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Unusual Regioselectivity in the Aldehyde Addition Reactions of Allenyl/Propargyl Zirconium Complexes Derived from γ-(2-Pyridyl)propargyl Ethers: Synthesis of Multisubstituted α-Hydroxyallenes

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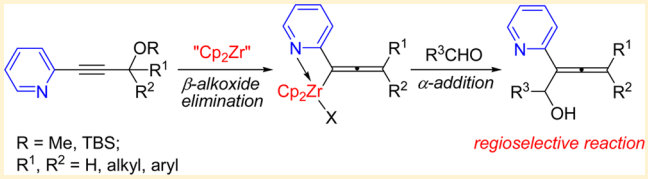
Supporting Information

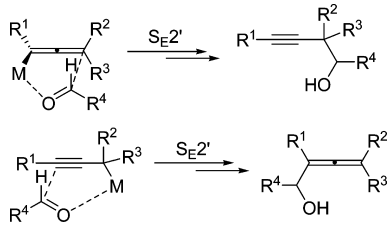
ABSTRACT: Zirconium-mediated reactions of γ-(2-pyridyl)-propargyl ethers with aldehydes afford α-hydroxyallenes selectively via the formation of allenyl/propargyl zirconium species. The reaction outcome is quite different to that of the reactions using propargylic ethers without a pyridyl group reported so far, in which homopropargyl alcohols were formed predominantly. The structure of allenylzirconium intermediate has been confirmed by X-ray crystal analysis which reveals an intramolecular Zr−N coordination. DFT calculations suggest that the smaller steric effect of the pyridine ring compared with the phenyl ring and its capability to form hydrogen bondings with hydrogen atoms of the Cp ligand and the aldehyde may account for the observed regioselectivity.



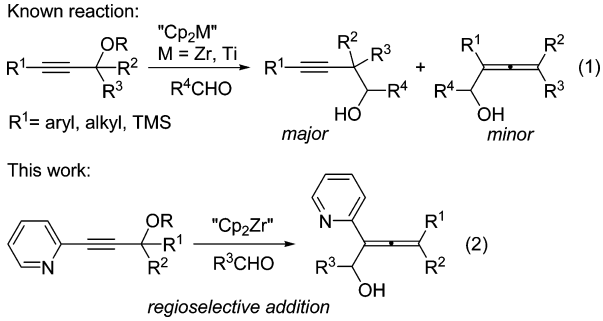
INTRODUCTION

Allenyl/propargyl metal complexes represent one of the most important classes of organometallics that can serve as useful intermediates in organic synthesis, for example, in the synthesis of highly complex molecules with biological and pharmaceutical interest.[1] However, due to the presence of the equilibrium between allenyl and propargyl metal species, regioselectivity control toward further C−C bond formation reactions is still an important issue.[2] Reaction of low-valent Group 4 metal complexes (M = Zr, Ti) with propargyl alcohol derivatives such as propargyl ethers, halides or carboxylates is a particularly attractive protocol for the generation of allenyl/propargyl metal species[3−5] via β-heteroatom elimination reactions.[3] The reactions of these allenyl/propargyl metals with electrophiles such as aldehydes could afford, in principle, two types of products, homopropargyl alcohols and α-hydroxyallenes.[3] Regioselectivity in these reactions depends mainly on the nature of the metal source and the substitution patterns of the propargylic precursors. It is generally accepted that these reactions proceed through a S_E2' process involving a chelate transition state as depicted in Scheme 1.[3b−g,4] That means, an allenyl metal give homopropargyl alcohols, while a propargyl metal produces the allene products. The reactions of allenyl/propargyl zirconium or titanium complexes with aldehydes usually afford homopropargyl alcohols as the major products (Scheme 2, eq 1), while the selective formation of α-hydroxyallenes is quite rare.[3f,g,4b,c] For example, Sato et al. reported that titanium-mediated reactions of propargyl bromides with aldehydes or ketones could afford α-hydroxyallenes as major products. However, only propargyl bromides bearing two hydrogen substituents at the propargyl position were successfully transformed into allenes.[3f] They have also shown that propargyltitanium could be selectively formed via reactions of the $Ti(O^iPr)_4/2\ ^iPrMgCl$ reagent with 1-alkynylcyclopropyl carbonate, which underwent further reac-

Scheme 1



Scheme 2



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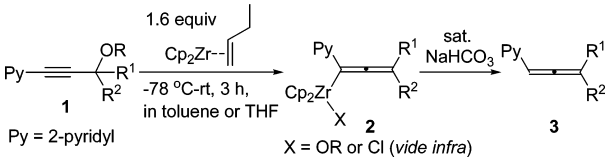
tions with aldehydes to afford allene products.[3g] Hoppe et al. developed an asymmetric synthesis of 4-hydroxyallenyl carbamates involving the formation of propargyltitanium species generated by asymmetric deprotonation of prochiral propargyl carbamates followed by transmetalation.[4b,c] Again, this reaction is restricted to the substrates of propargyl carbamates derived from primary alcohols. Recently, we reported a selective generation of the allenylzirconium complexes and their coupling reactions with aryl halides.[6] The preferential formation of the allenylzirconium species can be explained by the steric effects since it is less congested than the corresponding propargyl metal. Theoretical calculations also indicated that the large repulsion between the substituents at the propargylic position and the Cp rings decreases the interaction of the carbanion and the metal center, thus disfavoring the formation of propargylzirconium.[6] During our further investigations toward the nucleophilic addition reactions of allenylzirconium with aldehydes, we found that the use of a propargyl ether contains a pyridyl group on the alkyne terminus can dramatically change the regioselectivity (Scheme 2, eq 2). In this paper, we report a highly regioselective route for the synthesis of α-hydroxyallenes via α-addition of aldehydes to (2-pyridyl)-substituted allenylzirconium species. It is noted that there is no report for the formation of α-hydroxyallenes with high selectivities mediated by zirconium.

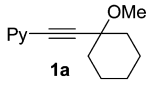
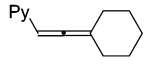
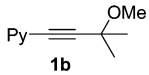
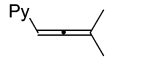
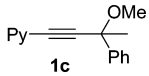
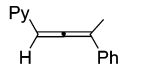
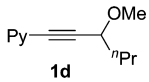
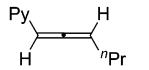
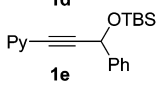
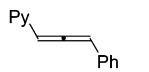
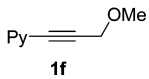
RESULTS AND DISCUSSION

Formation of Allenes through the Reactions of Cp_2ZrBu_2 with γ-(2-Pyridyl)propargyl Ethers. We envisioned that the existence of a functional group containing heteroatom like 2-pyridyl may also shift the equilibrium in favor of the allenylzirconium species due to its strong coordination ability with the metal, and highly regioselective reactions of these intermediates toward electrophiles are expected.[7] We then synthesized a series of γ-(2-pyridyl)propargyl methyl or silyl ethers **1**. The reaction of **1a** (R^1, R^2 = -$(CH_2)_5$-) with Negishi reagent "Cp_2ZrBu_2" in toluene was examined first. It was found that allene **3a** was formed in 78% yield as a sole product after hydrolysis (Table 1, entry 1). The reaction was suggested to be initiated by coordination of "Cp_2Zr" with propargyl ether to form zirconacyclopropene, which is followed by β-methoxide elimination to afford allenylzirconium **2**. The hydrolysis results also indicated that an allenylzirconium **2** was formed as a major zirconium intermediate. The typical results for allene **3** formation are shown in Table 1. It is noted that the reaction could also be performed in THF (the results are shown in the parentheses). Tertiary or secondary propargyl ether having alkyl or aryl substitutents on the propargylic position are suitable substrates (entries 1−5); however, secondary ether afforded lower yield in toluene than that in THF (entry 4). Primary substrate **1f** is also compatible for this reaction, furnishing terminal allene **3f** in 61% yield (entry 6).

Zirconium-mediated Reactions of γ-(2-Pyridyl)-propargyl Ethers with Aldehydes: Formation of α-Hydroxyallenes. Next we proceeded to examine the reactions with aldehydes in toluene. To our surprise, the reactions proceeded readily to provide the α-hydroxyallenes **4**, and there is no apparent formation of homopropargyl alcohols (Table 2). It should be noted that these addition reactions could not proceed well in THF. The regioselectivity observed in this study is in sharp contrast to the previously reported results of allenyl zirconium or titanium complexes bearing aryl, alkyl or TMS substituent on the α-position, in which homopropargyl

Table 1. Formation of Allenes by the Reaction of Cp_2ZrBu_2 with Propargyl Ethers



entry	propargyl ether	product		yield(%)[a]
1	 1a		3a	78 (83)
2	 1b		3b	80 (84)
3	 1c		3c	62 (61)
4[b]	 1d		3d	35 (58)
5	 1e		3e	(59)
6[c]	 1f		3f	(61)

[a]Isolated yields. Unless noted, all the reactions were carried out using 1.6 equiv of Negishi reagent in toluene at room temperature for 3 h. The yields obtained by using THF as solvent are shown in parentheses. [b]1.25 equiv of Negishi reagent was used. [c]1.1 equiv of Negishi reagent was used.

alcohol was formed predominantly through a S_E2' process.[3a−e] Typical results are shown in Table 2. The reaction could be applied to a wide range of aromatic aldehydes bearing electron-withdrawing or electron-donating groups. The functionalities such as $-NO_2$, $-CN$, $-CF_3$, $-OMe$ are well tolerated during the reaction. A thienyl aldehyde could also be used in this reaction, and the corresponding allene **4g** was formed in 62% yield (Table 2, entry 7). For the secondary ethers **1d** and **1e**, changing the solvent from THF to toluene before addition of aldehyde was necessary to achieve the satisfied yields (entries 11−12). However, when aliphatic aldehyde was used, the desired product **4m** was obtained in low yield (entry 13). The structure of hydroxyallenes was confirmed by X-ray single-crystal analysis of **4a**.[8] It should be noted that, in all cases, we could observe the formation of some side-products, which was not stable upon standing at room temperature. For example, in the case of Table 1, entry 1, 32% of these byproducts were isolated. The NMR indicated that it contains a mixture of two isomers without incorporation of a pyridine ring. According to NMR results, the side-products were defined as a mixture of (4-chlorophenyl)-(cyclopenta-1,3-dienyl)methanol and (4-chlorophenyl)(cyclopenta-1,4-dienyl)methanol derived by attack of Cp ligands to aldehydes. The participation of the Cp ligands in various type of reactions have been reported for Zr, Ti and Co cyclopentadienyl complexes.[9] In order to understand the effect of the 2-pyridyl group, we also synthesized a phenyl-substituted propargyl ether **5** to probe the reaction with aldehydes (Scheme 3). As expected, a homopropargyl alcohol **6** was obtained exclusively. The result also provided a circumstantial evidence for the directing effect of the 2-pyridyl group.

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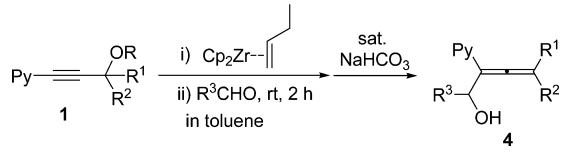
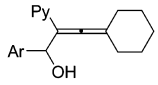
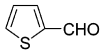
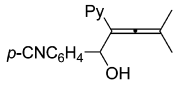
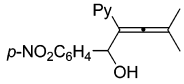
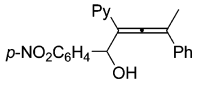
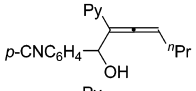
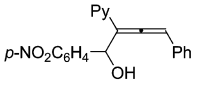
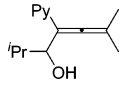
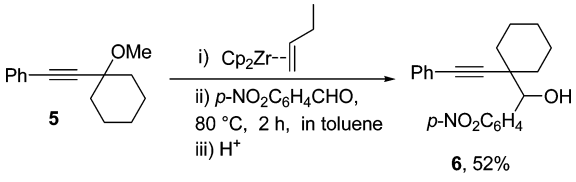
Table 2. Zirconium Mediated Reactions of γ-(2-Pyridyl)propargyl Ethers with Aldehydes



entry	substrate	R^3CHO	products		yields(%)[a]
1	**1a**	*p*-ClC_6H_4CHO		**4a** Ar= *p*-ClC_6H_4	56
2	**1a**	*p*-$NO_2C_6H_4CHO$	Ar= *p*-$NO_2C_6H_4$	**4b**	77
3	**1a**	*p*-CNC_6H_4CHO	Ar= *p*-CNC_6H_4	**4c**	61
4	**1a**	*p*-$CF_3C_6H_4CHO$	Ar= *p*-$CF_3C_6H_4$	**4d**	64
5	**1a**	*p*-$MeOC_6H_4CHO$	Ar= *p*-$MeOC_6H_4$	**4e**	45
6	**1a**	3,4,5-triMeOC_6H_2CHO	Ar= 3,4,5-triMeOC_6H_2	**4f**	74
7	**1a**		Ar= 2-thienyl	**4g**	62
8	**1b**	*p*-CNC_6H_4CHO		**4h**	73
9	**1b**	*p*-$NO_2C_6H_4CHO$		**4i**	74
10	**1c**	*p*-$NO_2C_6H_4CHO$		**4j**	50 (1.1:1)
11	**1d**	*p*-CNC_6H_4CHO		**4k**	52 (1.1:1)[b,c]
12	**1e**	*p*-$NO_2C_6H_4CHO$		**4l**	41 (2.3:1)[c]
13	**1b**	^{i}PrCHO		**4m**	14

[a]Isolated yields. The ratio of diastereomers is shown in parentheses. Unless noted, all the reactions were carried out using 1.6 equiv of Negishi reagent and 2.0 equiv of aldehyde in toluene. [b]1.25 equiv of Negishi reagent was used. [c]Allenylzirconium was prepared in THF, and the reaction with aldehydes was carried out by changing the solvent to toluene.

Scheme 3



Chacterization of the Allenylzirconium Intermediate. To have a deep insight into the molecular structure of the allenylzirconium intermediate, we isolated the zirconium complex **2a′** from the reaction of **1a** with Cp_2ZrBu_2 in THF. The X-ray crystal structure of **2a′** is shown in Figure 1. To our surprise, the ORTEP plot shows that it is an allenylzirconium chloride complex, but not an expected methoxide complex **2a**. The results indicated that a methoxide-halide exchange reaction occurred during the process, which was induced by in situ formed LiCl salt (Scheme 4). The two Cp rings and zirconium atom exhibit a bent structure, and the angles between the

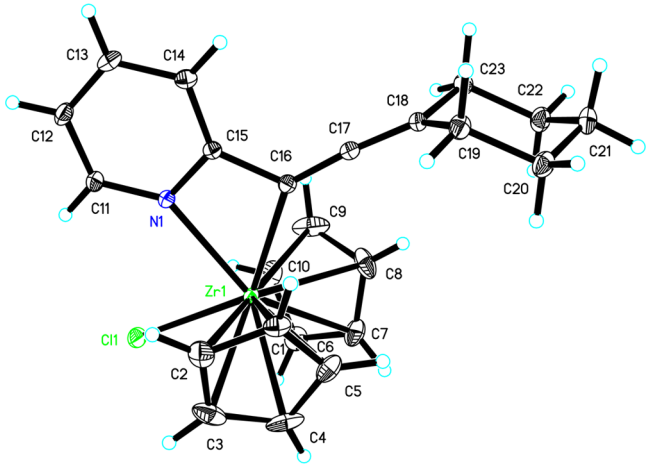
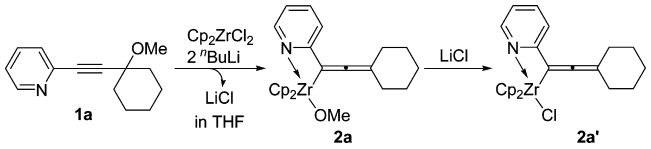


Figure 1. ORTEP drawing of complex **2a′**. Selected bond lengths (Å) and angles (deg): Zr1−N1 2.379(1), Zr1−Cl1 2.563 Zr1−C16 2.368(1), C15−C16 1.458(2), C16−C17 1.301(2), C17−C18 1.313(2), C16−Zr1−C5 87.76(5) C16−Zr1−N1 57.28(4), C15−C16−Zr1 96.06(8), C16−C17−C18 174.60(15), C15−N1−Zr1 98.63(8), N1−C15−C16 107.90(11).

Scheme 4



geometrical centers of both Cp rings and Zr center is 128.4°. The Zr−C16 distance of 2.368 Å is typical for Zr−C σ bond,[10] and the Zr−N bond length (2.379 Å) is in the typical range of pyridine *N*-coordination.[11] The chelate ring is nearly planar with a torsion angle of C16−C15−N1−Zr to be 3.4°. The allenic moiety is nearly linear (C16−C17−C18 174.6°). The ^{1}H NMR spectrum of **2a′** in C_6D_6 showed a singlet Cp resonance at 5.94 ppm, and an ortho proton adjacent to nitrogen in pyridine ring appeared at 9.01 ppm. The ^{13}C NMR spectrum showed peaks at 111.6 and 196.4 ppm assignable for Cp and ═C═ moiety, respectively. However, the in situ NMR of the same reaction in toluene revealed that the methoxide complex **2a** was formed as a major zirconium species (63% NMR yield) within 3 h. In this case, the methoxide-halide exchange reaction might be hampered due to the low solubility of LiCl in toluene.

Computational Studies. To rationalize the regioselectivity associated with the pyridine group in this reaction, density functional theory (DFT)[12] studies have been performed with GAUSSIAN09 program[13] using the M06[14] method. For Zr the Lanl2DZ basis set with Effective Core Potential (ECP)[15] was used; for the rest atoms, the 6-311+G** basis set was used. Harmonic vibration frequency calculations were carried out, the results show that all the optimized transition states with one imaginary frequency. The energy of the reactant complex is used as the zero point.[8] Substrates **5**, **1a** and *p*-$NO_2C_6H_4CHO$ were used in the calculation models. In the transition states, the cyclohexane tail of the allenic moiety may point "up" or "down". In most cases, the "up" type is more stable due to smaller intramolecular steric repulsion.

First, the reaction of the phenyl-substituted propargyl ether **5** was studied to be compared with. As shown in Figure 2, the

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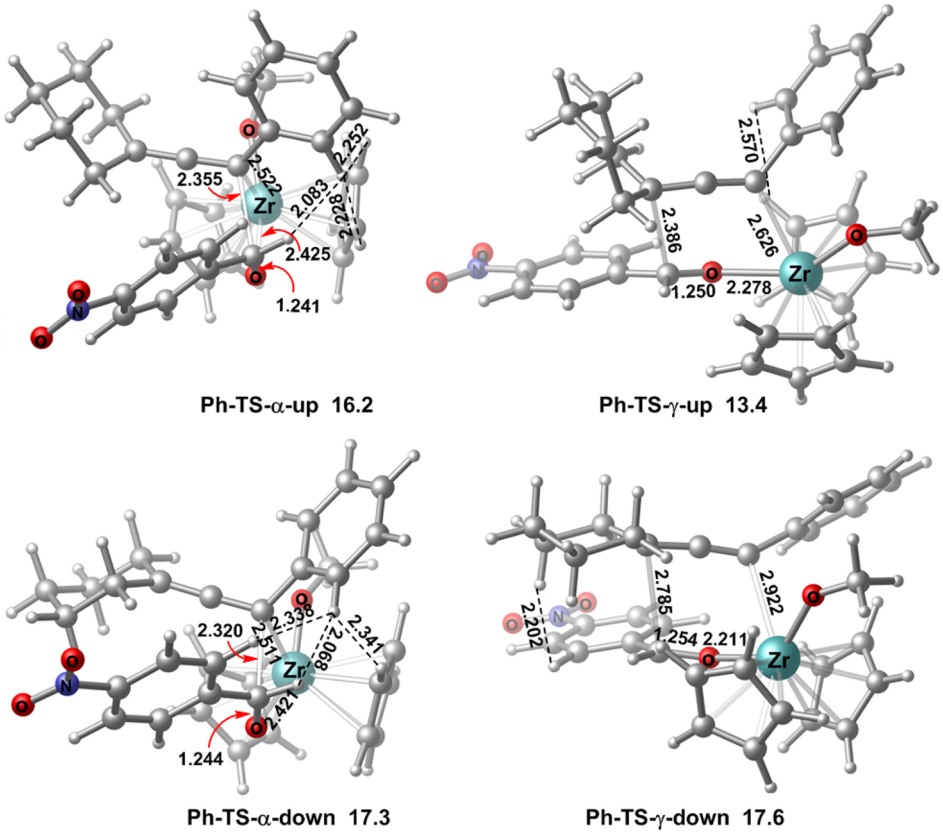

Figure 2. Optimized α- and γ-addition transition states of **5** with p-$NO_2C_6H_4CHO$. The selected bond lengths are in angstroms, and the relative free energies ΔG(298K) are in kcal/mol.

most favorable γ-addition transition state **Ph-TS-γ-up** is 2.8 kcal/mol lower in energy than the best α-addition transition state **Ph-TS-α-up**, indicating that the homopropargyl alcohol **6** is the dominant product. This result is consistent well with the experimental observations (Scheme 3). In **Ph-TS-α-up**, one of the *ortho*-hydrogen atoms of the phenyl group on the allenic moiety is close to the hydrogen atoms of the aldehyde (2.083 Å) and the Cp ring (2.252 Å, 2.228 Å). These distances are smaller than twice of the Van de Waals radius of hydrogen (2.400 Å),[16] showing that there are steric repulsions among the phenyl group, the Cp ring and the aldehyde. However, in the favorable transition state **Ph-TS-γ-up** the shortest H−H distance between the phenyl group on the allenic moiety and the Cp ring is 2.570 Å, larger than 2.400 Å, indicating there is no repulsion between them. **Ph-TS-α-down** and **Ph-TS-γ-down** are higher in energy. In these two structures, the collision of the cyclohexane tail of the allenic moiety with the phenly group of the aldehyde causes steric repulsion and entropy loss, which should account for their instabilities.

Likewise, for the pyridyl-substituted propargyl ether **1a**, four transition states were located (Figure 3). The most favorable γ-addition transition state **Py-TS-γ-up** is 0.6 kcal/mol higher than the best α-addition transition state **Py-TS-α-down**, indicating that the selectivity is reversed, the α-hydroxyallene **4** becomes the important product. This result is qualitatively consistent with the experimental observations (Table 2). Compared with the α-addition transition states **Ph-TS-α-down/up**, in **Py-TS-α-down/up**, one "C−H" moiety in the phenyl group is changed to "N" atom in the pyridyl group, the "steric *ortho*-hydrogen atom" does not exist any longer, releasing the steric energy to some extent. Furthermore, amazingly, the N atom of the pyridine ring can form hydrogen bondings[17] with the hydrogen atoms of the aldehyde (2.350, 2.621 Å in **Py-TS-α-down**) and the Cp ring (2.605 Å in **Py-TS-α-down**). Thus, the "steric repulsion" in **Ph-TS-α-down/up** becomes "stabilized attraction" in **Py-TS-α-down/up**, switching the regioselectivity.

To confirm that the pyridyl group in the transition state does not coordinate with the Zr center, the pyridyl-coordinated models **Py-TS-γ-up-N** and **Py-TS-γ-down-N** were also calculated. As shown in Figure 4, the coordination of the pyridine group will cause so large steric repulsion at the congested Zr center that the $^-$OMe anion is driven out of the coordination sphere. Compared with **Py-TS-γ-up**, the relative energy of **Py-TS-γ-up-N** increases dramatically by 28 kcal/mol. The transition states **Py-TS-α-up-N** and **Py-TS-α-down-N** were failed to be located possibly due to even larger steric repulsion. Therefore, the reverse of the regioselectivity originates from the following features of the pyridine ring: (a) has smaller steric effect compared with the phenyl ring; (b) the ability to form hydrogen bondings with hydrogen atoms of the Cp ligand and the substrate.

In summary, we have demonstrated that the nucleophilic addition reactions of pyridyl-substituted allenylzirconium species to aldehydes proceeds regioselectively at the α-position of the allenic moiety, leading to highly substituted α-hydroxyallenes. The regioselectivity is quite different to that of the reactions with allenyl/propargyl zirconium derived from propargylic ethers without a pyridyl group reported so far. DFT calculations suggest that the smaller steric effect of the pyridine ring and its capability to form hydrogen bondings with hydrogen atoms of the Cp ligand and the aldehyde may account for the observed regioselectivity.

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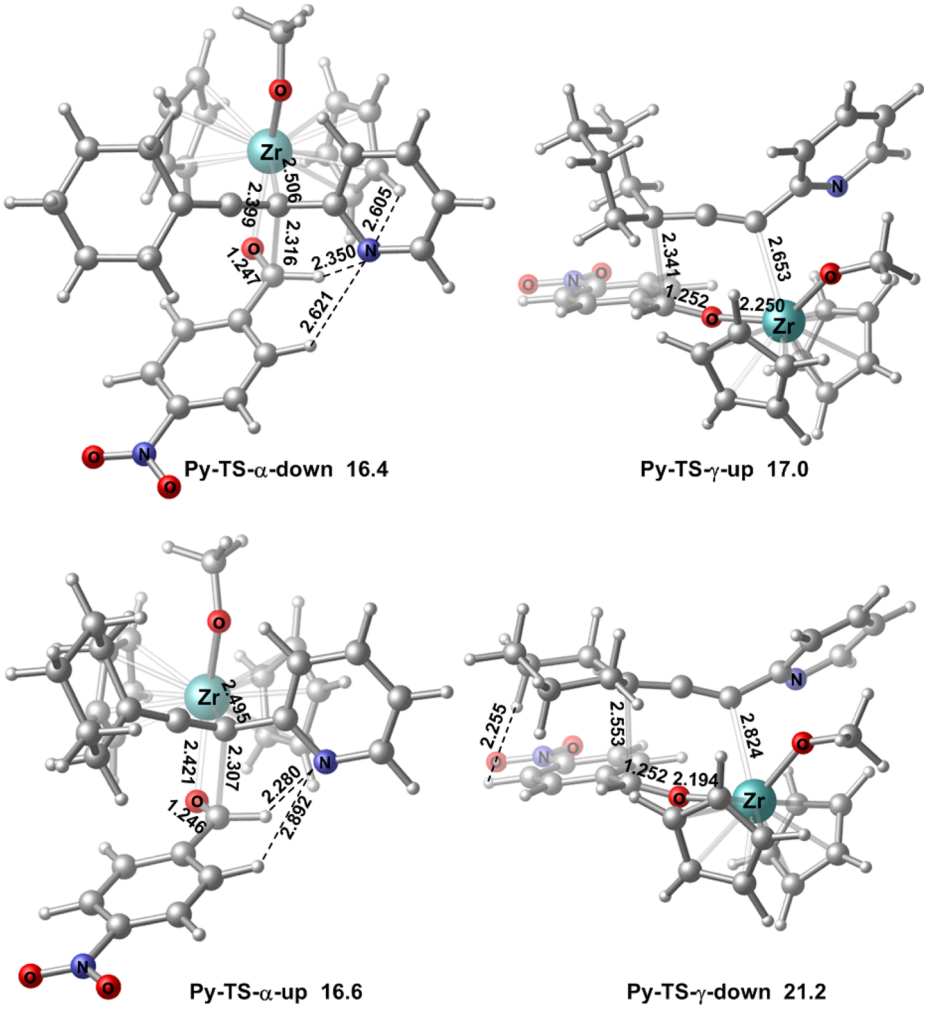

Figure 3. Optimized α and γ-addition transition states of **1a** with p-$NO_2C_6H_4CHO$. The selected bond lengths are in angstroms, and the relative free energies $\Delta G(298K)$ are in kcal/mol.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of Allenes by the Reaction of Cp_2ZrBu_2 with Propargyl Ethers. To a solution of Cp_2ZrCl_2 (234 mg, 0.8 mmol) in THF (5 mL) was added dropwise of n-BuLi (1.6 mmol, 1 mL, 1.6 M solution in hexane) at −78 °C. After stirring for 1 h at the same temperature, γ-(2-pyridyl)propargyl methyl ether **1** (0.5 mmol) was added and the reaction mixture was warmed up to room temperature and stirred for 3 h. The reaction was quenched with saturated $NaHCO_3$ solution and extracted with EtOAc. The extract was washed with water, brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel to afford the desired products.

2-(2-Cyclohexylidenevinyl)pyridine (3a). When THF was used as a reaction solvent, **3a** was obtained as a yellow oil in 83% yield by column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). When toluene was used as a reaction solvent, **3a** was obtained in 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.55−1.71 (m, 6H), 2.21−2.31 (m, 4H), 6.19−6.28 (m, 1H), 7.00−7.04 (m, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.56 (td, J = 7.8, 1.6 Hz, 1H), 8.49 (d, J = 4.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.82, 27.31, 30.82, 94.09, 106.74, 120.65, 120.75, 135.89, 149.11, 156.04, 201.54. HRMS (EI) calcd for $C_{13}H_{15}N$ 185.1204, found 185.1207. IR (neat) 2926, 2852, 1953, 1587, 1563, 1474, 1431, 831, 764, 740 cm^{-1}.

General Procedure for the Synthesis of α-Hydroxyallenes 4a−4j. To a suspension of Cp_2ZrCl_2 (234 mg, 0.8 mmol) in toluene (5 mL) was added dropwise of n-BuLi (1.6 mmol, 1 mL, 1.6 M solution in hexane) at −78 °C. After stirring for 1 h at the same temperature, γ-(2-pyridyl)propargyl methyl ether **1** (0.5 mmol) was added and the reaction mixture was warmed up to room temperature and stirred for 3 h. Aldehyde (1 mmol) was added and the reaction mixture was stirred for 2 h. The resulting mixture was quenched with saturated $NaHCO_3$ solution and extracted with EtOAc. The extract was washed with water, brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel to afford the desired products.

1-(4-Chlorophenyl)-3-cyclohexylidene-2-(pyridin-2-yl)prop-2-en-1-ol (4a). Column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1−10/1) afforded the title product as a yellow solid in 56% yield. Mp 119−120 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18−1.60 (m, 6H), 2.02−2.09 (m, 4H), 5.82 (s, 1H), 6.58 (br, 1H), 7.05−7.09 (m, 1H), 7.28 (d, J = 8.7 Hz, 2H), 7.37−7.42 (m, 3H), 7.56−7.62 (m, 1H), 8.43 (d, J = 5.1 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 25.63, 26.97, 27.08, 30.45, 30.58, 74.04, 106.90, 108.08, 121.05, 122.55, 127.78, 127.98, 132.34, 136.52, 141.64, 147.64, 156.89, 200.02. LRMS (EI) m/z 325 (M^+). Anal. Calcd for $C_{20}H_{20}ClNO$: C, 73.72; H, 6.19; N, 4.30. Found: C, 73.72; H, 6.22; N, 4.25. IR (neat) 3373, 3053, 2853, 1953, 1591, 1562, 1471, 1433, 1343, 1089, 1014, 802, 785, 743 cm^{-1}.

A Typical Procedure for the Synthesis of α-Hydroxyallenes 4k−4l. To a suspension of Cp_2ZrCl_2 (183 mg, 0.625 mmol) in THF (5 mL) was added dropwise of n-BuLi (1.25 mmol, 0.78 mL, 1.6 M solution in hexane) at −78 °C. After stirring for 1 h at the same temperature, γ-(2-pyridyl)propargyl methyl ether **1** (0.5 mmol) was

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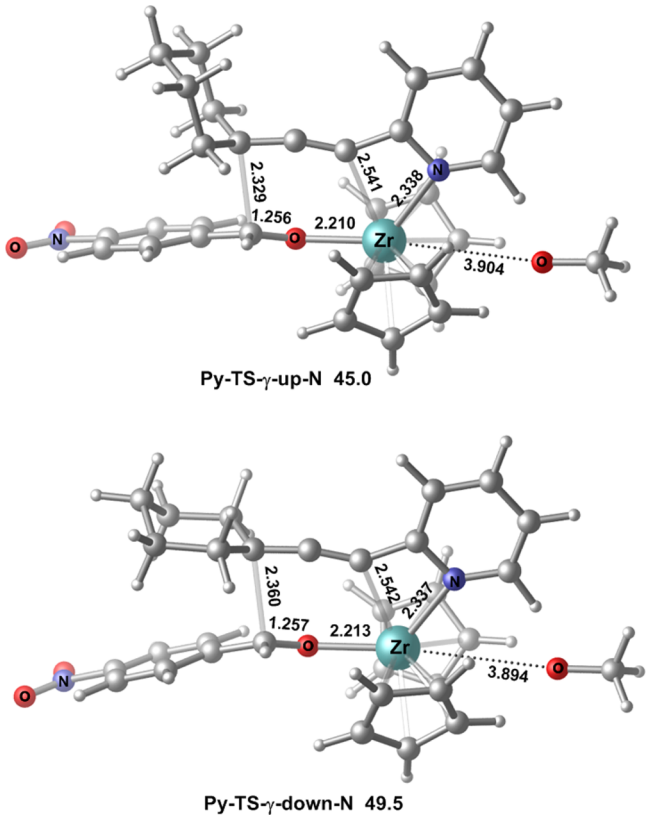

Figure 4. Optimized pyridine coordinated γ-addition transition states of **1a** with *p*-$NO_2C_6H_4CHO$. The selected bond lengths are in angstroms, and the relative free energies ΔG(298K) are in kcal/mol.

added and the reaction mixture was warmed up to room temperature and stirred for 3 h. The solvent was removed in vacuo, and then toluene (5 mL) was added. Aldehyde (1 mmol) was added and the reaction mixture was stirred for another 2 h. The resulting mixture was quenched with saturated $NaHCO_3$ solution and extracted with EtOAc. The extract was washed with water, brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel to afford the desired products.

4-(1-Hydroxy-2-(pyridin-2-yl)hepta-2,3-dien-1-yl)-benzonitrile (4k). Column chromatography on silica gel (petroleum ether/ethyl acetate =10/1, then petroleum ether/Et_3N = 10/1) afforded the title product as a yellow solid in 52% yield. The ratio of the two diastereomers is 1.1:1. ^{1}H NMR (400 MHz, $CDCl_3$) two isomers: δ 0.87 (t, J = 7.2 Hz), 1.33−1.38 (m), 1.97−2.03 (m), 5.52 (t, J = 7.2 Hz), 5.85 (s), 5.88 (s), 7.09−7.12 (m), 7.46 (d, J = 12.0 Hz), 7.59−7.65 (m), 8.43 (d, J = 5.2 Hz). The chemical shift of OH proton was not observed. ^{13}C NMR (100 MHz, $CDCl_3$) two isomers: δ 13.50, 13.51, 22.12, 22.16, 30.22, 30.31, 73.89, 74.08, 96.84, 96.86, 107.84, 107.92, 110.44, 110.46, 118.96, 121.44, 122.53, 122.55, 127.14, 127.20, 131.50, 136.71, 136.73, 147.66, 147.68, 148.26, 148.38, 155.62, 155.65, 205.00, 205.26. HRMS (EI) calcd for $C_{19}H_{18}N_2O$ 290.1419, found 290.1424. IR (neat) 3587, 2958, 2928, 2856, 2227, 1616, 1295, 1090, 742 cm^{-1}.

1-(4-Nitrophenyl)-4-phenyl-2-(pyridin-2-yl)buta-2,3-dien-1-ol (4l). 1.6 equiv Negishi reagent was used. Column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1) afforded the product as a yellow solid in 41% yield. The ratio of the two diastereomers is 2.3:1. ^{1}H NMR (400 MHz, $CDCl_3$) two isomers: δ 6.02 (s), 6.07 (s), 6.54−6.57 (m, 1H), 6.85 (s, 1H), 7.14−7.18 (m, 1H), 7.23−7.33 (m, 5H), 7.48−7.49 (m, 1H), 7.60−7.69 (m, 3H), 8.08−8.13 (m, 2H), 8.49−8.51 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) two isomers: δ 73.75, 74.51, 100.15, 111.66, 122.25, 123.07, 123.12, 126.93, 126.97, 127.15, 127.30, 127.99, 128.02, 128.85, 128.89, 131.76, 132.07, 137.13, 137.14, 147.02, 148.03, 148.05, 149.95, 150.00, 154.46, 207.57, 207.87. HRMS (EI) calcd for $C_{21}H_{16}N_2O_3$ 344.1161, found 344.1158. IR (neat) 3368, 2926, 2855, 1938, 1591, 1519, 1471, 1345, 1046, 747, 695 cm^{-1}.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details, NMR spectra of all new products, CIF files giving crystallographic data of compounds **2a′** and **4a**, the calculated reaction pathways, total energies and geometrical coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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