Short Note

Chloro(η²,η²-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 [RuCl₂(p-cymene)]₂ and the corresponding NHC/Ag(I) complex derived from a chiral benzimidazolium salt using the Ag₂O 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 [PdCl₂(NHC)] complex was synthesized by reacting an imidazolinium salt bearing a hydroxyalkyl sidearm with PdCl₂ in the presence of KOtBu [6]. Additionally, Grisi and coworkers synthesized a [PdCl₂(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(Me₂S)] in the presence of K₂CO₃ [8]. Furthermore, several research groups have successfully synthesized well-defined anionic alkoxide–NHC/metal (Cu, Ag, Ni, and Pd) complexes [9–11].

Scheme 1. List of monodentate hydroxyalkyl-functionalized NHC/metal complexes.
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 [RuCl₂(NHC)(p-cymene)] complex from the hydroxyalkyl-substituted benzimidazolium salt using the Ag₂O 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 Ag₂O at room temperature for 2 h. Subsequently, [RuCl₂(p-cymene)]₂ was introduced into the reaction vessel. After stirring the resultant reaction mixture at room temperature for 16 h, the corresponding [RuCl₂(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.](image)

(i) 2-Fluoronitrobenzene, NaHCO₃; ii) H₂, Pd/C, MeOH; (iii) CH(OEt)₃, p-TsOH+H₂O; (iv) R-X

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'Bu, K₂CO₃, and Ag₂O, 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 = C₂₅H₃₀ClN₂ORh) was clearly observed. In the ¹³C{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 sp² carbons of the cod ligand on complex 1b in the ¹³C{¹H} NMR spectrum. Additionally, four singlet signals for the sp³ 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 $\delta = 3.27$ 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.

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. $^1$H 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($^1$H) NMR in CDCl$_3$, (CD$_3$)$_2$SO, CD$_3$OD, or (CD$_3$)$_2$CO 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. $^1$H (400 MHz) and $^{13}$C($^1$H) (100 MHz) NMR spectra were acquired on a JEOL ECS-400 spectrometer (JEOL, Tokyo, Japan). Chemical shifts are reported downfield from TMS ($\delta = 0$ ppm) for $^1$H NMR. For $^{13}$C($^1$H) 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($^2$$^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): $^1$H NMR (400 MHz, CDCl$_3$): Major isomer: $\delta = 7.47$ (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$_2$OH), 6.33 (d, J = 15.6 Hz, 1H, CH$_2$Ph), 6.03 (d, J = 15.6 Hz, 1H, CH$_2$Ph), 5.18–5.16 (m, 1H, CH$_{cod}$), 5.12–5.07 (m, 1H, CH$_{cod}$), 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: $\delta = 7.39$ (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$_2$Ph), 6.37 (d, J = 15.6 Hz, 1H, CH$_2$Ph), 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($^1$H) NMR (100 MHz, CDCl$_3$): Major isomer: $\delta = 196.3$ (d, J$_{C-Rh}$ = 50.8 Hz, C$_{carbene}$), 135.6, 135.5, 128.7,
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$_2$Cl$_2$ / CH$_3$OH = 95/5). The desired azolium salt 2a was further purified by reprecipitating in CHCl$_3$ and CH$_3$CO$_2$H$_2$s, yielding a white solid (620 mg, 37% yield): $^1$H NMR (400 MHz, CDCl$_3$): δ = 8.96 (s, 1H, NCH$^+$), 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$_2$O), 5.09 (t, J = 6.5 Hz, 1H, OH), 4.05–3.95 (m, 2H, NCH and CH$_2$O), 1.64 (d, J = 6.7 Hz, 3H, CH$_3$O) ppm. $^{13}$C($^1$H) NMR (100 MHz, CDCl$_3$): δ = 140.9 (NCH$^+$), 135.2, 131.9, 131.3, 129.5, 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$_2$H$_2$Br$_2$N$_2$O: 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($^2$H$_2$,$^2$H$_2$-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$_2$CH), 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$_2$OH), 5.31 (br, 1H, CH$_2$O), 5.12–5.09 (m, 1H, CH$_2$OH), 4.27–4.19 (m, 1H, CH$_2$N), 4.15–4.10 (m, 1H, CH$_2$O), 3.50 (br, 1H, CH$_2$O), 3.27 (dd, J = 2.9 and 9.3 Hz, 1H, OH), 2.78 (br, 1H, CH$_2$O), 2.54–2.42 (m, 2H, CH$_2$O), 2.23–2.15 (m, 1H, CH$_2$O), 2.09 (br, 1H, CH$_2$O), 1.99 (br, 1H, CH$_2$O), 1.85–1.64 (m, 2H, CH$_2$O), 1.44–1.43 (m, 1H, CH$_2$O), 1.78 (d, J = 7.2 Hz, 3H, CH$_3$) ppm. Minor isomer: δ = 3.74 (br, 1H, CH$_2$O), 2.15 (br, 1H, CH$_2$O), 1.73 (d, J = 7.2 Hz, 3H, CH$_3$) ppm. Elemental analysis calculated (%) for C$_3$H$_3$Br$_2$N$_2$O$^+$H$_2$O: 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$_2$H$_2$S$_2$N$_2$OH$^+$, 477.1408, found, 477.1385. 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.

Author Contributions: Conceptualization, Methodology, and Writing—original draft preparation, S.S.; Investigation—experiments and analyses, S.M. and S.S.; Writing—review and editing, S.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: The data presented in this study are available in this article.

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

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