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Short Note

Chloro(η^2,η^2-cycloocta-1,5-diene){1-[(2-[(*S*)-1-(hydroxymethyl)-3-methylbutyl]amino)-2-oxoethyl]-3-(1-naphthalenylmethyl)benzimidazol-2-ylidene}rhodium(I)

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Abstract: Commercially available and air- and moisture-stable rhodium complex $[Rh(OH)(cod)]_2$ (**2**) was utilized in the synthesis of [RhX(cod)(NHC)] (**3**). The presence of an OH group in complex **2** serves as an internal base, facilitating the deprotonation of the C–H bond of the azolium ring in the hydroxyamide-substituted benzimidazolium salt **1**. This reaction between **1** and **2** proceeded in THF at room temperature without temperature control, affording the desired NHC/Rh complex **3** in excellent yield. The characterization of complex **3** was accomplished through NMR and HRMS analyses, revealing its existence as a diastereomeric mixture of two NHC/Rh complexes. Furthermore, its catalytic performance was briefly evaluated in the reaction between 2-naphthaldehyde (**5**) and phenylboronic acid (**6**).

Keywords: *N*-heterocyclic carbene; rhodium; azolium salt; deprotonation; internal base

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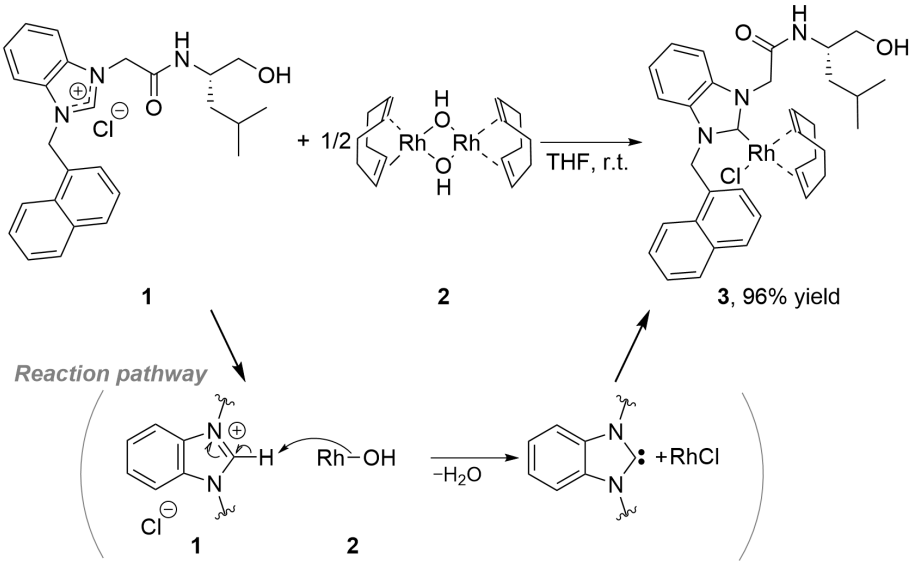
1. Introduction

Over the past two decades, *N*-heterocyclic carbenes (NHCs) have garnered significant attention as ligands for transition metals, since the decisive breakthrough was achieved in 1991 by Arduengo III et al. [1–6]. Typically derived from azolium salts through deprotonation, NHCs have been instrumental in the synthesis of complexes like [RhX(cod)(NHC)] (cod = η^2,η^2-1,5-cyclooctadiene, X = halogen), which are commonly prepared via one of two routes [7–9]. The first route involves the reaction of in situ-generated free carbenes with $[RhX(cod)]_2$, achieved through deprotonation using strong bases like KO^{t}Bu or potassium hexamethyldisilazide (KHMDS) [10,11]. This route requires thoroughly drying solvents and reagents and using an inert atmosphere. Herrmann et al. showed that the treatment of 1,3-dibenzylimidazolium bromide with $[RhCl(cod)]_2$ under the influence of K_2CO_3 at 70 °C for 20 h in water produced the corresponding [RhCl(cod)(NHC)] complex in almost quantitative yield [12]. The second route entails using a carbene transfer agent, the [AgX(NHC)] complex, derived from direct reactions of an azolium halide with Ag_2O [13,14]. However, this approach adds an extra synthetic step and risks contaminating the final product with unwanted silver, rendering both approaches multi-step and economically unfavorable.

Our recent findings demonstrate that the OMe group in the readily available $[Ir(OMe)(cod)]_2$ can serve as an internal base for deprotonation at the C_2 position of hydroxyamide-substituted benzimidazolium salt **1** [15]. Building upon this, we now turn our attention to the commercially available and easily accessible $[Rh(OH)(cod)]_2$ (**2**). We hypothesize that [RhCl(cod)(NHC)] complexes can be synthesized by reacting azolium chloride **1** with **2**, with water being the sole side product at room temperature without temperature control (Scheme 1).



Scheme 1. Synthesis of [RhCl(cod)(NHC)] complex **3**.

2. Results and Discussion

The hydroxyamide-substituted benzimidazolium salt **1** was synthesized following our previously reported procedure utilizing (*S*)-leucinol as the starting material [15]. Upon reacting compound **1** with $[Rh(OH)(cod)]_2$ (**2**) in THF, the desired monodentate [RhCl(cod)(NHC)] complex **3** was obtained in a 96% yield (Scheme 1). This reaction can be conducted at room temperature under standard laboratory conditions. Furthermore, complex **3** exhibits exceptional stability in the air and can be stored as a solid for at least one month at room temperature.

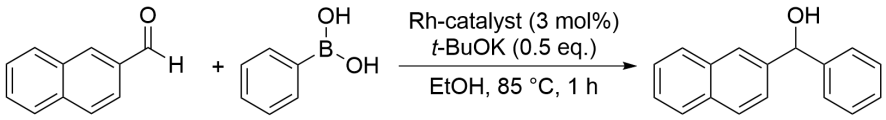
The characterization of the novel [RhCl(cod)(NHC)] complex **3**, isolated as an air-stable yellow solid, was straightforward using the obtained analytical and spectroscopic data (details are given in Section 3). Notably, the $^{13}C\{^1H\}$ NMR spectrum provided crucial insights, revealing a doublet signal at δ = 197.8 ppm, with a characteristic C–Rh coupling constant of 50.4 Hz for the carbene carbon atom. Furthermore, the $^{13}C\{^1H\}$ NMR spectrum of **3** indicated its existence as an 8:2 mixture of two NHC/Rh complexes, attributed to hindered carbene–metal bond rotation in the bulky cyclooctadiene (cod) ligand [16]. This was evident from the observation of two doublet signals for the sp^2 carbons (at δ = 101.6 and 101.4 ppm with a coupling constant of 5.6 Hz) and two doublet signals for the sp^2 carbons (at δ = 70.1 and 69.6 ppm with a coupling constant of 14.4 Hz) of cod observed in the $^{13}C\{1H\}$ NMR spectra. Four singlet signals for the sp^3 carbons of cod (at δ = 33.2, 31.9, 28.5, and 28.2 ppm) were also observed. Resonances corresponding to the carbonyl carbon (a singlet at δ = 167.1 ppm) and the isobutyl substituent (singlets at δ = 24.4 (CH), 22.7 (CH_3), and 21.5 (CH_3) ppm) of the hydroxyamide sidearm on the NHC ligand were also detected in the $^{13}C\{^1H\}$ NMR spectrum. Additionally, the disappearance of the signal of the proton in the C_2 position of the azolium salt **1** was observed in the ^1H NMR spectrum of **3**. The methyl group of the isobutyl substituent manifested as two doublet signals (at δ = 0.63 and 0.55 ppm with *J* = 6.4 Hz, respectively) in the ^1H NMR spectrum. Despite multiple attempts, suitable crystals for the structural determination of complex **3** via single-crystal X-ray diffraction were not obtained.

Owing to the complex NMR signals observed in **3**, we pursued the synthesis of another NHC/Rh complex, **4**, namely iodo(η^2,η^2-cycloocta-1,5-diene)(1,3-dimethylbenzimidazol-2-ylidene)rhodium(I), by reacting 1,3-dimethylbenzimidazolium iodide with **2** in 95% yield [17,18]. Notably, the $^{13}C\{^1H\}$ NMR spectrum of **4** revealed a doublet signal assigned to the carbene carbon atom at δ = 196.3 ppm with a coupling constant of 48.8 Hz. Additionally, two doublet signals for the sp^2 carbons (at δ = 98.0 ppm with *J* = 6.8 Hz and δ = 71.7 ppm

with J = 13.4 Hz) of cod were observed in the $^{13}C\{1H\}$ NMR spectra, along with two singlet signals at δ = 34.6 and 32.2 ppm attributed to the sp^3 carbon of cod.

Subsequently, the catalytic potential of [RhX(cod)(NHC)] complexes **3** and **4** was assessed. Shi et al. investigated asymmetric addition reactions of organoboronic acids to aldehydes catalyzed by a chiral monodentate NHC/Rh complex [19]. As depicted in Table 1, the treatment of 2-naphthaldehyde (**5**) with phenylboronic acid (**6**) in the presence of catalytic amounts of [RhCl(cod)(NHC)] complex (**3**, 3 mol%) and KO^{t}Bu (50 mol%) in EtOH at 85 °C for 1 h resulted in the production of naphthalen-2-yl(phenyl)methanol (**7**) in a 79% yield (entry 1). Similarly, NHC/Rh complex **4** facilitated the reaction, affording **7** in an 88% yield (entry 2). In contrast, utilizing $[RhCl(cod)]_2$ (**8**) as the catalyst led to a significantly lower yield of **7** (14%, entry 3), highlighting the efficacy of strong ligand-accelerated catalysis by NHCs. Although a racemic mixture of product **7** was obtained from the reaction of **5** and **6** catalyzed by [RhCl(cod)(NHC)] complex **3**, efforts to design a chiral NHC ligand for efficient catalytic enantioselective transformations are currently underway in our laboratory.

Table 1. Rh-catalyzed reaction between 2-naphthaldehyde (**5**) and phenylboronic acid (**6**) [1].



5 **6** (2 eq.) **7**

Entry	Catalyst	Yield (%) [2]
1	[RhCl(cod)(NHC)] (**3**)	79
2	[RhI(cod)(NHC)] (**4**)	88
3	$[RhCl(cod)]_2$ (**8**)	14

[1] Experimental details are given in Section 3. [2] Isolated yield.

3. Materials and Methods

All reagents and solvents were purchased from chemical suppliers and utilized without additional purification. ^1H (400 MHz) and $^{13}C\{1H\}$ (100 MHz) NMR spectra were acquired using a JEOL ECS-400 spectrometer (JEOL, Tokyo, Japan). Chemical shifts are reported downfield from TMS (δ = 0 ppm) for ^1H NMR. For $^3C\{^1H\}$ NMR, chemical shifts are reported relative to $CDCl_3$ as an internal reference. High-resolution mass spectrometry was conducted on a Bruker microTOF II instrument (Bruker Daltonik Gmbh, Bremen, Germany) employing electrospray ionization. Liquid chromatography (LC) analyses were performed using an Agilent 1260 Infinity HPLC system (Agilent Technologies, Santa Clara, CA, USA) equipped with a Daicel CHIRALCEL® OD-H column (IPA/Hexane = 10/90, flow rate: 0.8 mL/min).

*3.1. Chloro(η^2,η^2-Cycloocta-1,5-Diene){1-[(2-[(S)-1-(Hydroxymethyl)-3-Methylbutyl]Amino)-2-Oxoethyl]-3-(1-Naphthalenylmethyl)-Benzimidazol-2-Ylidene}Rhodium(I) (**3**)*

Azolium salt **1** (0.21 mmol, 95 mg) and $[Rh(OH)(cod)]_2$ (**2**, 0.1 mmol, 46 mg) were stirred in THF (2 mL) at room temperature under an argon atmosphere for 16 h. The reaction mixture was then passed through a short silica gel column using THF as the eluent. Subsequently, the filtrate was concentrated under reduced pressure using a rotary evaporator, affording [RhCl(cod)(NHC)] complex **3** as a yellow solid (128 mg, 96% yield). Additionally, the reaction of **1** with **2** could be performed under open-air conditions. The ^1H NMR (400 MHz, $CDCl_3$) results are as follows. Major isomer: δ = 8.34 (d, J = 8.2 Hz, 1H, NH), 7.96 (d, J = 8.2 Hz, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.73–7.42 (m, 3H), 7.32–6.96 (m, 6H), 6.85 (d, J = 7.2 Hz, 1H, CH_2Ar), 6.53 (d, J = 15.4 Hz, 1H, CH_2CO), 6.31 (d, J = 16.8 Hz, 1H, CH_2Ar), 5.12 (br, 1H, CH_{cod}), 5.12 (br, 1H, NHCH), 4.91 (d, J = 15.4 Hz, 1H, CH_2CO), 4.10-4.02 (br, 1H, CH_{cod}), 3.71–3.66 (m, 1H, CH_{cod}), 3.53–3.44 (m, 2H, CH_2OH and CH_{cod}),

3.31 (br, 1H, CH_2OH), 2.98 (t, J = 6.8 Hz, 1H, OH), 2.56–2.34 (m, 2H, CH_{2cod}), 2.18–2.06 (m, 1H, CH_{2cod}), 2.01–1.82 (m, 3H, CH_{2cod}), 1.66 (br, 1H, CH_{2cod}), 1.25 (br, 1H, CH_{2cod}), 1.22–1.15 (m, 1H, CH_{2iBu}), 1.06–0.99 (m, 1H, CH_{2iBu}), 0.96–0.92 (m, 1H, CH_{iBu}), 0.63 (d, J = 6.4 Hz, 3H, CH_{3iBu}), 0.55 (d, J = 6.4 Hz, 3H, CH_{3iBu}) ppm. Minor isomer: δ = 6.83 (d, J = 7.2 Hz, 1H, CH_2Ar), 6.48 (d, J = 15.4 Hz, 1H, CH_2CO), 6.28 (d, J = 16.8 Hz, 1H, CH_2Ar), 4.91 (d, J = 15.4 Hz, 1H, CH_2CO), 3.94 (br, 1H, CH_{cod}), 0.90 (d, J = 6.4 Hz, 3H, CH_{3iBu}), 0.87 (d, J = 6.4 Hz, 3H, CH_{3iBu}) ppm. The $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) results are as follows. Major isomer: δ = 197.8 (d, $J_{C\text{-}Rh}$ = 50.4 Hz, $C_{carbene}$), 167.1 (C=O), 134.9, 134.2, 133.5, 131.0, 130.4, 129.0, 128.3, 126.9, 126.2, 125.2, 123.5, 123.4, 123.1, 122.4, 110.9 (C of NHC ring), 110.2 (C of NHC ring), 101.6 (d, $J_{C\text{-}Rh}$ = 6.0 Hz, CH_{cod}), 101.4 (d, $J_{C\text{-}Rh}$ = 6.0 Hz, CH_{cod}), 70.1 (d, $J_{C\text{-}Rh}$ = 14.4 Hz, CH_{cod}), 69.6 (d, $J_{C\text{-}Rh}$ = 14.4 Hz, CH_{cod}), 65.4 (CH_2OH), 53.0 (NHCH), 50.4 (CH_2CO), 50.0 (NCH_2Ar), 39.2 (CH_{2iBu}), 33.2 (CH_{2cod}), 31.9 (CH_{2cod}), 28.5 (CH_{2cod}), 28.2 (CH_{2cod}), 24.4 (CH_{iBu}), 22.7 (CH_{3iBu}), 21.5 (CH_{3iBu}) ppm. Minor isomer: δ = 167.3 (C=O), 135.0, 134.3, 133.6, 131.1, 130.4, 128.2, 126.8, 126.2, 125.2, 123.3, 123.2, 110.8 (C of NHC ring), 110.5 (C of NHC ring), 101.2 (d, $J_{C\text{-}Rh}$ = 6.0 Hz, CH_{cod}), 65.3 (CH_2OH), 52.9 (NHCH), 51.1 (CH_2CO), 49.9 (NCH_2Ar), 33.0 (CH_{2cod}), 30.7 (CH_{2iBu}), 28.4 (CH_{2cod}), 28.4 (CH_{2cod}), 24.8 (CH_{3iBu}), 22.2 (CH_{3iBu}) ppm. HRMS (ESI-TOF), m/z: calculated for $C_{34}H_{41}N_3O_2Rh$ $[M\text{-}Cl]^+$ as 626.2248 and found to be 626.2245. The NMR spectrum can be found in the Supplementary Materials.

*3.2. Iodo(η^2,η^2-Cycloocta-1,5-Diene)(1,3-Dimethylbenzimidazol-2-Ylidene)Rhodium(I) (**4**)*

1,3-Dimethylbenzimidazolium iodide (0.21 mmol, 55 mg) and $[Rh(OH)(cod)]_2$ (**2**, 0.1 mmol, 46 mg) were stirred in THF (2 mL) at room temperature under an argon atmosphere for 16 h. The reaction mixture was then passed through a short silica gel column using THF as the eluent. Subsequently, the filtrate was concentrated under reduced pressure using a rotary evaporator, affording [RhI(cod)(NHC)] complex **4** as a yellow solid (92 mg, 95% yield). Compound **4** was reported in the literature [18]. The ^1H NMR (400 MHz, $CDCl_3$) results are as follows. δ = 7.29–7.21 (m, 4H), 5.34 (s, 2H, CH_{cod}), 4.20 (s, 6H, NCH_3), 3.52–3.51 (m, 2H, CH_{cod}), 2.40–2.38 (m, 4H, CH_{2cod}), 2.06–2.02 (m, 2H, CH_{2cod}), 1.88–1.84 (m, 2H, CH_{2cod}) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 196.3 (d, $J_{C\text{-}Rh}$ = 48.8 Hz, $C_{carbene}$), 135.3, 122.1, 109.0 (C of NHC ring), 98.0 (d, $J_{C\text{-}Rh}$ = 6.8 Hz, CH_{cod}), 71.7 (d, $J_{C\text{-}Rh}$ = 13.4 Hz, CH_{cod}), 34.6 (CH_{2cod}), 32.2 (CH_{2cod}), 29.4 (NCH_3) ppm. HRMS (ESI-TOF), m/z: calculated for $C_{17}H_{22}N_2Rh$ $[M\text{-}I]^+$ as 357.0832 and found to be 357.0832. The NMR spectrum can be found in the Supplementary Materials.

*3.3. General Procedure for the Catalytic Reaction of 2-Naphthaldehyde (**5**) with Phenylboronic Acid (**6**)*

Under an argon atmosphere, 2-naphthaldehyde (**5**, 0.75 mmol, 117 mg), phenylboronic acid (**6**, 1.5 mmol, 183 mg), KO^tBu (0.38 mmol, 42 mg), EtOH (0.75 mL), and the corresponding rhodium(I) complex (0.023 mmol, 3 mol%) were combined in a glass-capped sealed tube. The reaction mixture was then stirred at 85 °C for 1 h. After solvent evaporation, hexane was added to the resulting residue, forming gray precipitation. After filtration through a paper filter, the filtrate was concentrated under reduced pressure using a rotary evaporator, yielding a light-yellow liquid. The desired product, naphthalen-2-yl(phenyl)methanol (**7**), was subsequently purified from the residue via column chromatography on silica gel (Hexane/EtOAc = 8/2), affording a white solid.

4. Conclusions

In summary, novel rhodium complexes of the form [RhCl(cod)(NHC)] (**3**) were successfully synthesized in high yield via the reaction of azolium salt **1** with commercially available and readily accessible $[Rh(OH)(cod)]_2$ (**2**). The synthesized complexes were comprehensively characterized through analytical and spectroscopic methods. While rhodium complex **3** demonstrated catalytic activity in the addition reaction of 2-naphthaldehyde (**5**) with phenylboronic acid (**6**), its efficacy surpassed that of $[RhCl(cod)]_2$ (**8**). This enhanced

performance can likely be attributed to robust σ-donor electronic properties of the NHC ligand, which are anticipated to influence the catalytic cycle significantly.

Supplementary Materials: The following supporting information is available online. Figures S1–S3: ^{1}H NMR, ^{13}C{^{1}H} NMR, and HMQC-NMR of compound **3**. Figures S4 and S5: ^{1}H NMR and ^{13}C{^{1}H} NMR of compound **4**.

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Conflicts of Interest: The authors declare no conflicts of interest.

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