁶

^c Rest isomerized product **34** from starting material.

^d Also contains 15% dimeric product **35** (configuration not established).

^e A diastereomer of this ligand with (*R_dR_cR_c*) configuration also gave (*R*)-adduct in ~70% yield and 89% ee.