Chapter 2
Zirconocene-Mediated Cyclization of Bis(alkynyl)silanes and Nitriles: Synthesis of *N*-Heterocycles and Isolation, Characterization, and Synthetic Application of Zr/Si-Containing Reactive Intermediates

2.1 Introduction

The isolation and reactivity investigation of important intermediates in transition-metal-mediated or metal-catalyzed reactions are of general interest in both organometallic chemistry and synthetic organic chemistry. The research into organometallic reactive intermediates focuses on its structures, reaction patterns, and the relationship. On the one hand, these researches play an important role in the in-depth understanding of seemingly complicated reaction mechanisms. On the other hand, it can also lead to discovery of new synthetically useful reactions, such as new types of C–C and C–X bond formation or heterocycle synthesis (Fig. 2.1). However, generally the organometallic reactive intermediates are very reactive toward air, oxygen, and moisture and thus difficult to isolate and characterize.

Azaindoles are a class of heterocycles of considerable biological and pharmaceutical importance and have been frequently applied in natural product synthesis and as indole bioisosteres in the design of biologically active compounds [1, 2]. However, synthesis of azaindoles has remained a challenge for synthetic chemists both in academy and in pharmaceutical industry, since classical methods for synthesis of indole derivatives and related *N*-containing heterocycles do not work well on the synthesis of azaindole analogues, or at least work but not efficiently [1, 2]. In 2004, our research group reported a zirconocene-mediated intermolecular coupling reaction of one molecule of bis(alkynyl)silane with three molecules of organonitrile, which afforded 5-azaindoles upon hydrolysis of the reaction mixture (Scheme 2.1) [3].

In this one-pot reaction, five components are involved and integrated in a selective manner via an unknown pathway, involving cleavage of C≡N triple bonds and Si–C bonds [4–6]. We anticipated that novel and important reaction patterns might be involved. Thus, we expect to isolate and characterize the reactive intermediates ahead of hydrolysis process. Fortunately, we managed to isolate the intermediate in this process and illustrate the interesting and surprising mechanism which puts all the five

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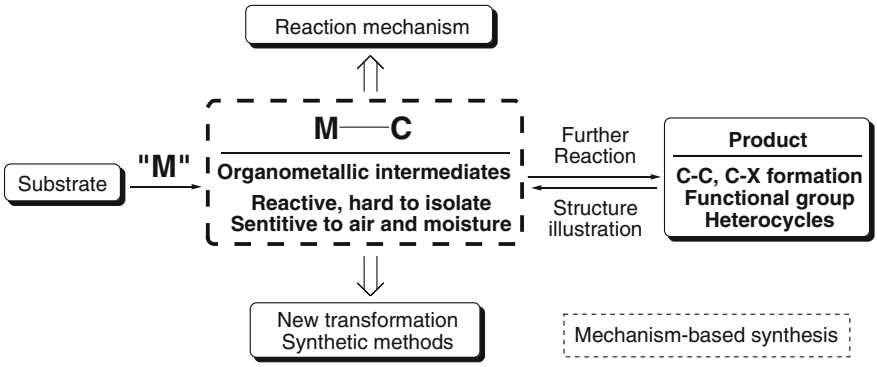
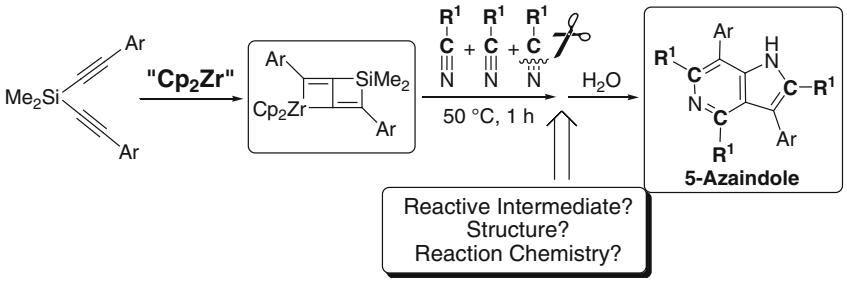


Fig. 2.1 Mechanism investigation and synthesis application based on chemistry of organometallic reactive intermediates



Scheme 2.1 Zirconocene-mediated intermolecular coupling reaction of bis(alkynyl)silane with three molecules of organonitriles affording 5-azaindoles

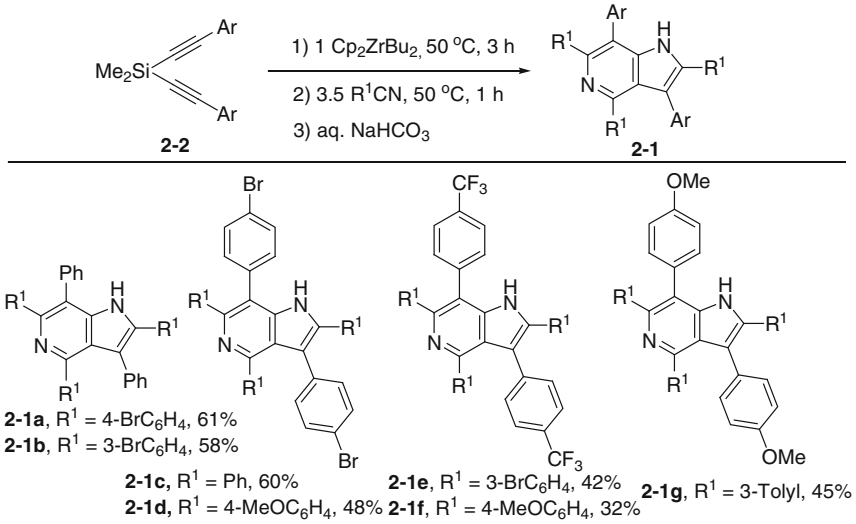
components together. In this chapter, the following researches are disclosed: (1) the scope of synthesis of 5-azaindoles and the further derivation; (2) isolation and characterization of Zr/Si-containing organometallic reactive intermediates; and (3) synthetically useful applications of these reactive intermediates toward synthesis of *N*-heterocycles.

2.2 Results and Discussion

2.2.1 Formation of 5-Azaindoles from One Molecule of Bis (alkynyl)silane with Three Molecules of the Same Organonitrile

Cp_2ZrBu_2 (Negishi reagent), as a very useful zirconocene (II) species, can be easily generated in situ from Cp_2ZrCl_2 and two equivalents of *n*-butyl lithium in toluene at −78 °C for 1 h [7]. Zirconocene (II) species promoted intermolecular coupling of

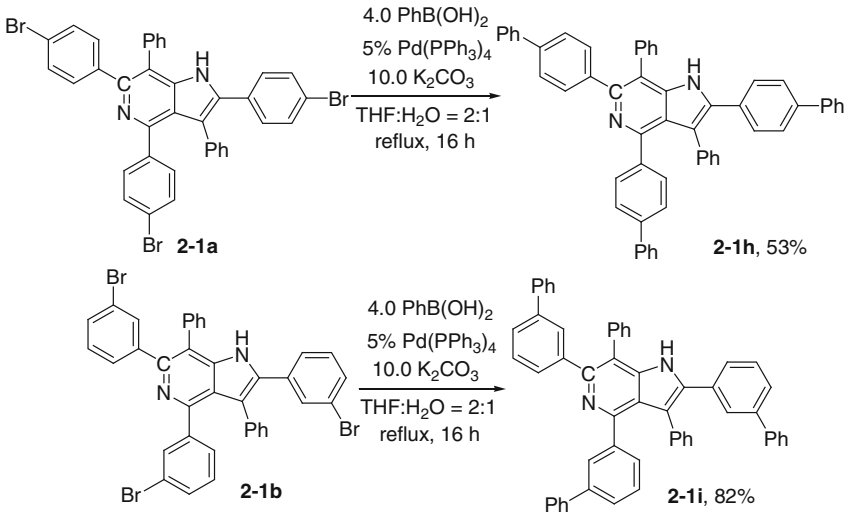
Table 2.1 Formation of 5-azaindoles from one molecule of bis(alkynyl)silane with three molecules of the same organonitrile (R^1CN)



bis(alkynyl)silane with three molecules of the same organonitriles [8, 9], to afford a 5-azaindole derivative upon hydrolysis (Table 2.1) [3]. Further investigation reveals that a wide variety of the bis(alkynyl)silane and organonitriles, especially those functionalized ones, can be applied in this procedure to afford 5-azaindole derivatives with diversified substitution patterns.

A variety of bis(arylalkynyl)silanes **2-2** could act as a suitable component as given in Table 2.1. In addition to Ph-substituted alkynes (**2-2a**), we also investigated substituted or functionalized bis(arylalkynyl)silanes, such as 4-Br (**2-2b**), 4-CF_3 (**2-2c**), and 4-OMe (**2-2d**). Bis(alkynyl)silanes with functional substituents (**2-2b**–**2-2d**) lead to the formation of azaindoles bearing various functional groups, however in lower yields. Electron-donating OMe group and electron-withdrawing CF_3 group on the aryl moiety of **2-2** could also be applied to afford their corresponding multi-functionalized azaindoles (**2-1e**–**2-1g**) in moderate to good yields, respectively. It should be noted that Br in **2-2b** survived this zirconocene-mediated conditions to give the azaindoles **2-1c**–**2-1d** in good yields.

A wide variety of organonitriles, either aliphatic or (hetero)aromatic with both electron-withdrawing groups and electron-donating groups, could be applied to afford 5-azaindoles in good isolated yields. Functionalized groups on the aromatic nitriles were tolerated in this process, albeit slightly lower yields were gained in comparison with PhCN. The 4-OMe- and 3-Br-substituted benzonitriles all gave good results to the corresponding azaindoles. However, as far as other functionalized or steric-hindered nitriles, such as 2-cyanopyridine, 9-cyanophenathracene, and 2-bromobenzonitrile, were concerned, only trace amount of azaindoles were observed.

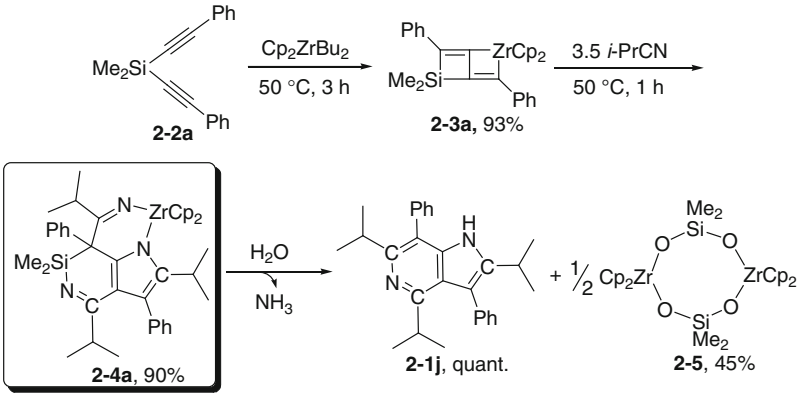


Scheme 2.2 Further application of 5-azaindoles: Suzuki coupling

The functionalized azaindoles with Br group could be further transformed to more complicated and diversified azaindoles. Thus, subjecting the Br-bearing azaindole **2-1a** or **2-1b** to Suzuki coupling condition with benzeneboronic acid gave their corresponding arylated azaindoles **2-1h** and **2-1i** in the respective 53 and 82 % isolated yield [10] (Scheme 2.2).

2.2.2 Isolation and Characterization of Zr/Si-Containing Organometallic Reactive Intermediates

In order to investigate the reaction mechanism in a pure and controllable system and get rid of LiCl generated in situ, we prepared and isolated the intermediate **2-3a** in 93 % yield. 3.5 Equivalents of *i*-PrCN were added to a toluene solution of **2-3a**. After the reaction mixture was stirred at 50 °C for 1 h, a red powder was isolated in 90 % yield, which was confirmed to be a very interesting and totally unexpected complex **2-4a** (Scheme 2.3). Single crystals of **2-4a** suitable for X-ray analysis were grown in benzene at room temperature. X-ray analysis of **2-4a** (Fig. 2.2) reveals its three-ring-fused structure composed of one 6-membered ring containing silicon and nitrogen, one 5-membered pyrrolo ring, and one 6-membered zirconacycle. The zirconium center is bonded with two Cp rings, one imine nitrogen atom, and one nitrogen atom of the pyrrolo ring. The silicon atom is bonded with one quaternary carbon atom, one imine nitrogen atom, and two methyl groups. Two imine carbon atoms neighboring the silicon and zirconium atoms in **2-4a** showed a singlet at δ = 183.9 and 188.2 ppm in the ^{13}C NMR spectrum in [D_6]benzene, respectively.



Scheme 2.3 Formation of zirconocene-containing intermediate **2-4a** from three molecules of nitrile and the hydrolysis reaction

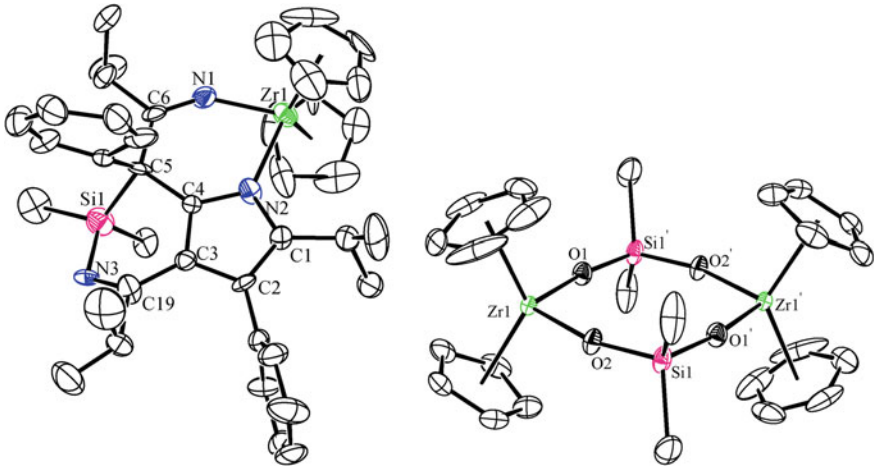
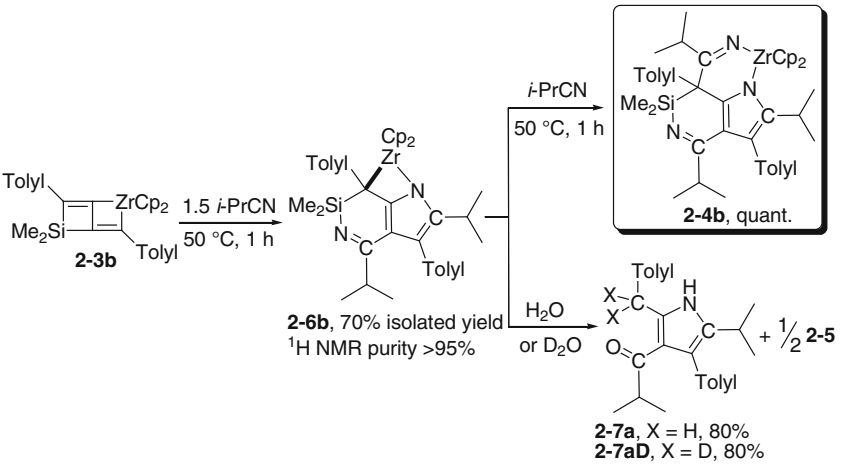


Fig. 2.2 ORTEP drawing of **2-4a** and **2-5** with 30 % thermal ellipsoids. Reproduced from Ref. [11] with the permission from Wiley

Hydrolysis of this isolated **2-4a** with a certain amount of H_2O afforded its corresponding 5-azaindole **2-2a** in a quantitative yield. In addition to **2-2a**, formation of NH_3 in the reaction solution was detected using in situ ^1H NMR spectra. Furthermore, the whereabouts of the Cp_2Zr moiety and the $SiMe_2$ moiety was determined by successful isolation of the cyclic zirconasiloxane **2-5**. This cyclic zirconasiloxane **2-5**, which was obtained in 45 % isolated yield, formed nice crystals suitable for X-ray structural analysis (Fig. 2.2).

With these results in hands, the author expected to understand more about the reaction mechanism. How is **2-4a** formed from the reaction of **2-3a** with *i*-PrCN? And what are the structures of reactive intermediates involving only one or two molecules

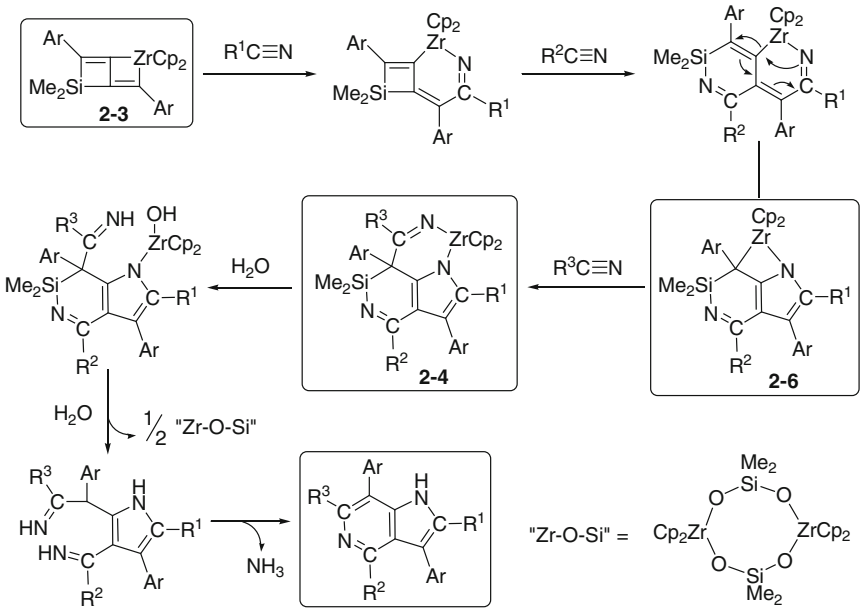


Scheme 2.4 Formation of zirconocene-containing intermediate **2-6b** from two molecules of nitrile and the hydrolysis reaction

of nitriles? The reaction of tolyl-substituted **2-3b** with 1.5 equivalents of *i*-PrCN in benzene at 50 °C for 1 h afforded a green solid **2-6b** in 70 % yield. Although single crystals of **2-6b** suitable for X-ray crystallographic analysis were not obtained, its ^{1}H and ^{13}C NMR data were rather informative for the elucidation of the structure. The imine carbon atoms in **2-6b** showed a singlet at $\delta = 181.5$, and the quaternary carbon atom linked by zirconium and silicon atoms gave a singlet at $\delta = 80.9$ ppm in the ^{13}C NMR spectrum in [D_6]benzene. Hydrolysis of **2-6b** with 1–3 equiv. of H_2O gave the compound **2-7** in 80 % yield after a short column chromatography. The cyclic zirconasiloxane **2-5** was also obtained in 45 % isolated yield (Scheme 2.4).

Based on all the above experimental results, we proposed a reaction mechanism for the formation of 5-azaindole (Scheme 2.5). Insertion of the C≡N triple bond of the first organonitrile (R^1CN) into one of the Zr–C bonds of **2-3** would afford the first intermediate, which might immediately undergo insertion of the C≡N triple bond of the second organonitrile (R^2CN) into one of the Si–C bonds. This intermediate is thermodynamically unstable and would undergo skeletal rearrangement through 1,2-shift of the Cp_2Zr moiety in the azazirconacyclic ring to afford the key intermediate **2-6**, which is stable enough at room temperature and could be characterized by ^{1}H NMR and ^{13}C NMR. The insertion chemistry of the C≡N triple bond of organonitriles into Zr–C bonds affording azazirconacycles and into Si–C bonds has been documented [12–14]. Insertion of the C≡N triple bond of the third organonitrile (R^3CN) to the Zr–C bond in **2-6** would lead to the formation of **2-4**.

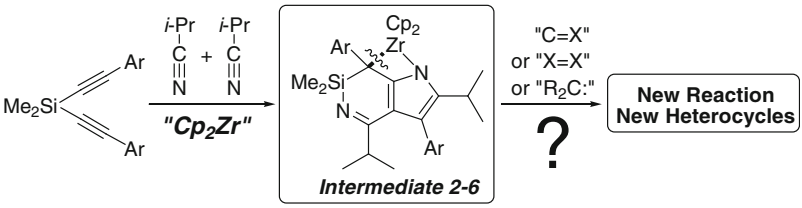
A proposed hydrolysis process of **2-4** leading to the formation of NH_3, 5-azaindole, and **2-5** is also shown in Scheme 2.5. Cleavage of the Zr–N (imine) bond in **2-4** by the first molecule of water and further hydrolysis with 2 molecules of water afforded the diimine. **2-5** was formed and eliminated through the coupling between the Me_2SiOH and Cp_2ZrOH moieties. The final product **2-2** was generated via the cyclization of the diimine, along with the loss of NH_3 [15].



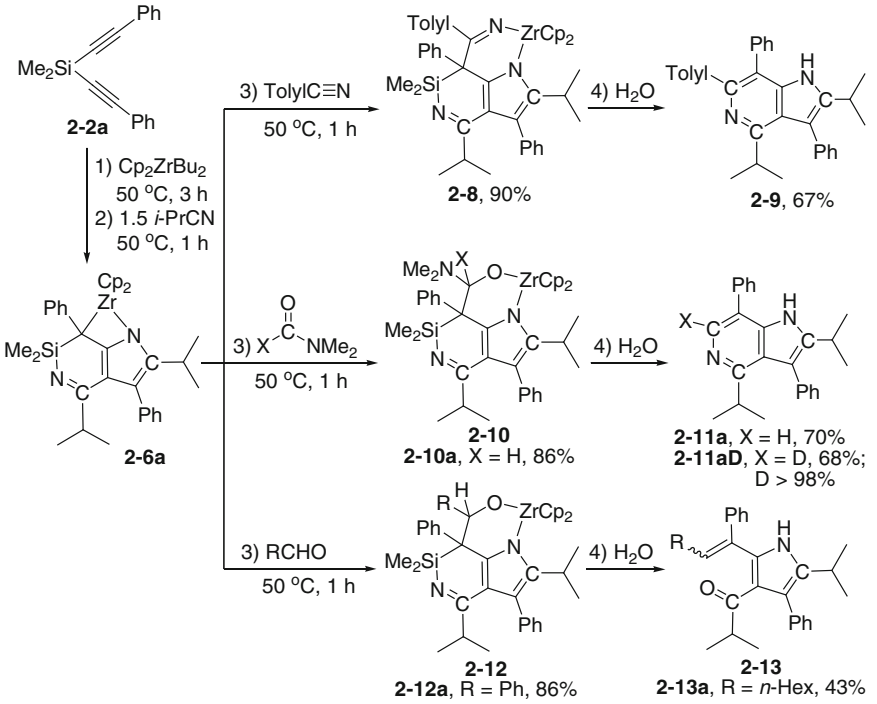
Scheme 2.5 Proposed reaction mechanism involving one bis(alkynyl)silane and three organonitriles

2.2.3 *Synthetic Application of Zr/Si-Containing Organometallic Reactive Intermediates*

The structural investigation of organometallic intermediates benefits the understanding of reaction mechanism and further reaction chemistry (Scheme 2.6). The reactive intermediate **2-6** features Zr–C(sp^3) bond, which was proved to be useful for further synthetic application. **2-6** could react with several unsaturated compounds or electrophiles such as isocyanide, formamide, acid chloride, and aldehyde, affording a series of *N*-heterocycles upon hydrolysis (Scheme 2.7).



Scheme 2.6 Reaction modes of intermediate **2-6**



Scheme 2.7 Reaction chemistry and synthetic application of **2-6**

Firstly, insertion of the third nitrile into reactive intermediate **2-6a** took place and afforded 5-azaindole with the same substituents on 2,4-positions and different substituent on 6-position. The azazirconacyclobutane-containing intermediate **2-6a** was isolated directly from reaction of **2-2a** with 1.5 equivalents of *i*-PrCN mediated by Cp_2ZrBu_2 in toluene solution (Scheme 2.7). Treatment of a benzene solution of **2-6a** with *p*-TolylCN at 50 °C for 1 h gave a deep brown solution, which was dried up under vacuum and then crystallized in THF/hexane mixed solvent to afford the complex **2-8** as brown crystals in 90 % isolated yield (Fig. 2.3). Single-crystal X-ray structural analysis of **2-8** clearly showed the three-ring-fused skeleton containing the Me_2Si and Cp_2Zr moieties. Hydrolysis of **2-8** gave 5-azaindole **2-9** quantitatively. 5-Azaindole **2-9** could also be obtained from one bis(alkynyl)silane, two molecules of *i*-PrCN, and one molecule of *p*-TolylCN in good isolated yields.

When a formamide Me_2NCHO was used instead of the third nitrile, 5-azaindole **2-11a** was obtained in 70 % isolated yield upon hydrolysis with saturated aq. $NaHCO_3$. When hydrolyzed with D_2O instead of saturated aq. $NaHCO_3$, again **2-11a** was obtained in a similar yield. The deuterium-labeled product **2-11aD** was not formed. When Me_2NCDO was used instead of Me_2NCHO, hydrolysis of the reaction mixture with aq. $NaHCO_3$ afforded the deuterated product **2-11aD** in 68 % isolated yield with D > 98 % (Scheme 2.7). These results indicate that the CH or CD moiety of the carbonyl groups (–CHO or –CDO) in formamides is incorporated

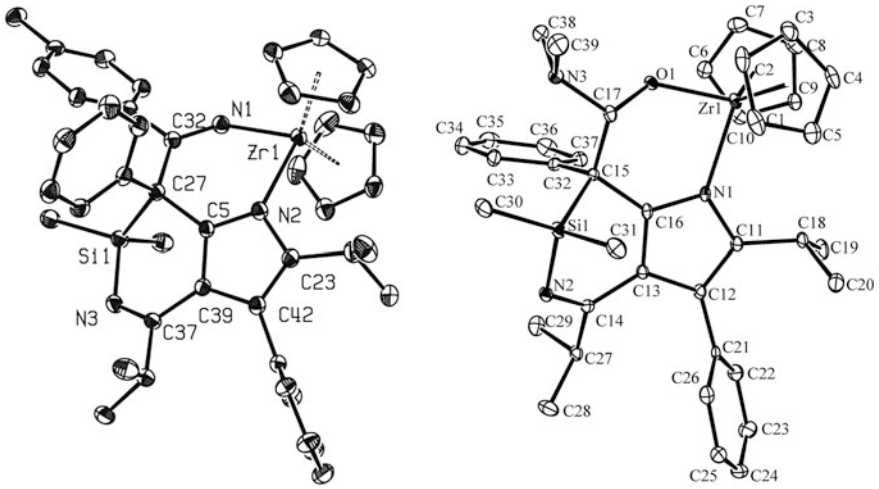


Fig. 2.3 X-ray structures of **2-8** and **2-10a.** Reproduced from Ref. [14] with the permission from Wiley

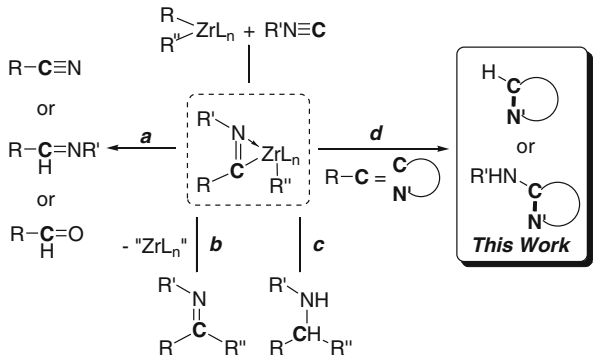
into the product. Other moieties in formamides were removed. Insertion of DMF into the Zr–C bond in **2-6a** has been demonstrated by isolation and characterization of the key intermediate **2-10a**, which is formed in 86 % isolated yield and characterized by X-ray single-crystal structural analysis (Fig. 2.3). Hydrolysis of **2-10a** with aq. $NaHCO_3$ gave azaindole **2-11a** in a quantitative yield.

When **2-6a** was treated with heptanal, formation of a new type of pyrrole derivative **2-13** was observed as a mixture of two isomers. When benzaldehyde was subjected to the reaction under the same condition, the reactive intermediate **2-12a** was isolated. Thus, the insertion of C=O bond of aldehyde into Zr–C bond in **2-6** is similar to the insertion reaction of DMF.

Besides, the reaction of **2-6a** with CO and alkynes (including diphenylacetylene, DMAD, and 4-octyne) did not show promising reactivity or no reaction occurred.

2.2.4 One-Pot Multi-component Coupling of Bis(alkynyl) silanes, Nitriles and Isocyanides and Synthesis of N*-Containing Heterocycles via Intramolecular Cyclization of Iminoacyl–Zr Intermediates*

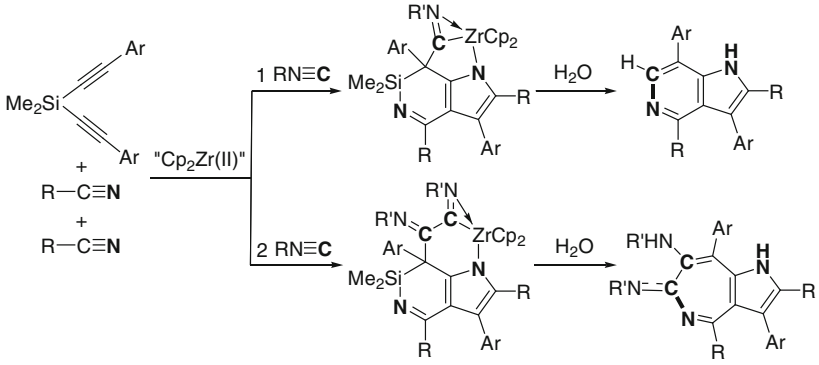
Isocyanide has been widely utilized as a key reagent in organic synthesis. Besides, the insertion of isocyanides into M–C bonds is one of the powerful means for carbon chain construction [16–34]. Insertion of isocyanide into M–C bonds afforded η^2-iminoacyl–metal intermediates, such as η^2-iminoacyl–Zr complexes [19–27], which can be conveniently converted to one-carbon elongated products such as imines, aldehydes, or nitriles via various chemical bond cleavage including Zr–C, C=N, and N–R′ bonds (Scheme 2.8) [29–32]. η^2-Iminoacyl–Zr complexes



Scheme 2.8 Reactivities of iminoacyl–Zr intermediates

also displayed other useful reactivities including reductive elimination [1, 2], -alkyl shift of non-acyl Zr–C bonds, and other types of rearrangements [28]. However, intramolecular cyclization of the iminoacyl–Zr intermediates yielding *N*-containing heterocycles has not been reported.

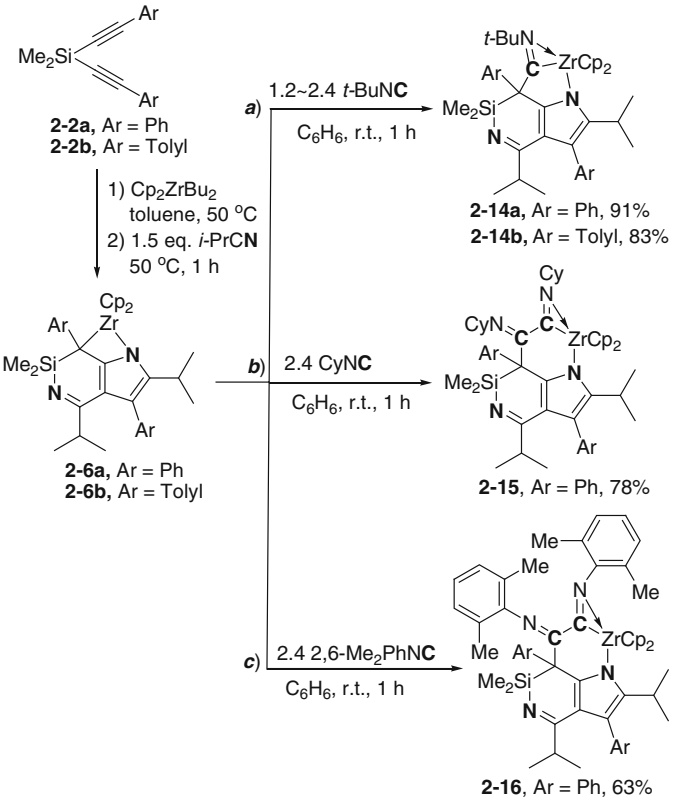
The author explored the reaction chemistry of intermediates **2-6** with isocyanides. Isocyanides bearing less-bulky and bulky substituents led to mono- and bis (iminoacyl)–Zr intermediates, respectively. Upon hydrolysis, the isolated mono (iminoacyl)–Zr intermediates underwent intramolecular cyclization to afford tetra-substituted 5-azaindoles, while intramolecular cyclization of bis(iminoacyl)–Zr intermediates led to the formation of dihydropyrrolo[3,2-*c*]azepines. Based on the above results, the author developed zirconocene-mediated multi-component coupling of bis(alkynyl)silanes, nitriles, and isocyanides. The structure of a bis(iminoacyl)–Zr intermediate, formed via insertion of two molecules of CyNC into the Zr–C bond, and structures of two dihydropyrrolo[3,2-*c*]azepines were characterized by single-crystal X-ray structural analysis (Scheme 2.9).



Scheme 2.9 One-pot synthesis of *N*-containing heterocycles by multi-component coupling of bis (alkynyl)silanes, nitriles, and isocyanides via intramolecular cyclization of iminoacyl–Zr intermediates

2.2.4.1 Isolation and Structural Characterization of Iminoacyl-Zr and Bis(iminoacyl)–Zr Intermediates via Mono- and Double Insertion of Isocyanides into Azazirconacycles

At room temperature, treatment of **2-6a** with 1.2 equivalents of aliphatic isocyanide *t*-BuNC led to the mono-insertion of isocyanide into the Zr–C(sp^3) σ bond giving **2-14a** in 91 % isolated yield (Scheme 2.10a). Even in the presence of excess amount of *t*-BuNC, only **2-14a** was obtained and the double-insertion product was not observed, probably due to the steric hindrance of *t*-Bu group. Similarly, the insertion of *t*-BuNC into tolyl-substituted **2-6b** gave **2-14b** under the same condition (Scheme 2.10b). However, when 2.4 equivalents of less steric-hindered isocyanide CyNC were used, the double-insertion product **2-15** was formed exclusively in 78 % isolated yield (Scheme 2.10b), showing that the steric hinderance of isocyanides strongly affects the insertion reaction. The double-insertion product **2-16** could also be obtained in good isolated yield when 2.4 equivalents of 2,6-dimethylphenyl isocyanide were used to react with **2-6a** (Scheme 2.10c). It should be noted that



Scheme 2.10 Formation of iminoacyl–Zr complexes by insertion of isocyanides into Zr–C(sp^3) bond

double insertion of isocyanides into Zr–C bonds is rare, and this work represents an efficient preparation of bis(iminoacyl)–Zr complexes [24–27].

These η^2-iminoacyl–Zr complexes **2-14**–**2-16** were all characterized by ^{1}H NMR and ^{13}C NMR spectra. The imine carbon atom neighboring the silicon in **2-14a** showed a singlet at δ = 186.88 ppm in the ^{13}C NMR spectrum in C_6D_6. In comparison, the characteristic carbon of η^2-iminoacyl–Zr moiety displayed a singlet at down-shielded δ = 234.17 ppm. The chemical shift of iminoacyl–Zr carbon in **2-14a** was comparable with that found in $Cp_2ZrCl(C(=N\mathit{t}Bu)C(Ph)=C(PPh_2)C{\equiv}CPh)$ (223.4 ppm) [19] and $Cp_2ZrCl(C(=N\mathit{t}Bu)CH_2SiMePhC(Ph)=CHPh)$ (228.77 ppm) [23]. The two imine carbons of bis(iminoacyl)–Zr moiety in **2-15** showed the respective singlet at δ = 164.95, 222.57 ppm in the ^{13}C NMR spectrum, which are consistent with those data in a reported bis(iminoacyl)–Zr complex [27]. Compared with mono(iminoacyl)–Zr carbon in **2-14a**, the iminoacyl carbon in **2-15** (222.57 ppm) appeared up-shielded in the ^{13}C NMR spectrum, probably due to the electron-withdrawing effect of the adjacent imino group. Similar to **2-15**, the two imine carbon atoms of bis(iminoacyl)–Zr moiety in **2-16** showed two singlets at δ = 180.93 and 237.10 ppm in the ^{13}C NMR spectra, respectively.

The structure of **2-15** was confirmed by single-crystal X-ray structural analysis, which featured four-ring-fused structure (Fig. 2.4). Zirconium center is bonded to a η^2-iminoacyl moiety in an "edge-on" fashion, forming a three-membered azazirconacycle [27]. The Zr1–N4 bond of 2.245(2) Å and the Zr–C18 bond of 2.175 (3) Å in Zr–C–N three-membered ring are close to the value of the reported bis(iminoacyl)–Zr complex [27]. The Zr1–N4 bond length of 2.245(2) Å is even shorter than the Zr1–N1 σ-bond of 2.347(2) Å, indicating a strong coordinative driving

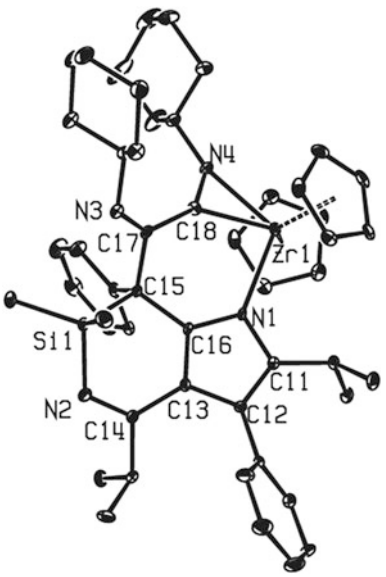


Fig. 2.4 ORTEP drawing of **2-15** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond length (Å): Zr1–N1 2.347(2), Zr1–N4 2.245(2), Zr1–C18 2.175(3), Si1–C15 1.924(3), Si1–N2 1.744(3), C13–C16 1.389(4), C15–C16 1.539(4), C15–C17 1.521(4), C17–C18 1.470(4), C17–N3 1.276(4), C18–N4 1.254(3). Reproduced from Ref. [35] with the permission from Wiley

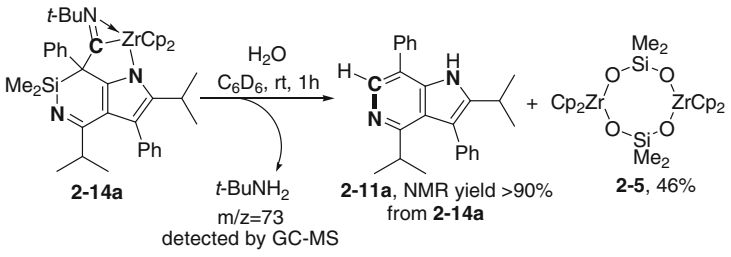
effect between Zr1 and N4 atoms. The bond length of two imine bonds C17–N3 and C18–N4 is 1.276(4) and 1.254(3) Å, respectively, demonstrating a strong C=N double-bond behavior.

2.2.4.2 Intramolecular Cyclization of η^2-Iminoacyl–Zr Complexes to Form Tetra-substituted 5-Azaindoles or Dihydropyrrolo[3,2-*c*]azepine Derivatives

Hydrolysis of the mono-insertion product **2-14a** with H_2O afforded a tetra-substituted 5-azaindole derivative **2-11a** in >90 % NMR yield, showing that the η^2-iminoacyl–Zr moiety cyclized with the *N*-silyl imine moiety by an unexpected C–N bond-forming fashion (Scheme 2.11). Along with **2-11a**, formation of *t*-$BuNH_2$ after quenching with water was detected using GC–MS. In addition, the Cp_2Zr moiety and the $SiMe_2$ moiety were coupled to form the cyclic zirconasiloxane **2-5**.

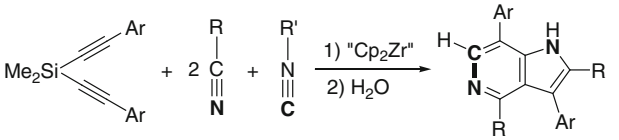
5-Azaindoles could be prepared conveniently in one pot via zirconocene-mediated multi-component coupling of bis(alkynyl)silanes, nitriles, and isocyanides as shown in Table 2.2. When bis(alkynyl)silane **2-2a**, *i*-PrCN, and *t*-BuNC were used, tetra-substituted 5-azaindole **2-11a** was formed in 63 % isolated yield, with only the isocyanide carbon atom being integrated into the product. The newly formed carbon–hydrogen bond was found to be originated from the hydrolysis process. Changing the isocyanide from *t*-BuNC to both aliphatic CyNC and aromatic 2,6-dimethylphenyl isocyanide led to the same 5-azaindole **2-11a** as main product in 65 and 54 % yields, respectively. In addition to *i*-PrCN, the scope of nitriles could be expanded to 2-methylbutyronitrile, CyCN and 1-phenyl cyclopropanecarbonitrile, affording their corresponding tetra-substituted 5-azaindoles **2-11b, 2-11c**, **2-11e**–**2-11f** in moderate to good isolated yields.

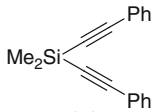
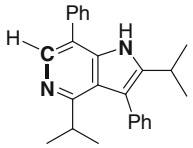
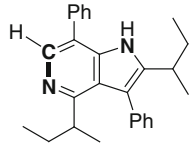
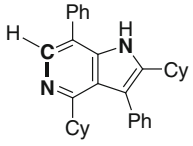
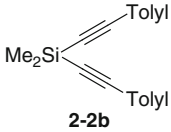
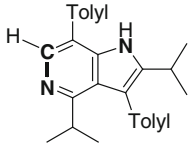
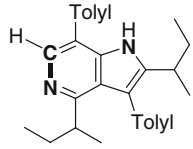
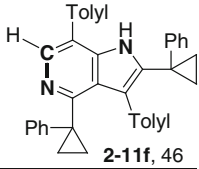
When the double-insertion intermediate **2-16** was hydrolyzed with water, two dihydropyrrolo[3,2-*c*]azepine derivatives **2-18a** and **2-19a** were obtained in 46 and 24 % yields, respectively (Scheme 2.12). Single-crystal X-ray structural analysis of **2-18a** and **2-19a** demonstrated their pyrrole-fused seven-membered azacycle (Fig. 2.5) [36]. The bond length of C6–N4 in **2-18a** is 1.277(7) Å, while the bond length of C47–N7 in **2-19a** is 1.481(3) Å. In their ^{13}C NMR spectra, the imine C6



Scheme 2.11 Hydrolysis of the iminoacyl–Zr intermediates **2-14a**

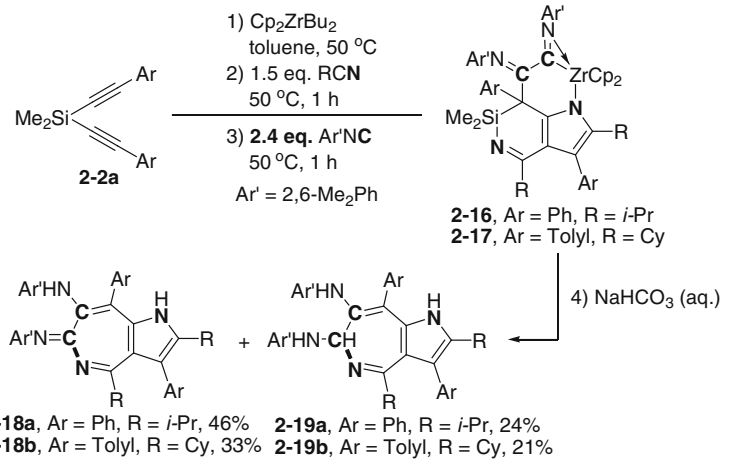
Table 2.2 Formation of 5-azaindoles **2-11** via zirconocene-mediated multi-component coupling of bis(alkynyl)silanes, nitriles, and isocyanides



entry	bis(alkynyl)silane **2-2**	RC**N**	R'N**C**	product **2-11** (yield/%) [a]
1	 **2-2a**	*i*-Pr—C**N**	*t*-BuN**C**	 **2-11a**, 63
2	**2-2a**	*i*-Pr—C**N**	CyN**C**	**2-11a**, 65 [b]
3	**2-2a**	*i*-Pr—C**N**	2,6-Me_2PhN**C**	**2-11a**, 54
4	**2-2a**		CyN**C**	 **2-11b,** 55
5	**2-2a**	Cy—C**N**	*t*-BuN**C**	 **2-11c**, 66
6	 **2-2b**	*i*-Pr—C**N**	*t*-BuN**C**	 **2-11d**, 41
7	**2-2b**		*t*-BuN**C**	 **2-11e**, 53
8	**2-2b**		*t*-BuN**C**	 **2-11f**, 46

[a] Isolated yields

[b] Main product yield, with trace amount of other products



Scheme 2.12 Intramolecular cyclization of bis(iminoacyl)–Zr complexes to form dihydropyrrolo [3,2-*c*]azepines

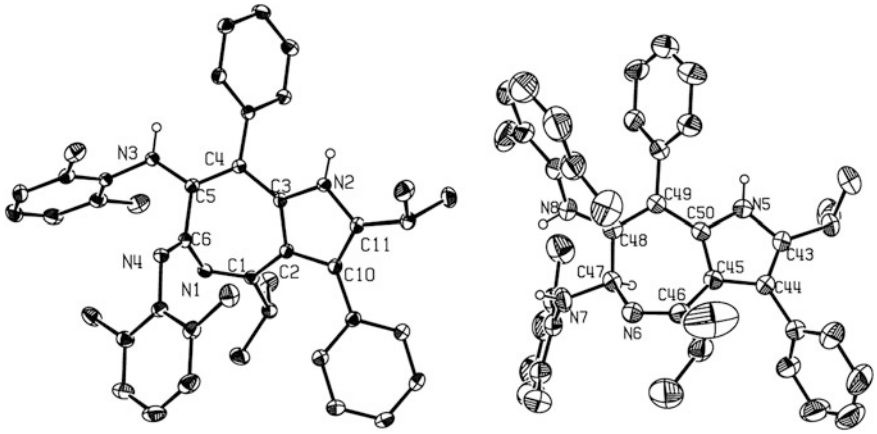


Fig. 2.5 ORTEP drawing of **2-18a** and **2-19a** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity except polar N–H bonds. Reproduced from Ref. [35] with the permission from Wiley

atom in **2-18a** shows a singlet at δ = 167.18 ppm, while the C47 atom in **2-19a** appears at 79.79 ppm. Dihydropyrrolo[3,2-*c*]azepine derivatives **2-18b** and **2-19b** could also be obtained. The hydrolysis mechanism from the bis(iminoacyl)–Zr intermediates to dihydropyrrolo[3,2-*c*]azepine derivatives **2-18** and **2-19** is not clear yet [37–39].

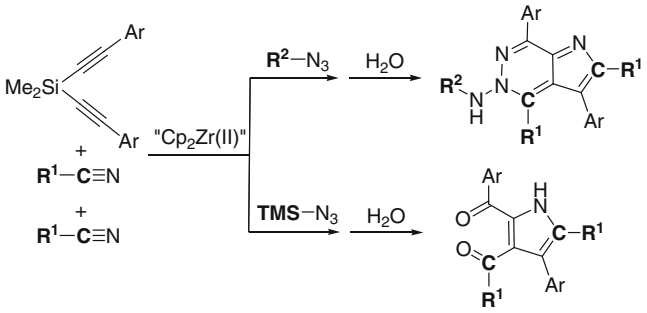
2.2.5 One-Pot Synthesis of Pyrrolo[3,2-d]pyridazines and Pyrrole-2,3-Diones via Zirconocene-Mediated Four-Component Coupling of Bis(alkynyl)silane, Nitriles, and Azide

Pyrrolo[3,2-*d*]pyridazines are a class of interesting and useful *N*-heterocycles [40–42]. However, synthetic methods for such heterocyclic compounds have been very much limited such as condensation of pyrrole-2,3-diones with hydrazine. There are no reports on one-pot multi-component synthesis of pyrrolo[3,2-*d*]pyridazines [43]. Moreover, synthetic methods for pyrrole-2,3-diones are also very limited [43]. On the other hand, transition-metal-mediated reactions of azides are of great importance and versatility in organic synthesis, because azides could be readily transformed into a wide variety of valuable *N*-containing natural products and medicinal agents [44–50].

Based on the mechanistic investigation and chemistry of reactive intermediates in zirconocene-mediated reactions, the author subjected organic azide to the reaction and developed a one-pot synthesis of pyrrolo[3,2-*d*]pyridazine derivatives via zirconocene-mediated cyclization of one bis(alkynyl)silane, two nitriles, and one azide. When $TMSN_3$ was used as a special azide, pyrrole-2,3-diones were isolated in high yields. These functionalized pyrrole-2,3-diones could be efficiently further transformed into pyrrole-fused heterocycles (Scheme 2.13).

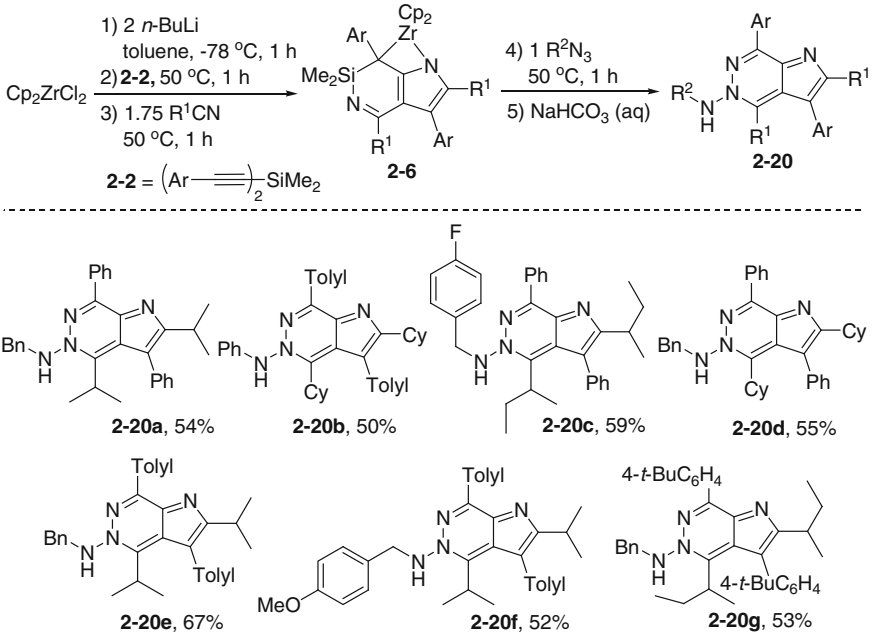
2.2.5.1 One-Pot Synthesis of Pyrrolo[3,2-*d*]pyridazine Derivatives via Zirconocene-Mediated Cyclization of One Bis(alkynyl) silane, Two Nitriles, and One Azide

As introduced in the previous section, reactive organometallic intermediates **2-6** were synthesized in situ in high yields via multi-component coupling of Cp_2ZrBu_2, bis(alkynyl)silane, and nitriles. Reaction of benzyl azide BnN_3 with **2-6a** (Ar = Ph,



Scheme 2.13 One-pot synthesis of pyrrolo[3,2-*d*]pyridazine or pyrrole-2,3-dione derivatives via zirconocene-mediated cyclization of one bis(alkynyl)silane, two nitriles, and one azide

Table 2.3 One-pot synthesis of pyrrolo[3,2-*d*]pyridazine derivatives via zirconocene-mediated cyclization of one bis(alkynyl)silane, two nitriles, and one azide



R^1 = *i*-Pr) at 50 °C for 1 h followed by quenching with saturated aqueous $NaHCO_3$ afforded a yellow solid **2-20a** in 54 % isolated yield (Table 2.3). The structure of product **2-20a** was confirmed by X-ray single-crystal structure analysis as a pyrrolo [3,2-*d*]pyridazine derivative (Fig. 2.6). Various aryl or benzyl azides with both electron-withdrawing groups (F) and electron-donating groups (MeO) could be applied to afford pyrrolo[3,2-*d*]pyridazine derivatives **2-20** in good isolated yields.

A proposed mechanism is shown in Scheme 2.14 for reaction of azides with reactive organometallic intermediate **2-6** and hydrolysis process affording the pyrrolo[3,2-*d*]pyridazine derivative. 1,1-Insertion of an azide into the C–Zr bond of **2-6** and delocalization leads to the formation of triazenido-ligated zirconium intermediate **2-21**. According to the literature, a 1,3-insertion of an azide into the C–Zr bond of **2-6** may be also possible to generate the intermediate **2-21** [52–54]. Although it is not clear that which one is formed in this reaction, only one insertion organometallic intermediate was obtained in 87 % isolated yield and was characterized by NMR spectroscopy. Hydrolysis of the insertion product, either **2-21a** or **2-21a′**, affords pyrrole derivatives **2-22** or **2-22′**. These intermediates **2-22** or **2-22′** would undergo cyclization of the triazene moiety with the imine C=N bond to afford **2-23** [55, 56]. Dehydration and aromatization of **2-23** led to the final product **2-20**.

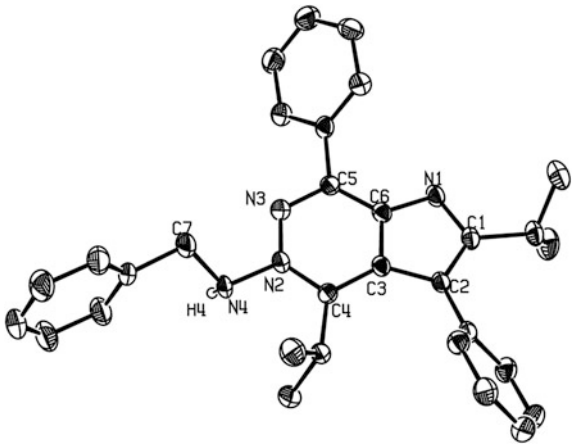
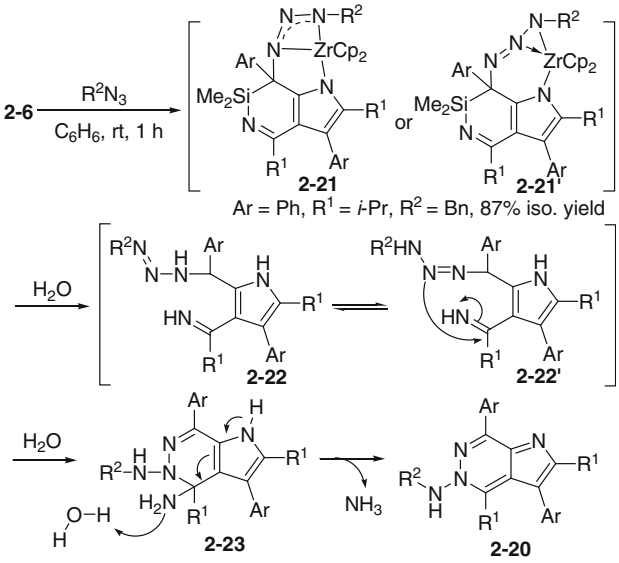


Fig. 2.6 Single-crystal X-ray structure of **2-20a**. Hydrogen atoms are omitted for clarity except polar N–H bonds. Selected bond length (Å): N1–C1 1.390(2), N1–C6 1.363(2), N2–N3 1.350(2), N2–C4 1.372(2), N3–C5 1.327(2), N4–N2 1.438(2). Reprinted with the permission from Ref. [51]. Copyright 2011 American Chemical Society

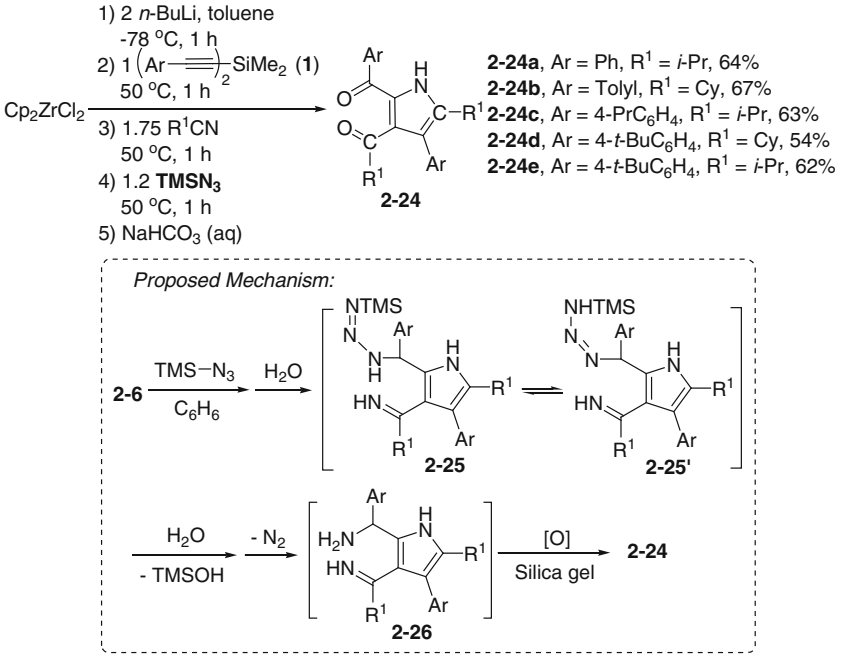


Scheme 2.14 Proposed mechanisms

2.2.5.2 One-Pot Synthesis of Pyrrole-2,3-Dione Derivatives via Zirconocene-Mediated Cyclization of One Bis(alkynyl) silane, Two Nitriles, and One $TMSN_3$

When $TMSN_3$ was used as an azide in this zirconocene-mediated reaction, pyrrolo [3,2-*d*]pyridazine derivative **2-20** was not isolated as product. Instead, pyrrole-2,3-diones **2-24** were formed in good isolated yields (Scheme 2.15). The structure of product **2-24a** was confirmed by single-crystal X-ray structural analysis (Fig. 2.7). Bis(alkynyl)silanes with functional groups as well as bulky nitriles such as *t*-BuCN could not lead to products **2-24** because their corresponding intermediates **2-6** could not be formed efficiently.

On mechanistic aspects, it is proposed that after insertion of $TMSN_3$ into the C–Zr bond, hydrolytic cleavage of N–Si and N–Zr bonds would give triazene **2-25** or **2-25′**. Hydrolysis of N-$SiMe_3$ bond followed by the elimination of dinitrogen would afford the imine **2-26**, which might be oxidized and hydrolyzed on the silica gel during column chromatography to give the final product pyrrole-2,3-dione **2-24** [57]. Although plenty of synthetic methods for pyrrole derivatives have been developed [58], synthetic methods for pyrrole-2,3-diones, which are highly functionalized pyrroles, are very rare.



Scheme 2.15 One-pot synthesis of pyrrole-2,3-diones **2-24** via zirconocene-mediated cyclization of bis(alkynyl)silane, nitriles, and $TMSN_3$

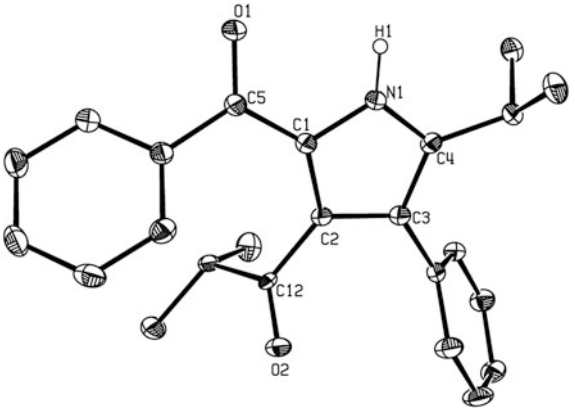
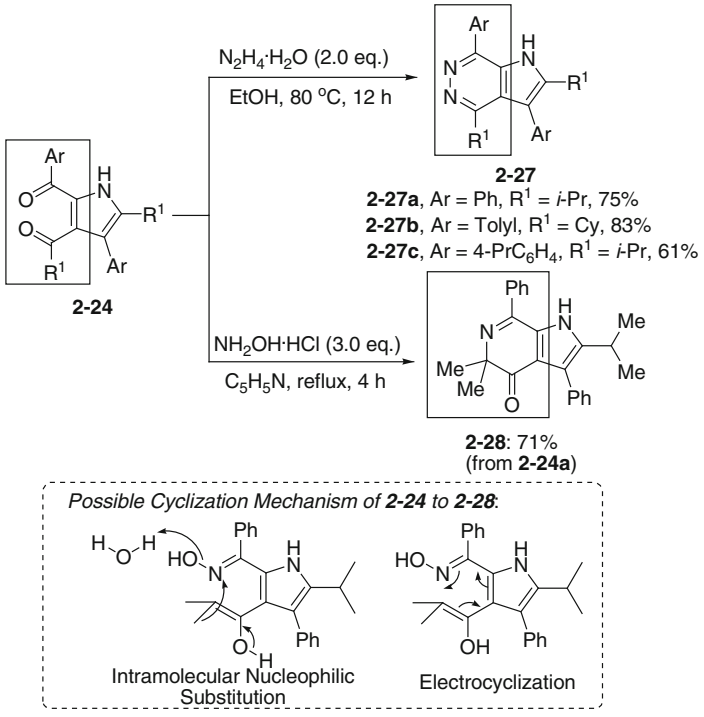


Fig. 2.7 Single-crystal X-ray structure of **2-24a**. Hydrogen atoms are omitted for clarity except polar N–H bonds. Reprinted with the permission from Ref. [51] Copyright 2011 American Chemical Society

Condensation of **2-24** with hydrazine hydrate and hydroxylamine hydrochloride was carried out. The pyrrole-fused heterocycles pyrrolo[3,2-*d*]pyridazine **2-27** and pyrrolo[2,3-*c*]pyridinone **2-28** were generated in high isolated yields, respectively (Scheme 2.16). These further applications of **2-24** demonstrate that the two carbonyl groups on the pyrrole ring of **2-24** are useful for the preparation of other valuable pyrrole-fused *N*-heterocyclic compounds [59, 60].



Scheme 2.16 Preparation of pyrrole-fused *N*-heterocyclic compounds via annulation of pyrrole-2,3-diones **2-24**

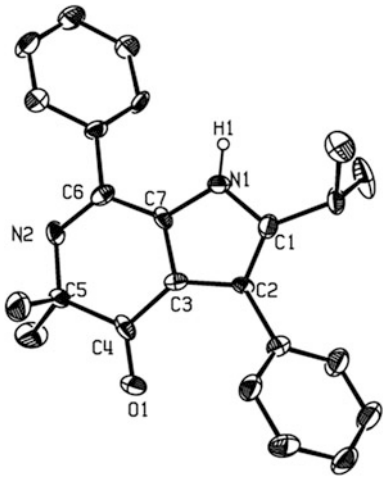


Fig. 2.8 Single-crystal X-ray structure of **2-28**. Hydrogen atoms are omitted for clarity except polar N–H bonds. Reprinted with the permission from Ref. [51]. Copyright 2011 American Chemical Society

Condensation of **2-24** with hydrazine hydrate in ethanol at 80 °C gave pyrrolo[3,2-*d*]pyridazines **2-27** as products. However, condensation of **2-24a** with hydroxylamine hydrochloride in refluxing pyridine led to the pyrrolo[2,3-*c*]pyridinone **2-28** as the single product, which was confirmed by single-crystal X-ray structural analysis (Fig. 2.8). The C_{sp3}–H bond of *i*-Pr was coupled with the in situ generated oxime moiety to form the pyridinone ring via intramolecular nucleophilic substitution or 6π-electrocyclization.

2.3 Summary

The author developed zirconocene-mediated one-pot multi-component synthesis of 5-azaindole derivatives from bis(alkynyl)silane and three molecules of nitriles. Isolation and characterization of Zr/Si-containing three-ring-fused organometallic complexes **2-4a** and **2-6** were achieved as three or two nitriles involved reactive intermediates, respectively. The 8-membered cyclic zirconasiloxane was characterized as fate of Cp_2Zr and Me_2Si in hydrolysis process. Ammonia was observed by NMR spectrum, showing that the nitrile C≡N bond was cleaved in hydrolysis process. Based on the reaction chemistry of reactive intermediates **2-6** with unsaturated compounds such as formamides, aldehydes, isocyanides, and azides, various *N*-heterocycles were synthesized, including 5-azaindoles, 3-acylpyrrole, dihydropyrrolo[3,2-*c*]azepines, pyrrolo[3,2-*d*]pyridazine, and pyrrolo[2,3-*c*]pyridinone derivatives.

2.4 Experimental Section

All reactions were conducted under a slightly positive pressure of dry nitrogen using standard Schlenk line techniques or under a nitrogen atmosphere in a Mikrouna Super (1220/750) glove box. The nitrogen in the glove box was constantly circulated through a copper/molecular sieves catalyst unit. The oxygen and moisture concentrations in the glove box atmosphere were monitored by an O_2/H_2O Combi-Analyzer to ensure that both were always below 1 ppm. Unless otherwise noted, all starting materials were commercially available and were used without further purification. Solvents were purified by an Mbraun SPS-800 Solvent Purification System and dried over fresh Na chips in the glove box.

Organometallic samples for NMR spectroscopic measurements were prepared in the glove box by use of J. Young valve NMR tubes (Wilmad 528-JY). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-400 spectrometer (FT, 400 MHz for ^{1}H; 100 MHz for ^{13}C) or a JEOL-AL300 spectrometer (FT, 300 MHz for ^{1}H; 75 MHz for ^{13}C) at room temperature, unless otherwise noted. High-resolution mass spectra (HRMS) were recorded on a Bruker Apex IV FTMS mass spectrometer using ESI (electrospray ionization). Microelemental analyses were performed on an Elemental Analyzer Vario EL apparatus.

Formation of 5-azaindoles Derivatives 2-1 from One Molecule of the Bis(alkynyl)silane with Three Molecules of Identical Organonitriles: To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.05 mmol, 307 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.1 mmol, 1.6 M, 1.32 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(alkynyl)silane (**2-2**) was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 3 h. After benzonitrile (3.5 mmol, 361 mg) was added, the reaction mixture was stirred at this temperature for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$, and the resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using hexane and diethyl ether (10:1) as the eluent.

2-1a: White solid, isolated yield 58 % (404 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.86–7.72 (m, 22H), 8.42 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 116.78, 118.34, 121.33, 121.56, 121.94, 122.62, 126.94, 127.33, 128.04, 128.10, 128.26, 128.63, 129.04, 129.51, 130.03, 130.07, 130.10, 130.44, 130.53, 130.96, 131.13, 132.74, 133.34, 133.56, 133.66, 134.83, 135.14, 140.96, 141.05, 142.34, 146.73, 151.42. HRMS calcd for $C_{37}H_{23}Br_3N_2$ 733.9391; found: 733.9388. Elemental Analysis Calcd (%) for $C_{37}H_{23}Br_3N_2$: C, 60.44; H, 3.15; N, 3.81. Found: C, 60.40; H, 3.35; N, 3.51.

2-1b: White solid, isolated yield 61 % (448 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.86–7.48 (m, 22H), 8.38 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 116.35, 117.88, 121.53, 121.80, 122.47, 126.62, 128.01, 128.16, 129.04,

129.54, 129.89, 130.02, 130.09, 130.57, 130.78, 130.85, 131.02, 131.87, 132.05, 133.98, 135.14, 135.46, 138.11, 139.27, 141.07, 146.99, 151.73. HRMS calcd for $C_{37}H_{23}Br_3N_2$ 733.9391; found: 733.9385. Elemental Analysis Calcd (%) for $C_{37}H_{23}Br_3N_2$: C, 60.44; H, 3.15; N, 3.81. Found: 60.24; H, 3.33; N, 3.67.

2-1c: White solid, isolated yield 60 % (393 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.74 (*d*, *J* = 7.8 Hz, 2H), 7.04–7.55 (m, 21H), 8.36 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 114.73, 116.37, 120.29, 121.27, 121.95, 127.13, 127.45, 127.80, 128.33, 128.49, 128.77, 129.53, 130.46, 130.71, 131.45, 131.80, 132.33, 132.49, 133.43, 134.96, 136.22, 139.23, 140.16, 148.69, 153.04. HRMS calcd for $C_{37}H_{24}N_2Br_2$ 656.0286; found: 656.0281.

2-1d: White solid, isolated yield 48 % (358 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.56 (*d*, *J* = 7.8 Hz, 2H), 6.73–6.82 (m, 6H), 7.11–7.25 (m, 6H), 7.28 (*d*, *J* = 8.4 Hz, 2H), 7.37 (*d*, *J* = 8.1 Hz, 2H), 7.55 (*d*, *J* = 7.5 Hz, 2H), 8.29 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 115.38, 117.11, 121.50, 122.24, 122.92, 124.85, 124.90, 124.95, 125.00, 126.46, 126.51, 126.56, 126.60, 127.61, 127.84, 128.97, 129.28, 130.37, 130.55, 130.61, 130.77, 130.91, 131.13, 131.79, 132.85, 132.92, 133.37, 135.68, 137.39, 139.09, 140.64, 140.68, 141.69, 147.35, 151.84. HRMS calcd for $C_{40}H_{30}Br_2N_2O_3$ 746.0603; found: 746.0597. Elemental Analysis Calcd (%) for $C_{40}H_{30}Br_2N_2O_3$: C, 64.36; H, 4.05; N, 3.75. Found: C, 64.53; H, 3.99; N, 3.60.

2-1e: White solid, isolated yield 42 % (365 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.91–7.77 (m, 20H), 8.46 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 115.38, 117.11, 121.50, 122.24, 122.92, 124.95, 125.00, 126.46, 126.51, 126.56, 126.60, 127.61, 127.85, 128.97, 129.28, 130.37, 130.55, 130.61, 130.77, 130.90, 131.13, 131.79, 132.85, 132.92, 133.37, 135.68, 137.39, 139.09, 140.64, 140.68, 141.69, 147.35, 151.84. HRMS calcd for $C_{39}H_{21}N_2F_6Br_2$ 869.9139; found: 869.9146. Elemental Analysis Calcd (%) for $C_{39}H_{21}N_2F_6Br_2$: C, 53.76; H, 2.43; N, 3.22. Found: C, 53.60; H, 2.68; N, 3.00.

2-1f: White solid, isolated yield 32 % (230 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.69 (s, 3H), 3.77 (s, 3H), 3.78 (s, 3H), 6.52 (*d*, *J* = 8.4 Hz, 2H), 6.75 (*d*, *J* = 8.7 Hz, 2H), 6.82 (*d*, *J* = 8.7 Hz, 2H), 7.00 (*d*, *J* = 8.1 Hz, 2H), 7.15 (*d*, *J* = 7.2 Hz, 4H), 7.26 (*d*, *J* = 8.4 Hz, 2H), 7.36 (*d*, *J* = 8.7 Hz, 2H), 7.55 (*d*, *J* = 8.4 Hz, 2H), 7.70 (*d*, *J* = 8.4 Hz, 2H), 8.30 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 55.10, 55.22, 55.32, 112.61, 113.34, 113.83, 114.34, 115.41, 120.98, 123.61, 124.37, 124.39, 124.44, 124.49, 126.20, 126.22, 126.30, 126.34, 129.91, 130.63, 130.71, 131.15, 131.72, 131.87, 132.61, 136.42, 138.86, 140.48, 148.02, 152.60, 158.99, 159.48, 159.80. HRMS calcd for $C_{42}H_{30}F_6N_2O_3$ 724.2161; found: 724.2166. Elemental Analysis Calcd (%) for $C_{42}H_{30}F_6N_2O_3$: C, 69.61; H, 4.17; N, 3.87. Found: C, 69.31; H, 4.36; N, 3.67.

2-1g: White solid, isolated yield 45 % (270 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.05 (s, 3H), 2.26 (s, 3H), 2.28 (s, 3H), 6.53–7.44 (m, 20H), 8.35 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.05, 21.43, 21.51, 55.26, 55.30,

113.11, 114.62, 115.59, 117.14, 121.42, 125.79, 126.71, 127.09, 127.26, 127.56, 127.66, 127.86, 128.24, 128.41, 128.64, 128.79, 130.97, 131.28, 131.74, 132.10, 133.42, 135.76, 136.33, 137.16, 138.24, 139.29, 140.55, 141.07, 148.00, 152.69, 158.00, 159.01. HRMS calcd for $C_{42}H_{36}N_2O_2$ 600.2777; found: 600.2768.

Formation of 5-Azaindoles 2-1h and 2-1i via Suzuki Coupling of 1n and 1o and Benzeneboronic Acid: To a mixture of **2-1b** (368 mg, 0.5 mmol) and benzeneboronic acid (244 mg, 2.0 mmol) in THF (5 mL) was added a solution of potassium carbonate (690 mg, 5.0 mmol) in water (2.5 mL). After the mixture was degassed and backfilled with nitrogen, $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) was added, and then, the reaction mixture was refluxed for 16 h. The mixture was extracted with dichloromethane and washed with brine (100 mL × 3). The organic extracts were dried with anhydrous $MgSO_4$. After the removal of the solvent, the residue was purified by column chromatography (silica gel, hexane, and ethyl acetate (10:1) as eluent) to afford **2-1i** as a white solid.

2-1h: White solid, isolated yield 53 % (385 mg), m.p. > 300 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.70–7.91 (m, 37H), 8.51 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 116.23, 117.61, 121.70, 125.77, 125.81, 126.11, 126.37, 126.92, 127.00, 127.04, 127.09, 127.12, 127.22, 127.61, 127.77, 127.84, 128.64, 128.67, 128.74, 128.85, 129.38, 129.91, 130.22, 130.79, 130.92, 131.00, 134.66, 135.63, 136.13, 138.50, 139.50, 139.61, 139.92, 140.14, 140.65, 140.97, 141.11, 141.46, 147.61, 152.55. HRMS calcd for $C_{55}H_{38}N_2$: 726.3035; found: 726.3096.

2-1i: White solid, isolated yield 82 % (300 mg). m.p. > 300 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.95–7.66 (m, 37H), 8.51 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 116.31, 117.79, 121.43, 125.74, 126.05, 126.30, 126.68, 126.80, 126.91, 126.94, 126.98, 127.12, 127.21, 127.47, 127.67, 127.80, 128.23, 128.27, 128.46, 128.51,128.69, 129.02, 129.43, 129.52, 129.62, 130.27, 130.83, 132.28, 134.48, 136.15, 136.25, 139.87, 140.02, 140.16, 140.29, 140.77, 141.06, 141.13, 141.34, 141.35, 147.88, 152.81. HRMS calcd for $C_{55}H_{38}N_2$: 726.3035; found: 726.3022. Elemental Analysis Calcd (%) for $C_{55}H_{38}N_2$: C, 90.88; H, 5.27; N, 3.85. Found: C, 90.72; H, 5.30; N, 4.08.

Isolation of 2-4a: In a 20-mL Schlenk tube, the *i*-PrCN (159 μL, 1.743 mmol) was added to the benzene solution of compound **2-3a** (240 mg, 0.498 mmol) with a syringe. After the reaction mixture was stirred at 50 °C for 1 h, it was dried up under vacuum and the residue was extracted with hexane. After filtering, the clear filtrate was reduced under vacuum to precipitate **2-4a** as red powder (309 mg, 0.448 mmol, 90 % yield).

2-4a: Red solid, isolated yield 90 % (309 mg, 0.448 mmol). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.28 (s, 3H, $SiMe_2$), 0.52 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 0.65 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 0.93 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.03 (s, 3H, $SiMe_2$), 1.11 (*t*, *J* = 6.4 Hz, 6H, $CHMe_2$), 1.47 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 2.03–2.10 (m, 1H, $CHMe_2$), 2.34–2.40 (m, 1H, $CHMe_2$), 2.72–2.78 (m, 1H, $CHMe_2$), 5.86 (s, 5H,

C_5H_4), 6.07 (s, 5H, C_5H_4), 6.95 (*t*, *J* = 7.2 Hz, 1H, C_6H_5), 7.06–7.19 (m, 6H, C_6H_5), 7.39 (*d*, *J* = 8.0 Hz, 2H, C_6H_5), 7.49 (*d*, *J* = 8.0 Hz, 1H, C_6H_5); ^{13}C NMR (100 MHz, C_6D_6): $\delta = -2.9$, 3.0, 19.3, 21.4, 21.9, 22.4, 22.5, 26.7, 35.6, 35.9, 36.3, 60.6, 111.3, 111.4, 120.6, 125.8, 126.2, 127.4, 127.6, 127.7, 129.3, 129.9, 131.4, 132.5, 140.9, 141.3, 142.6, 143.4, 183.9, 188.2. Anal. Calcd for $C_{40}H_{47}N_3SiZr$: C, 69.72; H, 6.87; N, 6.10. Found: C, 69.95; H, 6.60; N, 6.30. Single crystals of **2-4a** suitable for X-ray analysis were grown in benzene at room temperature for one week.

Isolation of 2-5: A J. Young valve NMR tube was charged with **2-4a** (69 mg, 0.1 mmol) and $CDCl_3$ (0.5 mL). 1–3 equivalents of H_2O were added to the $CDCl_3$ solution of **2-4a** with a syringe at room temperature, and then, the NMR tube was shaken immediately and stayed at room temperature. Single crystals of **2-5** suitable for X-ray analysis were grown after staying for one day. **2-5** was obtained in 45 % yield, which was insoluble in common organic solvents. Anal. Calcd for $C_{24}H_{32}O_4Si_2Zr_2$: C, 46.26; H, 5.18. Found: C, 46.20; H, 5.50.

Isolation of 2-6b: In a 20-mL Schlenk tube, the *i*-PrCN (70 μL, 0.765 mmol) was added to the benzene solution of compound **2-3b** (260 mg, 0.51 mmol) with a syringe. After the reaction mixture was stirred at 50 °C for 1 h, it was dried up under vacuum and the residue was extracted with hexane. After filtering, the clear filtrate was reduced under vacuum to precipitate **2-6b** as green powder, which was recrystallized at −40 °C to give **2-6b** in 70 % isolated yield. The purity of **2-6b** is >95 % determined by ^{1}H NMR spectroscopy.

2-6b: Green powder, isolated yield 70 % (210 mg) ^{1}H NMR (400 MHz, C_6D_6): $\delta = 0.22$ (s, 3H, $SiMe_2$), 0.76 (s, 3H, $SiMe_2$), 0.77 (*d*, *J* = 7.2 Hz, 3H, $CHMe_2$), 1.15 (*d*, *J* = 7.2 Hz, 3H, $CHMe_2$), 1.24 (dd, *J* = 7.2, 6.4 Hz, 6H, $CHMe_2$), 2.16 (s, 3H, 4-MeC_6H_4), 2.21 (s, 3H, 4-MeC_6H_4), 2.69–2.79 (m, 1H, $CHMe_2$), 3.05–3.16 (m, 1H, $CHMe_2$), 5.67 (s, 5H, C_5H_4), 5.74 (s, 5H, C_5H_4), 6.94–7.14 (m, 6H, 4-MeC_6H_4), 7.34 (*d*, *J* = 7.6 Hz, 2H, 4-MeC_6H_4); ^{13}C NMR (100 MHz, C_6D_6): δ = 4.3, 6.3, 21.5, 21.8, 21.9, 22.1, 24.6, 27.7, 32.4, 35.4, 80.9 (Zr–C), 111.1, 115.0, 124.1, 124.9, 125.7, 128.0, 128.8, 129.1, 129.2, 129.5, 130.6, 130.8, 131.7, 133.2, 136.2, 136.3, 153.7, 157.0, 181.5. Anal. Calcd for $C_{38}H_{44}N_2SiZr$: C, 70.42; H, 6.84; N, 4.32. Found: C, 70.02; H, 6.37; N, 4.00.

Isolation of 2-7: 2-6b was quenched with 1–3 equivalents of water, and the resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a white solid **2-7**, which was subjected to a short SiO_2 column using petroleum ether and diethyl ether (1:1) as the eluent.

2-7: White solid, isolated yield 80 %, m.p.: 168 °C. ^{1}H NMR ($CDCl_3$, Me_4Si): $\delta = 0.86$ (*d*, *J* = 6.9 Hz, 6H), 1.04 (*d*, *J* = 6.9 Hz, 6H), 2.28 (s, 3H), 2.40 (s, 3H), 2.45–2.62 (m, 1H), 2.72–2.30 (m, 1H), 4.22 (s, 2H), 6.68–7.32 (m, 8H), 7.81 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si): δ = 18.94, 21.07, 21.24, 22.88, 24.88, 33.37, 37.71, 119.87, 120.49, 128.94, 129.46, 129.80, 130.19, 133.54, 133.71, 135.04, 136.05, 136.13, 205.03. HRMS calcd for $C_{26}H_{31}NO$: 373.2406. Found: 373.2413.

Isolation of Reactive Intermediate 2-8 from Bis(alkynyl)silane, Two Molecules of *i*-PrCN, and *p*-TolylCN: In a 20-mL Schlenk tube, *p*-tolunitrile (60 μL, 0.50 mmol) was added to the benzene solution of compound **2-3a** (310 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at 50 °C for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, the solid was dried up under vacuum to precipitate **2-8** as brown powder (331 mg, 0.45 mmol, 90 % yield).

2-8: Brown powder, isolated yield 90 % (331 mg, 0.45 mmol) ^{1}H NMR (300 MHz, C_4D_8O, 25 °C): δ = 0.11 (s, 3H, $SiMe_2$), 0.17 (s, 3H, $SiMe_2$), 0.52 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.72 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.85 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.39 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 2.12–2.29 (m, 2H, $CHMe_2$), 2.34 (s, 3H, CH_3), 6.23 (s, 5H, C_5H_5), 6.45 (s, 5H, C_5H_5), 7.03 (s, 4H, C_6H_5), 7.13–7.37 (m, 9H, C_6H_5), 7.55 (*d*, *J* = 8.1 Hz, 2H, C_6H_5); ^{13}C NMR (75.4 MHz, C_4D_8O, 25 °C): δ = −5.0, 0.3, 18.5, 20.3, 21.0, 25.5, 26.2, 34.7, 35.6, 57.2, 111.3, 111.7, 119.6, 125.6, 125.8, 126.9, 127.0, 127.7, 127.9, 128.6, 128.7, 131.0, 132.1, 137.9, 138.6, 141.3, 142.7, 144.2, 145.0, 175.7, 185.7. Elemental Analysis Calcd (%) for $C_{48}H_{55}N_3OSiZr$: C, 71.24; H, 6.85; N, 5.19. Found: C, 70.84; H, 6.90; N, 5.00. Single crystals of **2-8** suitable for X-ray analysis were grown in tetrahydrofuran/hexane at room temperature for one week.

Isolation of 2-10a: In a 20-mL Schlenk tube, DMF (39 μL, 0.50 mmol) was added to the benzene solution of compound **2-6a** (310 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at 50 °C for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, *the solid was* dried up under vacuum to precipitate **2-10a** as yellow powder (298 mg, 0.43 mmol, 86 % yield).

2-10a: Yellow powder, isolated yield 86 % (298 mg, 0.43 mmol). ^{1}H NMR (300 MHz, C_4D_8O): δ = 0.30 (s, 3H, $SiMe_2$), 0.33 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 0.60 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.76 (s, 3H, $SiMe_2$), 1.01 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 1.58 (*t*, *J* = 6.6 Hz, 3H, $CHMe_2$), 1.92–2.10 (m, 2H, $CHMe_2$), 2.22 (s, 6H, NMe_2), 5.39 (s, 1H, CH), 6.45 (s, 5H, C_5H_5), 6.48 (s, 5H, C_5H_5), 7.06–7.39 (m, 9H, C_6H_5), 7.60 (*d*, *J* = 7.8 Hz, 1H, C_6H_5); ^{13}C NMR (75.4 MHz, C_4D_8O): δ = −4.1, 0.3, 18.0, 21.5, 22.1, 25.4, 35.1, 35.5, 42.1, 49.8, 100.3, 113.5, 114.1, 120.0, 124.7, 125.6, 125.8, 126.8, 127.1, 127.4, 128.1, 131.3, 131.4, 132.1, 140.7, 141.1, 141.4, 143.1, 195.0. Anal. Calcd for $C_{43}H_{55}N_3OSiZr$: C, 67.49; H, 7.24; N, 5.49. Found: C, 67.14; H, 7.51; N, 5.31. Single crystals of **2-10a**·THF suitable for X-ray analysis were grown in tetrahydrofuran at room temperature for three days.

Formation of 2-11: To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.05 mmol, 307 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.1 mmol, 1.6 M, 1.32 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane (**2-1a**) was added and warmed up to 50 °C for 3 h to yield **2-3a**. After *i*-PrCN (1.5 mmol, 0.135 ml) was added to the toluene solution of **2-3a**, the reaction mixture was stirred at 50 °C for 1 h. Then, *t*-BuNC (1.2 mmol, 100 mg) or CyNC (1.2 mmol, 131 mg) was added to the above reaction mixture. After

stirring at 50 °C for 1 h, it was quenched with saturated aqueous $NaHCO_3$ and extracted with diethyl ether for three times. The extract was washed with water and brine and dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to Al_2O_3 column using petroleum ether and diethyl ether (5:1) as the eluent to give **2-11a**. When *t*-BuNC was used and quenched by D_2O, **2-11aD** could be obtained through the similar procedure as shown above.

2-11a: White solid, isolated yield 70 % (247 mg), m.p.: 106–107 °C. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = 1.14 (*d*, *J* = 6.9 Hz, 6H), 1.22 (*d*, *J* = 6.9 Hz, 6H), 2.86–3.18 (m, 2H), 7.30–7.80 (m, 10H), 8.29 (s, 1H), 8.31 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si): δ = 22.03, 22.70, 25.59, 30.75, 113.71, 118.52, 121.84, 127.19, 127.73, 128.03, 128.22, 129.47, 131.06, 136.22, 136.58, 136.97, 139.31, 142.31, 159.95. HRMS calcd for $C_{25}H_{26}N_2$: 354.2096. Found: 354.2093.

2-11aD: White solid, isolated yield 56 % (197 mg), D > 98 %, m.p: 106 °C. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = 1.14 (*d*, *J* = 6.9 Hz, 6H), 1.22 (*d*, *J* = 6.9 Hz, 6H), 2.79–3.20 (m, 2H), 7.14–7.88 (m, 10H), 8.29 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si): δ = 22.03, 22.71, 25.58, 30.75, 113.70, 118.40, 121.83, 127.19, 128.03, 128.32, 129.48, 131.05, 136.20, 136.55, 136.94, 139.31, 142.28, 159.95. HRMS calcd for $C_{25}H_{25}N_2D$: 355.2156. Found: 355.2151.

Isolation of 2-12a: In a 20-mL Schlenk tube, PhCHO (50 μL, 0.50 mmol) was added to the benzene solution of compound **2-6a** (310 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at 50 °C for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, *the solid was* dried up under vacuum to precipitate **2-12a** as yellow powder.

2-12a: Yellow powder, isolated yield 93 % (336 mg, 0.465 mmol). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.66 (s, 3H, $SiMe_2$), 0.71 (s, 3H, $SiMe_2$), 0.89 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.08 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.12 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.53 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.68–1.75 (m, 1H, $CHMe_2$), 2.51–2.58 (m, 1H, $CHMe_2$), 5.63 (s, 1H, CH), 5.99 (s, 5H, C_5H_5), 6.18 (s, 5H, C_5H_5), 6.91 (*d*, *J* = 6.8 Hz, 2H, C_6H_5), 7.16–7.44 (m, 12H, C_6H_5), 7.78 (*d*, *J* = 7.2 Hz, 1H, C_6H_5); ^{13}C NMR (100 MHz, C_6D_6): δ = −3.3, 1.0, 18.8, 22.3, 23.3, 25.0, 25.5, 35.9, 36.0, 50.4, 88.4, 112.8, 113.9, 120.1, 125.5, 126.2, 127.1, 127.2, 127.6, 128.3, 128.6, 129.1, 131.7, 131.8, 132.4, 140.4, 141.2, 141.5, 142.1, 142.9, 186.1. Single crystals of **2-12a** suitable for X-ray analysis were grown in tetrahydrofuran at room temperature for a week.

Formation of 2-13: To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.05 mmol, 307 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.1 mmol, 1.6 M, 1.32 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane (**2-2a**) was added and warmed up to 50 °C for 3 h. After *i*-PrCN (1.5 mmol, 0.135 ml) was added, the reaction mixture was stirred at this temperature for 1 h. Then, *n*-heptanal (1.2 mmol, 137 mg) was added, and the

reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was performed for crude ^1H NMR to give the ratio of *trans* to *cis* of the product before purified by Al_2O_3 column, using petroleum ether and diethyl ether (2:1) as the eluent. Yellow liquid, total isolated yield (*trans* + *cis*) 43 % (190 mg) (*trans*/*cis* = 1: 0.5).

2-13: Yellow liquid, isolated yield 43 % (190 mg, *trans*/*cis* = 1:0.5). ^1H NMR ($CDCl_3$, Me_4Si): δ = 0.78 (*d*, *J* = 7.2 Hz, 12H), 0.81–0.93 (m, 6H), 1.00–1.54 (m, 28H), 2.03–2.30 (m, 4H), 2.54–3.12 (m, 4H), 5.99 (*t*, *J* = 7.5 Hz, 1H), 6.33 (*t*, *J* = 7.5 Hz, 1H),6.99–7.50 (m, 20H), 7.67 (s, 1H), 7.85 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si): δ = 13.99, 14.09, 18.65, 18.81, 22.59, 22.88, 23.04, 24.77, 24.88, 29.09, 29.56, 29.65, 29.92, 30.40, 31.68, 31.73, 38.19, 39.64, 120.84, 120.93, 122.53, 122.66, 126.20, 126.29, 126.36, 127.22, 127.34, 127.86, 127.93, 128.03, 128.12, 128.39, 128.61, 129.00, 129.76, 130.07, 130.36, 131.21, 131.23, 132.72, 133.14, 133.48, 133.50, 133.95, 134.27, 134.35, 135.17, 135.20, 135.86, 136.14, 136.17, 138.38, 140.63, 203.09, 205.74. HRMS calcd for $C_{31}H_{39}NO$: 441.3032; found: 441.3030.

Isolation of Iminoacyl–Zr Intermediate 2-14a from Bis(alkynyl)silane, Two Molecules of *i*-PrCN, and *t*-BuNC: In a 20-mL Schlenk tube, *t*-BuNC (56 μL, 0.50 mmol) was added to the benzene solution of compound **2-6a** (310 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at room temperature for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, *the solid was* dried up under vacuum to precipitate **2-14a** as yellow powder (319 mg, 0.455 mmol, 91 % yield).

2-14a: Yellow powder, isolated yield 91 % (319 mg). ^1H NMR (300 MHz, C_6D_6, 25 °C): δ = 0.38 (s, 3H, $SiMe_2$), 0.91 (s, 3H, $SiMe_2$), 1.11 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.18–1.28 (m, 15H, $CHMe_2$ + ^{t}Bu), 0.93 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.66 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 2.69–2.78 (m, 1H, $CHMe_2$), 3.03–3.12 (m, 1H, $CHMe_2$), 5.67 (s, 5H, C_5H_5), 5.71 (s, 5H, C_5H_5), 7.03–7.51 (m, 9H, C_6H_5), 7.88 (*d*, *J* = 7.2 Hz, 1H, C_6H_5); ^{13}C NMR (75.4 MHz, C_6D_6, 25 °C): δ = −2.97, 1.15, 14.32, 19.35, 22.66, 26.08, 30.08, 33.17, 35.36, 54.49, 60.89, 107.22, 108.08, 120.26, 124.20, 126.14, 126.34, 127.33, 127.54, 127.92, 129.68, 132.17, 132.88, 140.15, 141.35, 144.34, 156.76, 186.88, 234.17. Elemental analysis calcd (%) for $C_{41}H_{49}N_3SiZr$: C, 70.03; H, 7.02; N, 5.98. Found: C, 69.95; H, 7.20; N, 5.60.

2-14b: Yellow powder, isolated yield 83 % (302 mg). ^1H NMR (300 MHz, C_4D_8O, 25 °C): δ = 0.20 (s, 3H, $SiMe_2$), 0.68 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$ + $SiMe_2$), 0.73 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 1.05 (*d*, *J* = 7.2 Hz, 3H, $CHMe_2$), 1.61 (s, 9H, ^{t}Bu), 1.49 (*t*, *J* = 6.9 Hz, 3H, $CHMe_2$), 2.31 (s, 3H, CH_3), 2.36–2.43 (m, 1H, $CHMe_2$), 2.46 (s, 3H, CH_3), 3.04–3.14 (m, 1H, $CHMe_2$), 5.77 (s, 5H, C_5H_5), 6.85 (s, 5H, C_5H_5), 7.06–7.25 (m, 7H, C_6H_5), 7.54 (*d*, *J* = 7.5 Hz, 1H, C_6H_5); ^{13}C NMR (75.4 MHz, C_4D_8O, 25 °C): δ = −4.12, −0.13, 18.24, 20.07, 20.47, 21.76, 21.98,

25.29, 29.68, 32.75, 34.32, 61.09, 106.92, 107.80, 119.31, 123.33, 127.40, 127.60, 128.07, 129.32, 131.66, 132.28, 134.65, 135.10, 136.85, 138.10, 143.96, 156.42, 185.50. Elemental analysis calcd (%) for $C_{43}H_{53}N_3SiZr$: C, 70.63; H, 7.31; N, 5.75. Found: C, 70.42; H, 7.51; N, 5.40.

Isolation of Iminoacyl–Zr Intermediate 2-15 or 2-16 from Bis(alkynyl)silane, Two Molecules of *i*-PrCN, and Two Molecules of CyNC: In a 20-mL Schlenk tube, CyNC (124 μL, 1.0 mmol) was added to the benzene solution of compound **2-6a** (310 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at room temperature for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, *the solid was* dried up under vacuum to precipitate **2-15** or **2-16** as yellow powder (326 mg, 0.39 mmol, 78 % yield).

2-15: Yellow powder, isolated yield 78 % (326 mg). ^{1}H NMR (300 MHz, C_4D_8O, 25 °C): δ = 0.29 (s, 3H, $SiMe_2$), 0.39 (s, 3H, $SiMe_2$), 0.58 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.90 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 1.10 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 1.31 (*d*, *J* = 7.2 Hz, 3H, $CHMe_2$), 1.30–1.52 (m, 14H, $CHMe_2$ + C_6H_{11}), 1.70–2.00 (m, 11H, C_6H_{11}), 2.21–2.30 (m, 1H, $CHMe_2$), 2.78–2.87 (m, 1H, $CHMe_2$), 5.83 (s, 5H, C_5H_5), 6.06 (s, 5H, C_5H_5), 7.08–7.40 (m, 9H, C_6H_5), 7.73 (*d*, *J* = 7.5 Hz, 1H, C_6H_5); ^{13}C NMR (75.4 MHz, C_4D_8O, 25 °C): δ = −2.94, −1.48, 18.60, 22.20, 23.35, 24.25, 24.42, 24.76, 24.95, 25.25, 25.74, 32.16, 34.70, 35.07, 35.54, 50.90, 64.13, 68.07, 109.45, 110.31, 119.90, 124.79, 125.47, 126.30, 126.85, 127.08, 127.41, 128.07, 128.12, 132.78, 140.76, 141.16, 141.47, 143.99, 164.95, 183.63, 222.57. Elemental analysis calcd (%) for $C_{54}H_{70}N_4OSiZr$ (**2-15**·THF): C, 71.63; H, 7.45; N, 6.68. Found: C, 71.95; H, 7.81; N, 6.50. Single crystals of **2-15**·THF suitable for X-ray analysis were grown in tetrahydrofuran/hexane at room temperature for three days.

2-16: Yellow powder, isolated yield 63 % (277 mg). ^{1}H NMR (300 MHz, C_4D_8O, 25 °C): δ = 0.49 (s, 3H, $SiMe_2$), 0.54 (s, 3H, $SiMe_2$), 1.04 (*d*, *J* = 7.2 Hz, 3H, $CHMe_2$), 1.25 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.74 (s, 3H, 2,6-Me_2Ph), 1.90 (s, 3H, 2,6-Me_2Ph), 2.21 (s, 3H, 2,6-Me_2Ph), 2.44 (s, 3H, 2,6-Me_2Ph), 2.83–2.92 (m, 1H, $CHMe_2$), 3.07–3.16 (m, 1H, $CHMe_2$), 5.89 (s, 5H, C_5H_5), 5.92 (s, 5H, C_5H_5), 6.15–6.65 (m, 6H, 2,6-Me_2Ph), 7.32–7.40 (m, 8H, C_6H_5), 8.03 (*d*, *J* = 8.1 Hz, 2H, C_6H_5); ^{13}C NMR (75.4 MHz, C_4D_8O, 25 °C): δ = −0.97, 0.10, 0.43, 18.80, 19.47, 19.68, 20.81, 20.87, 21.59, 21.85, 25.66, 32.36, 33.51, 108.48, 109.17, 116.64, 118.15, 125.34, 126.03, 126.64, 126.98, 127.07, 127.15, 126.46, 127.64, 128.24, 129.04, 129.98, 130.19, 136.58, 138.41, 138.82, 139.14, 145.54, 151.96, 154.92, 161.63, 180.93, 184.93. Elemental analysis calcd (%) for $C_{54}H_{58}N_4SiZr$: C, 73.50; H, 6.63; N, 6.35. Found: C, 73.66; H, 6.48; N, 6.50.

Hydrolysis of Iminoacyl–Zr Intermediate 2-14a to Give 1*H*-Pyrrolo[3,2-*c*] pyridine 2-11a, *t*-BuNH$_2$, and Zirconasiloxane 2-5: Under a nitrogen atmosphere, a J. Young valve NMR tube was charged with **2-14a** (70 mg, 0.10 mmol) and C_6D_6 (0.5 mL). Three equivalents of H_2O (5.4 μL, 0.30 mmol) were added to the C_6D_6 solution of **2-14a** with a syringe at room temperature, and then, the NMR tube was shaken immediately. The mixture in NMR tube was monitored by ^{1}H and

^{13}C NMR spectroscopy, and **2-11a** was found to be the main product over 90 % yield by ^{1}H NMR. Then, the mixture was filtered in the glove box, and the filtrate was subjected to GC–MS. The obvious peak of *m/z* = 73 as the relative molecular weight of *t*-BuNH$_2$ was found. The residue was washed with diethyl ether for several times until it turned out to be a pale solid and further characterized by elemental analysis to be **2-5**.

Formation of 1*H*-Pyrrolo[3,2-*c*]pyridine 2-11 from One Molecule of the Bis (alkynyl)silane with Two Molecules of Nitrile and One Isocyanide. A General Procedure for the Formation of 2,4-Diisopropyl-3,7-di*p*-tolyl-1*H*-pyrrolo[3,2-*c*] pyridine (2-11d): To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.2 mmol, 350 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.4 mmol, 1.6 M, 1.5 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(*p*-tolylethynyl) dimethylsilane (**2-2b**) was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After *iso*-butyronitrile (1.5 mmol, 0.135 ml) was added, the reaction mixture was stirred at this temperature for 1 h. Then, *t*-BuNC (1.2 mmol, 100 mg, 136 μl) was added, and the reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, diethyl ether, and triethylamine (100:10:1) as the eluent to give product **2-11d**.

2-11b: White solid, isolated yield: 55 % (231 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.54–0.63 (m, 3H), 0.74–0.87 (m, 3H), 1.10–1.24 (m, 6H), 1.36–1.42 (m, 1H), 1.53–1.59 (m, 2H), 1.73–1.79 (m, 1H), 2.67–2.80 (m, 2H), 7.22–7.48 (m, 6H), 7.55 (*t*, *J* = 7.6 Hz, 2H), 7.64 (*d*, *J* = 7.6 Hz, 2H), 8.28 (s, 1H), 8.33 (Br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.12, 12.19, 12.21, 12.24, 19.36, 19.42, 20.91, 29.43, 29.47, 29.62, 29.71, 30.28, 32.50, 32.55, 37.51, 114.85, 114.94, 118.27, 122.56, 122.58, 127.07, 127.19, 127.45, 127.64, 127.87, 127.93, 127.95, 128.13, 128.16, 128.19, 128.32, 128.52, 128.93, 129.36, 131.07, 131.12, 131.39, 131.47, 131.85, 136.15, 136.18, 136.50, 137.03, 138.59, 139.13, 141.09, 141.16, 159.18, 159.24. HRMS: *m/z*: calcd for $C_{27}H_{31}N_2$ $[M + H]^+$: 383.2487; found: 383.2473.

2-11c: White solid, isolated yield: 66 % (287 mg), m.p.: 218–220 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.74–1.88 (m, 20H), 2.58–2.68 (m, 2H), 7.24–7.66 (m, 10H), 8.25 (s, 1H), 8.31 (Br, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 25.79, 26.00, 26.30, 26.60, 32.21, 33.27, 35.67, 41.30, 114.13, 118.64, 122.28, 127.33, 127.88, 128.16, 128.43, 129.64, 131.38, 136.43, 136.83, 137.03, 139.36, 141.76, 159.55. HRMS: *m/z*: calcd for $C_{31}H_{35}N_2$ $[M + H]^+$: 435.2800; found: 435.2780.

2-11d: White solid, isolated yield: 41 % (156 mg), m.p.: 181–184 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.14 (*d*, *J* = 6.9 Hz, 6H), 1.20 (*d*, *J* = 6.9 Hz, 6H),

2.44 (s, 3H), 2.45 (s, 3H), 2.95–3.13 (m, 2H), 7.24 (s, 4H), 7.36 (*d*, *J* = 7.8 Hz, 2H), 7.53 (*d*, *J* = 7.5 Hz, 2H), 8.25 (s, 1H), 8.32 (br, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 21.26, 21.35, 22.05, 22.70, 25.55, 30.61, 113.58, 118.47, 121.84, 128.08, 128.75, 130.14, 130.84, 133.03, 133.55, 136.70, 137.04, 137.56, 139.05, 142.34, 159.70. HRMS: *m/z*: calcd for $C_{27}H_{31}N_2$ $[M + H]^+$: 383.2487; found: 383.2469.

2-11e: White solid, isolated yield: 53 % (217 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.55–0.65 (m, 3H), 0.74–0.83 (m, 3H), 1.10–1.23 (m, 6H), 1.35–1.45 (m, 1H), 1.48–1.61 (m, 2H), 1.71–1.84 (m, 1H), 2.45 (s, 3H), 2.46 (s, 3H), 2.66–2.77 (m, 1H), 2.78–2.85 (m, 1H), 7.23 (s, 4H), 7.37 (*d*, *J* = 8.1 Hz, 2H), 7.54 (*d*, *J* = 7.8 Hz, 2H), 8.22 (br, 1H), 8.26 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 12.20, 12.29, 12.35, 19.57, 19.61, 21.05, 21.07, 21.29, 21.36, 29.58, 29.74, 29.77, 29.84, 32.54, 32.58, 37.52, 114.96, 115.05, 118.38, 122.84, 128.27, 128.83, 128.87, 128.92, 130.33, 131.16, 131.24, 131.46, 131.58, 133.32, 133.86, 136.82, 137.30, 137.71, 139.37, 141.20, 141.28, 159.40. HRMS: *m/z*: calcd for $C_{29}H_{35}N_2$ $[M + H]^+$: 411.2800; found: 411.2795.

2-11f: White solid, isolated yield: 46 % (487 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.83–1.38 (m, 8H), 2.30 (s, 3H), 2.45 (s, 3H), 6.56 (*d*, *J* = 7.8 Hz, 2H), 6.64–78 (m, 4H), 6.93 (*d*, *J* = 8.1 Hz, 2H), 7.01–7.25 (m, 6H), 7.36 (*d*, *J* = 7.8 Hz, 2H), 7.56 (*d*, *J* = 7.8 Hz, 2H), 8.36 (s, 1H), 8.50 (Br, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 17.79, 19.23, 21.27, 21.30, 22.19, 29.46, 117.98, 119.67, 124.11, 124.59, 125.06, 125.87, 125.95, 127.70, 127.86, 128.33, 128.56, 130.35, 131.33, 132.11, 133.23, 135.82, 138.01, 138.08, 139.40, 144.97, 145.97, 155.12. HRMS: *m/z*: calcd for $C_{39}H_{35}N_2$ $[M + H]^+$: 531.2800; found: 531.2783.

Formation of Dihydropyrrolo[3,2-*c*]azepine 2-18 and 2-19 from One Molecule of the Bis(alkynyl)silane with Two Molecules of *i*-PrCN and Two Molecules of 2,6-Dimethylphenyl Isocyanides. A General Procedure for the Formation of *N*-(2,6-dimethylphenyl)-6-(2,6-dimethylphenylimino)-2,4-diisopropyl-3,8-diphenyl-1,6-dihydropyrrolo[3,2-*c*]azepin-7-amine (2-18a) and N^6,N^7-bis(2,6-dimethylphenyl)-2,4-diisopropyl-3,8-diphenyl-1,6-dihydropyrrolo[3,2-*c*]azepine-6,7-diamine (2-19a): To a toluene (20 ml) solution of Cp_2ZrCl_2 (1.2 mmol, 350 mg) at −78 °C (dry ice/acetone) in a 50-ml Schlenk tube was added dropwise *n*-BuLi (2.4 mmol, 1.6 M, 1.5 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane (**2-2a**) was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After *i*-PrCN (1.5 mmol, 0.135 ml) was added, the reaction mixture was stirred at this temperature for 1 h. Then, 2,6-dimethylphenyl isocyanide (2.4 mmol, 314 mg) was added, and the reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, diethyl ether, and triethylamine

(100:7.5:1) as the eluent to give product **2-19a** and using petroleum ether, diethyl ether, and triethylamine (100:15:1) as the eluent to give product **2-18a**.

2-18a: Colorless crystal, isolated yield: 46 % (278 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.59 (*d*, *J* = 6.9 Hz, 6H, $CHMe_2$), 1.01 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.81 (s, 6H, Me), 2.23 (s, 6H, Me), 2.94–3.03 (m, 2H, $CHMe_2$), 6.08 (s, 1H, NH), 6.81 (*t*, *J* = 8.1 Hz, 4H, CH), 6.92 (*d*, *J* = 7.2 Hz, 2H, CH), 7.10–7.33 (m, 10H, CH), 7.44 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 17.76, 19.17, 20.73, 22.70, 24.77, 33.24, 106.65, 118.38, 118.61, 122.10, 125.27, 126.16, 127.05, 127.38, 127.80, 128.04, 128.09, 128.64, 129.72, 130.21, 134.36, 134.97, 135.18, 135.91, 136.27, 137.82, 147.28, 158.59, 167.17. HRMS: *m/z*: calcd for $C_{42}H_{45}N_4$ $[M + H]^+$: 605.3644; found: 605.3678. Single crystals of **2-18a**·1.5**DME** suitable for X-ray analysis were grown in 1,2-dimethoxyethane/diethyl ether at room temperature for three days.

2-18b: White solid, isolated yield: 33 % (235 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.57–0.63 (m, 2H, CH_2), 0.83–0.90 (m, 3H, CH_2), 1.05–1.14 (m, 4H, CH_2), 1.17–1.25 (m, 2H, CH_2), 1.37–1.45 (m, 3H, CH_2), 1.57–1.71 (m, 6H, CH_2), 1.75 (s, 6H, Me), 1.79–1.85 (m, 1H, CH), 2.22 (s, 6H, Me), 2.31 (s, 3H, Me), 2.35 (s, 3H, Me), 2.53–5.59 (m, 1H, CH), 5.97 (s, 1H, NH), 6.81 (*t*, *J* = 7.6 Hz, 4H, CH), 6.89 (*d*, *J* = 7.6 Hz, 2H, CH), 6.96 (*d*, *J* = 8.0 Hz, 2H, CH), 7.08 (*q*, *J* = 7.6 Hz, 4H, CH), 7.19 (*d*, *J* = 8.0 Hz, 2H, CH), 7.43 (Br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 17.72, 19.15, 21.12, 21.15, 25.71, 25.96, 26.11, 26.33, 30.97, 33.27, 34.81, 43.24, 106.47, 118.49, 118.76, 121.92, 125.14, 126.94, 127.79, 128.20, 128.67, 129.00, 129.37, 129.67, 130.05, 132.88, 133.36, 133.47, 135.18, 135.24, 135.54, 135.92, 136.99, 138.06, 147.41, 158.59, 168.16. HRMS: *m/z*: calcd for $C_{50}H_{57}N_4$ $[M + H]^+$: 713.4578; found: 713.4560.

2-19a: Yellow solid, isolated yield: 24 % (145 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.80 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.88 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.99 (*d*, *J* = 6.0 Hz, 3H, $CHMe_2$), 1.22 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.68 (s, 3H, Me), 2.35 (s, 3H, Me), 2.38–2.45 (m, 1H, $CHMe_2$), 2.57 (s, 6H, Me), 3.02–3.09 (m, 1H, $CHMe_2$), 4.33 (*d*, *J* = 5.1 Hz, 1H, CHNH), 4.68 (*d*, *J* = 5.1 Hz, 1H, CHNH), 6.39 (*d*, *J* = 7.5 Hz, 1H, CH), 6.57 (*t*, *J* = 7.2 Hz, 1H, CH), 6.75 (*d*, *J* = 7.2 Hz, 1H, CH), 6.85–7.34 (m, 13H, CH), 7.53 (Br, 1H, NH), 7.89 (br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 19.30, 19.99, 20.42, 22.28, 22.71, 23.03, 24.70, 33.04, 79.79, 101.03, 118.20, 118.97, 121.82, 123.35, 125.59, 125.83, 127.06, 127.43, 128.00, 128.55, 128.68, 128.77, 129.66, 129.72, 130.52, 130.60, 131.92, 133.62, 133.70, 136.38, 136.98, 137.04, 137.78, 147.01, 167.69. HRMS: *m/z*: calcd for $C_{42}H_{47}N_4$ $[M + H]^+$: 607.3801; found: 607.3794. Single crystals of **2-19a** suitable for X-ray analysis were grown in diethyl ether/hexane at room temperature for one week.

2-19b: Yellow solid, isolated yield: 21 % (150 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.55–0.67 (m, 1H, CH_2), 0.80–0.88 (m, 1H, CH_2), 0.94–1.05 (m, 5H, CH_2), 1.08–1.25 (m, 2H, CH_2), 1.43–1.61 (m, 9H, CH_2), 1.64 (s, 3H, Me), 1.72–1.77 (m, 1H, CH_2), 1.98–2.00 (m, 2H, CH), 2.14 (s, 3H, Me), 2.32 (s, 3H,

Me), 2.37 (s, 3H, Me), 2.56 (s, 3H, Me), 2.59–5.62 (m, 1H, CH), 4.27 (*d*, *J* = 5.2 Hz, 1H, CHNH), 4.63 (*d*, *J* = 5.2 Hz, 1H, CHNH), 6.35 (*d*, *J* = 7.6 Hz, 1H, CH), 6.53 (*t*, *J* = 7.6 Hz, 1H, CH), 6.62 (*d*, *J* = 7.6 Hz, 1H, CH), 6.73 (*t*, *J* = 8.0 Hz, 2H, CH), 6.77 (s, 2H, CH), 6.84 (t, *J* = 8.0 Hz, 1H, CH), 7.04 (*d*, *J* = 7.6 Hz, 2H, CH), 7.11 (*q*, *J* = 7.6 Hz, 4H, CH), 7.51 (Br, 1H, NH), 7.69 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 19.07, 19.33, 19.98, 20.94, 21.18, 25.76, 26.23, 26.31, 26.39, 26.47, 26.86, 30.89, 32.75, 33.03, 33.69, 34.70, 43.20, 79.85, 100.99, 118.31, 119.18, 121.73, 123.06, 126.98, 127.61, 128.11, 128.27, 12860, 128.70, 129.71, 130.26, 130.44, 131.94, 132.78, 133.07, 133.90, 134.11, 135.08, 135.19, 136.26, 137.93, 148.13, 167.01. HRMS: *m/z*: calcd for $C_{50}H_{59}N_4$ $[M + H]^+$: 715.4740; found: 715.4728.

Formation of pyrrolo[3,2-*d*]pyridazine 2-20 from One Molecule of the Bis (alkynyl)silane with Two nitriles and One Azide. A General Procedure for the Formation of N-benzyl-2, 4-diisopropyl-3, 7-diphenyl-5*H*-pyrrolo[3, 2-*d*]pyridazin-5-amine (2-20a): To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.2 mmol, 350 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.4 mmol, 1.6 M, 1.5 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane (**2-2a**) was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After *iso*-butyronitrile (1.75 mmol, 0.157 ml) was added, the reaction mixture was stirred at this temperature for 1 h. Then, BnN_3 (1.2 mmol, 154 mg) was added, and the reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, diethyl ether, and triethylamine (100:15:1) as the eluent to give product **2-20a**.

***N*-Benzyl-2,4-diisopropyl-3,7-diphenyl-5*H*-pyrrolo[3,2-*d*]pyridazin-5-amine (2-20a):** Yellow crystal, isolated yield 54 % (248 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.34 (*d*, *J* = 6.9 Hz, 6H, CH_3), 1.36 (*d*, *J* = 6.9 Hz, 6H, CH_3), 3.05–3.14 (m, 1H, C*H*Me_2), 3.48–3.57 (m, 1H, C*H*Me_2), 4.55 (*d*, *J* = 7.5 Hz, 2H, CH_2), 5.34 (*t*, *J* = 7.2 Hz, 1H, NH), 7.24–7.59 (m, 13H, CH), 8.81 (*d*, *J* = 6.9 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 19.88, 23.19, 28.55, 29.32, 56.63, 118.02, 126.70, 127.74, 127.91, 128.18, 128.22, 128.86, 128.93, 129.49, 129.78, 130.91, 135.21, 135.51, 137.50, 140.08, 145.31, 153.62, 168.22. HRMS calcd for $C_{31}H_{33}N_4$ $[M + H]^+$: 461.2705; found: 461.2761. Elemental Analysis Calcd (%) for $C_{31}H_{32}N_4$: C, 80.83; H, 7.00; N, 12.16. Found: C, 80.63; H, 7.20; N, 11.99. Single crystals of **2-20a** suitable for X-ray analysis were grown in hexane at room temperature for one day.

2,4-Dicyclohexyl-*N*-phenyl-3,7-di*p*-tolyl-5*H*-pyrrolo[3,2-*d*]pyridazin-5-amine (2-20b): Pale yellow crystal, isolated yield 50 % (277 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.21–2.17 (m, 20H, CH_2), 2.37 (s, 3H, CH_3), 2.45 (s, 3H, CH_3),

2.71–2.78 (m, 1H, CH), 3.00–3.16 (m, 1H, CH), 6.43 (*d*, *J* = 8.4 Hz, 2H, CH), 6.97 (*t*, *J* = 7.2 Hz, 1H, CH), 7.16–7.27 (m, 8H, CH), 7.75 (Br, 1H, NH), 8.47 (*d*, *J* = 8.1 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 21.34, 21.47, 25.40, 26.10, 26.36, 26.63, 29.23, 30.96, 33.13, 38.77, 39.91, 114.89, 118.77, 122.23, 127.90, 128.63, 128.92, 129.08, 129.81, 130.78, 132.00, 134.24, 136.24, 139.51, 139.89, 146.99, 147.12, 154.87, 167.50. HRMS calcd for $C_{38}H_{43}N_4$ $[M + H]^+$: 555.3488; found: 555.3486. Elemental Analysis Calcd (%) for $C_{38}H_{42}N_4$: C, 82.27; H, 7.63; N, 10.10. Found: C, 82.11; H, 7.89; N, 9.91.

2,4-Di-*sec*-butyl-*N*-(4-fluorobenzyl)-3,7-diphenyl-5*H*-pyrrolo[2,3-*d*]pyridazin-5-amine (2-20c): White solid, isolated yield 59 % (298 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 0.57–0.64 (m, 3H), 0.74–0.84 (m, 5H), 1.26–1.36 (m, 6H), 1.60–1.77 (m, 2H), 1.90–1.95 (m, 2H), 2.76–2.80 (m, 1H), 3.27–3.35 (m, 1H), 4.51 (*d*, *J* = 7.6 Hz, 2H, CH_2), 5.26 (*t*, *J* = 7.2 Hz, 1H, NH), 7.08 (*t*, *J* = 8.4 Hz, 2H), 7.23–7.55 (m, 10H), 8.85 (*d*, *J* = 7.2 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 12.36, 12.61, 12.72, 17.60, 17.73, 21.18, 21.22, 27.43, 27.46, 29.97, 30.15, 35.59, 35.65, 36.27, 36.30, 55.66, 115.68, 115.90, 119.12, 119.26, 126.67, 127.77, 127.86, 127.94, 128.21, 129.48, 129.76, 130.70, 130.79, 131.09, 131.17, 131.29, 131.33, 131.37, 131.40, 135.67, 137.63, 137.66, 139.98, 145.01, 145.05, 152.73, 152.81, 161.35, 163.81, 167.51, 167.58. HRMS calcd for $C_{33}H_{36}FN_4$ $[M + H]^+$: 507.2924; found: 507.2920. Elemental Analysis Calcd (%) for $C_{33}H_{35}FN_4$: C, 78.23; H, 6.96; N, 11.06. Found: C, 78.12; H, 7.09; N, 10.90.

***N*-Benzyl-2,4-dicyclohexyl-3,7-diphenyl-5*H*-pyrrolo[2, 3-*d*]pyridazin-5-amine (2-20d):** Yellow solid, isolated yield 55 % (297 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 0.66–2.24 (m, 20H, CH_2), 2.72–2.80 (m, 1H, C*H*), 3.03–3.11 (m, 1H, C*H*), 4.50 (*d*, *J* = 7.5 Hz, 2H, CH_2), 5.30 (*t*, *J* = 7.2 Hz, 1H, NH), 7.33–7.57 (m, 13H, CH), 8.83 (*d*, *J* = 6.9 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 25.89, 26.09, 26.42, 26.67, 29.41, 33.16, 38.89, 40.13, 56.80, 118.33, 126.68, 127.94, 128.15, 128.23, 128.84, 129.44, 129.76, 131.02, 135.25, 135.61, 137.73, 139.90, 145.33, 152.73, 167.23. HRMS calcd for $C_{37}H_{41}N_4$ $[M + H]^+$: 541.3331; found: 541.3320. Elemental Analysis Calcd (%) for $C_{37}H_{40}N_4$: C, 82.18; H, 7.46; N, 10.36. Found: C, 82.00; H, 7.93; N, 10.08.

***N*-Benzyl-2, 4-diisopropyl-3, 7-di*p*-tolyl-5*H*-pyrrolo[3, 2-*d*]pyridazin-5-amine (2-20e):** Yellow crystal, isolated yield 67 % (327 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.33 (*d*, *J* = 6.9 Hz, 6H, CH_3), 1.36 (*d*, *J* = 6.9 Hz, 6H, CH_3), 2.44 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.03–3.12 (m, 1H, $CHMe_2$), 3.53–3.62 (m, 1H, $CHMe_2$), 4.54 (*d*, *J* = 7.5 Hz, 2H, CH_2), 5.35 (*t*, *J* = 7.2 Hz, 1H, NH), 7.22–7.50 (m, 11H, CH), 8.72 (*d*, *J* = 8.1 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 19.91, 21.34, 21.54, 23.22, 28.49, 29.20, 56.68, 117.88, 127.54, 128.19, 128.66, 128.88, 128.97, 129.66, 130.75, 132.45, 134.34, 135.63, 136.14, 139.46, 139.98, 145.47, 153.55, 168.14. HRMS calcd for $C_{33}H_{37}N_4$ $[M + H]^+$: 489.3018; found: 489.3024. Elemental Analysis Calcd (%) for $C_{33}H_{36}N_4$: C, 80.94; H, 7.62; N, 11.44. Found: C, 80.63; H, 7.90; N, 11.21.

2,4-Diisopropyl-*N*-(4-methoxybenzyl)-3,7-di*p*-tolyl-5*H*-pyrrolo[2,3-*d*]pyridazin-5-amine (2-20f): Yellow oily solid, isolated yield 52 % (275 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.33 (*d*, *J* = 6.9 Hz, 6H, CH_3), 1.34 (*d*, *J* = 6.9 Hz, 6H, CH_3), 2.44 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.03–3.13 (m, 1H, $CHMe_2$), 3.52–3.61 (m, 1H, $CHMe_2$), 3.82 (s, 3H, OCH_3), 4.49 (*d*, *J* = 7.2 Hz, 2H, CH_2), 5.25 (*t*, *J* = 7.2 Hz, 1H, NH), 6.93 (*d*, *J* = 8.7 Hz, 2H, CH), 7.22–7.42 (m, 8H, CH), 8.72 (*d*, *J* = 6.9 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 19.91, 21.34, 21.54, 23.22, 28.46, 29.18, 55.29, 56.10, 114.17, 117.85, 127.49, 128.65, 128.97, 129.65, 130.36, 130.73, 132.45, 134.32, 136.12, 139.45, 139.94, 145.47, 153.55, 159.44, 168.06. HRMS calcd for $C_{34}H_{40}N_4O$ $[M + H]^+$: 519.3108; found: 519.3124.

***N*-Benzyl-2, 4-di-*sec*-butyl-3, 7-bis(4-*tert*-butylphenyl)-5*H*-pyrrolo[3, 2-*d*]pyridazin-5-amine (2-20g):** Yellow solid, isolated yield 53 % (312 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 0.76–0.85 (m, 4H, CH_2CH_3), 1.13–1.17 (m, 6H, $CHCH_3$), 1.39 (s, 9H, CMe_3), 1.40 (s, 9H, CMe_3), 1.61–1.70 (m, 3H, CH_2CH_3), 1.77–1.86 (m, 3H, CH_2CH_3), 2.77–2.87 (m, 1H, $CHCH_3$), 3.17–3.21 (m, 1H, $CHCH_3$), 4.53 (*d*, *J* = 7.2 Hz, 2H, CH_2), 5.27 (*t*, *J* = 7.2 Hz, 1H, NH), 7.23–8.72 (m, 11H, CH), 8.73 (*d*, *J* = 8.1 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = −0.82, 11.43, 11.87, 11.95, 16.42, 16.53, 20.48, 20.56, 26.43, 26.48, 29.16, 29.31, 30.52, 30.65, 33.73, 33.97, 34.74, 35.24, 55.71, 118.20, 118.30, 123.68, 123.73, 123.92, 124.46, 127.33, 127.51, 127.70, 128.04, 128.15, 128.60, 129.77, 129.93, 129.99, 130.17, 131.71, 133.57, 134.87, 139.15, 148.58, 151.54, 152.08, 152.16, 166.33, 166.39. HRMS calcd for $C_{41}H_{53}N_4$ $[M + H]^+$: 601.4270; found: 601.4274.

Isolation of Reactive Intermediate 2-21a or 2-21a′ with the Proposed Structure: In a 20-mL Schlenk tube, benzyl azide (59 mg, 0.5 mmol) was added to the benzene solution of compound **2-6a** (310 mg, 0.50 mmol). After the reaction mixture was stirred at room temperature for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, the solid was dried up under vacuum to precipitate **2-21a** or **2-21a′** as brown powder (328 mg, 0.43 mmol, 87 % yield). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.47 (s, 3H, $SiMe_2$), 0.59 (s, 3H, $SiMe_2$), 1.03 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.36 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 2.37–2.46 (m, 1H, $CHMe_2$), 2.73–2.82 (m, 1H, $CHMe_2$), 4.58 (s, 2H, CH_2Ph), 5.55 (s, 5H, C_5H_5), 5.76 (s, 5H, C_5H_5), 7.08–7.42 (m, 12H, C_6H_5), 7.57 (*d*, *J* = 7.5 Hz, 2H, C_6H_5), 7.75 (*d*, *J* = 6.9 Hz, 2H, C_6H_5); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −4.61, −1.38, 19.64, 22.28, 22.60, 26.11, 32.67, 35.63, 61.88, 65.59, 111.11, 111.58, 120.21, 123.07, 126.22, 126.43, 126.76, 127.34, 128.53, 128.73, 129.08, 132.25, 132.96, 139.36, 141.25, 143.48, 143.94, 144.48, 185.29. Elemental Analysis Calcd (%) for $C_{43}H_{47}N_5SiZr$: C, 68.57; H, 6.29; N, 9.30. Found: C, 68.46; H, 6.40; N, 9.18.

Formation of Pyrrole-2,3-diones 2-24 from One Molecule of the Bis(alkynyl)silane, Two Nitriles, and One $TMSN_3$. A General Procedure for the Formation of 1-(2-benzoyl-5-isopropyl-4-phenyl-1*H*-pyrrol-3-yl)-2-methylpropan-1-one (2-24a): To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.2 mmol, 350 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.4 mmol, 1.6 M, 1.5 ml) with a syringe. After the addition was complete, the reaction mixture

was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane (**2-2a**) was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After *iso*-butyronitrile (1.75 mmol, 0.157 ml) was added, the reaction mixture was stirred at this temperature for 1 h. Then, $TMSN_3$ (1.2 mmol) was added, and the reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, ethyl acetate, and triethylamine (100:15:1) as the eluent to give product **2-24a**.

1-(2-Benzoyl-5-isopropyl-4-phenyl-1*H*-pyrrol-3-yl)-2-methylpropan-1-one (2-24a): Yellow crystal, isolated yield 64 % (228 mg), m.p.: 135–136 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 0.55 (*d*, *J* = 6.9 Hz, 6H, CH_3), 1.24 (*d*, *J* = 6.9 Hz, 6H, CH_3), 2.09–2.18 (m, 1H, $CHMe_2$), 2.99–3.08 (m, 1H, $CHMe_2$), 7.26–7.77 (m, 10H, CH), 10.08 (Br, 1H, NH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 17.65, 22.40, 25.52, 43.44, 123.60, 127.07, 127.19, 128.00, 128.55, 129.17, 130.54, 131.99, 132.30, 133.71, 138.96, 142.65, 186.32, 206.07. IR (film): 1,689, 1,602 cm^{-1}. HRMS calcd for $C_{24}H_{26}NO_2$ $[M + H]^+$: 360.1964; found: 360.1952. Elemental Analysis Calcd (%) for $C_{24}H_{25}NO_2$: C, 80.19; H, 7.01; N, 3.90. Found: C, 80.36; H, 6.97; N, 3.68. Single crystals of **2-24a** suitable for X-ray analysis were grown in hexane/diethyl ether/ethyl acetate (2:1:1) at room temperature for one day.

(3-(Cyclohexanecarbonyl)-5-cyclohexyl-4-*p*-tolyl-1*H*-pyrrol-2-yl)(*p*-tolyl)methanone (2-24b): Yellow solid, isolated yield 67 % (315 mg), m.p.: 200–202 °C. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ = 0.79–1.88 (m, 20H, CH_2), 2.37 (s, 3H, Me), 2.39 (s, 3H, Me), 2.51–2.67 (m, 2H, CH), 7.14 (s, 4H, C_6H_4), 7.23 (*d*, *J* = 7.8 Hz, 2H, C_6H_4), 7.63 (*d*, *J* = 7.8 Hz, 2H, C_6H_4), 9.30 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 21.20, 21.53, 25.58, 26.21, 28.07, 32.81, 35.22, 53.32, 123.69, 127.18, 128.61, 129.10, 129.19, 130.29, 130.73, 131.76, 136.51, 136.58, 141.71, 142.79, 186.15, 205.37. IR (film): 1,685, 1,597 cm^{-1}. HRMS calcd for $C_{32}H_{38}NO_2$ $[M + H]^+$: 468.2903; found: 468.2907. Elemental Analysis Calcd (%) for $C_{32}H_{37}NO_2$: C, 82.19; H, 7.97; N, 3.00. Found: C, 82.10; H, 8.09; N, 2.97.

1-(5-Isopropyl-2-(4-propylbenzoyl)-4-(4-propylphenyl)-1H-pyrrol-3-yl)-2-methylpropan-1-one (2-24c): Yellow oil, isolated yield 63 % (264 mg). ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ = 0.55 (*d*, *J* = 6.9 Hz, 6H, $CHMe_2$), 0.90–0.97 (m, 6H, $CH_2CH_2CH_3$), 1.24 (*d*, *J* = 6.9 Hz, 6H, $CHMe_2$), 1.60–1.70 (m, 4H, $CH_2CH_2CH_3$), 2.10–2.19 (m, 1H, $CHMe_2$), 2.57–2.65 (m, 4H, $CH_2CH_2CH_3$), 2.99–3.09 (m, 1H, $CHMe_2$), 7.13–7.26 (m, 6H, C_6H_4), 7.68 (*d*, *J* = 8.1 Hz, 2H, C_6H_4), 9.88 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 13.68, 13.88, 17.64, 22.45, 24.27, 24.33, 25.40, 37.73, 37.98, 43.50, 123.52, 127.08, 127.99, 128.65, 129.28, 130.27, 130.82, 131.75, 136.55, 141.39, 142.29, 147.66, 186.02, 206.30. IR (film): 1,691, 1,597 cm^{-1}. HRMS calcd for $C_{30}H_{38}NO_2$ $[M + H]^+$: 444.2903; found: 444.2901.

(2-(4-*tert*-Butylbenzoyl)-4-(4-*tert*-butylphenyl)-5-cyclohexyl-1*H*-pyrrol-3-yl) (cyclohexyl)methanone (2-24d): Yellow oil, isolated yield 54 % (298 mg). ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ = 0.79–0.90 (m, 5H, C_6H_{11}), 1.05–1.20 (m, 6H, C_6H_{11}), 1.30 (s, 9H, CMe_3), 1.34 (s, 9H, CMe_3), 1.42–1.45 (m, 3H, C_6H_{11}), 1.62–1.75 (m, 6H, C_6H_{11}), 1.86–1.92 (m, 1H, C_6H_{11}), 2.53–2.59 (m, 1H, C_6H_{11}), 7.12 (*d*, *J* = 8.2 Hz, 2H, C_6H_4), 7.33 (*d*, *J* = 8.2 Hz, 2H, C_6H_4), 7.38 (*d*, *J* = 8.4 Hz, 2H, C_6H_4), 7.45 (*d*, *J* = 8.1 Hz, 2H, C_6H_4), 9.27 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 25.70, 25.91, 26.27, 29.83, 31.04, 31.34, 32.87, 34.47, 34.99, 35.34, 49.89, 123.82, 124.97, 125.28, 125.84, 128.85, 130.05, 130.73, 132.27, 136.73, 142.48, 149.45, 155.31, 180.90, 186.20. IR (film): 1,607, 1,558 cm^{-1}. HRMS calcd for $C_{38}H_{49}NO_2$ $[M + H]^+$: 551.3763; found: 551.3995.

1-(2-(4-*tert*-Butylbenzoyl)-4-(4-*tert*-butylphenyl)-5-isopropyl-1*H*-pyrrol-3-yl)-2-methylpropan-1-one (2-24e): Yellow solid, isolated yield 62 % (294 mg), ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ = 0.49 (*d*, *J* = 6.3 Hz, 6H, $CHMe_2$), 1.13 (*d*, *J* = 6.6 Hz, 6H, $CHMe_2$), 1.29 (s, 9H, CMe_3), 1.30 (s, 9H, CMe_3), 2.18–2.26 (m, 1H, $CHMe_2$), 2.92–3.01 (m, 1H, $CHMe_2$), 7.13 (*d*, *J* = 8.2 Hz, 2H, C_6H_4), 7.30 (*d*, *J* = 7.8 Hz, 2H, C_6H_4), 7.38 (*d*, *J* = 7.2 Hz, 2H, C_6H_4), 7.46 (*d*, *J* = 7.5 Hz, 2H, C_6H_4); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 17.84, 22.62, 25.14, 31.06, 31.32, 34.37, 34.76, 42.29, 122.05, 124.63, 125.54, 127.48, 127.89, 128.00, 129.87, 131.80, 137.03, 139.18, 149.02, 153.87, 170.02, 205.71. IR (film): 1,670, 1,609 cm^{-1}. HRMS calcd for $C_{32}H_{41}NO_2$ $[M + H]^+$: 471.3137; found: 471.3367.

Formation of Pyrrolo[3,2-*d*]pyridazines 2-27 from Pyrrole-2,3-diones 2-24 and Hydrazine Hydrate. A General Procedure for Preparation of 2,4-diisopropyl-3,7-diphenyl- 1*H*-pyrrolo[3,2-*d*]pyridazine (2-27a): In a 20-mL Schlenk tube, hydrazine hydrate (1.0 mmol, 0.057 mL) was added to the ethanol solution (5 mL) of compound **2-24** (180 mg, 0.5 mmol). After the reaction mixture was refluxed for 12 h, the solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, ethyl acetate, and triethylamine (100:30:1) as the eluent to give product **2-27a**.

2,4-Diisopropyl-3,7-diphenyl-1*H*-pyrrolo[3,2-*d*]pyridazine (2-27a): Yellow solid, isolated yield 75 % (133 mg), m.p.: 249–251 °C. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ = 1.21 (*d*, *J* = 7.2 Hz, 6H, $CHMe_2$), 1.24 (*d*, *J* = 7.2 Hz, 6H, $CHMe_2$), 3.05–3.14 (m, 2H, $CHMe_2$), 7.26–7.45 (m, 8H, C_6H_4), 7.81–7.84 (m, 2H, C_6H_4), 10.00 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 21.86, 22.32, 25.98, 30.25, 113.43, 122.37, 127.45, 128.02, 128.31, 128.63, 128.77, 129.60, 130.96, 135.04, 135.99, 145.32, 146.61, 160.36. HRMS calcd for $C_{24}H_{26}N_3$ $[M + H]^+$: 356.2127; found: 356.2123. Elemental Analysis Calcd (%) for $C_{24}H_{25}N_3$: C, 81.09; H, 7.09; N, 11.82. Found: C, 81.07; H, 7.15; N, 11.80.

2,4-Dicyclohexyl-3,7-di*p*-tolyl-1*H*-pyrrolo[3,2-*d*]pyridazine (2-27b): Yellow solid, isolated yield 83 % (192 mg), m.p.: >300 °C. ^{1}H NMR (THF-d8, Me_4Si) δ = 1.45–1.92 (m, 20H, CH_2), 2.58 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 2.89–2.93 (m, 2H, CH), 7.39–7.47 (m, 4H, CH), 7.39–7.47 (m, 4H, CH), 7.68–7.71 (m, 2H, CH), 7.83–7.86 (m, 2H, CH), 10.72 (Br, 1H, CH); ^{13}C NMR (THF-d8, Me_4Si) δ = 13.18,

19.19, 20.47, 25.88, 26.18, 26.46, 26.66, 29.75, 30.69, 32.22, 128.535, 128.69, 128.86, 130.67, 131.12, 132.75, 166.77. HRMS calcd for $C_{32}H_{38}N_3$ $[M + H]^+$: 464.3066; found: 464.3060. Elemental Analysis Calcd (%) for $C_{32}H_{37}N_3$: C, 82.89; H, 8.04; N, 9.06. Found: C, 82.78; H, 8.20; N, 8.99.

2,4-Diisopropyl-3,7-bis(4-propylphenyl)-1*H*-pyrrolo[3,2-*d*]pyridazine (2-27c): Yellow solid, isolated yield 61 % (134 mg), m.p.: 271–272 °C. ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) $\delta = 0.95$–1.21 (m, 6H, $CHMe_2$), 1.25 (*t*, $J = 9.5$ Hz, 6H, $CH_2CH_2CH_3$), 1.67–1.77 (m, 4H, $CH_2CH_2CH_3$), 2.63–2.71 (m, 4H, $CH_2CH_2CH_3$), 3.08–3.15 (m, 2H, $CHMe_2$), 7.26 (s, 4H, C_6H_4), 7.32 (*d*, $J = 8.1$ Hz, 2H, C_6H_4), 7.84 (*d*, $J = 8.0$ Hz, 2H, C_6H_4), 9.00 (Br, 1H, NH); ^{13}C NMR (100.0 MHz, $CDCl_3$, Me_4Si) δ = 13.31, 13.41, 21.45, 22.11, 23.92, 25.35, 29.84, 37.31, 37.41, 113.31, 122.00, 127.55, 127.74, 128.71, 129.00, 130.29, 131.45, 133.10, 141.47, 143.36, 144.79, 145.23, 159.99. HRMS calcd for $C_{30}H_{38}N_3$ $[M + H]^+$: 440.3066; found: 440.3060. Elemental Analysis Calcd (%) for $C_{30}H_{37}N_3$: C, 81.96; H, 8.48; N, 9.56. Found: C, 81.90; H, 8.53; N, 9.47.

Formation of Pyrrolo[2,3-*c*]pyridinone 2-28 from Pyrrole-2,3-diones 2-24 and Hydroxylamine Hydrochloride. In a 20-mL Schlenk tube, hydroxylamine hydrochloride (1.5 mmol, 104 mg) was added to the pyridine solution (10 mL) of compound **2-24a** (180 mg, 0.5 mmol). After the reaction mixture was refluxed for 4 h, the solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, ethyl acetate, and triethylamine (100:20:1) as the eluent to give product **2-28**.

2-Isopropyl-5,5-dimethyl-3,7-diphenyl-1*H*-pyrrolo[2,3-*c*]pyridin-4(5*H*)-one (2-28): Yellow crystal, isolated yield 71 % (126 mg), m.p.: 274–276 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ = 1.28 (*d*, J = 4.0 Hz, 6H, $CHMe_2$), 1.57 (s, 6H, CMe_2), 3.23–3.30 (m, 1H, $CHMe_2$), 7.30–7.46 (m, 5H, C_6H_5), 7.61–7.63 (m, 3H, C_6H_5), 7.74–7.76 (m, 2H, C_6H_5), 8.27 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 22.76, 24.92, 26.96, 69.54, 118.13, 119.89, 127.04, 127.39, 127.85, 129.43, 130.00, 130.15, 130.52, 132.98, 136.97, 140.13, 152.88, 201.55. IR (film): 1,648 cm^{-1}. HRMS calcd for $C_{24}H_{25}N_2O$ $[M + H]^+$: 357.1967; found: 357.1962. Elemental Analysis Calcd (%) for $C_{24}H_{24}N_2O$: C, 80.87; H, 6.79; N, 7.86. Found: C, 80.81; H, 6.86; N, 7.86. Single crystals of **2-28** suitable for X-ray analysis were grown in dichloromethane/ethyl acetate (1:1) at room temperature for one day.

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