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Short Note

Chloro(η^2,η^2-cycloocta-1,5-diene){1-benzyl-3-[(*S*)-2-hydroxy-1-methylethyl]benzimidazol-2-ylidene}rhodium(I)

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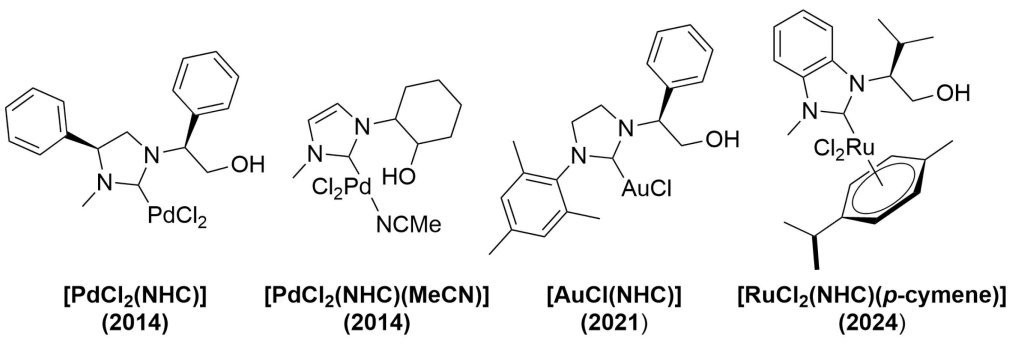
Abstract: Previously, we demonstrated the synthesis of a well-defined hydroxyalkyl-functionalized *N*-heterocyclic carbene (NHC)/Ru(II) complex through the transmetalation reaction between $[RuCl_2(p\text{-cymene})]_2$ and the corresponding NHC/Ag(I) complex derived from a chiral benzimidazolium salt using the Ag_2O method. In this study, we successfully synthesized [RhX(cod)(NHC)] complexes through a one-pot deprotonation route. The hydroxyalkyl-substituted benzimidazolium salt reacted with $[Rh(OH)(cod)]_2$ in THF at room temperature, affording the corresponding monodentate NHC/Rh(I) complex in nearly quantitative yield. The rhodium complex was characterized using NMR, HRMS measurement, and elemental analysis.

Keywords: *N*-heterocyclic carbene; rhodium; azolium salt; hydroxyalkyl substituent

1. Introduction

Recently, there has been considerable interest in the transition metal complex having an *N*-heterocyclic carbene (NHC) ligand with hydroxyalkyl sidearms, owing to the numerous expected applications of complexes incorporating chiral NHC ligands in asymmetric catalysis [1–5]. Scheme 1 showcases representative monodentate NHC/metal complexes, the structural formulas of which have been elucidated through various analyses. In 2014, a $[PdCl_2(NHC)]$ complex was synthesized by reacting an imidazolinium salt bearing a hydroxyalkyl sidearm with $PdCl_2$ in the presence of KO^tBu [6]. Additionally, Grisi and coworkers synthesized a $[PdCl_2(NHC)(MeCN)]$ complex through transmetalation from the corresponding bis(NHC)/Ag complex [7]. Structural characterization of the NHC/Pd complex was performed using X-ray diffraction studies. Fiksdahl and coworkers reported the synthesis of an [AuCl(NHC)] complex by allowing a hydroxyalkyl-substituted imidazolinium salt derived from (*S*)-2-phenylglycinol to react with $[AuCl(Me_2S)]$ in the presence of K_2CO_3 [8]. Furthermore, several research groups have successfully synthesized well-defined anionic alkoxide–NHC/metal (Cu, Ag, Ni, and Pd) complexes [9–11].



[PdCl$_2$(NHC)] (2014) **[PdCl$_2$(NHC)(MeCN)] (2014)** **[AuCl(NHC)] (2021)** **[RuCl$_2$(NHC)(*p*-cymene)] (2024)**

Scheme 1. List of monodentate hydroxyalkyl-functionalized NHC/metal complexes.

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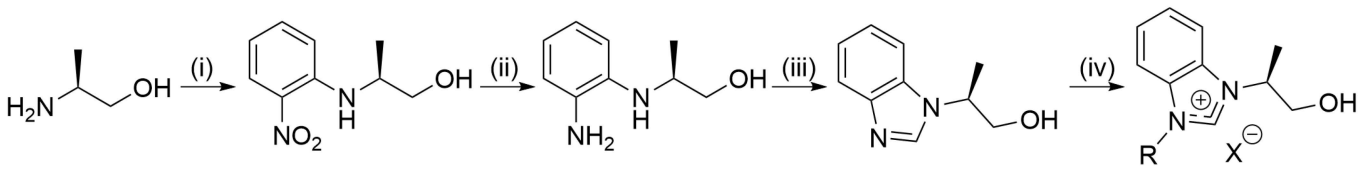
Previously, we showed a highly enantioselective allylic alkylation reaction catalyzed by copper species bearing a chiral hydroxyalkyl-functionalized NHC ligand derived from naturally occurring α-amino acids [12]. During this investigation, we successfully synthesized a novel [$RuCl_2$(NHC)(*p*-cymene)] complex from the hydroxyalkyl-substituted benzimidazolium salt using the Ag_2O method (Scheme 1). The monodentate NHC/Ru(II) complex was obtained utilizing the following experimental procedure: specifically, an azolium salt derived from (*S*)-valinol was reacted with Ag_2O at room temperature for 2 h. Subsequently, [$RuCl_2$(*p*-cymene)]$_2$ was introduced into the reaction vessel. After stirring the resultant reaction mixture at room temperature for 16 h, the corresponding [$RuCl_2$(NHC)(*p*-cymene)] complex was obtained in a 62% yield (Scheme 1). Here, we present the synthesis and characterization of an NHC/Rh(I) complex featuring a hydroxyalkyl-functionalized NHC ligand. The desired [RhX(cod)(NHC)] complexes were synthesized via a one-pot deprotonation route by reacting benzimidazolium salt with [Rh(OH)(cod)]$_2$.

2. Results and Discussion

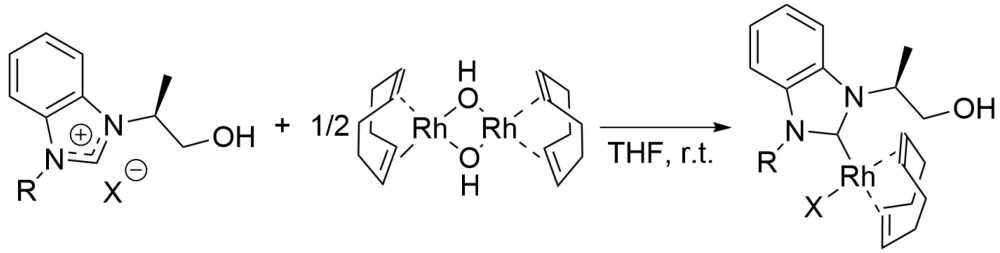
Hydroxyalkyl-functionalized benzimidazolium salts were synthesized from commercially available chiral β-amino alcohols using Ishida and Saigo's synthetic route (Scheme 2) [13]. The synthesis started with a nucleophilic substitution reaction between 2-fluoronitrobenzene and (*S*)-alaninol, yielding (*S*)-2-[*N*-(2-nitrophenyl)amino]propan-1-ol. Subsequent reduction of the nitro compound produced 2-[*N*-(2-aminophenyl)amino]propan-1-ol. Then, the condensation reaction between the resulting diamino compound and triethyl orthoformate afforded 2-(benzimidazol-1-yl)propan-1-ol. Finally, coupling the azole with an alkyl halide (R-X) produced the corresponding hydroxyalkyl-substituted benzimidazolium salt. In this study, we synthesized two azolium salts, **1a** and **2a**, derived from benzyl chloride and benzhydryl bromide, respectively. Further details are provided in Section 3.



Scheme 2. Synthetic route to hydroxyalkyl-substituted benzimidazolium salt.

In previous investigations, the synthesis of NHC/metal (Pd, Au, and Ru) complexes involved treating a hydroxyalkyl-substituted azolium salt with appropriate bases such as KO^{t}Bu, K_2CO_3, and Ag_2O, as outlined in the introductory section (Section 1). In this study, we showed a synthetic approach for the NHC/Rh complex using the following one-pot deprotonation route: treatment of azolium salt **1a** with [Rh(OH)(cod)]$_2$ in THF at room temperature afforded monodentate [RhCl(cod)(NHC)] complex **1b** in nearly quantitative yield (Scheme 3). Complex **1b**, isolated as an air-stable yellow solid, was characterized by analyzing the acquired analytical and spectroscopic data (further details are provided in Section 3). In the HRMS (ESI-TOF) measurement, the $[M-Cl]^+$ ion (M = $C_{25}H_{30}ClN_2ORh$) was clearly observed. In the $^{13}C\{^1H\}$ NMR spectrum, a doublet signal at δ = 196.3 ppm with a typical C–Rh coupling constant of 50.8 Hz was observed for the carbene carbon atom. Complex **1b** was found to exist as a 75:25 mixture of two NHC/Rh complexes. Enders et al. observed the hindered rotation of the carbene-metal bond in an NHC/Rh complex, which contained a bulky cyclooctadiene ligand [14]. The four doublet signals at δ = 100.7 ppm (*J* = 6.7 Hz), 99.9 ppm (*J* = 6.7 Hz), 70.0 ppm (*J* = 14.4 Hz), and 68.5 ppm (*J* = 14.4 Hz) were attributed to the four non-equivalent sp^2 carbons of the cod ligand on complex **1b** in the $^{13}C\{1H\}$ NMR spectrum. Additionally, four singlet signals for the sp^3 carbons of cod at δ = 33.8, 31.5, 29.5, and 27.6 ppm were observed. In the ^1H NMR spectrum, the doublet signal assigned to the methyl group adjacent to the chiral carbon center of **1b** appeared at δ = 1.78 ppm with a coupling constant of 7.6 Hz. Furthermore, the hydroxy group at the

NHC sidearm was observed at δ = 3.27 ppm. This strongly suggests that [RhCl(cod)(NHC)] complex **1b** possesses an *N*-hydroxyalkyl functional group, indicating that an anionic alkoxide-tethered NHC/Rh(I) complex is not formed under these reaction conditions.



1a (R = CH_2Ph, X = Cl)
2a (R = $CHPh_2$, X = Br)

1b, 99% yield
2b, 70% yield

Scheme 3. Synthesis of [RhX(cod)(NHC)] complexes **1b** and **2b**.

Similarly, [RhBr(cod)(NHC)] complex **2b** was synthesized by reacting **2a** featuring an *N*-$CHPh_2$ wingtip with $[Rh(OH)(cod)]_2$ in THF. Notably, following the reaction, a substantial amount of yellow precipitate formed. Subsequent simple filtration and washing with ether yielded the desired NHC/Rh(I) complex **2b** in its pure form. This differs from the preparation of complex **1b**. ^1H NMR, HRMS measurements, and elemental analysis strongly supported the chemical structure of **2b** (details are provided in Section 3). However, attempts to measure $^{13}C\{^1H\}$ NMR in $CDCl_3$, $(CD_3)_2SO$, CD_3OD, or $(CD_3)_2CO$ failed owing to the poor solubility of **2b**.

3. Materials and Methods

All reagents, including $[Rh(OH)(cod)]_2$ 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 on a JEOL ECS-400 spectrometer (JEOL, Tokyo, Japan). Chemical shifts are reported downfield from TMS (δ = 0 ppm) for ^1H NMR. For $^{13}C\{^1H\}$ 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 (ESI). Elemental analyses were carried out at Osaka University. An azolium salt, specifically 1-benzyl-3-[(*S*)-2-hydroxy-1-methylethyl]benzimidazolium bromide (**1a**), was synthesized following our previously reported procedure [12].

3.1. Chloro(η^2,η^2-cycloocta-1,5-diene){1-benzyl-3-[(S)-2-hydroxy-1-methylethyl]-benzimidazol-2-ylidene}rhodium(I) (**1b**)

1-Benzyl-3-[(S)-2-hydroxy-1-methylethyl]-benzimidazolium chloride (**1a**) (0.21 mmol, 64 mg) and $[Rh(OH)(cod)]_2$ (0.1 mmol, 46 mg) were stirred in THF (2 mL) at room temperature for 16 h under Ar. After passing through a short silica gel column using THF as a solvent, the filtrate was evaporated using a rotary evaporator, yielding [RhCl(cod)(NHC)] complex **1b** as a yellow solid (103 mg, 99% yield): ^1H NMR (400 MHz, $CDCl_3$): Major isomer: δ = 7.47 (d, J = 8.8 Hz, 1H), 7.34–7.27 (m, 5H), 7.14 (td, J = 0.8 and 10.0 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 6.63–6.54 (m, 1H, CH_2OH), 6.33 (d, J = 15.6 Hz, 1H, CH_2Ph), 6.03 (d, J = 15.6 Hz, 1H, CH_2Ph), 5.18–5.16 (m, 1H, CH_{cod}), 5.12–5.07 (m, 1H, CH_2OH), 4.22–4.12 (m, 1H, CHN), 4.11–4.09 (m, 1H, CH_{cod}), 3.68–3.65 (m, 1H, CH_{cod}), 3.52–3.26 (m, 1H, CH_{cod}), 3.27–3.26 (m, 1H, OH), 2.59–2.43 (m, 2H, CH_{2cod}), 2.37–2.28 (m, 1H, CH_{2cod}), 2.19–2.06 (m, 3H, CH_{2cod}), 1.92–1.83 (m, 2H, CH_{2cod}), 1.78 (d, J = 7.6 Hz, 3H, CH_3) ppm. Minor isomer: δ = 7.39 (d, J = 8.8 Hz, 1H), 7.18–7.12 (m, 1H), 6.93 (d, J = 8.0 Hz, 1H), 6.48 (d, J = 15.6 Hz, 1H, CH_2Ph), 6.37 (d, J = 15.6 Hz, 1H, CH_2Ph), 4.08–4.06 (m, 1H, CH_{cod}), 3.57 (br, 1H, CH_{cod}), 1.66 (d, J = 7.6 Hz, 3H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): Major isomer: δ = 196.3 (d, $J_{C\text{-}Rh}$ = 50.8 Hz, $C_{carbene}$), 135.6, 135.5, 128.7,

127.7, 126.9, 122.3, 122.3, 111.4 (C of of NHC ring), 111.3 (C of of NHC ring), 100.7 (d, J_{C-Rh} = 6.7 Hz, CH_{cod}), 99.9 (d, J_{C-Rh} = 6.7 Hz, CH_{cod}), 70.0 (d, J_{C-Rh} = 14.4 Hz, CH_{cod}), 68.5 (d, J_{C-Rh} = 14.4 Hz, CH_{cod}), 63.7 (NCH), 59.4 (CH_2O), 52.5 (CH_2Ph), 33.8 (CH_{2cod}), 31.5 (CH_{2cod}), 29.5 (CH_{2cod}), 27.6 (CH_{2cod}), 16.3 (CH_3) ppm. Minor isomer: δ = 196.4 (d, J_{C-Rh} = 50.8 Hz, $C_{carbene}$), 135.9, 134.7, 128.7, 127.6, 126.8, 122.4, 111.1 (C of the NHC ring), 99.3 (d, J_{C-Rh} = 6.7 Hz, CH_{cod}), 98.5 (d, J_{C-Rh} = 6.7 Hz, CH_{cod}), 63.8 (NCH), 58.4 (CH_2O), 32.9 (CH_{2cod}), 30.7 (CH_{2cod}), 28.9 (CH_{2cod}), 27.9 (CH_{2cod}), 17.0 (CH_3) ppm. HRMS (ESI-TOF), *m*/*z*: calculated for $C_{25}H_{30}N_2ORh$ [M-Cl]$^+$, 477.1408, found, 477.1385. The NMR spectrum can be found in the Supplementary Materials.

3.2. 1-[(S)-2-hydroxy-1-methylethyl]-3-(diphenylmethyl)benzimidazolium Bromide (**2a**)

A mixture of (S)-2-benzimidazol-1-yl-propan-1-ol (4.2 mmol, 740 mg) and benzhydryl bromide (4.0 mmol, 989 mg) in toluene (18 mL) was stirred at 110 °C for 72 h. The solvent was evaporated under reduced pressure upon completion of the reaction, resulting in a brown liquid. The product obtained from the residue was isolated via column chromatography on silica gel (CH_2Cl_2/CH_3OH = 95/5). The desired azolium salt **2a** was further purified by reprecipitating in $CHCl_3$ and $CH_3CO_2C_2H_5$, yielding a white solid (620 mg, 37% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.86 (s, 1H, $NCHN^+$), 7.93 (d, J = 8.5 Hz, 1H), 7.55 (t, J = 7.9 Hz, 1H), 7.48–7.38 (m, 12H), 7.24 (d, J = 8.5 Hz, 1H), 5.20–5.16 (m, 1H, CH_2O), 5.09 (t, J = 6.5 Hz, 1H, OH), 4.05–3.95 (m, 2H, NCH and CH_2O), 1.64 (d, J = 6.7 Hz, 3H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 140.9 ($NCHN^+$), 135.2, 131.9, 131.3, 129.5, 129.4, 129.4, 129.3, 128.6, 128.4, 127.0, 126.9, 114.9 (C of azolium), 114.3 (C of azolium), 66.5 (NCH), 62.9 (OCH_2), 57.4 (NCH_2), 16.7 (CH_3) ppm. Elemental analysis calculated (%) for $C_{23}H_{23}BrN_2O$: C 65.25, H 5.48, N 6.62; found: C 65.15, H 5.44, N 6.56. The NMR spectrum can be found in the Supplementary Materials.

3.3. Bromo(η^2,η^2-cycloocta-1,5-diene){1-[(S)-2-hydroxy-1-methylethyl]-3-diphenylmethylbenzimidazol-2-ylidene}rhodium(I) (**2b**)

Azolium bromide **2a** (0.137 mmol, 58 mg) and $[Rh(OH)(cod)]_2$ (0.065 mmol, 30 mg) were stirred in THF (2 mL) at room temperature for 16 h under Ar. After the reaction, a yellow precipitate formed. The resulting yellow solid was collected by filtration and washed with ether. The desired [RhBr(cod)(NHC)] complex **2b** was obtained as a yellow solid (58 mg, 70% yield): ^{1}H NMR (400 MHz, $CDCl_3$): Major isomer: δ = 8.75 (s, 1H, Ph_2CH), 7.47 (d, J = 8.2 Hz, 1H), 7.41–7.39 (m, 5H), 7.37–7.35 (m, 2H), 7.25–7.23 (m, 3H), 7.09 (t, J = 7.7 Hz, 1H), 6.89 (t, J = 7.9 Hz, 1H), 6.74 (d, J = 8.2 Hz, 1H), 6.56–6.50 (m, 1H, CH_2OH), 5.31 (br, 1H, CH_{cod}), 5.12–5.09 (m, 1H, CH_2OH), 4.27–4.19 (m, 1H, CHN), 4.15–4.10 (m, 1H, CH_{cod}), 3.50 (br, 1H, CH_{cod}), 3.27 (dd, J = 2.9 and 9.3 Hz, 1H, OH), 2.78 (br, 1H, CH_{cod}), 2.54–2.42 (m, 2H, CH_{2cod}), 2.23–2.15 (m, 1H, CH_{2cod}), 2.09 (br, 1H, CH_{2cod}), 1.99 (br, 1H, CH_{2cod}), 1.85–1.64 (m, 2H, CH_{2cod}), 1.44–1.43 (m, 1H, CH_{2cod}), 1.78 (d, J = 7.2 Hz, 3H, CH_3) ppm. Minor isomer: δ = 3.74 (br, 1H, CH_{cod}), 2.15 (br, 1H, CH_{2cod}), 1.73 (d, J = 7.2 Hz, 3H, CH_3) ppm. Elemental analysis calculated (%) for $C_{31}H_{34}BrN_2ORh{\cdot}H_2O$: C 57.16, H 5.57, N 4.30; found: C 57.54, H 5.31, N 4.45. HRMS (ESI-TOF), *m*/*z*: calculated for $C_{31}H_{34}N_2Rh$ [M-Br]$^+$, 553.1721, found, 553.1723. The NMR spectrum can be found in the Supplementary Materials.

4. Conclusions

In summary, two rhodium complexes featuring hydroxyalkyl-functionalized NHC ligands were successfully synthesized by treating the corresponding benzimidazolium salts with $[Rh(OH)(cod)]_2$ via a one-pot deprotonation route. This is a new addition to hydroxyalkyl-functionalized NHC/metal complexes. Further investigations are underway to explore the preparation of conformationally stable anionic alkoxide–NHC/metal complexes and their potential applications in enantioselective transformation reactions.

Supplementary Materials: The following supporting information information is available online. Figures S1 and S2: ^{1}H NMR and ^{13}C{^{1}H} NMR of compound **1b**; Figures S3 and S4: ^{1}H NMR and ^{13}C{^{1}H} NMR of compound **2a**; and Figure S5: ^{1}H NMR and HMRS of compound **2b**.

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

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