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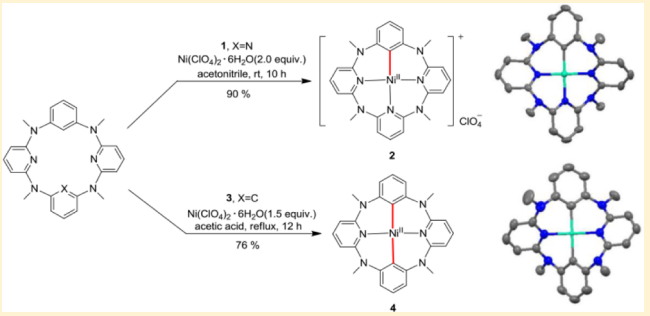
Macrocyclic Aryl−Nickel(II) Complexes: Synthesis, Structure, and Reactivity Studies

Chi Yang, Wen-Di Wu, Liang Zhao,* and Mei-Xiang Wang*

The Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology (Ministry of Education), Department of Chemistry, Tsinghua University, Beijing 100084, People's Republic of China

Supporting Information

ABSTRACT: The synthesis, characterization, and reactivity of the monoaryl−Ni(II) compound **2** and the diaryl−Ni(II) compound **4** formed through the direct electrophilic metalation of two macrocyclic azacalix[*m*]arene[*n*]pyridine ligands are described. Compound **4** was much more stable in protic solvents and acids than the monoaryl−Ni(II) compound **2**. Moreover, **2** can react with a variety of nucleophiles, resulting in the formation of C−C, C−O, C−Br, and C−N bonds. In contrast, compound **4** exhibited very inert reactivity upon reaction with a large numberof nucleophiles. Interestingly, compound **2** was also capable of reacting with several less bulky alkyl halides to form new C−C bonds, while the same procedure is inapplicable to **4**. The study reported in this work provides a thorough investigation on the reactivity of aryl−Ni(II) species that should facilitate comprehension of the detailed mechanism of nickel-catalyzed C−H functionalization.



INTRODUCTION

From the standpoints of economics and versatility, nickel is a privileged metal for the direct conversion of C−H bonds into C−C, C−O, C−N, and C−halogen bonds.[1] In contrast to its precious-metal congeners Pd and Pt, nickel is widely recognized as a low-cost and sustainable commodity metal. The unique electron configuration of Ni ($[Ar]4s^23d^8$), different from that of Pd ($[Kr]4d^{10}$) and Pt ($[Xe]4f^{14}5d^96s^1$), engenders the nickel element with a wide range of oxidation states from 0, +1, +2, and +3[2] to the recently reported +4,[3] which greatly increases its chemical versatility in catalytic reactions. Therefore, the use of nickel in C−H functionalization processes has recently received particular attention.[4] Many unique transformations have been reported for the functionalization of sp^2 and sp^3 C−H bonds.[5] For example, Hiyama and co-workers have reported indole C−H bond activation by $Ni(COD)_2$ followed by the insertion of different alkynes to yield a series of hydroheteroarylation products.[6] A similar transformation was also reported by Chatani to synthesize various isoquinolone derivatives.[7] In addition to the Ni(0) compounds, Ni(II) salts can also be utilized in C−H functionalizations. Miura and co-workers have reported nickel(II)-catalyzed direct C−H arylation and alkenylation of heteroarenes with organosilicon reagents.[8] A postulated catalytic mechanism involved several steps, including electrophilic aromatic metalation, transmetalation, reductive elimination, and oxidation by Ni(II). In addition, despite the absence of a C−H activation step, Fu's seminal work reported a novel Ni(I/II/III) catalytic cycle for nickel-catalyzed Negishi arylations of propargylic bromides.[9] However, despite the great number of Ni-catalyzed organic transformations, relatively high catalyst loading, high temperature requirements, and limitations in substrate scope restrict the practicality of the nickel-catalyzed C−H functionalization. Obviously, insightful comprehension of the detailed mechanism of the nickel-catalyzed C−H activation and the subsequent C−C and C−heteroatom bond formation would be very helpful in improving the catalytic efficiency of various nickel catalysts.

In the reported nickel-catalyzed aryl C−H bond functionalization reactions,[4] aryl−Ni(II) complexes are thought to be the key intermediate regardless of their generation by oxidative addition or direct electrophilic aromatic metalation. In most cases, subsequent reductive elimination of the intermediates derived from the ligand exchange of aryl−Ni(II) complexes with various nucleophiles accounts for the generation of the final C−C and C−heteroatom coupling compounds. Kochi and co-workers have previously synthesized a series of arylalkylnickel(II) complexes and systematically investigated the kinetics of the reductive elimination step.[10] Recently, Itami and co-workers detailedly investigated the mechanism of the Ni(0)-catalyzed C−H/C−O coupling of benzoxazole and naphthalen-2-yl pivalate by isolating the key C−O oxidative addition intermediate $Ar-Ni^{II}-OR$.[11] Nevertheless, to date the systematic reactivity studies of aryl−Ni(II) complexes have remained very poor. Herein we report the syntheses of two aryl−Ni(II) compounds formed through the direct electrophilic metalation of two macrocyclic azacalix[*m*]arene[*n*]pyridine ligands (*m*, *n* = 1, 3 and 2, 2).[12] The structure and

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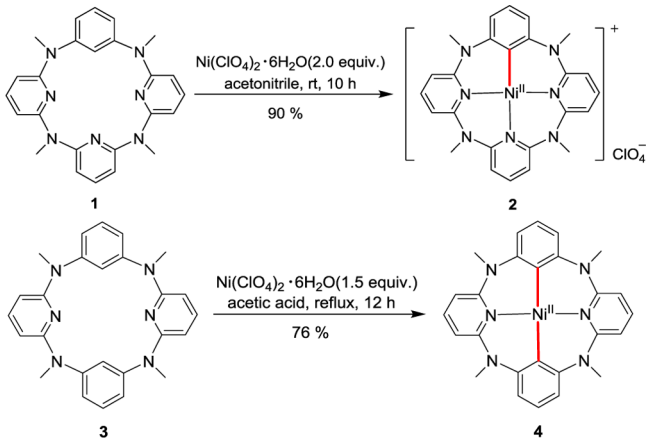
physicochemical properties of the monoaryl−Ni(II) compound **2** and the diaryl−Ni(II) compound **4** have been thoroughly characterized by different techniques, including X-ray crystallography, X-ray photoelectron spectroscopy (XPS), and cyclic voltammetry (CV). In contrast to the chemical passivity of the diaryl−Ni(II) compound **4**, the monoaryl−Ni(II) compound **2** can react with a large number of nucleophiles and electrophiles to construct C−C, C−O, C−N, and C−Br bonds. Elucidation of the reactivity difference between monoaryl− and diaryl−Ni(II) compounds provides basic information for understanding Ni-catalyzed or -mediated C−H functionalization reactions.

RESULTS AND DISCUSSION

Synthesis and Characterization of Aryl−Ni(II) Compounds 2 and 4. We have recently shown that the azacalix[1]arene[3]pyridine **1** can undergo electrophilic aromatic metalation to generate arylcopper(II) compounds.[13] According to a similar procedure (Scheme 1), reaction of **1** with 2 equiv of $Ni(ClO_4)_2$ in acetonitrile at room temperature resulted in the formation of the monoaryl−Ni(II) compound **2** as a yellow powder in 90% yield. However, the same procedure was unsuccessful in the metalation of azacalix[2]arene[2]pyridine **3**. We therefore referred to the previous synthetic procedure of aryl−Pd(II) complexes[14] and carried out the synthesis of the diaryl−Ni(II) compound **4** in acetic acid at elevated temperature. Finally, compound **4** was obtained in 76% yield.

Scheme 1. Synthesis of Monoaryl−Ni(II) Compound 2 and Diaryl−Ni(II) Compound 4



Crystals of compound **2** of quality suitable for X-ray crystallography were obtained by diffusing diethyl ether into the dichloromethane/methanol solution of **2**. As shown in Figure 1, the crystal structure of **2** contains the encapsulated nickel atom Ni1 coordinated by a deprotonated azacalix[1]arene[3]pyridine. A perchlorate counteranion is located at the top of the nickel atom but at a distance far beyond that of a Ni−O coordination bond. Ni1 exhibits a typical square-planar coordination configuration, which is evidenced by the linear ∠N1−Ni1−N5 and ∠N3−Ni1−C24 bond angles of 178.6(2) and 178.3(2)°. It is notable that the Ni1−C24 bond length (1.881(5) Å) is approximately 0.02 Å shorter than the other three Ni−N bond lengths in the range of 1.897(4)−1.908(5) Å. Upon the occurrence of coordination, the azacalix[1]arene[3]pyridine macrocycle adjusts its 1,3-alternate conformation in the free state[12] to this saddlelike conformation in **2**. In this way, the four coordinated atoms are almost located on the same plane with a very small deviation of 0.023 Å.

In the crystal structure of **4**, the azacalix[2]arene[2]pyridine macrocycle adopts a similar saddle conformation, thus constituting a square-planar coordination geometry for the nickel atom (deviation ∼0.035 Å) as well. The two C−Ni bond lengths Ni1−C6 = 2.001 (7) Å and Ni1−C19 = 2.017(7) Å are shorter than the Ni−N bond lengths (2.043(5)−2.045(5) Å). In general, due to electrostatic interaction the doubly deprotonated azacalix[2]arene[2]pyridine macrocycle in **4** should form a more compact coordination environment in comparison to that of azacalix[1]arene[3]pyridine in **2**. A survey of the biaryl−bipyridine nickel compounds reported in the literature[15] suggests that the Ni−C and Ni−N bond lengths in these compounds lie in the range of 1.85−2.00 Å, comparable to the values in complex **2**. We speculate that the abnormally elongated bond lengths in **4** may be ascribed to the unique cyclic skeleton of the azacalix[2]arene[2]pyridine. A detailed structural comparison of the macrocyclic ligands in **2** and **4** indicates that the separation between two opposite bridging nitrogen atoms in **2** is about 0.4 Å shorter than the values in **4**, suggesting a more curved conformation of the macrocycle in **2**. The more planar conformation of azacalix[2]arene[2]pyridine in **4** may be attributed to the fact that the

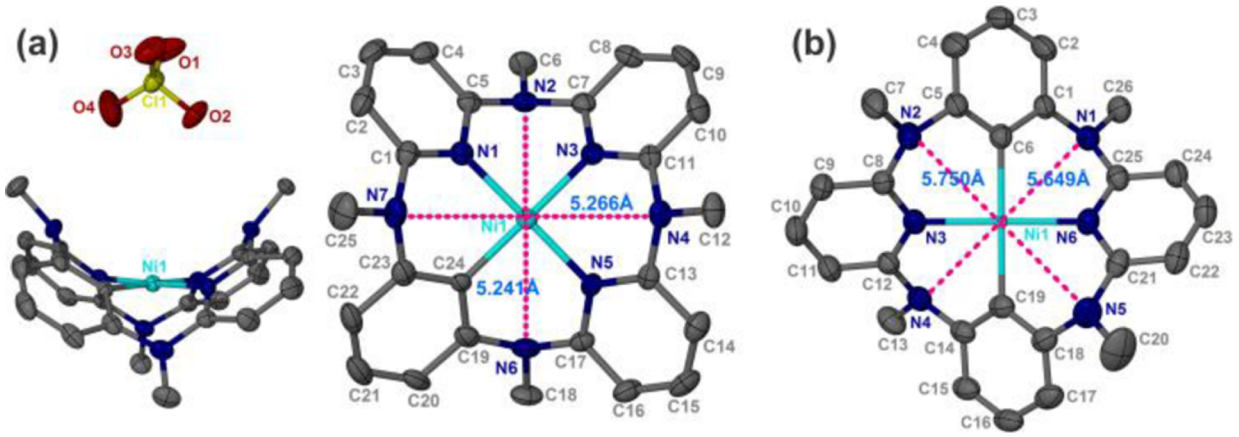


Figure 1. X-ray crystal structure of (a) the monoaryl−Ni(II) compound **2** and (b) the diaryl−Ni(II) compound **4** with ellipsoids at the 40% probability level.

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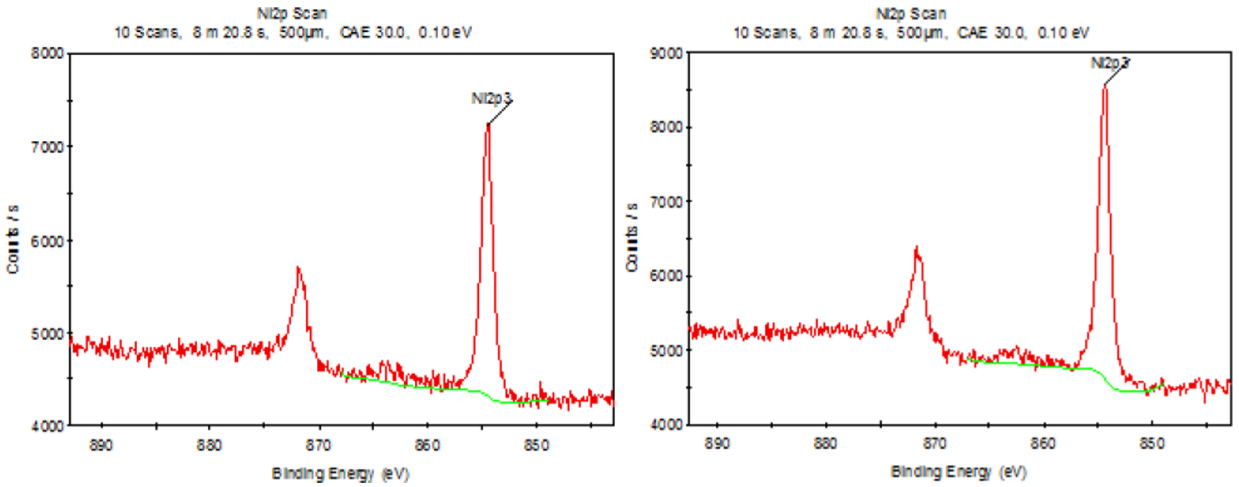

Figure 2. XPS spectra of (left) **2** and (right) **4**.

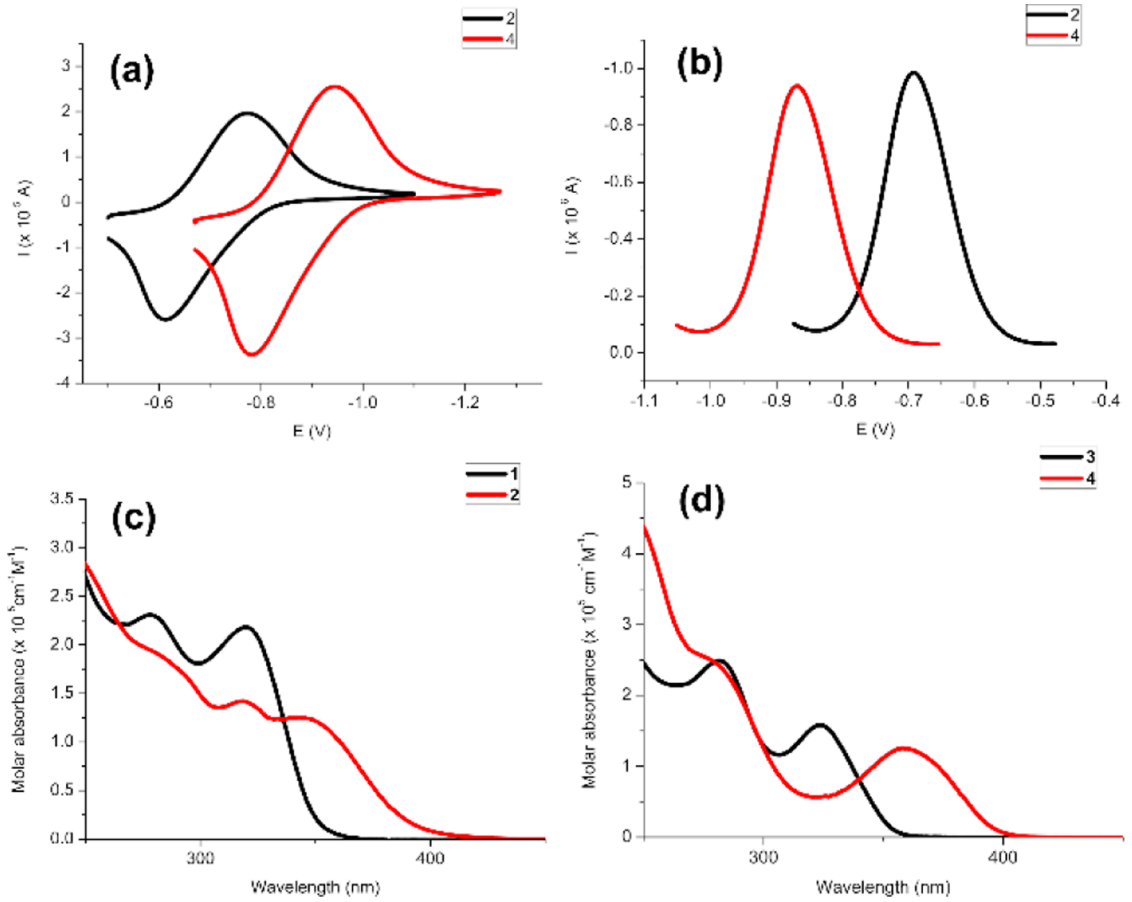

Figure 3. (a) Cyclic voltammograms of **2** and **4** in CH_3CN at 298 K. (b) DPV of **2** and **4** in CH_3CN at 298 K. The concentration of **2** and **4** is 2.0×10^{-3} M. (c) UV/vis spectra of **1** and **2** in CH_3CN at 298 K. (d) UV/vis spectra of **3** and 4 in CH_3CN at 298 K. The concentration of **2** and **4** in (c) and (d) is 2.0×10^{-5} M.

separated N−N and C−C arrangement can weaken the electrostatic and dipole−dipole repulsion.

In order to ensure the +2 oxidation state of the nickel center in **2** and **4**, the XPS measurement was conducted. As shown in Figure 2, the XPS spectra revealed a pair of peaks for each sample (854.4 and 871.6 eV for **2** and 854.5 and 871.8 eV for **4**), which were assigned to the typical $2p_{2/3}$ and $2p_{1/2}$ peaks of the nickel(II) on the basis of previously reported data.[16]

To understand the physicochemical properties of compounds **2** and **4**, their electrochemistry and absorption spectra were investigated. The redox properties were examined by means of CV and differential pulse voltammetry (DPV). As shown in Figure 3a, cyclic voltammograms of **2** and **4** showed a similar reversible redox couple resulting from one-electron reduction and oxidation of the nickel(II) center. The half-wave reduction potentials ($E_{1/2}$) measured by CV agreed quite well with the values obtained by means of DPV (Figure 3b). The

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Table 1. Summary of Physicochemical Properties of 2 and 4

	λ_{max}, nm (ε)[a]	λ_{max}, nm (ε)	λ_{max}, nm (ε)	E_g^{opt}, eV][b]	$E_{1/2}$, mV[c]	HOMO, eV][d]	LUMO, eV][e]
2	285 (1.85)	318 (1.42)	345 (1.25)	2.77	−693	−4.24	−1.47
4	282 (2.45)	358 (1.26)		3.02	−867	−4.01	−0.99

[a]ε is given in units of 10^4 M^{-1} cm^{-1}. [b]$E_g^{opt} = 1240/\lambda_{abs}^{onset}$. [c]Reduction potentials measured by cyclic voltammetry with ferrocene as the standard. [d]HOMO = $-(E_{ox}^{onset} + 4.8$ eV). [e]LUMO = HOMO + E_g^{opt}.

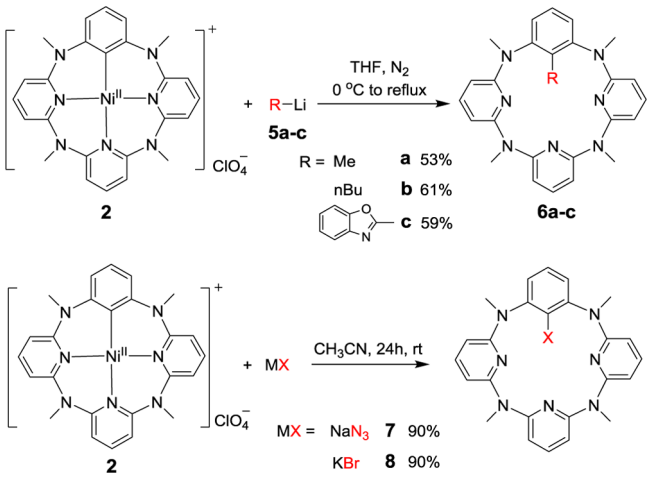
acquired data indicated that compound **2** had a higher $E_{1/2}$ potential of −693 mV in comparison to that of compound **4** (−867 mV). This implied that compound **2** had a greater tendency to be reduced than compound **4**, thus possibly favoring the reductive elimination step. The UV/vis spectra of **2** in acetonitrile exhibited three absorption bands at λ_{max} 285, 318, and 345 nm with molar extinction coefficients (ε) of around 1.25−1.85 × 10^4 M^{-1} cm^{-1} (Table 1). Relative to the three absorption bands of the neat azacalix[1]arene[3]pyridine, all absorption bands of **2** were shifted bathochromically. As for the diaryl−Ni(II) compound **4**, its UV/vis spectra included two absorption bands at λ_{max} 282 and 358 nm with molar extinction coefficients (ε) of 2.45 × 10^4 and 1.26 × 10^4 M^{-1} cm^{-1} (Table 1). A red shift of the absorption bands in comparison with those of the azacalix[2]arene[2]pyridine was observed as well.

From the absorption spectra and the reduction potentials, the estimated energy gap between the LUMO and HOMO (E_g) and both the HOMO and LUMO energy levels of **2** and **4** were obtained and summarized in Table 1. The energy gap of **4** is 0.25 eV larger than that of **2**, while the LUMO orbital of **2** is approximately 0.5 eV lower than that of **4**. In general, the reaction of **2** with nucleophiles, which is mostly related to the LUMO orbital of **2**, is expectedly more favored than that of **4**.

Reactivity Comparison between 2 and 4 with Nucleophiles and Electrophiles. We next embarked on the reactivity studies of the monoaryl−Ni(II) compound **2** and the diaryl−Ni(II) compound **4**. First, the stabilities of **2** and **4** in solution were quite different. In protic solvents such as methanol compound **2** was gradually protonated to give the neat azacalix[1]arene[3]pyridine ligand **1**. The use of acetic acid accelerated this process and generated **1** quantitatively within 4 h. In contrast, compound **4** was stable in protic solvents and even on heating in mild acids. Only the strong acid trifluoroacetic acid can drive the protonated transformation of **4**.

We next employed various nucleophiles, including organolithium reagents, azide, halide, phenol, and hydroxyl, to react with **2** and **4** with the aim of elucidating the reaction difference of these two organonickel(II) compounds. Organolithium reagents **5a−c** were first applied to react with **2** to produce alkylated or arylated azacalix[1]arene[3]pyridine compounds **6a−c** (Scheme 2). Optimization of reaction conditions revealed that the best yield of 60% was achieved when 2 equiv of organolithium was used and the reaction was conducted at 0 °C to reflux temperature, no matter what kind of organolithium (alkyl- or aryllithium) was utilized. However, it has to be pointed out that this carbon−carbon bond formation reaction is time consuming. Generally, over 60 h is necessary for total conversion. Moreover, a similar reaction procedure was applicable to the formation of C−N and C−Br bonds as well. When 2 equiv of sodium azide and potassium bromide was respectively reacted with **2** in acetonitrile, after 24 h the azido- or bromo-substituted azacalix[1]arene[3]pyridine derivatives **7** and **8** were obtained in high yield (90%). In sharp contrast, reaction of the diaryl−Ni(II) compound **4** with the

Scheme 2. Cross-Coupling Reaction between Ar−Ni(II) Complex 2 and Different Nucleophiles



aforementioned nucleophiles (organolithium reagents, NaN_3, and KBr) under the same reaction conditions did not produce any coupling products.

The C−O bond formation was also attempted by conducting the reaction of **2** with different alcohols and phenol in the presence of bases (Table 2). With reference to our previously

Table 2. Reaction Conditions of 2 with O-Containing Nucleophiles

Nu (amt, equiv)	solvent	base (amt, equiv)	temp	time, h	yield, %
MeOH (2)	acetonitrile	DBU (2)	reflux	48	trace
i-PrOH (2)	acetonitrile	DBU (2)	reflux	48	trace
MeONa (2)	acetonitrile		reflux	48	trace
PhOH (2)	acetonitrile	DBU (2)	reflux	48	67
KOH (4)	DMSO/H_2O 30/1		room temp	6	82[a]

[a]The parent macrocyclic azacalix[1]arene[3]pyridine was isolated in 15% yield after workup.

reported C−O coupling reaction of the aryl−Cu(III) analogue of **2**,[17] we carried out the reaction of **2** with methanol in refluxing acetonitrile with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base. Only a trace amount of methoxy-substituted azacalix[1]arene[3]pyridine derivative was obtained. Isopropyl alcohol gave the same negative result. Moreover, it is puzzling that the direct use of CH_3ONa also cannot facilitate the C−O bond formation. In contrast, under the same conditions the cross-coupling reaction between phenol and **2** afforded compound **9** in 67% yield. We hypothesize that very different dissociation constants of $CH_3O^-Na^+$ and $[PhO^-][H\text{-}DBU]^+$ in the organic solvent acetonitrile may account for their biased performance in the C−O coupling reaction. The latter compound has a larger dissociation constant due to the existence of the organic cationic species $[H\text{-}DBU]^+$. Remark-

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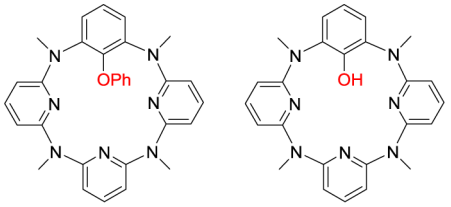
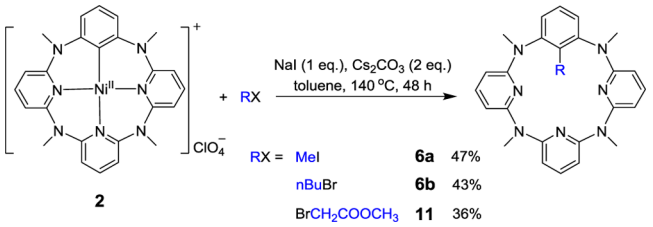
ably, when the typical ionic compound potassium hydroxyl was employed in a mixed solvent of dimethyl sulfoxide (DMSO) and water, a good yield (82%) for the formation of hydroxyl-substituted compound **10** was achieved. Therein water is prerequisite for this reaction. Unfortunately, there were no C−O coupling reactions taking place between **4** and the oxygen-containing nucleophiles.



9 **10**

In addition to the above diverse nucleophiles, it is amazing to find that the monoaryl−Ni(II) complex **2** can react with alkyl halides (Scheme 3). To date, the alkylation of aryl−metal

Scheme 3. Cross-Coupling Reaction between Ar−Ni(II) Complex 2 and Alkyl Halides

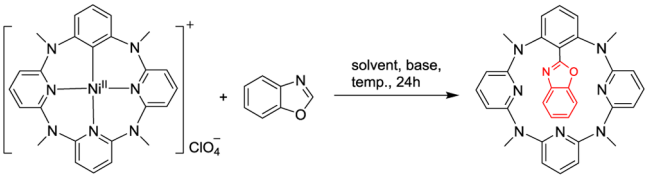


2

complexes via the oxidative addition of alkyl halides is quite limited,[7c−e,f] since such a process involves unfavorable formation of a high-valence metal center and the resulting alkyl metal complexes tend to favor β-hydride elimination rather than the desired reductive elimination. When **2** was mixed with methyl iodide in toluene in the presence of the two additives sodium iodide and cesium carbonate and the mixture was heated to 140 °C for 48 h, the alkylation product **6a** was obtained in 47% yield. It should be pointed out that the two additives are necessary for this transformation. The reactions for the two other primary alkyl halides ^{n}BuBr and $BrCH_2COOMe$ also worked very well according to the same procedure. However, the reaction of **2** with ^{t}BuCl did not produce any desired coupling products, implying a detrimental effect of the bulky group of alkyl halides. Until now, the mechanism of the reaction between aryl−Ni(II) and electrophiles is still unknown. No reactions took place between **4** and alkyl halides.

Biaryl Coupling Reaction between 2 and Benzoxazole. Recently, Itami and co-workers separated an aryl−Ni(II) compound via the oxidative addition of Ni(0) by a C−O bond.[11] They reported that this aryl−Ni(II) species is responsible for the following C−H bond activation of the heterocyclic benzoxazole. We thus attempted to investigate whether **2** and **4** can also be applied in this transformation to realize C−H functionalization. As shown in Table 3 (entry 1), the monoaryl−Ni(II) compound **2** was initially mixed with benzoxazole and cesium carbonate in acetonitrile in a sealed tube. When the mixture was heated for 24 h, the benzoxazole-decorated macrocycle compound **6c** was obtained in 23% yield (entry 1). The use of other solvents such as toluene, 1,4-

Table 3. Optimization of the Reaction Conditions for 2 and Benzoxazole



2 **6c**

entry	solvent	base (amt, equiv)	temp, °C	yield, %
1	acetonitrile	Cs_2CO_3 (1)	100	23
2	toluene	Cs_2CO_3 (1)	100	17
3	dioxane	Cs_2CO_3 (1)	100	15
4	THF	Cs_2CO_3 (1)	100	none
5	DMSO	Cs_2CO_3 (1)	100	29
6	DMF	Cs_2CO_3 (1)	100	45
7	DMF	K_2CO_3 (1)	100	25
8	DMF	K_3PO_4 (1)	100	none
9	DMF	*t*-BuOK (1)	100	19
10	DMF	DIPEA (1)	100	none
11	DMF	Et_3N (1)	100	23
12	DMF	DBU (1)	100	13
13	DMF	DABCO (1)	100	14
14	DMF	Cs_2CO_3 (0.2)	100	8
15	DMF	Cs_2CO_3 (0.5)	100	38
16	DMF	Cs_2CO_3 (1.5)	100	30
17	DMF	Cs_2CO_3 (2)	100	32
18	DMF	Cs_2CO_3 (1)	90	14
19	DMF	Cs_2CO_3 (1)	110	34 (mess)
20	DMF	Cs_2CO_3 (1)	120	23 (mess)

dioxane, THF, and DMSO did not improve the yield. Finally, *N*,*N*-dimethylformamide (DMF) was chosen as the reaction medium, since it gave the best yield (45%). Screening of other bases, such as the inorganic bases K_2CO_3, K_3PO_4, and *t*-BuOK and organic bases including diisopropylethylamine (DIPEA), Et_3N, DBU, and 1,4-diazabicyclo[2.2.2]octane (DABCO) revealed that cerium carbonate was a suitable base for this transformation. Interestingly, the unique role of Cs_2CO_3 was also mentioned in Itami's work.[18] Decreasing or increasing the amount of Cs_2CO_3 was detrimental to the reaction. We also attempted to utilize other heterocycles such as oxazole, thiazole, and benzothiazole to realize the formation of biaryl carbon−carbon bonds. However, these substrates were all inapplicable to this reaction.

CONCLUSIONS

In summary, we have reported the facile synthesis of aryl−Ni(II) complexes by the direct electrophilic metalation of azacalixaromatic macrocycles. The structure and properties of the two aryl−Ni(II) complexes **2** and **4** were fully characterized. The reactivity difference between the monoaryl−Ni(II) compound **2** and the diaryl−Ni(II) compound **4** have been systematically investigated through conducting the coupling reactions with various nucleophiles and electrophiles. The reactivity study will hopefully spur the development of new synthetic methodologies by using cheap Ni(II) salts. Detailed mechanistic studies for the transformations reported in this work are still in progress.

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EXPERIMENTAL SECTION

General Procedures. All of the anhydrous solvents were purified and dried via the reported standard process. Unless otherwise noted, all the glassware used in reactions was dried in an oven. Commercially available reagents were used as received. Reactions were monitored by TLC, which was performed on precoated glass-backed silica gel plates and visualized under UV light. Silica gel (200−300 mesh) was used to perform flash column chromatography. A JEOL ECX-400 400 MHz spectrometer was used to record ^{1}H NMR and ^{13}C NMR spectra using $CDCl_3/CD_3CN$ as solvent, and abbreviations are used to describe NMR spectral data as follows: chemical shift (ppm), coupling constant (J, Hz), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). The electron spray ionization mass spectra (ESI-MS) were recorded on an Esquire-LC-00136 spectrometer, and high-resolution electrospray ionization (ESI) mass spectra were recorded on a Thermo Fisher Exactive mass spectrometer. Infrared spectra were recorded using a PerkinElmer Spectrum 100 FT-IR spectrometer in an anhydrous environment. UV spectra were recorded using a PerkinElmer Lamber35 UV/vis spectrophotometer at room temperature.

Synthesis of 2. To a solution of reactant **1** (212 mg, 0.5 mmol) in anhydrous acetonitrile (50 mL) was added a solution of $Ni(ClO_4)_2\cdot 6H_2O$ (274 mg, 1.0 mmol) in 5 mL of acetonitrile slowly with a syringe pump within 1 h. After addition was complete, the solution was stirred for 10 h until the reactant **1** disappeared. Solvent was removed under reduced pressure without heating, and a yellow-green mixture was obtained. Chloroform (30 mL) was then added, the resulting mixture was centrifuged, and the supernatant was removed. These operations were repeated another two times, and then methanol was used for the centrifugation. The solid from centrifugation was dried to give the yellow powder **2** in 90% yield: mp >300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (t, J = 8.1 Hz, 1 H), 8.10 (t, J = 7.8 Hz, 2 H), 7.50 (t, J = 7.8 Hz, 1 H), 7.39 (d, J = 7.8 Hz, 2 H), 7.32 (d, J = 7.8 Hz, 2 H), 7.19 (d, J = 7.8 Hz, 2 H), 7.07 (t, J = 7.8 Hz, 4 H), 3.68 (s, 6 H), 3.53 (s,6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4 (s), 152.3 (s), 151.9 (s), 145.7 (s), 144.0 (s), 139.2 (s), 137.0 (s), 131.4 (s), 115.9 (s), 112.5 (s), 110.9 (s), 109.8 (s), 38.5 (s), 38.2 (s); IR (KBr, cm^{-1}) ν 1578, 1484, 1423, 1341, 1091; ESI-MS m/z $[M - ClO_4^-]^+$: 480.2. HRMS (ESI) calcd for $C_{25}H_{24}N_7Ni$ $[M - ClO_4^-]^+$ 480.1447, found 480.1435. Anal. Calcd for $C_{25}H_{24}ClN_7NiO_4$: C, 51.71; H, 4.17; N, 16.89. Found: C, 51.66; H, 4.19; N, 16.85.

Synthesis of 4. A mixture of azacalix[2]arene[2]pyridine **3** (211 mg, 0.50 mmol) and $Ni(ClO_4)_2\cdot 6H_2O$ (274 mg, 0.75 mmol) in acetic acid was stirred and refluxed in 15 mL of acetic acid for 12 h. When **3** was consumed, which was monitored by TLC analysis, the reaction mixture was cooled to room temperature. The solvent was removed, and the residue was dissolved in dichloromethane and washed with water (2 × 10 mL) and saturated brine (2 × 15 mL). The organic phase was dried over anhydrous $MgSO_4$. After filtration and concentration under vacuum, the residue was recrystallized in a mixture of dichloromethane, methanol, and hexane to give pure **4** (182 mg, yield: 76%) as a yellow powder: mp >300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (t, J = 8.2 Hz, 2 H), 7.12 (t, J = 7.8 Hz, 2 H), 6.81 (t, J = 7.8 Hz, 4 H), 6.68 (t, J = 7.8 Hz, 4 H), 3.46 (s, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7 (s), 145.8 (s), 140.8 (s), 138.0 (s), 125.1 (s), 109.4 (s), 105.7 (s), 40.3 (s); IR (KBr, cm-1) ν 1576, 1451, 1415,1316, 1116; ESI-MS $[M + H]^+$ m/z 480.1; HRMS calcd for $C_{26}H_{25}N_6Ni$ $[M + H]^+$ 479.1494, found 479.1484. Anal. Calcd for $C_{26}H_{24}N_6Ni$: C, 65.17; H, 5.05; N, 17.54. Found: C, 65.13; H, 5.08; N, 17.57.

Synthesis of 6a or 6b (Method A). A mixture of **2** (116 mg, 0.2 mmol) and 20 mL of anhydrous THF was stirred at 0 °C for 0.5 h in a 50 mL three-neck round-bottom flask. Then 134 μL of lithium methide (3 M in diethoxymethane) or 161 μL of n-butyllithium (2.5 M in n-hexane) was injected slowly into the reaction mixture over 5 min. The reaction mixture was stirred for 10 min at 0 °C and 10 min at room temperature and then refluxed for 72 h under an Ar atmosphere until the starting compound **2** was consumed. The reaction mixture was cooled to room temperature, and saturated NH_4Cl was added slowly. The resulting mixture was extracted with dichloromethane (3 × 15 mL), and the organic phase was then washed with water (3 × 15 mL) and saturated brine (3 × 15 mL) and dried over anhydrous $MgSO_4$. After filtration and concentration, the residue was flash-chromatographed on a silica gel column (petroleum ether/ethyl acetate/dichloromethane 12/2/1) to afford the products: **6a** (55 mg, 53%) as a white solid, mp 230−232 °C (lit.[19] mp 230−232 °C); **6b** (59 mg, 61%) as a white solid, mp 182−184 °C (lit.[19] mp 182−184 °C).

Synthesis of 6c (Method A). At −78 °C and under an N_2 atmosphere, 161 μL n-butyllithium (2.5 M in hexane) was injected into a 10 mL Schlenk tube and then 1 mL of a THF solution of benzoxazole (47.6 mg, 0.4 mmol) was injected slowly into the n-butyllithium and the mixture stirred for 0.5 h at −78 °C. The resulting mixture was then slowly added to a mixture of **2** (116 mg, 0.2 mmol) and 10 mL of THF inside a three-neck round-bottom flask under N_2 pressure and at a temperature of −78 °C within 30 min. After the addition, the reaction temperature was raised to room temperature and then the mixture was refluxed for 60 h until compound **2** was consumed (monitored by TLC). The reaction mixture was cooled to room temperature, and saturated NH_4Cl was added slowly. The resulting mixture was extracted with dichloromethane (3 × 15 mL), and the organic phase was then washed with water (3 × 15 mL) and saturated brine (3 × 15 mL) and dried over anhydrous $MgSO_4$. After filtration and concentration, the residue was flash chromatographed on a silica gel column (petroleum ether/ethyl acetate 6/1) to afford **6c** (64 mg, 59%): mp 278−279 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (m, 1 H), 7,59 (m, 1 H), 7.43 (t, J = 8.0 Hz, 2 H), 7.40−7.37 (m, 2 H), 7.14 (t, J = 7.6 Hz, 1 H), 6.88 (dd, J = 6.8 Hz, J = 7.2 Hz, 1 H), 6.81−6.80 (m, 2 H), 6.56 (d, J = 8.0 Hz, 2 H), 6.09 (d, J = 8.0 Hz, 2 H), 6.03 (d, J = 8.0 Hz, 2 H), 3.26 (s, 6 H), 3.10 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9 (s), 158.8 (s), 157.4 (s), 152.6 (s), 150.0 (s), 140.7 (s), 140.1 (s), 139.1 (s), 137.4 (s), 137.3 (s), 128.5 (s), 125.7 (s), 124.7 (s), 124.5 (s), 120.7 (s), 120.2 (s), 111.1 (s), 96.1 (s), 94.7 (s), 38.4 (s), 36.3 (s); IR (KBr, cm^{-1}) ν 1584, 1572, 1466, 1419, 1365, 1248, 1130; HRMS (ESI) calcd for $C_{32}H_{29}N_8O$ $[M + H]^+$ 541.2464, found 541.2464. Anal. Calcd for $C_{32}H_{28}N_8O$: C, 71.09; H, 5.22; N, 20.73. Found: C, 71.12; H, 5.27; N, 20.70.

Synthesis of 7 or 8. Under an N_2 atmosphere, a mixture of **2** (116 mg, 0.2 mmol) and sodium azide or potassium bromide (0.4 mmol) in dried acetonitrile (20 mL) was stirred for 24 h at room temperature in a 50 mL three-neck round-bottom flask until all **2** was consumed. Then 10 mL of ammonia was added. The resulting mixture was extracted with dichloromethane (3 × 15 mL), and the organic phase was then washed with water (3 × 15 mL) and saturated brine (3 × 15 mL) and dried over anhydrous $MgSO_4$. After filtration and concentration, the residue was flash-chromatographed on a silica gel column (petroleum ether/ethyl acetate/dichloromethane 12/2/1) to afford the target products: **7** (80 mg, 91%) as a white powder, mp 171−172 °C (lit.[20] mp 170−171 °C); **8** (93 mg, 93%) as a white powder, mp 257−258 °C (lit.[21] mp 257−258 °C).

Synthesis of 9. Under an N_2 atmosphere, a mixture of **2** (116 mg, 0.2 mmol), phenol (0.4 mmol), and DBU (0.4 mmol) in dried acetonitrile (20 mL) was refluxed for 48 h in a 50 mL three-neck round-bottom flask until all **2** was consumed. Then 10 mL of ammonia was added. The resulting mixture was extracted with dichloromethane (3 × 15 mL), and the organic phase was then washed with water (3 × 15 mL) and saturated brine (3 × 15 mL) and dried over anhydrous $MgSO_4$. After filtration and concentration, the residue was flash-chromatographed on a silica gel column (petroleum ether/ethyl acetate/dichloromethane 12/2/1) to afford **9** as a white solid: mp 228−229 °C (lit.[17] mp 228−229 °C).

Synthesis of 10. In a 25 mL three-neck round-bottom flask, **2** (58 mg, 0.1 mmol) was dissolved in 10 mL of $DMSO/H_2O$ (30/1) mixed solvent, and potassium hydroxide solid (22.4 mg, 0.4 mmol) was added in one portion. The mixture was stirred at room temperature for 6 h until **2** was consumed (monitored by TLC). A 5 mL portion of water was poured into the flask, and hydrochloric acid (0.1 M) was added until the solution became neutral. Dichloromethane was used to extract the organic materials. Then the organic phase was washed with

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water (3 × 10 mL) and saturated brine (3 × 10 mL) and dried over anhydrous $MgSO_4$. After filtration and concentration, the residue was first flash-chromatographed on a silica gel column using petroleum ether/ethyl acetate (3/1) mixed solvent as eluent to afford the crude product. Then the crude product was flash-chromatographed again on a silica gel column using petroleum ether/ethyl acetate (10/1) as eluent to afford **10** as a white solid in 90% yield: mp 207−208 °C (lit.[12c] mp 207−208 °C).

Synthesis of 6a,b (Method B) or 11: General Procedure. In the glovebox, a 35 mL sealed tube was charged with compound **2** (116 mg, 0.2 mmol), electrophilic reagents (1.2 mmol), cesium carbonate powder (65 mg, 0.2 mmol), sodium iodide (30 mg, 0.2 mmol), and 15 mL of toluene (anhydrous and deoxgenized). Then the sealed tube was moved out of the glovebox and the mixture was heated to 140 °C and stirred. After 48 h, the reaction mixture was cooled to room temperature and insoluble substances were removed by filtration. Toluene was removed under reduced pressure, and 20 mL of dichloromethane was added. The resulting organic phase was washed with water (5 × 10 mL) and saturated brine (2 × 10 mL) and dried over anhydrous $MgSO_4$. After filtration and concentration, the residue was flash-chromatographed on a silica gel column (petroleum ether/ethyl acetate/dichloromethane 12/2/1) to afford product **6a** (47%), **6b** (43%), or **11** (36%). Data for **11** (as yellow powder): mp 204−206 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (t, J = 8.0 Hz, 2 H), 7.14 (t, J = 7.4 Hz, 1 H), 6.89 (dd, J = 6.8 Hz, J = 6.8 Hz, 1 H), 6.81−6.78 (m, 2 H), 6.54 (d, J = 7.8 Hz, 2 H), 6.06 (d, J = 8.0 Hz, 2 H), 6.00 (d, J = 8.0 Hz, 2 H), 3.84 (s, 2 H),3.79 (s, 3 H), 3.26 (s, 6 H), 3.10 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8 (s), 158.8 (s), 158.7 (s), 157.4 (s), 141.0 (s), 139.1 (s), 137.4 (s), 137.3 (s), 128.0 (s), 124.0 (s), 120.5 (s), 96.0 (s), 94.1 (s), 38.4 (s), 36.3 (s); IR (KBr, cm^{-1}) ν 2902, 1742, 1598, 1567, 1474, 1421, 1248, 1133; HRMS [ESI] calcd for $C_{28}H_{30}N_7O_2$ $[M + H]^+$ 496.2461, found 496.2460. Anal. Calcd for $C_{28}H_{29}N_7O_2$: C, 67.86; H, 5.90; N, 19.78. Found: C, 67.84; H, 5.88; N, 19.74.

Synthesis of 6c (Method C). In the glovebox, a 5 mL sealed tube was charged with compound **2** (116 mg, 0.2 mol), cesium carbonate powder (65 mg, 0.2 mmol), benzoxazole (47.6 mg, 0.4 mmol), and 1.5 mL of DMF. Then the sealed tube was moved out of the glovebox and the mixture was heated to 100 °C and stirred. After 24 h, the reaction mixture was cooled to room temperature and insoluble substances were removed by filtration. Dichloromethane (20 mL) was added to the filtrate, and the resulting organic phase was washed with water (5 × 10 mL) and saturated brine (2 × 10 mL) and dried over anhydrous $MgSO_4$. After filtration and concentration, the residue was flash-chromatographed on a silica gel column (petroleum ether/ethyl acetate 6/1) to afford **6c** (49 mg, yield 45%).

X-ray Crystal Structure Determination. X-ray-quality single crystals of **2** (an orange plate) and **4** (a yellow plate) were obtained by careful diffusion of diethyl ether into a dichloromethane/methanol (a 1/1 mixture) solution of **2** and slow evaporation of a dichloromethane/methanol/hexane solution (a 4/1/2 mixture) of **4** at room temperature. Intensity data for analysis were collected with Mo Kα radiation (λ = 0.71073 Å) on a Rigaku Saturn 724+ CCD diffractometer under a cold nitrogen steam (T = 173 K). Both structures were solved by direct methods using the SHELXS-97 program and refined by full-matrix least squares on all F^2 values. Crystal data for **2** (CCDC-1420173): $C_{25}H_{24}ClN_7NiO_4$, monoclinic, M_r = 580.67, space group $P2/n$, a = 13.884 Å, b = 8.603 Å, c = 20.772 Å, β = 108.36°, V = 2354.9 Å^3, Z = 4, D_c = 1.638 g/cm^3, R1 ($I > 2\sigma(I)$) = 0.0806, wR2 (all data) = 0.1798, goodness of fit 1.231. Crystal data for **4** (CCDC-1420247): $C_{26}H_{24}N_6Ni$, monoclinic, M_r = 479.22, space group $C2/c$, a = 27.248 Å, b = 8.617 Å, c = 21.659 Å, β = 106.98°, V = 4846.0 Å^3, Z = 8, D_c = 1.309 g/cm^3, R1 ($I > 2\sigma(I)$) = 0.0885, wR2 (all data) = 0.2636, goodness of fit 1.130. Anisotropic refinement was applied to all non-hydrogen atoms. The disordered solvent molecule dichloromethane was removed from the crystal structure of **4**.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.5b00733.

NMR spectra and XPS and CV data for the compounds and X-ray crystallographic data for **2** and **4** (PDF)

X-ray crystallographic data for **2** and **4** (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail for L.Z.: zhaolchem@mail.tsinghua.edu.cn.

*E-mail for M.-X.W.: wangmx@mail.tsinghua.edu.cn.

Notes

The authors declare no competing financial interest.

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