Regio- and Stereoselective Coupling of Heteroaryl-Substituted Alkynes: New Insights into the Mechanism of Zirconium-Mediated Cyclodimerization of Alkynes and a Facile Route to 3-Methylenecyclobutenes

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The cyclodimerization of (2-pyridyl)alkynes tethered with an amino group mediated by zirconium was achieved cleanly under controlled reaction conditions. This methodology provided an efficient route for the synthesis of tetrasubstituted cyclobutenes with high regio- and diastereoselectivity when the reaction was quenched by water. However, by quenching with saturated $NaHCO_3$ solution, a 3-methylenecyclobutene derivative was readily constructed. The effect of other quenching reagents on the product distribution was also investigated. This cyclization/elimination was influenced strongly by the nature of the substituent on the amino group. The reaction worked well with aryl/methyl-, aryl/benzyl-, or diaryl/aminomethyl-substituted alkynes, giving generally good yields of the corresponding products. Conversely, the phenyl/hydrogen or dialkyl (except **1k**) substitutions on nitrogen gave either lower chemical yields or different products. The zirconium intermediate was isolated successfully, which has been fully characterized by NMR experiments and mass analysis. Extensive NMR experiments (DEPT, COSY, HMQC, and HMBC) revealed its structure is in agreement with that of zirconacyclopentadiene, and this structure was further confirmed by DFT calculations. Subsequent cyclization to yield a cyclobutadiene skeleton was induced by the attack of the coordinative species. This is different with the reactions of late transition metal mediated cyclodimerization of alkynes (e.g., Co) via direct reductive elimination. To account for the formation of 3-methylenecyclobutenes, an E1cb reaction pathway was suggested.

Introduction

The cyclodimerization reactions of alkynes are very important processes from both the synthetic and mechanistic points of view, which also represent a useful strategy for the construction of four-membered-ring derivatives.[1] The synthetic approaches for alkyne cyclodimerization mainly include (i) thermolysis at high temperature with or without a trapping reagent;[2] (ii) Lewis acid (AlX_3) promoted cyclodimerization to afford aluminum halide σ complexes of cyclobutadienes;[3] (iii) reactions of alkynes with metal carbonyl derivatives;[4] (iv) reactions of alkynes with coordination complexes and inorganic salts;[5] and (v) syntheses via precursors derived indirectly from alkynes.[6] Among these methods, transition-metal-mediated inter- or intramolecular cyclodimerization of alkynes has received considerable attention, which, in most cases, results in the formation of η^4-cyclobutadiene-metal complexes. For the purposes of practical utility in organic synthesis or material science, Co complexes have been intensively studied. For example, numerous polycyclic,[7a−d] superphane,[7e−g] multiply ethynylated,[7h−j] dendritic,[7k] and polymeric derivatives[7l] of cyclobutadiene-cobalt complexes have been synthesized by interaction of $CpCo(CO)_2$ with functionalized alkynes.[7] Although still being debated,[8] the widely accepted mechanism for this type of cyclization is shown in Scheme 1,[9] which involves a sequential replacement of the CO ligand by acetylene to yield first a monoacetylene complex **A**, then a diacetylene complex **B**, which undergo an oxidative coupling to convert into a 16-electron metallacyclopentadiene **C**. A reductive elimination of metallacycle **C** or **D** affords the

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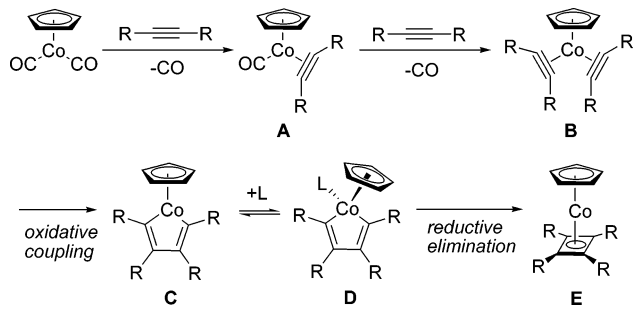
Scheme 1



cyclobutadiene-metal complex **E**. Several intermediates including mono(alkyne)cobalt complexes[10] and metallacyclopentadiene of type **D** with a further ligand L[11] were isolated and characterized by means of X-ray analyses. The newly formed cyclobutadienes are typically not readily released from metal complexes. This fact makes these cycloadditions of limited value in the generation of the free species for synthetic use.

Zirconacyclopentadiene-Mediated Cyclodimerization. Due to the similarity of the alkyne-interaction process with cobalt and zirconium, we envisioned that zirconacyclopentadienes could also be good precursors for ring formation to give cyclobutadiene-metal complexes through reductive elimination. The zirconocene-coupling route using dialkylzirconocenes Cp_2ZrBu_2 (Negishi reagent) or Cp_2ZrEt_2 (Takahashi reagent) has proven to be a powerful methodology for oxidative coupling of alkynes.[12] The readily formed zirconacyclopentadienes are very useful intermediates in organic synthesis. However, prior to our study,[13] there is no report of direct cyclodimerization of two alkynes in this system. It is obvious that the key problem is how to achieve the reductive elimination. Although this step is very common for late transition metals, it has not been well studied for early transition metal compounds such as Ti and Zr. Only a few reductive couplings of organozirconium compounds have been reported, such as migratory insertion reactions of zirconacycles with CO,[14] photolysis or oxidation of diphenylzirconocene,[15] alkynyl−phenyl coupling via ate-complexation, etc.[16]

Ligand-Induced Reductive Elimination. It was known that a ligand or a directing group (often containing a heteroatom moiety) could induce reductive elimination in titanium or zirconium chemistry.[17−19] Rothwell had reported that the mono-η^2-iminoacyl compound Ti(OAr-2,6-*i*-Pr_2)$_2$(η^2-*t*-BuNCCH_2Ph)-(CH_2Ph) reacted with pyridine to produce the reductive elimination product Ti(OAr-2,6-*i*-Pr_2)$_2$[η^2-*t*-BuNC(CH_2Ph)$_2$](py).[17] Takahashi had demonstrated that reductive elimination of α-alkynyl-substituted zirconacyclopentenes can proceed to give cyclobutenes, which might be driven by strong coordination of an α-alkynyl triple bond with the zirconium center.[18] Majoral had also pointed out that the α-phosphino group in an iminoacyl zirconacycle could induce reductive elimination.[19] Very recently, we reported a facile cyclization of 2-pyridyl-substituted zirconacyclopentadienes to tetrasubstituted cyclobutenes, which would represent an advance in zirconium-mediated cyclodimerization of alkynes (Scheme 2).[13] The noteworthy features are that (i) it realizes a complete regio- and stereoselective incorporation of the alkynes to afford *trans*-cyclobutenes; (ii) the stereoselectivity of products can be changed by choosing different quenching reagents; and (iii) the decomplexation of the intermediacy of the coordinated zirconium group appears to be fairly easy. However, the mechanism for cyclization and the beneficial effects of the 2-pyridyl group have not been clarified yet. In this paper, we present the results of our new investigations concerning the extension of this method for the formation of 3-methylenecyclobutenes and our efforts aimed at clarifying the role of the 2-pyridyl group.

Results and Discussion

Cyclodimerization of *N*-(2-Alkynyl)amines. In conjunction with a program directed toward the investigation of the intermediate of alkyne cyclodimerization, we were particularly interested in 2-pyridyl-substituted propargylic amine substrates since the tethered amino group might stabilize the highly reactive zirconium intermediates. The requisite *N*-(2-alkynyl)amines were easily synthesized by Sonogashira coupling[20] of the corresponding heteroaryl bromides with propargylamines using 1% $PdCl_2$-(PPh_3)$_2$ and 2% CuI in Et_3N or Et_2NH solvent.[21] The yields of this process range from 66% to 91%. It should be noted that these substrates must be purified twice before use by column chromatography or by recrystallization in order to remove the

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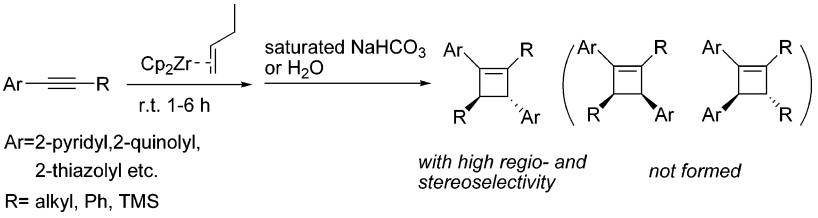
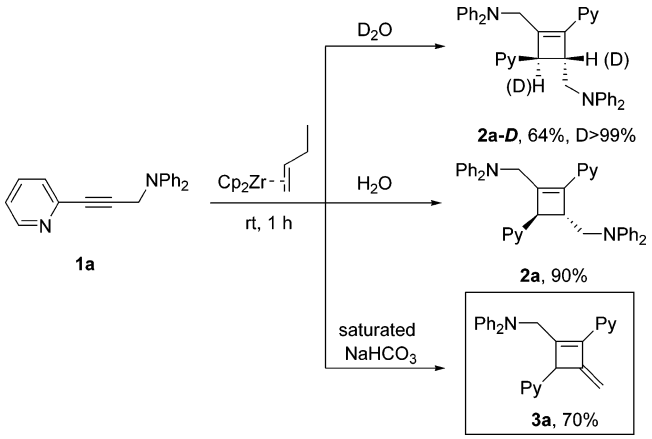
Scheme 2



Scheme 3



colored impurities.[22] Our investigation began with an examination of the reaction between diphenyl(3-pyrid-2-ylprop-2-ynyl)-amine **1a** with Negishi reagent "Cp_2ZrBu_2" (Scheme 3). Treatment of alkyne **1a** with Cp_2ZrBu_2 at room temperature for 1 h followed by quenching the reaction mixture using water afforded *trans*-cyclobutene **2a** in 90% isolated yield. The reaction was highly stereoselective (>99%), and the byproducts such as the *cis*-isomer or its regioisomer derived from head-to-head coupling were not detected. The stereochemistry of **2a** was established on the basis of the coupling constants in its proton NMR spectrum. A slice of the ^{1}H NMR spectrum in the region of 3.4−3.6 ppm unequivocally exhibited the signals with a negligibly small coupling constant (<1 Hz) between the cyclobutene ring protons. The deuteration experiment of the reaction mixture of **2a** revealed the formation of dideuterated compound *trans*-**2a**-*D* in 64% yield with high (>99%) deuterium incorporation. Interestingly, when the reaction was quenched by saturated $NaHCO_3$ solution, 3-methylenecyclobutene derivative **3a** was readily formed in 70% yields. The structure of **3a** was further confirmed by X-ray crystallographic analysis of its mono(1-methyl)pyridium salt **4** prepared by the reaction of **3a** with methyl iodide (Figure 1). It is noteworthy that the isolated **2a** did not transform to **3a** under basic conditions. Since it is known that elimination of the disubstituted aminomethyl group was usually achieved by H_2O_2/pyrolysis at high temperature (100−160 °C),[23] the formation of **3a** here must relate to some reactive zirconium intermediates.

We proceeded to examine the scope of this cyclization/elimination in terms of the alkyne substituent (Table 1). 2-Pyridyl alkyne **1b**, with a phenyl and a methyl group on the nitrogen, undergoes cyclization smoothly and afforded 79% yield of **3b**. The electronic effect of substitution on the aromatic ring has also been examined. Virtually no significant differences in the reaction time or the yields have been observed using an amine bearing methyl (1 h, 79%), chlorine (2 h, 74%), and methoxy (2 h, 71%) substituted aromatic ring (Table 1, entries 3−5). Introducing a benzyl group on the nitrogen of the aniline gave **3f** in 65% yield. 5-Methylpyridyl-substituted substrates **1g** and **1h** afforded the corresponding cyclobutenes **3g** and **3h** in 69% and 73% yields, respectively. The reaction also proceeded smoothly with 2-quinolylalkyne **1i**, furnishing **3i** in 64% yield (Table 1, entry 9). The quinolylalkyne **1j**, bearing a diphenylamino group, afforded **3j** in 47% yield, together with a 30% yield of *trans*-cyclobutene **2j**. However, alkynes **1l** and **1m**, bearing diethyl or a secondary amino group, failed to give the desired product. Instead, a complicated reaction mixture (entry 12) or the linear butadiene **5a** was formed as a major product in low yield (entry 13), respectively. These results indicated that the nature of the substituent on nitrogen had a strong influence on the cyclization reactions. The reaction worked well with aryl/methyl-, aryl/benzyl-, or diaryl/aminomethyl-substituted alkynes, giving generally good yields of the corresponding products. Conversely, the phenyl/hydrogen or dialkyl (except **1k**) substitutions on nitrogen gave either lower chemical yields or different products, which cannot be improved even at higher temperature (50 °C) and a prolonged reaction time. Interestingly, when a pyridyl alkyne tethered with a heterocycle group such as 1-(3-(pyridin-2-yl)prop-2-ynyl)-1*H*-indole was used, the cyclodimerization reaction smoothly occurred to afford **2n** in 87% yield (Scheme 4).

Effect of the 2-Pyridyl Group. We have been assuming the coordination effect as an origin for ring cyclization, as mentioned in a previous paper.[13] When alkynes such as aryl/alkyl alkyne, 3-pyridylalkyne, or 2-thienylalkyne were employed, the reaction failed to give cyclobutenes; instead, butadienes were formed as the sole products (Scheme 5). These results provided circumstantial evidence for the directing effect of the 2-pyridyl group on the alkyne.

Organometallic Intermediates. It seems certain that the cyclization reaction proceeded through 2-pyridyl group-induced reductive elimination of the initially formed zirconacyclopentadienes, and the cyclobutadienyl zirconium complex is expected to be detected. To get further insight into the role of the pyridyl

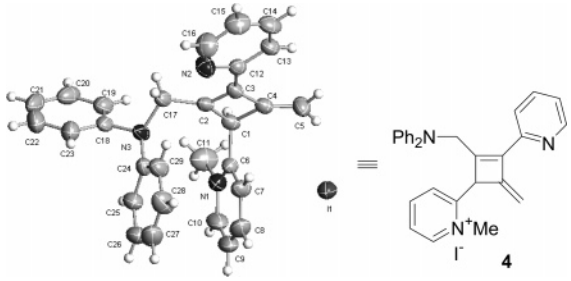


Figure 1. Crystal structure of compound **4**.

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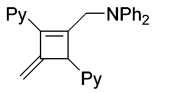
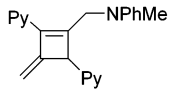
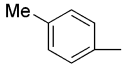
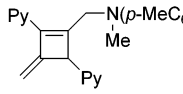
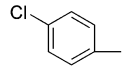
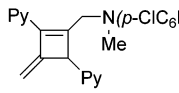
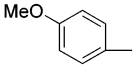
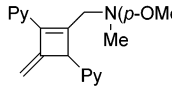
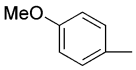
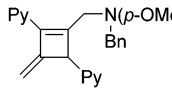
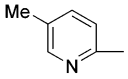
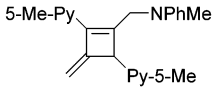
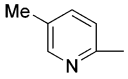
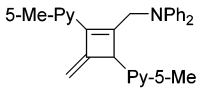
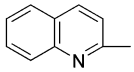
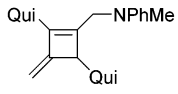
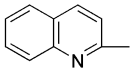
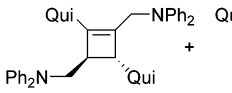
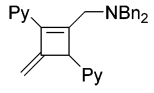
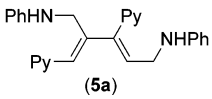
Table 1. Selective Formation of Trisubstituted 3-Methylenecyclobutenes via Alkyne Cyclodimerization

Entry	Ar—≡—NR^1R^2	Ar	R^1	R^2	Product	Yield[a]
1	(**1a**)		Ph	Ph	 (**3a**)	70
2	(**1b**)		Ph	Me	 (**3b**)	79
3	(**1c**)			Me	 (**3c**)	79
4	(**1d**)			Me	 (**3d**)	74
5	(**1e**)			Me	 (**3e**)	71
6	(**1f**)			Bn	 (**3f**)	65[b]
7	(**1g**)		Ph	Me	 (**3g**)	69
8	(**1h**)		Ph	Ph	 (**3h**)	73
9	(**1i**)		Ph	Me	 (**3i**)[c]	64
10	(**1j**)		Ph	Ph	 (**2j**)[c], 30% + (**3j**)[c], 47%	
11	(**1k**)		Bn	Bn	 (**3k**)	78[d]
12	(**1l**)		Et	Et	— [e]	
13	(**1m**)		Ph	H	 (**5a**)	30%

[a] Isolated yields. Unless noted, all the reactions were carried out at room temperature for 1−3 h using 1.1 equiv of Cp_2ZrBu_2. [b] 1.25 equiv of Cp_2ZrBu_2 was used. [c] Qui = 2-quinolyl. [d] The product was concomitant with dibenzylamine. [e] Complicated reaction mixture.

groups, we investigated two reactions of 2-pent-1-ynylpyridine (**1n**) and the *N*-(2-alkynyl)amine (**1a**) with Cp_2ZrBu_2 by NMR. In each reaction, we found an obvious generation of a new zirconium complex **10n** or **10a**, which was formed in 67% and 95% NMR yield, respectively. Although our attempts to obtain a single crystal suitable for X-ray crystal analysis failed, those two samples prepared via recrystallization (**10n**) or by solvent evaporation in vacuo (**10a**) have provided rather clean and single dominant sets of ^{1}H and ^{13}C NMR spectral data (see Supporting Information). To our surprise, in the ^{13}C NMR spectrum of complexes **10n** and **10a**, there was no resonance in the region of 70−100 ppm, which is typical for the cyclobutadiene carbons in a cyclobutadiene-metal complex, e.g., 73.1 ppm for tetrakis-(4-pyridyl)cyclobutadienecyclopentadienyl cobalt;[24] 94.5 and 71.5 ppm for a naphthoquinone-fused cyclobutadiene ruthenium complex.[25] Extensive NMR experiments (DEPT, COSY, HMQC,

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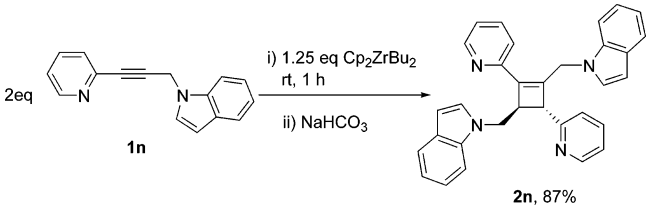
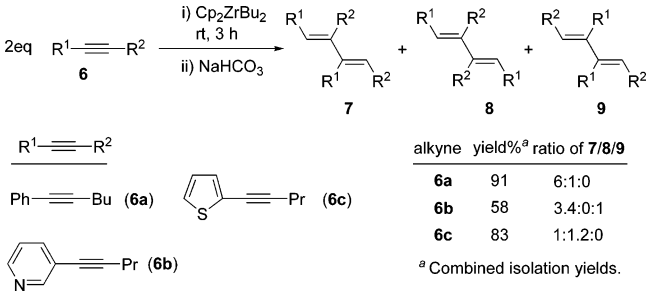
Scheme 4



Scheme 5



and HMBC) revealed its structure is in agreement with that of zirconacyclopentadiene or the allenyl structure of **10n′** (Figure 2). The representative NMR assignments of complex **10n** and important correlations established by HMBC experiments are shown in Figure 2. In the ^{1}H NMR spectrum of **10n**, the most interesting feature is the quite different chemical shifts of *ortho* protons adjacent to nitrogen in two pyridine rings. One of them appeared at 8.73 ppm, which is close to that found in free pyridylalkynes (8.40 ppm); however, another one shifts to 7.38 ppm. These change in chemical shifts exceed more than 1.3 ppm, which indicates that two "different" pyridine rings exist in complex **10n**. It is noteworthy that the vicinal coupling constants between 2-H, 3-H, and 4-H in one pyridine group are no longer equal as in free alkynes (7.8 Hz); ^3J(2-H, 3-H) is decreased to 7.2 Hz and ^3J(3-H, 4-H) is raised to 8.4 Hz. This indicates that, upon complexation, the aromaticity of a pyridine subunit may be reduced and one of the double bonds in the pyridine ring isomerizes to an exocyclic double bond to afford an allenyl structure of **10n′**.[26] A similar dearomatization of the pyridine ring was observed in zirconocene and *rac*-[1,2-ethylene-1,1′-bis(η^5-tetrahydroindenyl)]zirconium complexes of 2-vinylpyridine.[26] The ^{1}H NMR spectrum of **10n** also showed a singlet peak at 5.74 ppm, and its ^{13}C NMR spectrum revealed one singlet at 106.6 ppm, which were assigned to cyclopentadienyl ligands. Additionally, a signal at 207.4 ppm is assignable to the =CZr moiety, which is typical for an alkenyl-zirconium carbon of a zirconocene fragment.[27] However, the chemical shift of another Zr−C(sp^2) carbon has shifted to 159.1 ppm. The chemical shifts observed for **10a** are very similar to complex **10n**, in particular the ^{13}C NMR shifts. The high-resolution mass spectra (MALDI) of these two complexes are all in agreement with their compositions; molecular ions $[M + H]^+$ are observed for each of them. Interestingly, it was found that quenching the reaction mixture using 2 equiv of D-(−)-pantolactone afforded the linear product **5b** in 58% yield, while only a trace amount of cyclobutene was observed under this condition (Scheme 6). This experiment provided additional evidence in support of the intermediacy of the zirconacyclopentadiene **10n**.

To better understand the structure of intermediate **10**, density functional theory (DFT) studies have been performed with the GAUSSIAN03 program[28] using the B3LYP[29] method. For C, H, and N, the 6-311+G** basis set was used; for Zr, the Lanl2DZ basis set with effective core potential (ECP)[30] was used. First, the allenyl structure **10n′** was explored (Figure 2). In this model, methyl groups were used instead of propyl groups. The results indicate that this structure is unstable and always converged to a structure in which C6 coordinated with the Zr atom (Figure 3), i.e., the structure **10n** in Figure 2. Harmonic vibration frequency calculation was carried out, and this structure is shown to be a minimum (has no imaginary frequencies). With this model, atomic charges were calculated by NBO natural bonding analysis,[31] and ^{13}C and ^{1}H chemical shifts were computed by the gauge including atomic orbital (GIAO) method.[32] Selected results are shown in Figure 3.

The calculated NMR shifts are in good agreement with the experimental values. The most interesting thing is the large difference of the ^{13}C chemical shifts of C6 (159.1) and C9 (207.4), which seem to be the same type of carbon. The calculated NBO atomic charge of C6 is −0.433, much larger than that of C9 (−0.246), indicating that the shielding effect of the large electron density on C6 causes the chemical shift to move upfield.

In the optimized structure, Py1 coordinated with the Zr atom; consequently, it is coplanar with Zr, C6, and C7, and the dihedral angle N1−C5−C6−Zr is only −3.3°. This indicates that Py1 can be conjugated with C6. The C5−C6 bond has some double-bond characteristics (1.434 Å). Py2 is rotated off this plane, and the dihedral angle N2−C20−C8−C7 is −67.0°. The C6−Zr bond length is 2.237 Å, even stronger than the C9−Zr bond (2.379 Å).

To find out the origin of the large electron density on C6, the three models in Figure 4 were studied. In model **A**, the

(26) Thomas, D.; Baumann, W.; Spannenberg, A.; Kempe, R.; Rosenthal, U. *Organometallics* **1998**, *17*, 2096. (b) Spannenberg, A.; Arndt, P.; Baumann, W.; Burlakov, V. V.; Rosenthal, U.; Becke, S.; Weiss, T. *Organometallics* **2004**, *23*, 3819.

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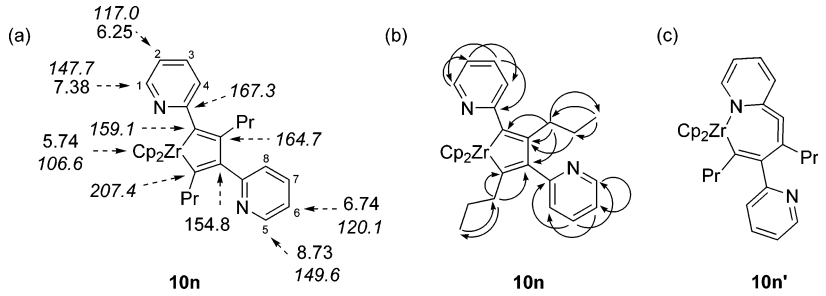
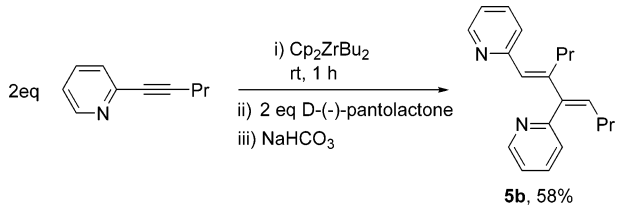


Figure 2. (a) Representative proton and carbon (italics) NMR assignments of **10n**. (b) Representative correlations of **10n** established by HMBC experiments. (c) Proposed structure of **10n′**.

Scheme 6



coordination effect of Py1 can be excluded. This model is nonplanar, but the two pyridines are conjugated to some extent with the two double bonds. The NBO charge distribution shows that C6 has larger negative charges than C9. This apparently can be explained by resonance electronic effects of the two pyridine rings and the hyperconjugation effect of the two methyl groups. In model **B**, the positions of Py1 and Py2 are equivalent, but Py1 is twisted with C6 and C7 and Py2 is coplanar with C9 and C8 (dihedral angle N1−C11−C6−C7 is −149.4°, dihedral angle N2−C10−C9−C8 is 0.8°). Consequently, C9 has larger negative charges than C6. This result indicates that good conjugation will increase resonance electronic effects. In model **C**, Py1 is rotated to −67.0° (the same as that of Py2 in Figure 3) with the Zr−C6−C7 plane. The conjugation effect of Py1 with C6−C7−C8−C9 is reduced. As a result, the difference of the negative charges on C6 and C9 decreased from 0.187 (see Figures 3, 4) to 0.079. So the resonance electron effects should mainly account for the larger negative charges on C6.

Mechanistic Considerations. On the basis of the above results, we propose a plausible mechanism of the Zr-mediated cyclodimerization of 2-pyridylalkynes as depicted in Scheme 7. (i) Oxidative coupling of the two coordinated alkynes affords unsymmetrically substituted zirconacyclopentadiene **10**, in which a pyridyl group may coordinate with zirconium through its nitrogen atom. The high regioselectivity may be caused by a cooperation of steric and electronic effects. (ii) The complex **10** is the major organozirconium species that can be observed during the reaction, and this suggests that the cyclization to a cyclobutadiene skeleton occurred only after hydrolysis. Indeed, treatment of purified **10a** with 10 equiv of H_2O resulted in the formation of **2a** in excellent yield (>99% NMR yield). Thus (iii) coordination of H_2O to the zirconium center "pushes" the ring rearrangement to generate N-donor-stabilized η^2-cyclobutadiene complex **12**. This result indicates that water acts as a coordinating ligand to induce the cyclization. To account for the *trans* selectivity of **2**, an external electrophilic attack of water at the face opposite the metal on the coordinated alkene is suggested. The protonation proceeded at the carbon atom in the α-position to the pyridine ring to give **13** or **14**, which affords *trans*-**2** by a second protonation. The complex **13** was further stabilized by a intramolecular pyridyl group, which may be formed preferentially over **14**. This was supported by a stepwise hydrolysis/deuteriolysis experiment as mentioned in a previous paper.[13] When using *N*-(2-alkynyl)amines as substrates and quenching the reaction by $NaHCO_3$ solution, 3-methylenecyclobutene derivative **3** was formed. The result indicated that the product distribution was strongly affected by quenching reagents. To further understand the fact that HCO_3^- facilitates the elimination of an amino group, several anions and various kinds of quenching reagents were studied. It was found that **2a** was formed as a major product by quenching with 10% NaOH (>99% NMR yield), 10% Na_2CO_3 (89% NMR yield), or 10% of KOH, K_2CO_3, KOAc, or K_3PO_4 solution (detected by TLC), whereas **3a** was formed as a major product by quenching with MeOH (94% isolated yield), (+)-camphoric acid (85% isolated yield), 3 N HCl (then neutralized with aqueous NaOH, 75% isolated yield), or 10% KH_2PO_4, EtOH, *t*-BuOH, or benzoic acid (detected by TLC). Although we still need to wait for further investigations to explain all the above results, those reactions suggested an E1cb pathway for elimination of an amino group. In the presence of $NaHCO_3$, KH_2PO_4, HCl, etc., protonation of the amine may occur, which makes it a better leaving group. It was also found that diphenylamine was isolated in 71% yield in the reaction of **2a**.

Conclusion

In summary, a novel zirconium-mediated cyclodimerization of (2-pyridyl)alkynes tethered with an amino group has been described. It was found that upon quenching the reaction mixture with water, a tetrasubstituted cyclobutene with high regio- and diastereoselectivity was formed. However, by quenching with saturated $NaHCO_3$ solution, a 3-methylenecyclobutene derivative was readily constructed. More importantly, we have succeeded in isolating the zirconium intermediate, which has been fully characterized by NMR experiments and mass analysis. Extensive NMR experiments (DEPT, COSY, HMQC, and HMBC) revealed its structure is in agreement with that of zirconacyclopentadiene, and this structure was further confirmed by DFT calculations. Subsequent cyclization to yield a cyclobutadiene skeleton was induced by the attack of the coordinative species. This is different from the reactions of late transition metal mediated cyclodimerization of alkynes (e.g., Co) via direct reductive elimination. To account for the formation of 3-methylenecyclobutenes, an E1cb reaction pathway was suggested. The present findings not only allow us to better understand the reactivity of 2-pyridyl-substituted alkynes but also provide a foundation on which to further develop more efficient cyclization reactions promoted by directing groups.

Experimental Section

General Method. See the Supporting Information.

Synthesis and Characterization of Compounds 1a−n, 2a, 2a-*D*, 2j, 2n, 4, and 5a. See the Supporting Information.

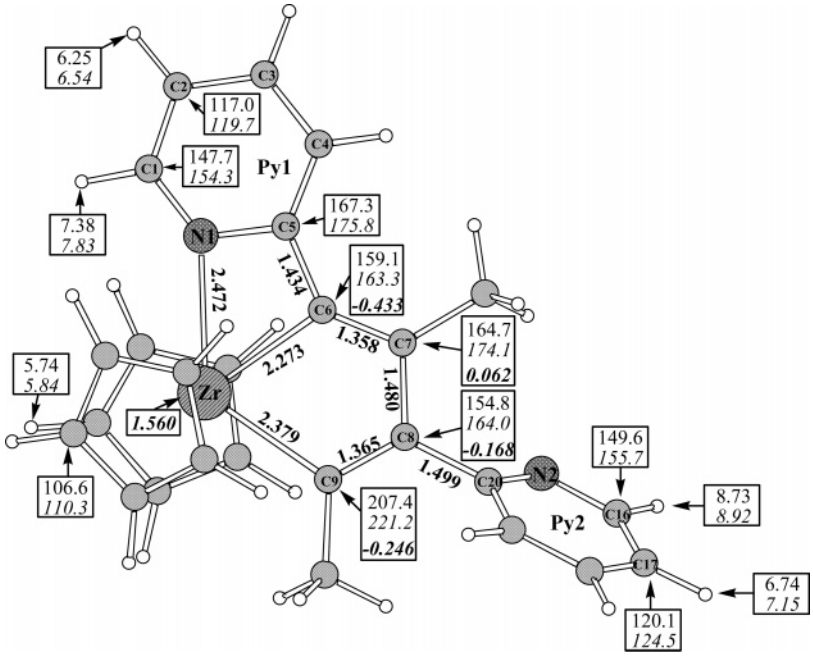


Figure 3. Optimized structure of **10n** (in this model, methyl groups were used instead of propyl groups), selected ^{13}C and ^{1}H chemical shifts (normal for experimental values, italic for calculated results), NBO atomic charges (bold italic), and bond lengths (bold). Both the geometry optimization and the NMR studies were calculated at the B3LYP/6-311+G**/Lanl2DZ level.

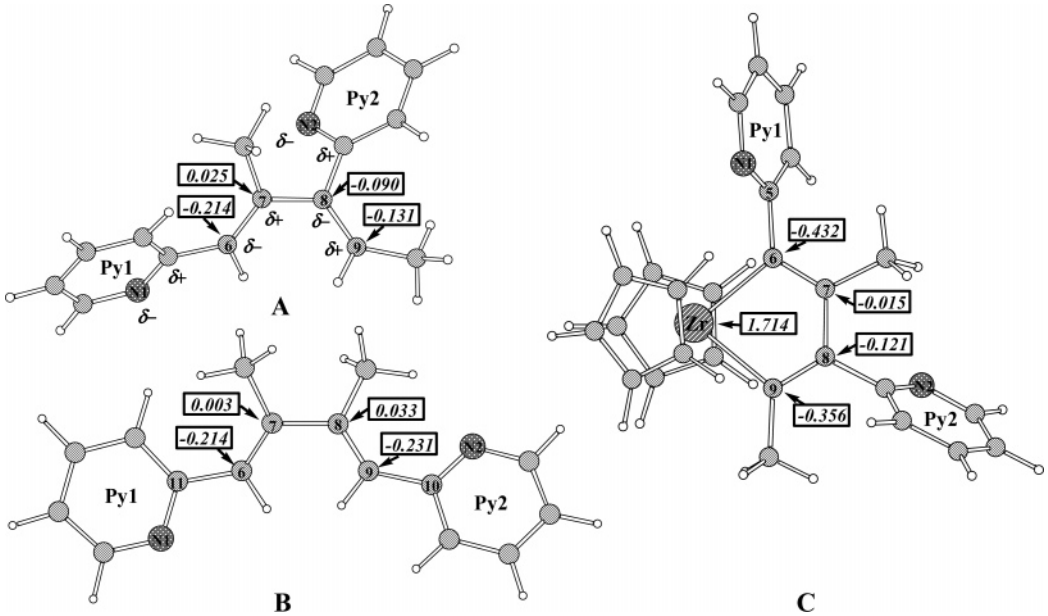


Figure 4. Optimized structures of models **A**, **B**, and **C** with selected NBO atomic charges, calculated at the B3LYP/6-311+G**/Lanl2DZ level.

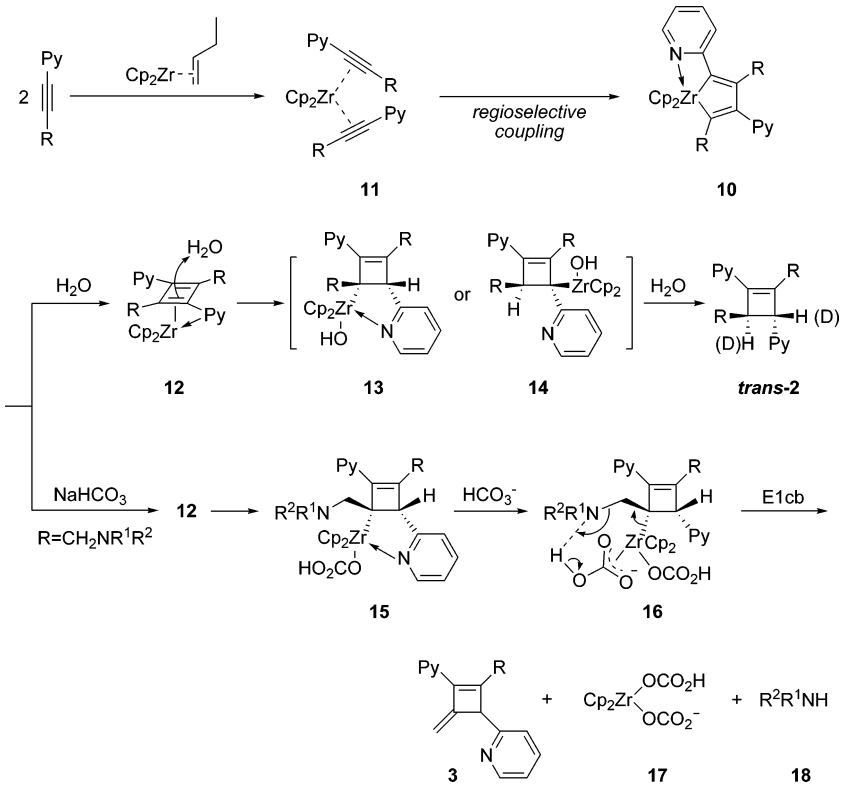
A Typical Procedure for the Preparation of 3-Methylenecyclobutene Derivatives 3. To a solution of Cp_2ZrCl_2 (0.32 g, 1.1 mmol) in THF (5 mL) was added *n*-BuLi (1.38 mL, 2.2 mmol, 1.6 M solution in hexane) at −78 °C. After stirring for 1 h at the same temperature, alkyne **1a** (2 mmol) was added and the reaction mixture was warmed to room temperature and stirred for 1−3 h. The resulting orange-brown solution was quenched with saturated $NaHCO_3$ solution and extracted with ethyl acetate. The extract was washed with water and brine and dried over Na_2SO_4. The solvent was evaporated in vacuo, and the residue was purified by chromatography on silica gel. 3-Methylenecyclobutene **3a** was formed in 70% isolated yield.

1-(Diphenylaminomethyl)-2,4-dipyridyl-3-methylenecyclobut-1-ene (3a). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) afforded the title product in 70% isolated yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 4.40 (s,1H), 4.54 (s, 1H), 4.96 (d, J = 18.0 Hz, 1H), 5.15 (s, 1H), 5.43 (d, J = 18.3 Hz, 1H), 6.79−6.88 (m, 6H), 6.96−7.09 (m, 6H), 7.17 (dd, J = 7.5, 4.8 Hz, 1H), 7.39 (td, J = 7.8, 1.8 Hz, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.68 (td, J = 7.8, 1.8 Hz, 1H), 8.45 (d, J = 4.5 Hz, 1H), 8.68 (dt, J = 5.1, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 50.40, 56.24, 97.81, 120.61, 120.99, 121.44, 122.08, 122.12, 128.78, 135.94, 136.05, 142.84, 146.82, 147.88, 149.13, 149.69, 151.79, 154.98, 159.43; HRMS (MALDI/DHB) for $C_{28}H_{24}N_3$ $[M + H]^+$ calcd 402.1970, found 402.1965.

Diphenylamine was isolated in 71% yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 5.67 (br, 1H), 6.89−6.94 (m, 2H), 7.03−7.07 (m, 4H), 7.22−7.29 (m, 4H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 117.73, 120.93, 129.29, 143.02.

1-(*N*-Methylanilinylmethyl)-2,4-dipyridyl-3-methylenecyclobut-1-ene (3b). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) afforded the title product in 79% isolated

Scheme 7



yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.72 (s, 3H), 4.36 (s, 1H), 4.51-(d, J = 18.6 Hz, 1H), 4.56 (s, 1H), 4.95 (d, J = 17.7 Hz, 1H), 5.17 (s, 1H), 6.57−6.60 (m, 3H), 7.04−7.09 (m, 4H), 7.18 (ddd, J = 7.6, 5.1, 0.9 Hz, 1H), 7.43−7.49 (m, 2H), 7.70 (td, J = 7.8, 1.8 Hz, 1H), 8.51−8.52 (ddd, J = 4.7, 1.8, 0.9 Hz, 1H), 8.68−8.70 (m, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 38.97, 50.08, 56.20, 97.93, 111.98, 116.01, 121.56, 122.01, 122.09, 122.16, 128.78, 136.02, 136.08, 142.98, 146.88, 148.90, 149.19, 149.69, 151.82, 155.05, 159.50; HRMS (MALDI/DHB) for $C_{23}H_{22}N_3$ $[M + H]^+$ calcd 340.1814, found 340.1808.

1-(*N*-Tolyl-*N*-methylaminomethyl)-2,4-dipyridyl-3-methylenecyclobut-1-ene (3c). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) afforded the title product in 79% isolated yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.20 (s, 3H), 2.71 (s, 3H), 4.35 (s, 1H), 4.43 (d, J = 18.0 Hz, 1H), 4.56 (s, 1H), 4.93 (d, J = 17.7 Hz, 1H), 5.17 (s, 1H), 6.52 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 7.08−7.11 (m, 2H), 7.18−7.22 (m, 1H), 7.46−7.53 (m, 2H), 7.71 (td, J = 7.8, 1.2 Hz, 1H), 8.53 (d, J = 4.5 Hz, 1H), 8.70 (d, J = 4.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 20.07, 39.08, 50.26, 56.17, 97.82, 112.32, 121.46, 121.94, 122.05, 122.06, 125.12, 129.26, 135.95, 135.99, 142.90, 146.88, 146.93, 149.13, 149.60, 151.80, 155.17, 159.54; HRMS (MALDI/DHB) for $C_{24}H_{24}N_3$ $[M + H]^+$ calcd 354.1970, found 354.1965.

1-(*N*-Methyl-4-chloroanilinylmethyl)-2,4-dipyridyl-3-methylenecyclobut-1-ene (3d). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) afforded the title product in 74% isolated yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.70 (s, 3H), 4.32 (s, 1H), 4.54 (d, J = 15.9 Hz, 1H), 4.56 (s, 1H), 4.90 (d, J = 18.3 Hz, 1H), 5.16 (s, 1H), 6.48 (d, J = 9.0 Hz, 2H), 6.97 (d, J = 9.3 Hz, 2H), 7.03−7.08 (m, 2H), 7.17−7.21 (m, 1H), 7.43−7.49 (m, 2H), 7.70 (td, J = 7.8, 1.8 Hz, 1H), 8.49 (ddd, J = 4.8, 1.8, 0.9 Hz, 1H), 8.68 (ddd, J = 4.8, 1.8, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, Me_4-Si) δ 39.16, 50.10, 56.21, 98.14, 113.06, 120.69, 121.63, 121.90, 122.05, 122.28, 128.46, 136.05, 136.15, 143.24, 146.72, 147.40, 149.13, 149.69, 151.68, 154.36, 159.29; HRMS (MALDI/DHB) for $C_{23}H_{21}ClN_3$ $[M + H]^+$ calcd 374.1424, found 374.1419.

1-(*N*-Methyl-4-methoxyanilinylmethyl)-2,4-dipyridyl-3-methylenecyclobut-1-ene (3e). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) afforded the title product in 71% isolated yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.71 (s, 3H), 3.70 (s, 3H), 4.35 (s, 1H), 4.41 (d, J = 17.4 Hz, 1H), 4.56 (s, 1H), 4.87 (d, J = 17.1 Hz, 1H), 5.17 (s, 1H), 6.55−6.58 (m, 2H), 6.65−6.69 (m, 2H), 7.06−7.10 (m, 2H), 7.17−7.22 (m, 1H), 7.46−7.52 (m, 2H), 7.70 (td, J = 7.8, 1.8 Hz, 1H), 8.51−8.53 (m, 1H), 8.68−8.70 (m, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 39.60, 50.87, 55.66, 56.34, 97.96, 113.91, 114.42, 121.56, 122.00, 122.19, 136.07, 136.09, 143.19, 143.95, 147.01, 149.21, 149.70, 151.31, 151.89, 155.19, 159.62; HRMS (MALDI/DHB) for $C_{24}H_{24}N_3O$ $[M + H]^+$ calcd 370.1919, found 370.1914.

1-(*N*-Benzyl-4-methoxyanilinylmethyl)-2,4-dipyridyl-3-methylenecyclobut-1-ene (3f). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) afforded the title product in 65% isolated yield (1.25 equiv of Cp_2ZrBu_2 was used): ^{1}H NMR ($CDCl_3$, Me_4Si) δ 3.67 (s, 3H), 4.12 (d, J = 16.5 Hz, 1H), 4.28 (d, J = 16.8 Hz, 1H), 4.41 (s, 1H), 4.48 (d, J = 17.7 Hz, 1H), 4.56 (s, 1H), 4.95 (d, J = 17.7 Hz, 1H), 5.16 (s, 1H), 6.58−6.65 (m, 4H), 7.05−7.11 (m, 4H), 7.14−7.21 (m, 4H), 7.43−7.47 (m, 2H), 7.68 (td, J = 7.8, 1.2 Hz, 1H), 8.53 (d, J = 4.8 Hz, 1H), 8.66 (d, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 48.75, 55.52, 55.94, 56.26, 97.89, 114.35, 114.44, 121.60, 122.03, 122.11, 122.15, 126.49, 126.70, 128.22, 136.06, 138.94, 143.14, 143.26, 146.91, 149.13, 149.65, 151.42, 151.76, 155.37, 159.57; HRMS (MALDI/DHB) for $C_{30}H_{28}N_3O$ $[M + H]^+$ calcd 446.2232, found 446.2227.

1-(*N*-Methylanilinylmethyl)-2,4-di(5-methylpyridyl)-3-methylenecyclobut-1-ene (3g). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) afforded the title product in 69% isolated yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.26 (s, 3H), 2.37 (s, 3H), 2.74 (s, 3H), 4.36 (s, 1H), 4.50 (d, J = 16.8 Hz, 1H), 4.53 (s, 1H), 4.88 (d, J = 17.7 Hz, 1H), 5.13 (s, 1H), 6.55−6.62 (m, 3H), 6.98 (d, J = 8.1 Hz, 1H), 7.05 (dd, J = 8.7, 7.5 Hz, 2H), 7.25−7.29 (m, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.50 (dd, J = 8.7 Hz, 1.2 Hz, 1H), 8.33 (bs, 1H), 8.52 (bs, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 18.05, 18.42, 39.06, 50.00, 55.53, 97.78, 112.01, 115.95, 121.54, 121.65, 128.74, 131.05, 131.83, 136.51, 137.08, 143.14, 147.17, 148.88, 148.93, 149.22, 150.25, 153.77, 156.44; HRMS (MALDI/DHB) for $C_{25}H_{26}N_3$ $[M + H]^+$ calcd 368.2127, found 368.2121.

1-(Diphenylaminomethyl)-2,4-di(5-methylpyridyl)-3-methylenecyclobut-1-ene (3h). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) afforded the title product in 73% isolated yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.24 (s, 3H), 2.36 (s, 3H), 4.36 (s, 1H), 4.51 (s, 1H), 4.94 (d, J = 18.6 Hz, 1H), 5.11 (s, 1H), 5.36 (d, J = 18.0 Hz, 1H), 6.79−6.89 (m, 7H), 7.03−7.10 (m, 4H), 7.12−7.24 (m, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.49−7.52 (m, 1H), 8.27−8.28 (m, 1H), 8.51−8.52 (m, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 18.02, 18.41, 50.35, 55.89, 97.49, 120.66, 120.91, 121.49, 121.64, 128.76, 130.69, 131.71, 136.46, 136.57, 142.89, 147.27, 147.95, 149.25, 149.40, 150.23, 153.85, 156.57; HRMS (MALDI/DHB) for $C_{30}H_{28}N_3$ [M + H]$^+$ calcd 430.2283, found 430.2278.

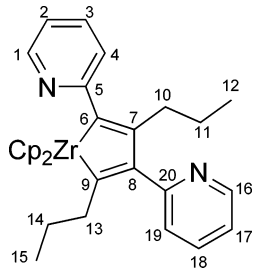
1-(*N*-Methylanilinylmethyl)-2,4-di(quinolin-2-yl)-3-methylenecyclobut-1-ene (3i). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) afforded the title product in 64% isolated yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.75 (s, 3H), 4.68 (s, 1H), 4.71 (s, 1H), 4.79 (d, J = 18.0 Hz, 1H), 5.01 (d, J = 18.0 Hz, 1H), 5.38 (s, 1H), 6.56 (t, J = 7.2 Hz, 1H), 6.62 (d, J = 8.4 Hz, 2H), 6.98 (dd, J = 8.7, 7.5 Hz, 2H), 7.22 (d, J = 7.5 Hz, 1H), 7.46 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.62−7.74 (m, 4H), 7.80 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.7 Hz, 1H), 8.06 (d, J = 8.4 Hz, 1H), 8.16 (t, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 39.23, 50.61, 57.37, 99.28, 112.10, 116.11, 119.55, 120.16, 125.81, 126.60, 127.02, 127.19, 127.40, 127.49, 128.80, 129.00, 129.11, 129.60, 129.70, 135.91, 136.30, 143.77, 146.64, 147.70, 148.25, 148.84, 151.81, 156.28, 160.03; HRMS (MALDI/DHB) for $C_{31}H_{26}N_3$ [M + H]$^+$ calcd 440.2127, found 440.2121.

1-(Diphenylaminomethyl)-2,4-di(quinolin-2-yl)-3-methylenecyclobut-1-ene (3j). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) afforded the title product in 47% isolated yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 4.69 (s, 1H), 4.73 (s, 1H), 5.26 (d, J = 18.3 Hz, 1H), 5.35 (s, 1H), 5.50 (d, J = 18.3 Hz, 1H), 6.73 (td, J = 7.2, 0.6 Hz, 2H), 6.89−6.97 (m, 8H), 7.18 (d, J = 8.4 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.62−7.75 (m, 4H), 7.79−7.84 (m, 2H), 8.01 (d, J = 8.7 Hz, 1H), 8.13−8.20 (m, 2H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 50.91, 57.46, 99.17, 119.49, 120.14, 120.68, 121.03, 125.73, 126.64, 127.01, 127.14, 127.30, 127.50, 128.77, 128.99, 129.02, 129.64, 129.72, 135.85, 136.32, 143.75, 146.56, 147.66, 147.83, 148.27, 151.78, 156.30, 159.99; HRMS (MALDI/DHB) for $C_{36}H_{28}N_3$ [M + H]$^+$ calcd 502.2283, found 502.2278.

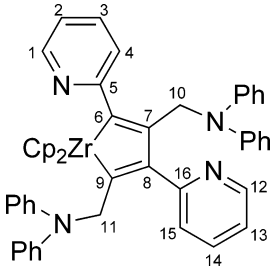
1-(Dibenzylaminomethyl)-2,4-dipyridyl-3-methylenecyclobut-1-ene (3k). Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) afforded the title product (concomitant with dibenzylamine) in 78% isolated yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 3.34 (d, J = 13.5 Hz, 2H), 3.56 (d, J = 15.9 Hz, 1H), 3.79 (d, J = 13.8 Hz, 2H), 3.89 (d, J = 15.9 Hz, 1H), 4.63 (s, 1H), 4.75 (s, 1H), 5.23 (s, 1H), 7.11−7.19 (m, 12H), 7.22−7.36 (m, 20H), 7.44 (d, J = 7.8 Hz, 1H), 7.51 (td, J = 7.8, 1.8 Hz, 1H), 7.65 (td, J = 7.8, 1.8 Hz, 1H), 8.57−8.59 (m, 1H), 8.62−8.65 (m, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 50.25, 52.94, 56.73, 58.84, 98.14, 121.57, 121.70, 122.14, 122.51, 126.64, 126.98, 127.99, 128.18, 128.37, 128.54, 135.92, 136.28, 139.09, 139.89, 144.55, 147.28, 149.33, 149.59, 151.84, 155.20, 159.98; HRMS (MALDI/DHB) for $C_{30}H_{28}N_3$ [M + H]$^+$ calcd 430.2282, found 430.2278.

Bn_2NH: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.15 (s), 3.81 (s), 7.32−7.34 (m).

1,3-Dipropyl-2,4-dipyridyl-1,3-butadiene (5b). To the reaction mixture of 2-pent-1-ynyl-pyridine (**1n**) with Cp_2ZrBu_2 was added D-(−)-pantolactone (2 equiv). After stirring for 1 h at room temperature, the mixture was quenched with saturated $NaHCO_3$ solution and extracted with ethyl acetate. Column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) afforded the title product in 58% isolated yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.86 (t, J = 7.2 Hz, 3H), 0.94 (t, J = 7.2 Hz, 3H), 1.43 (sex, J = 7.2 Hz, 2H), 1.55−1.67 (m, 2H), 1.97 (q, J = 7.2 Hz, 2H), 2.67−2.73 (m, 2H), 6.10 (t, J = 7.5 Hz, 1H), 6.14 (s, 1H), 7.03 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H), 7.13 (d, J = 7.8 Hz, 1H), 7.19 (ddd, J = 7.5, 5.1, 1.2 Hz, 1H), 7.22−7.25 (m, 1H), 7.56 (td, J = 7.8, 1.8 Hz, 1H), 7.68 (td, J = 7.8, 1.8 Hz, 1H), 8.54−8.57 (m, 1H), 8.67−8.69 (m, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.73, 14.17, 22.35, 22.74, 30.42, 31.43, 120.62, 121.48, 124.11, 124.96, 128.17, 132.14, 135.60, 135.89, 143.01, 147.23, 149.00, 149.37, 157.13, 158.91; HRMS (MALDI/DHB) for $C_{20}H_{25}N_2$ [M + H]$^+$ calcd 293.2018, found 293.2012.



Zirconium Complex 10n. NMR yield: 67%. To a solution of Cp_2ZrCl_2 (0.16 g, 0.55 mmol) in hexane (5 mL) was added *n*-BuLi (0.69 mL, 1.1 mmol, 1.6 M solution in hexane) at −78 °C. After stirring for 1 h at the same temperature, the reaction mixture was warmed to 0 °C and stirred for 15 min. 2-(Pent-1-ynyl)pyridine (1 mmol) was added at −30 °C, and the reaction mixture was warmed to room temperature and stirred for 3 h. Then the solution was filtered, the filtrate was concentrated in vacuo, and *n*-hexane was added. Pure **10n** was obtained as an orange solid by recrystallization in *n*-hexane: ^{1}H NMR (C_6D_6, 600 MHz) δ 0.81 (t, J = 7.2 Hz, 3H, H-15), 0.85 (t, J = 7.2 Hz, 3H, H-12), 1.40−1.47 (m, 2H, H-14), 1.52 (sex, J = 7.2 Hz, 2H, H-11), 2.40−2.43 (m, 2H, H-13), 2.54 (t, J = 7.2 Hz, 2H, H-10), 5.74 (s, 10H, Cp), 6.25 (ddd, J = 7.2, 5.4, 1.2 Hz, 1H, H-2), 6.74 (ddd, J = 7.2, 4.8, 1.2 Hz, 1H, H-17), 6.77 (d, J = 8.4 Hz, 1H, H-4), 6.97 (ddd, J = 8.4, 7.2, 1.8 Hz, 1H, H-3), 7.11 (dt, J = 7.2, 1.2 Hz, 1H, H-19), 7.25 (td, J = 7.8, 2.4 Hz, 1H, H-18), 7.38 (ddd, J = 5.4, 1.8, 1.2 Hz, 1H, H-1), 8.73 (ddd, J = 4.8, 1.8, 1.2 Hz, 1H, H-16); ^{13}C NMR (C_6D_6, 75.5 Hz) δ 14.63 (C-12), 15.97 (C-15), 22.72 (C-11), 24.30 (C-14), 35.16 (C-10), 41.28 (C-13), 106.56 (Cp), 116.99 (C-4), 117.02 (C-2), 120.08 (C-17), 124.76 (C-19), 134.97 (C-18), 136.49 (C-3), 147.65 (C-1), 149.59 (C-16), 154.80 (C-8), 159.05 (C-6), 163.28 (C-20), 164.73 (C-7), 167.28 (C-5), 207.38 (C-9); HRMS (MALDI/DHB) for $C_{30}H_{33}N_2Zr$ [M + H]$^+$ calcd 511.1691, found 511.1685.



Zirconium Complex 10a. NMR yield: 95%. The solvent was evaporated in vacuo after the general procedure, and dry ether (5 mL) was added, followed by stirring for 10 min. After filtration the filtrate was concentrated in vacuo, and **10a** was obtained as an orange solid: ^{1}H NMR (C_6D_6) δ 4.52 (s, 2H, H-10), 4.71 (s, 2H, H-11), 5.59 (s, 10H, Cp), 6.16−6.20 (m, 1H, H-2), 6.54 (dd, J = 4.8, 1.8 Hz, 1H, H-13), 6.75−6.80 (m, 2H, Ph-H), 6.83−6.89 (m, 3H, 3,4-H, Ph-H), 6.92−7.11 (m, 12H, 15,14-H, Ph-H), 7.15−7.23 (m, 8H, H-1, Ph-H), 8.60 (d, J = 4.8 Hz, 1H, H-12); ^{13}C NMR (C_6D_6) δ 53.32 (C-10), 63.34 (C-11), 107.58 (Cp), 118.31 (C-2), 119.13 (C-4), 120.37 (C-13), 121.59 (Ph), 121.76 (Ph), 122.29 (Ph), 122.55 (Ph), 124.82 (C-15), 128.89 (Ph), 129.12 (Ph), 134.90 (C-14), 136.50 (C-3), 147.04 (C-1), 149.14 (Ph), 149.29 (C-12), 151.27

(Ph), 152.83 (C-8), 155.72 (C-6 or C-7), 162.80 (C-16), 165.42 (C-5), 166.68 (C-7 or C-6), 199.25 (C-9); HRMS (MALDI/DHB) for $C_{50}H_{43}N_4Zr$ $[M + H]^+$ calcd 789.2535, found 789.2529.

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Supporting Information Available: Experimental details and spectroscopic characterization of compounds **1a**−**m**, **2a**, **2a**-***D***, **2j**, **2n**, **4**, and **5a** and CIF files giving crystallographic data of **4**. Calculated total energies and geometrical coordinates of structure **10n**, models A, B, and C. This material is available free of charge via the Internet at http://pubs.acs.org.

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