Electrochemical Reduction

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Synthesis and Electrochemical Reduction of a Ruthenium Complex Bearing an *N*,*N*-Bis[(benzo[*g*][1,5]naphthyridin-2-yl)methyl]propane-2-amine Ligand as an NAD^+/NADH-Type Redox Site**

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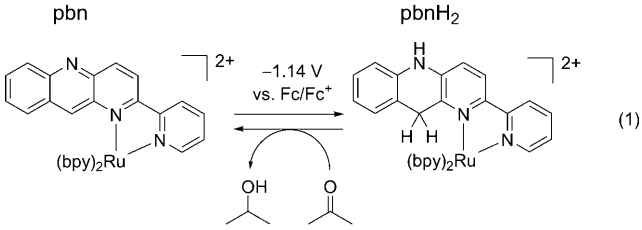
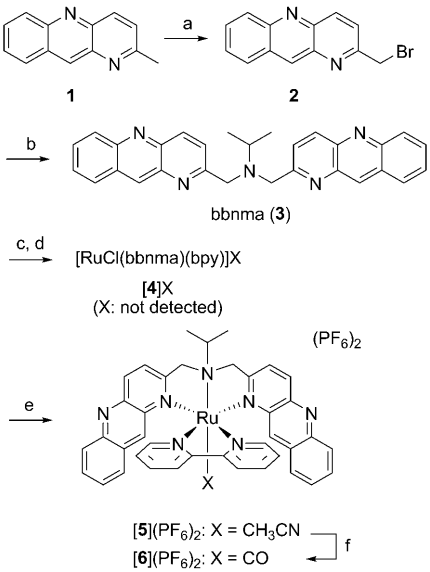
Hydrogenation is one of the most important chemical transformations for a wide range of materials, and a variety of metal hydrides have been used in catalytic hydrogenation reactions with hydrogen gas.[1] As an alternative, electrocatalytic reduction is a clean process and has advantages in terms of cost, regulation of reactivity of catalysts by choosing applied potentials, and handling compared with the use of stoichiometric amounts of common reducing agents, such as $LiAlH_4$. In addition, reduction without the use of hydrogen gas makes the manipulation simple and safe, both in laboratory and industrial reactions. Metal hydride compounds are generally sensitive to water because of their high reactivity. Conversely, the nicotinamide adenine dinucleotide redox couple (NAD^+/NADH) functions as a reservoir/source of two electrons and one proton, and plays key roles in various biological redox reactions.[2] To mimic the efficiency and versatility of the NAD^+/NADH redox couple, a variety of model reactions have been conducted using NADH model compounds.[3] However, the reactions reported so far have been stoichiometric in nature. We have reported the synthesis of 2-(2-pyridyl)benzo[*g*][1,5]naphthyridine (pbn) and its ruthenium complex $[Ru(bpy)_2(pbn)](PF_6)_2$ (bpy = 2,2′-bipyridine), the latter of which underwent a pbn-localized redox reaction at −1.14 V (versus the ferrocene/ferrocenium (Fc/Fc^+) couple) in CH_3CN/AcOH/NaOAc to afford $[Ru(bpy)_2(pbnH_2)](PF_6)_2$ as an NADH-type two-electron reductant. The ruthenium–$pbnH_2$ complex catalytically reduced acetone to give 2-propanol with regeneration of the Ru-pbn complex under acidic conditions [Eq. (1)].[4]



(1)

To expand the utility of the NAD^+/NADH-type redox reaction by benzo[*g*][1,5]naphthyridine for a variety of materials, we designed a new tridentate ligand, *N*,*N*-bis-[(benzo[*g*][1,5]naphthyridin-2-yl)methyl]propane-2-amine (denoted as bbnma) which incorporates two benzo[*g*]-[1,5]naphthyridines tethered to a tertiary amine, and its complex with ruthenium and bipyridine, namely $[Ru(bbnma)(bpy)L](PF_6)_2$ (L = CH_3CN, CO). The ligand bbnma is designed to create a space, not only to introduce substrates, such as ketones, imines, and related unsaturated compounds including CO and CO_2, onto the ruthenium center by substitution of a monodentate ligand, but also to place such substrates forcibly in the vicinity of the two NADH-type hydride sources on bbnma, coordinated in a facial fashion. Herein, we report the synthesis of a novel ruthenium complex having a new type of NAD^+/NADH-type ligand (bbnma) and its electrochemical reduction and structural characterization.

The syntheses of bbnma and its ruthenium complexes are summarized in Scheme 1. 2-(Bromomethyl)benzo[*g*]-



Scheme 1. Synthesis of $[Ru(bbnma)(bpy)(CO)](PF_6)_2$. Reagents and conditions: a) NBS, AIBN, CCl_4, reflux, 68%; b) $iPrNH_2$, K_2CO_3, CH_3CN/CH_2Cl_2, 25 °C, 68%; c) $[RuCl(bpy)(CH_3CN)_3]PF_6$, $CH_3OCH_2CH_2OH$, 95 °C; d) Alumina column chromatography; e) $NaPF_6$, CH_3CN/H_2O, 25 °C, 60% from **3**; f) CO (20 atm), CH_2Cl_2/EtOH, 25 °C, 98%.

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[1,5]naphthyridine (**2**) was prepared in 68% yield by treatment of 2-methylbenzo[*g*][1,5]naphthyridine (**1**)[5] with 1.1 equivalents of *N*-bromosuccinimide (NBS) and 0.1 equivalents of 2,2′-azobis(isobutyronitrile) (AIBN) in refluxing CCl_4 for 6 h. The reaction of **2** with 0.5 equivalents of isopropylamine in the presence of excess potassium carbonate in CH_2Cl_2/CH_3CN (1/1 v/v) at 25 °C for 24 h gave bbnma (**3**) in 68% yield. An equimolar mixture of **3** and $[RuCl(bpy)(CH_3CN)_3]PF_6$ in 2-methoxyethanol was stirred at 95 °C for 12 h. Subsequent column chromatography on alumina afforded the ruthenium chloride complex $[\mathbf{4}]^+X^-$ (X = mixture of Cl^- and PF_6^-). The cation $[\mathbf{4}]^+$ was characterized by ESI mass spectrometry and ^{1}H NMR spectroscopy. The chloride ligand on $[\mathbf{4}]^+$ was readily substituted by acetonitrile in CH_3CN/H_2O (5:1 v/v) containing excess sodium hexafluorophosphate at 25 °C, to afford $[Ru(bbnma)(bpy)(CH_3CN)](PF_6)_2$ ($[\mathbf{5}](PF_6)_2$) in 60% yield from **3**.

The crystal structure of $[\mathbf{5}]^{2+}$ (Figure 1) exhibited a distorted octahedral cooordination geometry around the Ru center formed by coordination of bbnma, bpy, and acetonitrile ligands. The bbnma ligand coordinated to ruthenium in a facial fashion through the tertiary nitrogen and 1- and 1′-nitrogen atoms of the benzo[*g*][1,5]naphthyridine moieties. Coordination of the bbnma and acetonitrile ligands was highly distorted from octahedral geometry, presumably as a result of the steric repulsion between the two benzonaphthyridine moieties and the coordinated acetonitrile molecule. The bond angles of N3-Ru1-N8 and Ru1-N8-C40 are 171.75(9) and 168.8(2)°, respectively. Conversely, the ^{1}H NMR spectrum of $[\mathbf{5}](PF_6)_2$ in CD_2Cl_2 at 25 °C showed that the signals of two sets of methyl, methylene, or aromatic protons were equivalent on the NMR timescale. The acetonitrile complex $[\mathbf{5}](PF_6)_2$ gave $[Ru(bbnma)(bpy)(CO)](PF_6)_2$ ($[\mathbf{6}](PF_6)_2$) in MeOH under 20 atm CO at 25 °C for 3 days (Scheme 1). Interestingly, during the purification of $[\mathbf{6}](PF_6)_2$ by column chromatography on neutral alumina with an eluent of CH_2Cl_2/CH_3OH (20:1), deprotonation of one methylene group with formation of a covalent bond between the ruthenium and nitrogen centers occurred, to give *rac*-$[\mathbf{7}]^+$, accompanied by a change in the color of the complex from brown to red [Eq. (2)]. The mass spectrum of *rac*-$[\mathbf{7}]^+$ displayed the parent signal at *m*/*z* 728.2, with a monocationic mass pattern, and the ^{1}H NMR spectrum showed olefinic proton signals (H^a and H^b) at $\delta = 4.52$ (s), 6.65 (d, $J = 9.8$ Hz), and 6.37 ppm (d, $J = 9.8$ Hz), with desymmetrization of two methyl groups ($\delta = 1.10$ and 0.52 ppm) and aromatic proton signals (16 different signals). The ν(CO) band of *rac*-$[\mathbf{7}]^+$ was detected at 1955 cm^{-1} in the IR spectrum. Treatment of a solution of *rac*-$\mathbf{7}^+$ in CH_2Cl_2 with aqueous sodium hexafluorophosphate regenerated $[\mathbf{6}](PF_6)_2$ quantitatively [Eq. (2)]. The carbonyl complex $[\mathbf{6}](PF_6)_2$ displayed the ν(CO) band at 1984 cm^{-1} in the IR spectrum. The ESI-MS and ^{1}H NMR spectroscopic data of $[\mathbf{6}](PF_6)_2$ also support the similar structure of the acetonitrile complex.

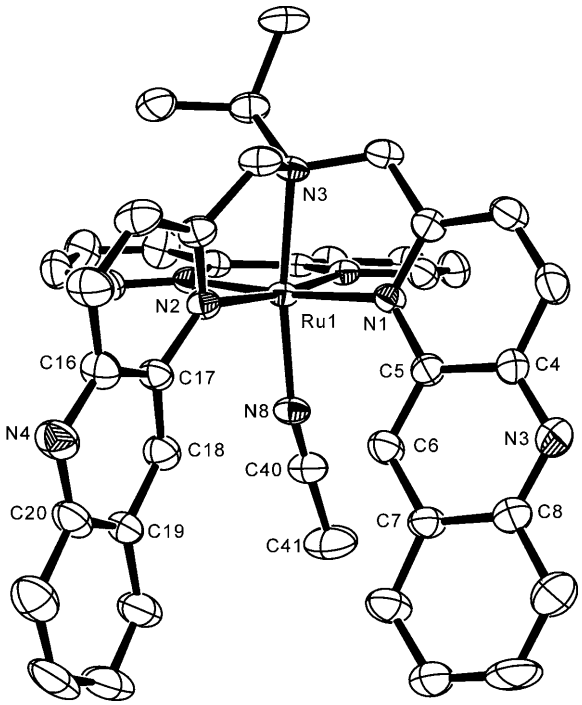
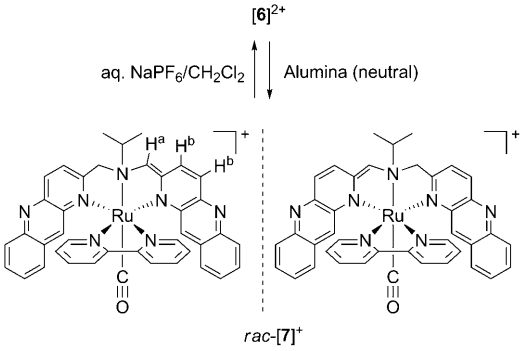


Figure 1. ORTEP representation of $[\mathbf{5}]^{2+}$ with thermal ellipsoids set at 50% probability. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: Ru1–N1 2.089(2), Ru1–N2 2.145(2), Ru1–N3 2.1256(18), Ru1–N8 2.0703(19), C5–C6 1.382(4), C6–C7 1.393(3), C17–C18 1.378(3), C18–C19 1.411(4); N3-Ru1-N8 171.75(9), Ru1-N8-C40 168.8(2).



(2)

The cyclic voltammogram (CV) of $\mathbf{6}(PF_6)_2$ (1 mM; Figure 2) shows four cathodic waves ($E_{pc} = -1.0$ (broad), −1.27, −1.35, and −1.61 V vs. $Ag/AgNO_3$ 0.1M) and four anodic ones ($E_{pa} = +0.30$, 0 (broad), −1.13, and −1.50 V) in the presence of LiOTf (0.1M) in 2-propanol/CH_2Cl_2 (1:1 v/v, gray line). The nearly reversible couple at $E_{pc} = -1.61$ V and $E_{pa} = -1.50$ V is assigned to a bipyridine-based redox reaction. Two of the remaining three cathodic waves ($E_{pc} = -1.0$ (broad), −1.27 and −1.35 V) would be correlated with the reductions of two benzo[*g*][1,5]naphthyridine groups of bbnma, since analogous $[Ru(bbnp)(terpy)]^{2+}$ (bbnp = 2,6-bis(benzo[*g*][1,5]naphthyridin-6-yl)-4-*tert*-butylpyridine, terpy = 2,2′:6′,2″-terpyridine) displays two bbnp-localized redox couples in CH_3CN.[6] The complexes $[\mathbf{6}]^{2+}$ and *rac*-$[\mathbf{7}]^+$ coexisted in CH_3OH [Eq. (2)], and an addition of excess acid into the solution completely shifted the equilibrium to $[\mathbf{6}]^{2+}$ owing to the suppressed deprotonation of the methylene

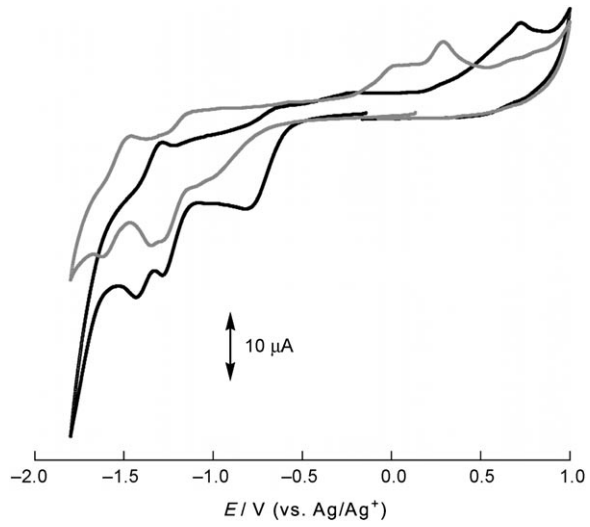
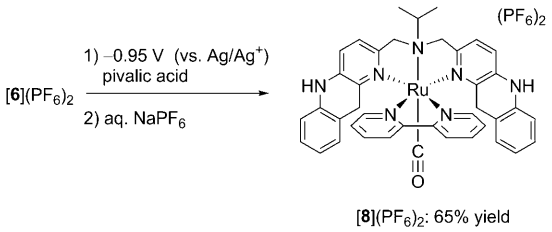


Figure 2. Cyclic voltammograms of 1 mM $[\mathbf{6}](PF_6)_2$ in 0.1 M LiOTf/(2-propanol/CH_2Cl_2 (1:1 v/v)) under Ar in the absence (gray line) and in the presence (black line) of pivalic acid.

groups of bbnma.[7] Two irreversible anodic waves at $E_{pa} = 0$ (broad) and $+0.30$ V are associated with oxidations of *rac*-$[\mathbf{7}]^+$ and its deprotonated form, or those of $[\mathbf{6}]^{2+}$, alongside deprotonation of the bbnma methylene groups.[8] On addition of 10 equivalents of pivalic acid to the solution these anodic waves disappear (black line), and the reversible bipyridine-based redox couple at $E_{1/2} = -1.55$ V in 2-propanol/CH_2Cl_2 (gray line) shifts to -1.49 V (black line). Furthermore, the three cathodic waves ($E_{pc} = -1.0$ (broad), -1.27, and -1.35 V) that correlate with the bbnma-based reduction (gray line) become two cathodic waves ($E_{pc} = -0.81$ (broad) and -1.28 V) in the presence of the acid (black line). Based on the redox behavior of similar complexes, [Ru(bbnp)-(terpy)]$^{2+}$ and [Ru(bpy)$_2$(pbn)]$^{2+}$, in the presence of proton sources,[6] broad cathodic and anodic waves at $E_{pc} = -0.81$ V and $E_{pa} = +0.72$ V, respectively, are assigned to the reduction of benzo[*g*][1,5]naphthyridine, affording 5,10-dihydrobenzo[*g*][1,5]naphthyridine, and the reverse oxidation reaction, respectively. In fact, the controlled-potential electrolysis of $[\mathbf{6}](PF_6)_2$ at -0.95 V (vs. Ag/Ag^+) in the same media proceeded smoothly, and the cathodic current stopped completely upon consumption of 4.5 molar equivalents of electricity.[9] The ESI mass spectrum of the complex obtained by electrolysis and subsequent anion exchange with aqueous $NaPF_6$ displayed a parent signal at $m/z = 366.6$ with a dicationic mass pattern corresponding to an increase of 4 mass units, based on $[\mathbf{6}]^{2+}$. The ^{1}H NMR spectrum of a solution of the same complex in CD_2Cl_2 had lost the singlet signal corresponding to the aromatic proton at the 10-position of the benzo[*g*][1,5]naphthyridine groups, with two new singlet signals at $\delta = 6.94$ (NH, 2H) and 4.20 ppm (CH_2, 4H). The addition of CD_3OD to the solution resulted in the disappearance of the signal at $\delta = 6.94$ ppm. The signal at $\delta =$ 4.20 ppm split into two sets of doublets ($\delta = 4.14$ and 4.08 ppm, $J = 17.1$ Hz) at -30 °C. These results suggest that the electrochemical reduction of $[\mathbf{6}]^{2+}$ in the presence of pivalic acid produces [Ru(bbnmaH$_4$)(bpy)(CO)]$(PF_6)_2$ ($[\mathbf{8}](PF_6)_2$), bearing two 5,10-dihydrobenzo[*g*][1,5]naphthyridines groups [Eq. (3)]. The exact structure of $[\mathbf{8}](PF_6)_2$ was determined by single-crystal X-ray diffraction of the complex (Figure 3).



(3)

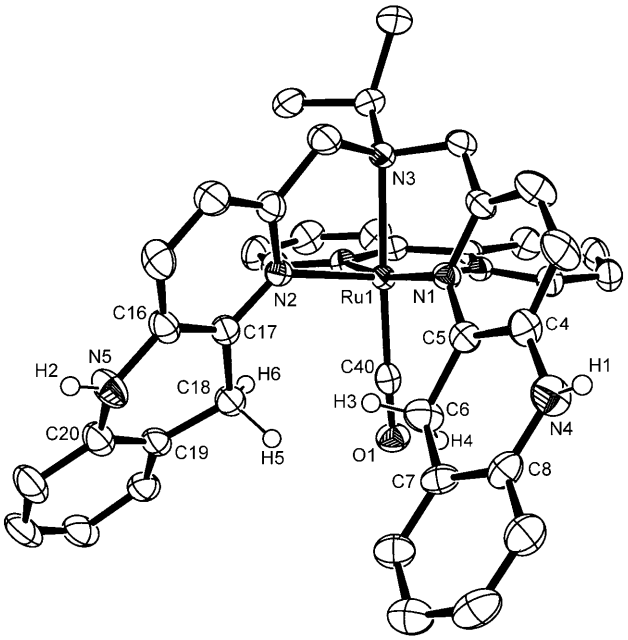


Figure 3. An ORTEP representation of $[\mathbf{8}]^{2+}$ with thermal ellipsoids set at 50% probability. Hydrogen atoms, except for those at N4, N5, C6, and C18 are omitted for clarity. Selected bond lengths, interatomic distances [Å], and angles [°]: Ru1–N1 2.1259(18), Ru1–N2 2.1365(19), Ru1–N3 2.207(2), Ru1–C40 1.853(2), C5–C6 1.499(3), C6–C7 1.498(3), C17–C18 1.516(3), C18–C19 1.492(3); C40–H3 2.84(2), C40–H4 2.41(2), C40–H5 2.59(2), C40–H6 2.55(2); N3-Ru1-C40 177.85(9), Ru1-C40-O1 173.8(2).

The bond lengths of C5–C6, C6–C7, C17–C18, and C18–C19 (1.499(3), 1.498(3), 1.516(3), and 1.492(3) Å, respectively) are longer than the corresponding bond lengths in the acetonitrile complex $[\mathbf{5}](PF_6)_2$ (1.378(3)–1.411(4) Å), clearly indicating the occurrence of the four-electron reduction in the 5- and 10-positions of both benzo[*g*][1,5]naphthyridine moieties. The hydrogen atoms at the 10-position are located close to the CO ligand. The distances C40–H3, C40–H4, C40–H5, and C40–H6 (2.84(2), 2.41(2), 2.59(2), and 2.55(2) Å, respectively) are shorter than the total of the van der Waals radii of hydrogen and carbon atoms.[10] Thus, the reduction of the bbnma ligand successfully creates a NADH-type hydride source in the vicinity of the carbonyl carbon atom.

In summary, the complex $[\mathbf{6}](PF_6)_2$ was synthesized in 12 steps from commercially available 3-aminoquinoline in 3% overall yield. The bbnma/bbnmaH_4 redox reaction suggests a new method for intramolecular hydride-transfer reactions. Studies on multielectron reductions of unsaturated compounds with $[\mathbf{6}]^{2+}$ are currently underway.

Experimental Section

See the Supporting Information for experimental details and characterization data of compounds **2**–**8**, including X-ray diffraction studies. CCDC 691510 ($[\mathbf{5}](PF_6)_2$) and 691511 ($[\mathbf{8}](PF_6)_2$) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

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[7] The major signal of the ESI-MS spectrum of $[\mathbf{6}](PF_6)_2$ in CH_3OH was $m/z = 728.2$ (*rac*-$\mathbf{7}^+$) rather than $m/z = 364.2$ ($[\mathbf{6}]^{2+}$). An addition of ten equivalents of pivalic acid to the CH_3OH solution resulted in disappearance of the $m/z = 728.2$ (*rac*-$[\mathbf{7}]^+$) peak, and the parent peak of $[\mathbf{6}]^{2+}$ ($m/z = 364.2$) became the major signal.

[8] The controlled potential electrolysis of $[\mathbf{6}](PF_6)_2$ at $+0.50$ V in 2-propanol/CH_2Cl_2 resulted in degradation of the complex, since the ESI-MS spectra of the oxidation products showed elimination of a benzo[*g*][1,5]naphthyridine group from the complex. The similar electrolysis at -0.10 V under otherwise the same conditions also caused decomposition of the complex without affording $[\mathbf{8}]^+$. Thus, 2-propanol did not work as a proton source in the reduction of $[\mathbf{6}]^{2+}$.

[9] The electrolysis of $[\mathbf{6}](PF_6)_2$ at -1.30 V in the presence of ten equivalents of pivalic acid in 2-propanol/CH_2Cl_2 consumed more than five molar equivalents of electricity. Attempts to identify the reduction product were not successful as a result of the extreme lability of the product.

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