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Mechanistic Insights into N—N Bond Cleavage in Catalytic Guanylation Reactions between 1,2-Diarylhydrazines and Carbodiimides

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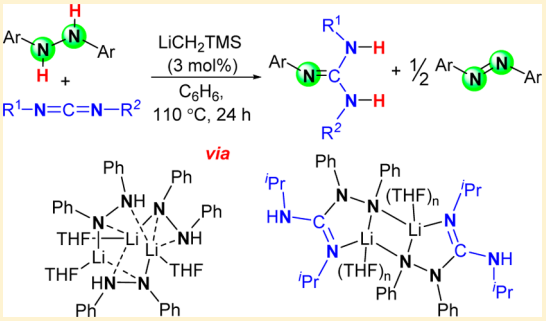
Supporting Information

ABSTRACT: Cleavage of the N—N bond in 1,2-diarylhydrazine was achieved through an alkyllithium-catalyzed guanylation reaction of 1,2-diarylhydrazine with carbodiimide, affording guanidine and azo compounds. This N—N bond cleavage via thermal rearrangement was driven by an intramolecular proton shift. No reductants, oxidants, bases, or external protons were needed. The proposed mechanism has been well elucidated by the isolation, characterization, and reaction studies of two important amido lithium intermediates and an ArHN-substituted guanidine.



INTRODUCTION

In recent years, there has been significant growth in the study of N—N bond cleavage in hydrazines because of its importance in biological nitrogen fixation[1,2] and organic synthesis.[3−5] In the case of biological nitrogen fixation, evidence has shown that only η^1-coordinated hydrazines can be converted into ammonia by N—N bond cleavage, in which both the variable oxidation states on the Mo center and an external proton are required (Scheme 1*a*).[2] In organic synthesis, known methods for N—N bond cleavage of hydrazines mainly involve reductive cleavage,[3] oxidative cleavage in which one of the substrate nitrogen atoms is substituted by a carbonyl group,[4] or base-promoted eliminative cleavage (Schemes 1*b*−*d*).[5] In all of these processes, a stoichiometric amount of reductants, oxidants, and bases are required. In addition, N—N bond cleavage of hydrazines has also been discovered and applied to Benzidine rearrangement[6] and Fischer indole synthesis.[7] In these two metal-free transformations, N—N bond cleavage is promoted by external protons (Schemes 1*e* and 1*f*).

We have been interested in catalytic guanylation reactions of various amines with carbodiimides to prepare guanidines.[8−12] In this catalytic guanylation reaction, an amine that acts as a nucleophile is added to a carbodiimide. Metal-catalyzed aminoguanylation reactions between 1,1-disubstituted hydrazines and carbodiimides giving amino guanidines have been reported;[9g,10b] however, we envisioned that 1,2-diarylhydrazines could be alternative nucleophiles for catalytic guanylation reactions if cleavage of the N—N bond in 1,2-diarylhydrazine occurred. Herein, we report cleavage of the N—N bond of 1,2-diarylhydrazines in alkyllithium-catalyzed guanylation reactions of 1,2-diarylhydrazines with carbodiimides to give guanidines and azo compounds (Scheme 1). In this N—N bond cleavage process, no additives including reductants, oxidants, bases, or external protons were required. The reaction mechanism was investigated through the isolation, characterization, and reaction studies of two important amido lithium intermediates and an ArHN-substituted guanidine.

RESULTS AND DISCUSSION

Catalytic Guanylation Reaction of 1,2-Diarylhydrazine with Carbodiimide. *a. Condition Screening.* A 1:1 reaction between 1,2-diphenylhydrazine (PhNHNHPh) and *N,N′*-diisopropylcarbodiimide (DIC) was performed. No reaction would take place without catalysts even at 110 °C for 24 h (Table 1, entry 1). However, when the half-sandwich rare-earth catalyst (1 mol %) [{$Me_2Si(C_5Me_4)(NPh)$}$Y(CH_2SiMe_3)(thf)_2$] (**1**)[11i] or [$Cp^{4PrPh}Y(CH_2SiMe_3)_3$][$Li(thf)_3(OEt_2)$] (**2**)[11c] was added to the mixture of 1,2-diphenylhydrazine and DIC, the guanidine product PhN=C(NH^iPr_2)$_2$ (**3a**) and *trans*-azobenzene (*trans*-PhN=NPh) were obtained instead of the expected product ^{i}PrN=C(NH^iPr)NPhNHPh (**4**) (Table 1, entries 2 and 3). Other rare-earth catalysts such as $Y(CH_2SiMe_3)_3(thf)_2$ or alkali-metal catalysts such as $LiCH_2TMS$, $LiN(TMS)_2$, $NaN(TMS)_2$, and $KN(TMS)_2$[10g] all could serve as excellent catalyst precursors to give **3a** and *trans*-azobenzene (Table 1, entries 4−8, respectively). Other solvents such as THF and toluene afforded similar results.

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Scheme 1. Different Modes of N—N Bond Cleavage of Hydrazines

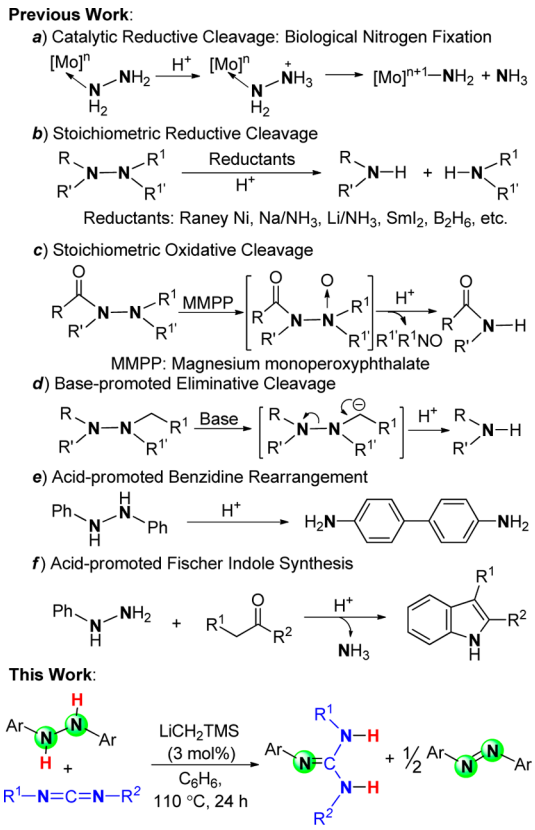
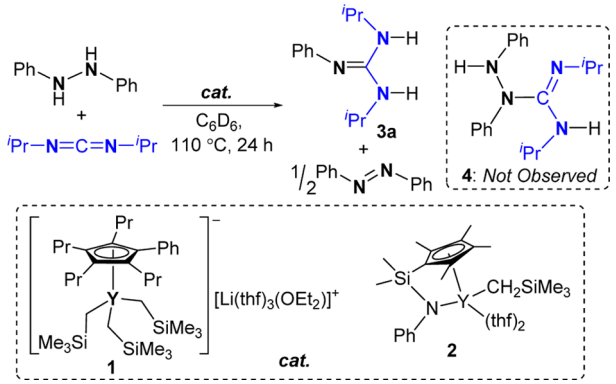


Table 1. Screening of the Catalytic Activity of the Reaction between PhNHNHPh and DIC[a]

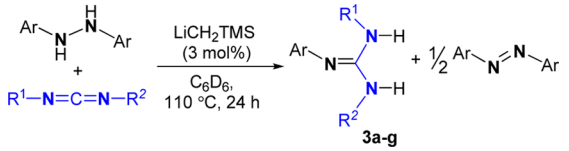


entry	catalyst	loading (mol %)	yield (%)[b]
1	none	0	0
2	**1**	1	84
3	**2**	1	96
4	$Y(CH_2TMS)_3(thf)_2$	1	44
5	$LiCH_2TMS$	3	96
6	$LiN(TMS)_2$	3	97
7	$NaN(TMS)_2$	3	88
8	$KN(TMS)_2$	3	93

[a]Conditions: PhNHNHPh, 0.20 mmol; DIC, 0.20 mmol. [b]Yields were determined by ^{1}H NMR spectroscopy.

b. Substrate Scope. $LiCH_2TMS$ was chosen as the catalyst precursor for the reaction between 1,2-diarylhydrazine and various carbodiimides. Representative results are shown in Table 2. For isopropyl-, cyclohexyl-, phenyl-, and tolyl-substituted carbodiimides, their corresponding guanidines could all be obtained in moderate to good yields (Table 2).

Table 2. Substrate Scope of the Catalytic Guanylation Reaction between ArNHNHAr and Carbodiimides[a]



entry	R^1	R^2	Ar	yield (%)
1	^{i}Pr	^{i}Pr	Ph	**3a**: 89
2	Cy	Cy	Ph	**3b**: 93
3	Ph	Ph	Ph	**3c**: 71
4	^{i}Pr	^{i}Pr	Tol	**3d**: 82
5	Cy	Cy	Tol	**3e**: 88
6	Tol	Tol	Tol	**3f**: 96
7	^{i}Pr	^{i}Pr	*o*-MeC_6H_4	**3g**: 85
8	^{i}Pr	^{i}Pr	4-ClC_6H_4	**3h**: 93
9	^{i}Pr	^{i}Pr	4-BrC_6H_4	**3i**: 64
10	^{i}Pr	^{i}Pr	4-^{t}BuC_6H_4	**3j**: 46

[a]Conditions: ArNHNHAr, 1.0 mmol; carbodiimides, 1.0 mmol.

When the reaction of 1-methyl-1-phenylhydrazine or 1,1-diphenylhydrazine with DIC was tested under the present conditions, only amino guanidines, which were similar to those of the work of Gade and Bergman, were observed. The present reaction mode between 1,2-disubstituted arylhydrazines and carbodiimides is different from that of catalytic amino-guanylation reactions between 1,1-disubstituted hydrazines and carbodiimides in which N—N bond cleavage is not observed.[9g,10b]

Mechanistic Studies on N—N Bond Cleavage. Cleavage of the N—N bond in 1,2-diarylhydrazine has apparently taken place in the aforementioned catalysis process. However, the reaction conditions applied in this study are totally different from the known conditions that are used for the cleavage of N—N bonds in hydrazines. To explore this reaction mechanism, a stoichiometric reaction was performed (Scheme 2). Initially, the reaction between $LiCH_2TMS$ and PhNHNHPh in THF at room temperature yielded the lithium hydrazide PhNHNPhLi (**5**). Recrystallization of **5** in THF/hexane solution afforded the THF-coordinated complex **5′** in 97% yield (Scheme 2*a*). **5′** was characterized by ^{1}H and ^{13}C NMR spectra. Single crystal X-ray diffraction analysis indicated that **5′** was a solid-state, unsymmetric trimer (Figure 1). Li1 took a five-coordinate mode bonded by one thf and four N atoms, whereas Li2 adopted a four-coordinate fashion bonded by one thf and three N atoms. In contrast, Li3 bonded to one thf and two N atoms.

Heating the benzene solution of **5′** at 110 °C for 24 h did not lead to any change in ^{1}H NMR spectra, indicating that the N—N bond cleavage did not occur at this step. Then, 1 equiv of DIC was added to the benzene solution of **5′** at room temperature. After the sample had been mixed for 4 h, a large amount of white powder **6** precipitated. Via evaporation of the THF/hexane solution of **6**, single crystals of **6′** were obtained (Scheme 2*b*).[13] X-ray analysis revealed that **6′** was a centrosymmetric dimer (Figure 2). The bridged Li atom adopted a distorted tetrahedral coordination environment and

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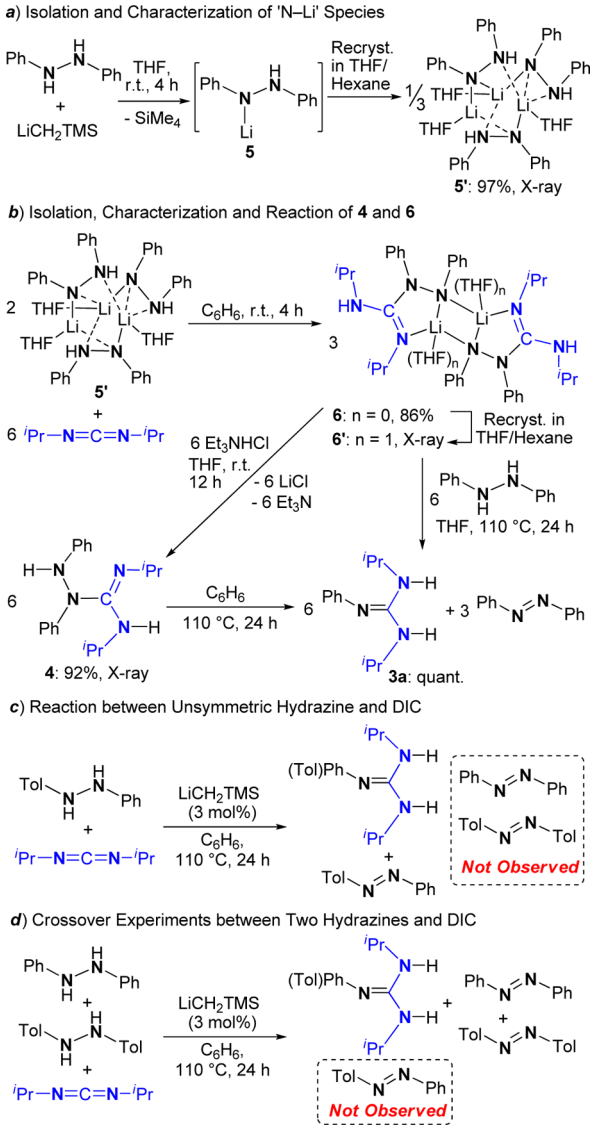
Scheme 2. Mechanistic Studies



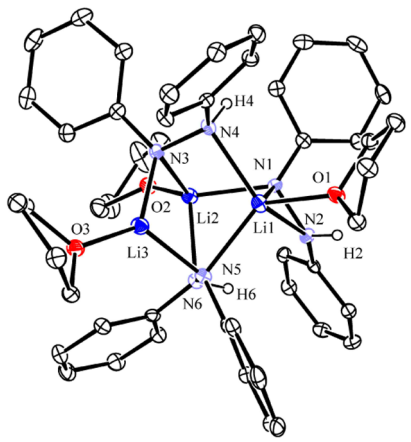


Figure 1. ORTEP drawing of $5'\cdot C_6H_{14}$ with 30% thermal ellipsoids. Hexane and hydrogen atoms, except those connected to N atoms, are omitted for clarity.

was supported by one thf and two guanidino-amide ligands; both of the guanidino-amide ligands adopted the $\eta^1{:}\mu^2$ mode.

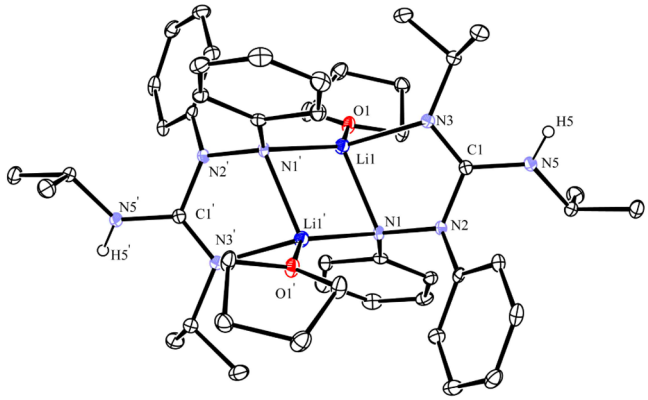


Figure 2. ORTEP drawing of **6′** with 30% thermal ellipsoids. Hydrogen atoms, except those connected to N atoms, are omitted for clarity.

The length of the C1—N3 bond (1.292(2) Å) was significantly shorter than that of the C1—N5 bond (1.376(2) Å) or the C1—N2 bond (1.406(2) Å), which indicated that C1—N3 was a double bond. The formation of **6** could involve two steps: the nucleophilic addition of lithium hydrazide from **5′** to the central carbon of DIC, followed by proton transfer from the PhNH moiety to the ^{i}PrN═C moiety. This process might be driven by the increasing acidity of PhNH due to coordination of the Lewis-acidic lithium and the stability of the fused [5.4.5] ring. Both **5′** and **6** showed comparable catalytic activity with $LiCH_2TMS$ in the aforementioned guanylation reaction.

The thermal stability of **6** was also examined by heating it in THF solution at 110 °C for 24 h; no change in ^{1}H NMR spectra was detected. Then, the stoichiometric reaction between **6** and PhNHNHPh was conducted in THF. After 24 h at room temperature, the mass spectrum data of the reaction mixture showed the existence of both **4** and N—N bond cleaved product **3a**. When the reaction between **6** and PhNHNHPh was conducted at 110 °C for 24 h, **3a** and *trans*-PhN═NPh were cleanly formed with a trace amount of **4** in the ^{1}H NMR spectrum. If **6** was treated with 1 equiv of Et_3NHCl at room temperature, **4** was obtained in 92% yield (Scheme 2*b* and Figure 3). Being different from **5′** and **6**, **4** was

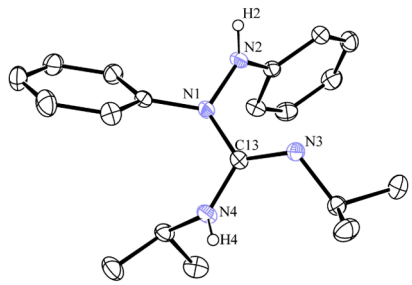


Figure 3. ORTEP drawing of **4** with 30% thermal ellipsoids. Hydrogen atoms, except those connected to N atoms, are omitted for clarity.

not stable at elevated temperatures. When **4** was heated at 110 °C for 24 h, it quantitatively transformed to **3a** and *trans*-PhN═NPh. This experiment clearly showed that cleavage of the N—N bond should occur during further transformation of **4**.

The catalytic reaction of unsymmetric hydrazine (TolNHNHPh) and DIC was performed in the presence of $LiCH_2TMS$ (3 mol %) at 110 °C for 24 h (Scheme 2*c*). In

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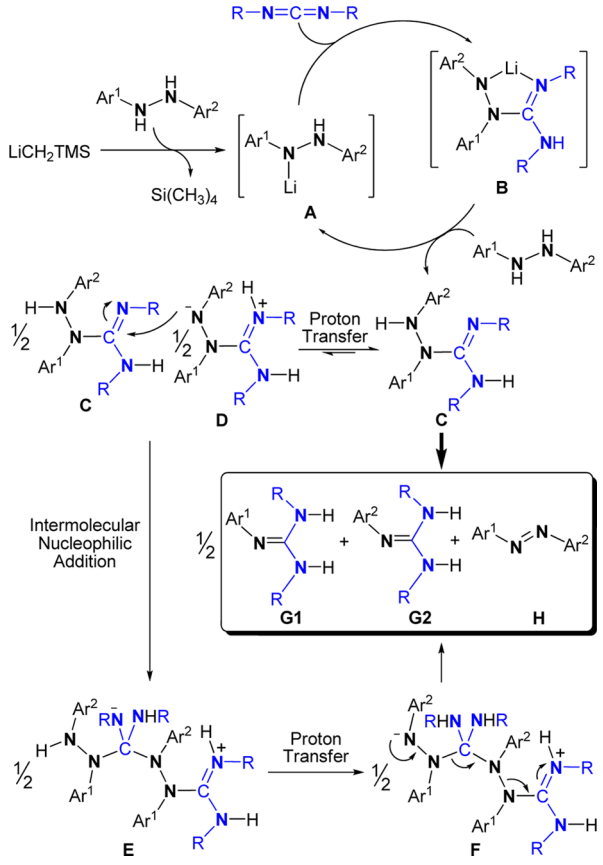
addition to guanidines PhN=C(NH^{i}Pr$_2$)$_2$ and TolN=C-(NH^{i}Pr$_2$), only one azo complex (TolN=NPh) was detected by a GC/MS spectrometer. Furthermore, the crossover experiment among PhNHNHPh, TolNHNHTol, and DIC showed that TolN=NPh was not observed (Scheme 2*d*). These results showed that formation of the azo complex ArN=NAr should come from the proton abstraction of 0.5 equiv of ArNHNHAr; the other half of ArNHNHAr should undergo N—N bond cleavage.

Based on this experimental evidence, a possible mechanism is proposed in Scheme 3. Deprotonation of 1,2-diarylhydrazine by

Scheme 3. A Possible Mechanism for the Catalytic Guanylation Reaction of 1,2-Diarylhydrazine with Carbodiimides



LiCH$_2$TMS affords lithium hydrazide **A**. Nucleophilic attack of **A** on carbodiimide should give **B**. In the presence of Ar^{1}NHNHAr^2, **B** is protonated to give guanidine **C** and regenerate the active species **A**. Then, an intramolecular proton shift in **C** gives **D**. This is likely driven by the strong basicity of the guanidine unit. The intermolecular nucleophilic addition between **C** and **D** should give the adduct **E**, which undergoes proton transfer to yield **F**. An intramolecular rearrangement in **F** gives the final products **G1**, **G2**, and the azo-compound **H**. During the rearrangement of **F**, the N—N bond from one hydrazine unit is cleaved, whereas the N—N bond from the other hydrazine unit furnishes the N=N bond of **H**.

CONCLUSIONS

In summary, we have disclosed the first alkyllithium-catalyzed guanylation reaction of 1,2-diarylhydrazine with carbodiimides to give guanidine and azo compounds. The N—N bond cleavage of 1,2-diarylhydrazine, which was driven by an intramolecular proton shift, did not require a variable oxidation state on a metal center and/or additives. The basicity of the guanidino group played an important role in this cleavage process. The isolation, characterization, and reaction studies of two important amido lithium intermediates and an ArHN-substituted guanidine give strong support to the proposed mechanism.

EXPERIMENTAL SECTION

General Methods. All reactions were conducted under slightly positive dry nitrogen pressure using standard Schlenk line techniques or under a nitrogen atmosphere in a glovebox. The nitrogen in the glovebox was constantly circulated through a copper/molecular sieves catalyst unit. The oxygen and moisture concentrations in the glovebox atmosphere were monitored by an O_2/H_2O Combi-Analyzer to ensure both were always below 1 ppm. Unless otherwise noted, all starting materials were commercially available and were used without further purification. TolNHNHPh, TolNHNHTol, and *o*-MeC$_6$H$_4$NHNHC$_6$H$_4$Me-*o* were prepared according to known procedures.[14] Solvents were purified by a solvent purification system and dried over molecular sieves in a glovebox. Organometallic samples for NMR spectroscopic measurements were prepared in a glovebox by the use of J. Young valve NMR tubes (Wilmad 528-JY). ^{1}H and ^{13}C NMR spectra were recorded on a 500 MHz (FT, 500 MHz for ^{1}H, 125 MHz for ^{13}C) or 400 MHz (FT, 400 MHz for ^{1}H, 100 MHz for ^{13}C) spectrometer at room temperature. Mass spectra (MS) were recorded on a GC/MS spectrometer using an EI source. High-resolution mass spectra (HRMS) were recorded on an FTMS mass spectrometer using an ESI source.

Typical Procedures for the Catalytic Guanylation Reaction between 1,2-Diarylhydrazine and Carbodiimides. *a. NMR Tube Reaction.* In a glovebox, a J. Young valve NMR tube was charged with catalyst (0.002 or 0.006 mmol), C$_6$D$_6$ (0.5 mL), PhNHNHPh (36.8 mg, 0.20 mmol), and DIC (25.3 mg, 0.20 mmol). The tube was taken out of the glovebox and then heated at 110 °C in an oil bath for 24 h. Formation of **3a** was monitored by ^{1}H NMR spectra.

b. Preparative Scale Reaction. In a glovebox, a benzene solution (1 mL) of LiCH$_2$TMS (2.8 mg, 0.03 mmol) and a benzene solution (5 mL) of PhNHNHPh (184.2 mg, 1.00 mmol) were added to a Schlenk tube. Then, a benzene solution (3 mL) of DIC (126.2 mg, 1.00 mmol) was added to the above reaction mixture. The Schlenk tube was removed from the glovebox, and the mixture was stirred at 110 °C for 24 h. After the solvent was removed under vacuum, an orange−red residue was purified by silica-gel column chromatography using petrol ether and EtOAc as eluents to give colorless solid **3a** (196.0 mg, 0.89 mmol) in 89% yield. The NMR data of **3a**−**g** were consistent with previous reports.[11c,f,15]

3a: colorless solid[11c] (89% yield, 196 mg, 1 mmol scale); ^{1}H NMR (500 MHz, C$_6$D$_6$, Me$_4$Si) δ 0.90 (d, J = 6.1 Hz, 12H), 3.65 (br, 4H), 6.92 (t, J = 7.3 Hz, 1H), 7.14 (d, J = 8.1 Hz, 2H), 7.25 (t, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, C$_6$D$_6$, Me$_4$Si) δ 23.2, 43.3, 121.5, 123.7, 129.7, 149.8, 151.3.

3b: colorless solid[11c] (93% yield, 277 mg, 1 mmol scale); ^{1}H NMR (400 MHz, CDCl$_3$, Me$_4$Si) δ 1.04−1.20 (m, 6H), 1.30−1.40 (m, 4H), 1.58−1.62 (m, 2H), 1.66−1.71 (m, 4H), 1.99−2.02 (m, 4H), 3.41 (br, 2H), 6.85 (d, J = 8.0 Hz, 2H), 6.92 (t, J = 7.3 Hz, 1H), 7.24 (t, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, C$_6$D$_6$, Me$_4$Si) δ 25.2, 25.9, 34.0, 50.4, 121.4, 123.8, 129.6, 149.4, 151.8.

3c: colorless solid[15] (71% yield, 204 mg, 1 mmol scale); ^{1}H NMR (400 MHz, CDCl$_3$, Me$_4$Si) δ 7.03 (t, J = 7.3 Hz, 3H), 7.18 (d, J = 7.5 Hz, 6H), 7.28 (t, J = 7.8 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$, Me$_4$Si) δ 121.4, 123.1, 129.2, 142.2, 145.0. The NH signal was not observed in the ^{1}H NMR spectrum.

3d: colorless solid[11f] (82% yield, 191 mg, 1 mmol scale); ^{1}H NMR (400 MHz, CDCl$_3$, Me$_4$Si) δ 1.15 (d, J = 6.3 Hz, 12H), 2.28 (s, 3H), 3.57 (br, 2H), 3.74−3.77 (m, 2H), 6.74 (d, J = 7.9 Hz, 2H), 7.04 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$, Me$_4$Si) δ 20.8, 23.4, 43.3, 123.3, 129.9, 130.5, 147.4, 150.4.

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3e: colorless solid[11f] (88% yield, 276 mg, 1 mmol scale); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 1.04−1.19 (m, 6H), 1.29−1.38 (m, 4H), 1.57−1.69 (m, 6H), 1.98−2.00 (m, 4H), 2.27 (s, 3H), 3.40 (br, 2H), 3.65 (br, 2H), 6.74 (d, J = 7.8 Hz, 2H), 7.03 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 20.8, 24.9, 25.7, 33.8, 50.2, 123.4, 129.8, 130.5, 147.5, 150.3.

3f: colorless solid[11f] (96% yield, 317 mg, 1 mmol scale); ^{1}H NMR (400 MHz, C_6D_6, Me_4Si) δ 2.08 (s, 9H), 5.68 (br, 2H), 6.90 (d, J = 7.8 Hz, 6H), 7.04 (d, J = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, C_6D_6, Me_4Si) δ 20.7, 121.8, 130.0, 132.2, 140.8, 145.5.

3g: colorless solid[11f] (85% yield, 99.5 mg, 0.50 mmol scale); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 1.15 (d, J = 6.3 Hz, 12H), 2.15 (s, 3H), 3.53−3.76 (m, 4H), 6.78 (d, J = 7.7 Hz, 1H), 6.88 (t, J = 7.2 Hz, 1H), 7.08 (t, J = 7.0 Hz, 1H), 7.14 (d, J = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 18.1, 23.4, 43.4, 122.1, 123.3, 126.7, 130.5, 131.7, 147.5, 149.5.

3h: colorless solid[11f] (93% yield, 119.7 mg, 0.50 mmol scale); ^{1}H NMR (400 MHz, C_6D_6, Me_4Si) δ 0.86 (d, J = 6.4 Hz, 12H), 3.35 (br, 2H), 3.57 (br, 2H), 6.86 (d, J = 8.6 Hz, 2H), 7.17 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, C_6D_6, Me_4Si) δ 23.2, 43.2, 124.9, 126.3, 129.7, 149.8, 150.2.

3i: colorless solid[11f] (64% yield, 95.0 mg, 0.50 mmol scale); ^{1}H NMR (400 MHz, C_6D_6, Me_4Si) δ 0.85 (d, J = 6.4 Hz, 12H), 3.34 (br, 2H), 3.56 (br, 2H), 6.81 (d, J = 8.6 Hz, 2H), 7.31 (d, J = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, C_6D_6, Me_4Si) δ 23.2, 43.3, 113.9, 125.4, 132.6, 149.8, 150.6.

3j: colorless solid[11c] (46% yield, 63.0 mg, 0.50 mmol scale); ^{1}H NMR (400 MHz, C_6D_6, Me_4Si) δ 0.92 (d, J = 6.3 Hz, 12H), 1.27 (s, 9H), 3.70 (br, 4H), 7.09−7.13 (m, 2H), 7.30−7.34 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6, Me_4Si) δ 23.2, 31.7, 34.2, 43.3, 123.2, 126.4, 143.6, 148.6, 149.9.

Catalytic Guanylation Reaction of Unsymmetric 1,2-Diarylhydrazine and DIC. In a glovebox, a benzene solution (1 mL) of $LiCH_2TMS$ (0.6 mg, 0.006 mmol) and a benzene solution (3 mL) of TolNHNHPh (39.7 mg, 0.20 mmol) were added to a Schlenk tube. Then, a benzene solution (3 mL) of DIC (25.2 mg, 0.20 mmol) was added to the above reaction mixture. The Schlenk tube was removed from the glovebox, and the mixture was stirred at 110 °C for 24 h. The reaction was monitored by GC/MS spectrometry; for azo complexes, only the peak of m/z = 196 was observed. The ^{1}H NMR and ^{13}C NMR spectra of the isolated azo complex also indicated the formation of TolN═NPh.

Preparation of 5′. A THF solution (∼1 mL) of $LiCH_2TMS$ (282.6 mg, 3.0 mmol) was added to a THF solution (15 mL) of PhNHNHPh (552.6 mg, 3.0 mmol); the solution turned light green immediately. The mixture was stirred for 4 h at room temperature. Evaporation of volatiles gave a light green powder. The powder was washed with hexane and recrystallized in THF/hexane at −20 °C. After the sample had been dried under a vacuum, **5′**·C_6H_{14} was obtained as a white powder (848 mg, 0.97 mmol, 97% yield). Single crystals of **5′**·C_6H_{14} suitable for X-ray analysis could be grown from THF/hexane for 2 days at room temperature: ^{1}H NMR (500 MHz, C_6D_6, Me_4Si) δ 0.88 (t, J = 7.0 Hz, 6H), 1.19−1.21 (m, 12H), 1.23−1.27 (m, 8H), 3.31 (t, 12H), 5.66 (br, 3H), 6.71 (br, 18H), 7.09−7.12 (m, 12H); ^{13}C NMR (125 MHz, C_6D_6, Me_4Si) δ 14.3, 23.0, 25.3, 31.9, 68.7, 113.3, 116.7, 129.7, 155.3. The hexane in the unit cell was partially pumped away, and therefore, the hexane integral was not accurate. The aromatic carbon may degenerate in solution.

Preparation of 6. A benzene solution (10 mL) of **5′** (848 mg, 0.97 mmol) was added to a benzene solution of DIC (367 mg, 2.9 mmol). After the sample had been stirred for 4 h, a large amount of white powder precipitated; then, the solvent was decanted. The residual white solid was washed by benzene three times. Any residual solvent was removed under vacuum. **6** was obtained as a white powder (787 mg, 2.49 mmol, 86% yield): ^{1}H NMR (400 MHz, THF-d_8) δ 1.08−1.13 (m, 24H), 3.41−3.58 (m, 2H), 3.90 (br, 2H), 4.56 (d, J = 6.9 Hz, 2H), 5.80 (br, 2H), 6.21 (br, 2H), 6.35 (br, 2H), 6.64−6.67 (m, 6H), 6.99 (t, J = 7.6 Hz, 4H), 7.13 (d, J = 7.4 Hz, 4H); ^{13}C NMR (100 MHz, THF-d_8) δ 19.8, 21.8, 43.4, 43.7, 104.8, 108.9, 115.7, 116.8, 125.4, 126.7, 148.9, 156.4, 161.4. Single crystals of **6′** suitable for X-ray analysis could be grown from THF/hexane for 2 days at room temperature.

Preparation of 4. Et_3NHCl (275 mg, 2.0 mmol) was added to a THF solution (5 mL) of **6** (633 mg, 2.0 mmol) at room temperature. The mixture was stirred overnight, and the solvent was removed under reduced pressure. The residue was extracted with toluene three times. Then, the extract was dried under vacuum. The residual solid was washed by hexane. **4** was obtained as a white solid (573 mg, 1.84 mmol, 92% yield) after any remaining hexane was removed under reduced pressure. Single crystals of **4** suitable for X-ray analysis could be grown from THF/hexane at room temperature: ^{1}H NMR (500 MHz, CD_2Cl_2, Me_4Si) δ 1.02 (br, 12H), 3.57 (br, 2H), 3.66 (br, 1H), 6.85 (t, J = 7.3 Hz, 1H), 6.94 (d, J = 7.9 Hz, 2H), 6.98 (t, J = 7.4 Hz, 1H), 7.19−7.23 (m, 4H), 7.25 (t, J = 7.9 Hz, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2, Me_4Si) δ 24.2, 46.1, 114.8, 119.0, 120.8, 122.8, 129.1, 129.3, 148.9, 149.9. One signal of NH was not observed in the ^{1}H NMR spectrum, and one signal of carbon was not observed in the ^{13}C NMR spectrum. HRMS m/z: $[M + H]^+$ calcd for $C_{19}H_{27}N_4$, 311.2230; found, 311.2234.

X-ray Crystallographic Studies. Crystals of **4**, **5′**, and **6′** suitable for X-ray analysis were grown as described above. The crystals were wrapped in mineral oil and then frozen at low temperature. Data collections for **4** were performed at 180 K on a SuperNova diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). Data collections for **5′** and **6′** were performed at 100 K on a SuperNova diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). Using Olex2,[16a] the structures of **4**, **5′**, and **6′** were solved with the Superflip structure solution program using Charge Flipping[16b] and refined with the XL refinement package using least-squares minimization. Refinement was performed on F^2 anisotropically for all of the non-hydrogen atoms by the full-matrix least-squares method. The hydrogen atoms connected to N atoms in **5′** were identified according to difference electron density. Other hydrogen atoms were placed at the calculated positions and were included in the structure calculation without further refinement of their parameters. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre with supplementary publication numbers: CCDC 1017747 (**4**), CCDC 1017748 (**5′**·C_6H_{14}), and CCDC 1017749 (**6′**). These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. The thermal ellipsoid plots in the figures were drawn by Ortep-3 v1.08.[16c]

■ ASSOCIATED CONTENT

Supporting Information

Additional NMR data, copies of ^{1}H NMR and ^{13}C NMR spectra of all new compounds, crystallographic tables, and X-ray crystallographic data in cif format. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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