Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Organometallic Chemistry 689 (2004) 4820–4832
Journal of Organometallic Chemistry
www.elsevier.com/locate/jorganchem

Cyclometalated *N*,*N*-dimethylbenzylamine ruthenium(II) complexes $[Ru(C_6HR^1R^2R^3\text{-}o\text{-}CH_2NMe_2)(bpy)(RCN)_2]PF_6$ for bioapplications: synthesis, characterization, crystal structures, redox properties, and reactivity toward PQQ-dependent glucose dehydrogenase

Ronan Le Lagadec [a,*], Laura Rubio [a], Larissa Alexandrova [b], Rubén A. Toscano [a], Ekaterina V. Ivanova [c], Rolandas Meškys [d], Valdas Laurinavičius [d], Michel Pfeffer [e], Alexander D. Ryabov [*,f]

[a] *Instituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, Coyoacán, 04511 México DF, Mexico*
[b] *Instituto de Investigaciones en Materiales, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, Coyoacán, 04511 México DF, Mexico*
[c] *Department of Chemistry, Moscow State University, 119899 Moscow, Russia*
[d] *Laboratory of Bioanalysis, Institute of Biochemistry, Mokslininku 12, Vilnius 2600, Lithuania*
[e] *UMR 7513, Laboratoire de Synthèses Métallo-Induites, Université Louis Pasteur, 4, rue Blaise Pascal, 67000 Strasbourg, France*
[f] *Department of Chemistry, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, PA 15213, USA*

Received 12 August 2004; accepted 24 September 2004
Available online 22 October 2004

Abstract

Cyclometalated derivatives of ring-substituted *N*,*N*-dimethylbenzylamines with controlled redox potentials as potent mediators of bioelectrochemical electron transport are reported. The cycloruthenation of $R^1R^2R^3C_6H_2CH_2NMe_2$ (R^1, R^2, R^3 = H, Me, ^{t}BuO, MeO, NMe_2, F, CF_3, CN, NO_2) by $[(\eta^6\text{-}C_6H_6)RuCl(\mu\text{-}Cl)]_2$ in the presence of NaOH/KPF_6 in acetonitrile or pivalonitrile affords cyclometalated complexes $[(\eta^6\text{-}C_6H_6)Ru(C_6HR^1R^2R^3\text{-}o\text{-}CH_2NMe_2)(RCN)]PF_6$ [R = Me (**1**) and R = CMe_3 (**2**)] in good yields. Reactions of complexes **1** and **2** with 2,2′-bipyridine (bpy) in acetonitrile or pivalonitrile result in dissociation of η^6-bound benzene and the formation of $[Ru(C_6HR^1R^2R^3\text{-}o\text{-}CH_2NMe_2)(bpy)(RCN)_2]PF_6$ [R = Me (**3**) and R = CMe_3 (**4**)]. All new compounds have been fully characterized by mass spectrometry, $^1H/^{13}C$ NMR, and IR spectroscopy. An X-ray crystal structural investigation of complex **1** ($R^1/R^2/R^3$ = H/H/H) and two complexes of type **3** ($R^1/R^2/R^3$ = MeO/H/H, MeO/MeO/H) has been performed. Acetonitrile ligands of **3** are mutually *cis* and the σ-bound carbon is *trans* to one of the bpy nitrogens. Measured by the cyclic voltammetry in MeOH as solvent, the redox potentials of complexes **3** for the $Ru^{II/III}$ feature cover the range 320–720 mV (versus Ag/AgCl) and correlate linearly with the Hammett ($\sigma_p^+ + \sigma_m$) constants. Complexes **3** mediate efficiently the electron transport between the active site of PQQ-dependent glucose dehydrogenase (PQQ = pyrroloquinoline quinone) and a glassy carbon electrode. Determined by cyclic voltammetry the second order rate constant for the oxidation of the reduced (by D-glucose) enzyme active site by Ru^{III} derivative of **3** ($R^1/R^2/R^3$ = H) (generated electrochemically) is as high as 4.8×10^7 M^{-1} s^{-1} at 25 °C and pH 7.

Keywords: Cyclometalation; Ruthenium complexes; Electrochemistry; Electron transfer; Kinetics; PQQ-dependent glucose dehydrogenase

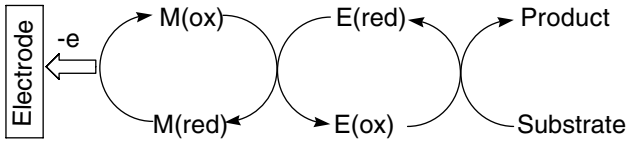
* Corresponding author. Tel.: +52 555 622 4515; fax: +52 555 616 2203.
E-mail address: ronan@seridor.unam.mx (R. Le Lagadec).

0022-328X/$ - see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.jorganchem.2004.09.056

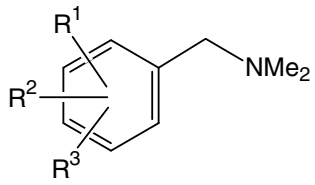
1. Introduction

Since Cope and Siekman discovery in 1965 [1], cyclometalated transition metal complexes have found numerous applications. The most impressive progress has been achieved in fine organic synthesis [2–5], metal-complex [6–9] and biochemically inspired catalysis [10,11]. Recently, we have disclosed a new sphere for using cyclometalated ruthenium and osmium compounds. The σ-bound arene ring affects tremendously redox potentials of the complexes and this allows to design and prepare the species, which are capable of exchanging electrons with the active sites of redox enzymes [12–15]. Therefore, the complexes appear to be promising mediators for the electron transport between redox enzymes and an electrode for their further incorporation into amperometric biosensors, i.e. bioanalytical devices, the principle of action of which is shown in Scheme 1 [16,17].

Specifically, cationic cyclometalated ruthenium(II) derivatives of 2-phenylpyridine and *N*,*N*-dimethylbenzylamine have been preliminary communicated [12]. The *N*,*N*-dimethylbenzylamine derivatives appear particularly interesting due to a rather uncomplicated preparation of a series of related ligands with various ring-substituents – electron-donating and electron-withdrawing. Both are potentially interesting. Electron-richer complexes are advantageous as low potential mediators for amperometric biosensors (Scheme 1) but electron-poorer species are preferred as "oxidative" mediators used in enzyme-catalyzed oxidations such as an oxidative degradation of lignin [17]. Here, we report on the synthesis, structural characterization, and systematic investigation of a large variety of ruthenium(II) compounds with cyclometalated ring-substituted *N*,*N*-dimethylbenzylamine ligands shown in Chart 1. This work has demonstrated that by changing the ring-substituents the redox potential of the ruthenium complex is tunable within a 400 mV range and predictable in terms of the Hammett formalism. It is demonstrated that the complexes exchange electrons with PQQ-dependent glucose dehydrogenase (PQQ = pyrroloquinoline quinone) and the rate constant determined by cyclic voltammetry reach the level of 10^7 M^{-1} s^{-1}.



Scheme 1. Principle of action of a typical amperometric biosensor based on the mediated electron transfer. Formed after reacting with substrate, reduced enzyme E(red) cannot be oxidized directly by electrode. A small mediator M(ox) can reach the shielded enzyme active site, get an extra electron, and deliver it to electrode.



Amine	R^1	R^2	R^3
a	H	H	H
b	4-Me	H	H
c	3-Me	4-Me	H
d	4-MeO	H	H
e	3-MeO	H	H
f	3-MeO	4-MeO	H
g	3-MeO	5-MeO	H
h	2-MeO	3-MeO	4-MeO
i	3-MeO	4-MeO	5-MeO
j	4-F	H	H
k	3-CF_3	H	H
l	4-CF_3	H	H
m	4-^{t}Bu	H	H
n	4-NMe_2	H	H
o	4-NO_2	H	H
p	4-CN	H	H

Chart 1. Substituted *N*,*N*-dimethylbenzylamines $R^1R^2R^3C_6H_2CH_2NMe_2$ used in this work.

2. Experimental

2.1. Materials and methods

All reactions were performed under the atmosphere of dry argon using a standard Schlenk technique. *N*,*N*-Dimethylbenzylamine, 3-methoxy-*N*,*N*-dimethylbenzylamine, 2,2′-bipyridine and potassium hexafluorophosphate were purchased from Aldrich and used as received. HPLC grade solvents were dried using conventional methods and distilled under nitrogen prior to use. The dimer $[(\eta^6\text{-}C_6H_6)RuCl(\mu\text{-}Cl)]_2$ [18], complex **1a** [19], and substituted *N*,*N*-dimethylbenzylamines **b**–**d** and **f**–**p** were prepared as described [20]. PQQ-dependent glucose dehydrogenase was purified from *Erwinia* sp. 34-1 (specific activity 12 U mg^{-1}) and used as a solution in 0.02 M the same buffer containing 10% glycerol [21].

Satisfactory analytical data (C, H, N) were obtained for all Ru complexes subjected to a combustion analysis performed by the Service Central de Microanalyse du CNRS, Strasbourg (France). Mass spectra were obtained using a JEOL JMS-SX102A instrument with *m*-nitrobenzyl alcohol as the matrix (FAB^+) mode, *m*/*z* [relative abundance (%) throughout]. Infra-red spectra were recorded on a Nicolet FTIR MAGNA 750 instrument in KBr disks (*v* are in

cm^{-1} throughout). Unless otherwise stated all NMR spectra were recorded in CD_3CN using a JEOL GX 300 spectrometer (^1H at 300.5311 and ^{13}C at 75.5757 MHz). The δ scale is used throughout; chemical shifts are in ppm and the coupling constants are in Hz. Two-dimensional shift-correlated experiments (COSY, HETCOR) were used to unambiguously assign the chemical shifts.

Cyclic voltammograms of the ruthenium(II) complexes were run using a PC-interfaced IPC BAS 50W Electrochemical Analyzer (Bioanalytical System Inc., USA) usually in MeOH as a solvent containing 0.1 M $(n\text{-}Bu)_4NClO_4$ as a supporting electrolyte at 25 °C and a scan rate 0.1 V s^{-1}. A three-electrode scheme was applied with working glassy carbon, Ag/AgCl reference, and auxiliary Pt electrodes. The working electrode was always polished with a diamond paste before use. Electrochemical measurements involving GDH were performed on a PC-interfaced potentiostat–galvanostat IPC-4 (Institute of Physical Chemistry, RAS, Moscow, Russia) in aqueous solution at 25 °C. Before measurements the working electrode was polished with a diamond paste and rinsed with ethanol and distilled water. Anodic peak currents (i_o) were obtained from cyclic voltammograms in the absence of the enzyme. Catalytic currents (i_{cat}) were obtained in the presence of GDH and D-glucose. The rate constants k were calculated from the slopes of linear plots of the ratio (i_{cat}/i_o) against ([GDH]/v)$^{1/2}$ (v is the scan rate).

2.2. Synthesis of cycloruthenated complexes

2.2.1. Complexes **1b–p**

A suspension of $[(\eta^6\text{-}C_6H_6)RuCl(\mu\text{-}Cl)]_2$ (0.200 g, 0.4 mmol), the amine (0.8 mmol), NaOH (0.031 g, 0.8 mmol) and KPF_6 (0.292 g, 1.6 mmol) in 15 ml of acetonitrile was stirred at room temperature for 15 h. The resulting dark yellow suspension was filtered over Al_2O_3 using acetonitrile as an eluent. The yellow band was collected, concentrated under vacuum to about 5 ml, and diethyl ether (50 ml) was added. The microcrystalline yellow material was filtered off, washed with diethyl ether (210 ml), and dried under vacuum.

2.2.1.1. Complex ***1b***. Yield: 51%. MS: 369(8) $[(M + H)]^{+\cdot}$, 328(15) $[(M + H) - NCMe]^+$, 250(5) $[M - NCMe - C_6H_6]^{+\cdot}$, IR: 839 (s, PF_6^-). ^1H NMR: 7.91 (s, 1H, H6), 6.87 (d, 1H, $^3J = 7.4$, H3), 6.77 (d, 1H, $^3J = 7.4$, H4), 5.62 (s, 6H, C_6H_6), 3.66 (d, 1H, $^2J = 13.4$, CH_2), 3.22 (d, 1H, $^2J = 13.4$, CH_2), 2.97 (s, 3H, NMe_2), 2.69 (s, 3H, NMe_2), 2.32 (s, 3H, Me), 1.95 (m, 3H, $MeCN/CD_3CN$). ^{13}C NMR: 162.14, 143.73, 139.53 (C6), 135.18, 124.56 (C4), 122.53 (C3), 118.08, 87.99 (C_6H_6), 71.99 (CH_2), 57.80 (NMe_2), 55.52 (NMe_2), 20.40 (Me), 0.67 (NC*Me*).

2.2.1.2. Complex ***1c***. Yield: 56%. MS: 383(13) $[(M + H)]^{+\cdot}$, 342(100) $[(M + H) - NCMe]^+$, 264(24) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$, IR: 840 (s, PF_6^-). ^1H NMR: 7.84 (s, 1H, H6), 6.77 (s, 1H, H3), 5.60 (s, 6H, C_6H_6), 3.64 (d, 1H, $^2J = 13.5$, CH_2), 3.16 (d, 1H, $^2J = 13.5$, CH_2), 2.98 (s, 3H, NMe_2), 2.67 (s, 3H, NMe_2), 2.26 (s, 3H, Me), 2.14 (s, 3H, Me), 1.95 (m, 3H, $MeCN/CD_3CN$). ^{13}C NMR: 158.37, 144.28, 139.86 (C6), 133.92, 131.62, 123.95 (C3), 118.08, 87.82 (C_6H_6), 71.88 (CH_2), 57.74 (NMe_2), 55.51 (NMe_2), 18.66 (Me), 18.39 (Me), 0.67 (NC*Me*).

2.2.1.3. Complex ***1d***. Yield: 46%. MS: 344(97) $[(M + H) - NCMe]^+$, 266(15) $[M^+ - NCMe - C_6H_6]^{+\cdot}$. IR: 839 (s, PF_6^-). ^1H NMR: 7.61 (d, 1H, $^4J = 2.4$, H6), 6.92 (d, 1H, $^3J = 7.9$, H3), 6.52 (dd, 1H, $^3J = 7.9$, $^4J = 2.4$, H4), 5.63 (s, 6H, C_6H_6), 3.80 (s, 3H, MeO), 3.62 (d, 1H, $^2J = 13.5$, CH_2), 3.24 (d, 1H, $^2J = 13.5$, CH_2), 2.91 (s, 3H, NMe_2), 2.72 (s, 3H, NMe_2), 1.95 (m, 3H, $MeCN/CD_3CN$). ^{13}C NMR: 163.95, 157.49, 138.95, 124.63 (C6), 123.02 (C3), 118.04, 108.47 (C4), 88.09 (C_6H_6), 71.95 (CH_2), 57.79 (NMe_2), 55.35 (NMe_2), 54.77 (MeO), 0.66 (NC*Me*).

2.2.1.4. Complexes ***1e*** *and* ***1′e*** *(1:1 mixture).* Yield: 48%. MS: 385(10) $[(M + H)]^{+\cdot}$, 344(75) $[(M + H) - NCMe]^+$, 266(17) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 839 (s, PF_6^-). ^1H NMR: 7.93 (d, 1H, $^3J = 8.2$, H6), 6.98 (t, 1H, $^3J = 7.4$, H′4), 6.73 (d, 1H, $^3J = 8.2$, H5), 6.68 (d, 1H, $^3J = 7.4$, H′3 or H′5), 6.65 (d, 1H, $^3J = 7.4$, H′3 or H′5), 6.64 (s, 1H, H3), 5.75 (s, 6H, C_6H_6), 5.60 (s, 6H, C_6H_6), 3.89 (s, 3H, MeO), 3.70 (s, 3H, MeO), 3.68 (d, 2H, $^2J = 14.0$, 2 CH_2), 3.38 (d, 1H, $^2J = 13.7$, CH_2), 3.20 (d, 1H, $^2J = 14.03$, CH_2), 2.99 (s, 3H, NMe_2), 2.84 (s, 3H, NMe_2), 2.76 (s, 3H, NMe_2), 2.68 (s, 3H, NMe_2), 1.95 (m, 6H, $MeCN/CD_3CN$). ^{13}C NMR: 164.92, 162.57, 157.26, 155.70, 148.28, 147.48, 138.85 (C6), 125.13 (C′4), 118.35, 115.96 (C′3 or C′5), 111.82 (C′3 or C′5), 109.26 (C3), 108.57 (C5), 87.70 (C_6H_6), 87.38 (C_6H_6), 73.41(CH_2), 72.16 (CH_2), 57.80 (NMe_2), 72.16 (CH_2), 55.55 (NMe_2), 55.30 (MeO), 55.10 (NMe_2), 54.75 (MeO), 0.63 (NC*Me*), 0.63 (NC*Me*).

2.2.1.5. Complex ***1f***. Yield: 55%. MS: 560(1) $[(M + H) + PF_6]^+$, 415(10) $[(M + H)]^{+\cdot}$, 374(21) $[(M + H) - NCMe]^+$, 296(4) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 839 (s, PF_6^-). ^1H NMR: 7.57 (s, 1H, H6), 6.66 (s, 1H, H3), 5.62 (s, 6H, C_6H_6), 3.89 (s, 3H, MeO), 3.68 (s, 3H, MeO), 3.62 (d, 1H, $^2J = 13.5$, CH_2), 3.20 (d, 1H, $^2J = 13.5$, CH_2), 2.94 (s, 3H, NMe_2), 2.71 (s, 3H, NMe_2), 1.95 (m, 3H, $MeCN/CD_3CN$). ^{13}C NMR: 152.13, 147.07, 146.57, 138.24, 122.43, 118.28, 107.83, 87.70 (C_6H_6), 72.17 (CH_2), 57.75 (NMe_2), 55.89 (MeO), 55.57 (NMe_2), 55.32 (MeO), 0.66 (NC*Me*).

2.2.1.6. Complex ***1g***. Yield: 56%. MS: 560(1) $[(M + H) + PF_6]^+$, 415(5) $[(M + H)]^{+\cdot}$, 374(71) $[(M + H) - NCMe]^+$, 296(20) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 838 (s, PF_6^-). ^1H NMR: 6.36 (d, 1H, $^4J = 2.5$, H3 or H5), 6.31 (d, 1H, $^4J = 2.2$, H3 or H5), 5.72 (s, 6H, C_6H_6), 3.88 (s, 3H, MeO), 3.71 (s, 3H, MeO), 3.62 (d, 1H, $^2J = 13.5$, CH_2), 3.20 (d, 1H, $^2J = 13.5$, CH_2), 2.91 (s, 3H, NMe_2), 2.71 (s, 3H, NMe_2), 1.95 (m, 3H, MeCN/CD_3CN). ^{13}C NMR: 165.31, 158.67, 148.17, 138.18, 118.18, 100.97, 96.44, 88.12 (C_6H_6), 73.25 (CH_2), 57.65 (NMe_2), 55.20 (NMe_2), 55.09 (MeO), 54.85 (MeO), 0.66 (NC*Me*).

2.2.1.7. Complex ***1h***. Yield: 46%. MS: 590(1) $[(M + H) + PF_6]^+$, 445(10) $[(M + H)]^{+\cdot}$, 404(100) $[(M + H) - NCMe]^+$, 326(22) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 840 (s, PF_6^-). ^1H NMR: 7.41 (s, 1H, H6), 5.64 (s, 6H, C_6H_6), 3.92 (s, 3H, MeO), 3.72 (s, 3H, MeO), 3.68 (s, 3H, MeO), 3.56 (d, 1H, $^2J = 14.0$, CH_2), 3.41 (d, 1H, $^2J = 14.0$, CH_2), 2.94 (s, 3H, NMe_2), 2.73 (s, 3H, NMe_2), 1.95 (m, 3H, MeCN/CD_3CN). ^{13}C NMR: 156.62, 151.32, 148.57, 138.65, 131.01, 118.14 (C6), 118.03, 88.00 (C_6H_6), 68.26 (CH_2), 60.29 (MeO), 60.18 (MeO), 58.08 (NMe_2), 56.01 (NMe_2), 55.50 (MeO), 0.66 (NC*Me*).

2.2.1.8. Complex ***1i***. Yield: 42%. MS: 590(2) $[(M + H) + PF_6]^+$, 445(9) $[(M + H)]^{+\cdot}$, 404(100) $[(M + H) - NCMe]^+$, 326(23) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 837 (s, PF_6^-). ^1H NMR: 6.54 (s, 1H, H3), 5.72 (s, 6H, C_6H_6), 3.83 (s, 3H, MeO), 3.80 (s, 3H, MeO), 3.72 (s, 3H, MeO), 3.59 (d, 1H, $^2J = 13.5$, CH_2), 3.32 (d, 1H, $^2J = 13.5$, CH_2), 2.82 (s, 3H, NMe_2), 2.76 (s, 3H, NMe_2), 1.95 (m, 3H, MeCN/CD_3CN). ^{13}C NMR: 158.95, 150.95, 144.18, 141.91, 140.77, 118.03, 110.50, 103.99 (C3), 87.35 (C_6H_6), 73.43 (CH_2), 60.51 (MeO), 59.98 (MeO), 57.73 (NMe_2), 55.72 (MeO), 55.00 (NMe_2), 0.66 (NC*Me*).

2.2.1.9. Complex ***1j***. Yield: 44%. MS: 373(22) $[(M + H)]^{+\cdot}$, 332(55) $[(M + H) - NCMe]^+$, 254(8) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 839 (s, PF_6^-). ^1H NMR: 7.79 (dd, 1H, $^3J_{HF}$ 9.6, $^4J_{HH}$ 2.5, H6), 6.99 (dd, 1H, $^3J_{HH}$ 8.2, $^4J_{HF}$ 5.7, H3), 6.68 (ddd, 1H, $^3J_{HF}$ 9.4, $^3J_{HH}$ 8.2, $^4J_{HH}$ 2.5, H4), 5.66 (s, 6H, C_6H_6), 3.65 (d, 1H, $^2J = 13.5$, CH_2), 3.30 (d, 1H, $^2J = 13.5$, CH_2), 2.93 (s, 3H, NMe_2), 2.73 (s, 3H, NMe_2), 1.95 (m, 3H, MeCN/CD_3CN). ^{13}C NMR: 165.40, 160.63 (d, $^1J = 244.4$, CF), 142.65, 124.86 (d, $^2J = 17.9$, C6), 123.49 (d, $^3J = 7.5$, C3), 118.23, 109.94 (d, $^2J = 20.2$, C4), 88.31 (C_6H_6), 71.83 (CH_2), 57.90 (NMe_2), 55.50 (NMe_2), 0.65 (NC*Me*).

2.2.1.10. Complex ***1k***. Yield: 37%. MS: 423(35) $[(M + H)]^+$, 382(100) $[(M + H) - NCMe]^+$, 304(12) $[M - NCMe - C_6H_6]^{+\cdot}$. IR: 1328 (m, CF_3), 1112 (m, CF_3), 839 (s, PF_6^-). ^1H NMR: 8.24 (d, 1H, $^3J = 7.7$, H6), 7.34 (d, 1H, $^3J = 7.7$, H5), 7.29 (s, 1H, H3), 5.68 (s, 6H, C_6H_6), 3.73 (d, 1H, $^2J = 14.0$, CH_2), 3.39 (d, 1H, $^2J = 14.0$, CH_2), 2.96 (s, 3H, NMe_2), 2.74 (s, 3H, NMe_2), 1.95 (m, 3H, MeCN/CD_3CN). ^{13}C NMR: 170.14, 147.96, 139.42, 128.21, 127.88, 127.56, 122.04, 118.81, 117.30, 88.59 (C_6H_6), 72.01 (CH_2), 58.08 (NMe_2), 55.66 (NMe_2), 0.68 (NC*Me*).

2.2.1.11. Complex ***1l***. Yield: 41%. MS: 423(40) $[(M + H)]^+$, 382(100) $[(M + H) - NCMe]^+$, 304(15) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 1316 (m, CF_3), 1112 (m, CF_3), 839 (s, PF_6^-). ^1H NMR: 8.33 (d, 1H, $^4J = 1.0$, H6), 7.27 (dd, 1H, $^3J = 7.7$, $^4J = 1.0$, H4), 7.14 (d, 1H, $^3J = 7.7$, H3), 5.70 (s, 6H, C_6H_6), 3.73 (d, 1H, $^2J = 14.3$, CH_2), 3.39 (d, 1H, $^2J = 14.3$, CH_2), 2.97 (s, 3H, NMe_2), 2.74 (s, 3H, NMe_2), 1.95 (m, 3H, MeCN/CD_3CN). ^{13}C NMR: 163.62, 151.65, 134.74, 122.78, 120.67, 118.50, 88.42 (C_6H_6), 72.06 (CH_2), 58.09 (NMe_2), 55.70 (NMe_2), 0.66 (NC*Me*).

2.2.1.12. Complex ***1m***. Yield: 50%. MS: 370(62) $[(M + H) - NCMe]^+$, 292(11) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 840 (s, PF_6^-). ^1H NMR: 8.09 (d, 1H, $^4J = 1.9$, H6), 7.00 (dd, 1H, $^3J = 8.0$, $^4J = 1.9$, H4), 6.91 (d, 1H, $^3J = 8.0$, H3), 5.63 (s, 6H, C_6H_6), 3.65 (d, 1H, $^2J = 13.7$, CH_2), 3.25 (d, 1H, $^2J = 13.7$, CH_2), 2.94 (s, 3H, NMe_2), 2.71 (s, 3H, NMe_2), 1.95 (m, 3H, MeCN/CD_3CN), 1.37 (s, 9H, ^{t}Bu). ^{13}C NMR: 161.98, 148.52, 143.88, 135.64 (C6), 122.30 (C3), 120.88 (C4), 118.13, 87.98 (C_6H_6), 72.10 (CH_2), 57.88 (NMe_2), 55.37 (NMe_2), 34.40, 31.01 (^{t}Bu), 0.67 (NC*Me*).

2.2.1.13. Complex ***1n***. Yield: 23%. MS: 543(5) $[(M + H) + PF_6]^+$, 398(11) $[(M + H)]^{+\cdot}$, 357(40) $[(M + H) - NCMe]^+$, 279(13) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 838 (s, PF_6^-). ^1H NMR: 7.43 (d, 1H, $^4J = 2.5$, H6), 6.78 (d, 1H, $^3J = 8.2$, H3), 6.34 (dd, 1H, $^3J = 8.2$, $^4J = 2.5$, H4), 5.56 (s, 6H, C_6H_6), 3.54 (d, 1H, $^2J = 13.5$, CH_2), 3.15 (d, 1H, $^2J = 13.5$, CH_2), 2.89 (s, 6H, NMe_2), 2.84 (s, 3H, NMe_2), 2.68 (s, 3H, NMe_2), 1.95(m, 3H, MeCN/CD_3CN). ^{13}C NMR: 163.32, 149.38, 135.06, 123.45 (C6), 122.79 (C3), 118.31, 108.96 (C4), 87.92 (C_6H_6), 72.10 (CH_2), 57.70 (NMe_2), 55.18 (NMe_2), 40.47(NMe_2),0.67 (NC*Me*).

2.2.1.14. Complex ***1o***. Yield: 11%. MS: 359(46) $[(M + H) - NCMe]^+$, 281(4) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 1511 (m, NO_2), 1340 (m, NO_2), 837 (s, PF_6^-). ^1H NMR: 8.80 (d, 1H, $^4J = 2.2$, H6), 7.80 (dd, 1H, $^3J = 8.23$, $^4J = 2.5$, H4), 7.18 (d, 1H, $^3J = 8.2$, H3), 5.73 (s, 6H, C_6H_6), 3.74 (d, 1H, $^2J = 14.5$, CH_2), 3.46 (d, 1H, $^2J = 14.5$, CH_2), 2.95 (s, 3H, NMe_2), 2.77 (s, 3H, NMe_2), 1.95 (m, 3H, MeCN/CD_3CN). ^{13}C NMR: 164.71, 154.98, 146.23, 132.44 (C6), 123.01

(C3), 119.16 (C4), 118.70, 88.61 (C_6H_6), 72.10 (CH_2), 58.27 (NMe_2), 55.71 (NMe_2), 0.66 (NC*Me*).

2.2.1.15. Complex ***1p***. Yield: 11%. MS: 525(1) $[(M + H) + PF_6]^+$, 380(8) $[(M + H)]^{+\cdot}$, 339(16) $[(M + H) - NCMe]^+$, 261(5) $[(M + H) - NCMe - C_6H_6]^{+\cdot}$. IR: 2217 (m, CN), 838 (s, PF_6^-). ^{1}H NMR: 8.39 (d, 1H, $^4J = 1.6$, H6), 7.32 (dd, 1H, $^3J = 7.7$,$^4J = 1.6$, H4), 7.11 (d, 1H, $^3J = 7.7$, H3), 5.70 (s, 6H, C_6H_6), 3.72 (d, 1H, $^2J = 14.5$, CH_2), 3.39 (d, 1H, $^2J = 14.5$, CH_2), 2.95 (s, 3H, NMe_2), 2.74 (s, 3H, NMe_2), 1.95 (m, 3H, MeCN/CD_3CN). ^{13}C NMR: 163.84, 152.81, 141.84 (C6), 127.61 (C4), 122.98 (C3), 119.91, 118.24, 109.17, 88.50 (C_6H_6), 72.25 (CH_2), 58.17 (NMe_2), 55.69 (NMe_2), 0.66 (NC*Me*).

2.2.2. Complex ***2a***

The same procedure as for complexes **1** was applied using pivalonitrile instead of acetonitrile. Yield: 35%. MS: 314(100) $[(M + H) - NC^tBu]^+$, 236(25) $[(M + H) - NC^tBu - C_6H_6]^{+\cdot}$. IR: 839 (s, PF_6^-). ^{1}H NMR: 8.04 (d, 1H, $^3J = 7.4$, H6), 7.06–6.92 (m, 3H, H3 +H4 +H5), 5.62 (s, 6H, C_6H_6), 3.69 (d, 1H, $^2J = 13.7$, CH_2), 3.27 (d, 1H, $^2J = 13.7$, CH_2), 2.96 (s, 3H, NMe_2), 2.71 (s, 3H, NMe_2), 1.32 (s, 9H, NC^{t}Bu). ^{13}C NMR: 162.40, 146.86, 138.67, 126.41, 123.49, 122.55, 118.19, 87.54 (C_6H_6), 72.59 (CH_2), 57.61 (NMe_2), 55.80 (NMe_2), 28.08, 27.45 (^{t}Bu).

2.2.3. Complexes ***3a–p***

A solution of complex **1** (about 100 mg) and one equivalent of 2,2′-bipyridine in 15 ml of acetonitrile was stirred at room temperature for 12 h. The resulting deep purple solution was evaporated to dryness under reduced pressure and the residue was purified by column chromatography on Al_2O_3 using dichloromethane as an eluent. The purple band was collected and evaporated to dryness. Dark purple crystals were obtained by the slow diffusion of diethyl ether into a concentrated solution of the purple solid in a mixture of CH_2Cl_2:MeCN (1:1).

2.2.3.1. Complex ***3a***. Yield: 53%. MS: 619(3) $[(M + H) + PF_6]$, 474(15) $[(M + H)]$, 433(4) $[M - NCMe]$, 392(25) $[M - 2NCMe]$, 349(7), 257(3). IR: 2264 (m, NCMe), 840 (s, PF_6^-). ^{1}H NMR: 9.52 (dd, 1H, $^3J = 6.0$, $^4J = 1.6$, H6″), 8.69 (dd, 1H, $^3J = 5.5$, $^4J = 1.1$, H6′), 8.65 (d, 1H, $^3J = 8.2$, H3″), 8.53 (d, 1H, $^3J = 7.7$, H3′), 8.17 (td, 1H, $^3J = 7.7$, $^4J = 1.1$, H4″), 7.92 (td, 1H, $^3J = 8.2$, $^4J = 1.6$, H4′), 7.86–7.80 (m, 2H, H5″+H6), 7.36 (ddd, 1H, $^3J = 7.1$, $^3J = 6.0$, $^4J = 1.6$, H5′), 7.08 (td, 1H, $^3J = 7.1$, $^4J = 1.1$, H5), 7.00 (d, 1H, $^3J = 7.2$, H3), 6.85 (td, 1H, $^3J = 7.1$, $^4J = 1.1$, H4), 3.88 (d, 1H, $^2J = 13.8$, CH_2), 3.30 (d, 1H, $^2J = 13.8$, CH_2), 2.45 (s, 3H, NCMe), 2.18 (s, 3H, NMe_2), 2.07 (s, 3H, NCMe), 1.36 (s, 3H, NMe_2). ^{13}C NMR: 168.46, 159.49, 155.80, 153.17 (C6′), 150.65 (C6″), 148.03, 137.61 (C6), 135.96 (C4″), 134.96 (C4′), 126.52 (C5″), 125.43 (C5′), 125.28 (C5), 122.82 (C3′), 122.60 (C3″), 120.76 (C3), 120.27 (C4), 118.03, 73.02 (CH_2), 52.00 (NMe_2), 50.46 (NMe_2), 4.00 (NC*Me*), 3.16 (NC*Me*).

2.2.3.2. Complex ***3b***. Yield: 51%. MS: 633(8) $[M^+ + PF_6^-]$, 488(36) $[M^+]$, 447(10) $[M^+ - NCMe]$, 406(100) $[M^+ - 2NCMe]$. IR: 2258 (m, NCMe), 841 (s, PF_6^-). ^{1}H NMR: 9.33 (dd, 1H, $^3J = 5.2$, $^4J = 0.8$, H6″), 8.65 (dd, 1H, $^3J = 5.4$, $^4J = 0.8$, H6′), 8.41 (d, 1H, $^3J = 8.2$, H3″), 8.28 (d, 1H, $^3J = 8.0$, H3′), 8.06 (td, 1H, $^3J = 7.8$, $^4J = 1.6$, H4″), 7.80 (td, 1H, $^3J = 7.8$, $^4J = 1.6$, H4′), 7.72 (ddd, 1H, $^3J = 7.4$, $^3J = 5.5$, $^4J = 1.1$, H5″), 7.66 (d, 1H, $^4J = 1.1$, H6), 7.24 (ddd, 1H, $^3J = 7.4$, $^3J = 5.8$, $^4J = 1.4$, H5′), 6.89 (d, 1H, $^3J = 7.4$, H3), 6.68 (dd, 1H, $^3J = 7.4$, $^4J = 1.2$, H4), 3.84 (d, 1H, $^2J = 13.5$, CH_2), 3.26 (d, 1H, $^2J = 13.5$, CH_2), 2.44 (s, 3H, NCMe), 2.37 (s, 3H, Me), 2.16 (s, 3H, NMe_2), 2.08 (s, 3H, NCMe), 1.35 (s, 3H, NMe_2). ^{13}C NMR: 159.51, 155.81, 153.81 (C6′), 150.61 (C6″), 144.89, 138.43 (C6), 135.91 (C4″), 134.90 (C4′), 133.95, 126.49 (C5″), 125.40 (C5′), 122.79 (C3′), 122.58 (C3″), 121.15 (C4), 120.53 (C3), 118.25, 72.79 (CH_2), 51.95 (NMe_2), 50.38 (NMe_2), 20.92 (Me), 4.01 (NC*Me*), 3.19 (NC*Me*).

2.2.3.3. Complex ***3c***. Yield: 48%. MS: 647(5) $[M^+ + PF_6^-]$, 502(29) $[M^+]$, 461(5) $[M^+ - NCMe]$, 420(62) $[M^+ - 2NCMe]$. IR: 2250 (m, NCMe), 841 (s, PF_6^-). ^{1}H NMR: 9.33 (d, 1H, $^3J = 4.7$, H6″), 8.68 (d, 1H, $^3J = 4.7$, H6′), 8.40 (d, 1H, $^3J = 8.0$, H3″), 8.27 (d, 1H, $^3J = 8.2$, H3′), 8.06 (td, 1H, $^3J = 8.0$, $^4J = 1.5$, H4″), 7.80 (td, 1H, $^3J = 7.8$, $^4J = 1.6$, H4′), 7.72 (ddd, 1H, $^3J = 7.4$, $^3J = 5.2$, $^4J = 1.4$, H5″), 7.57 (s, 1H, H6), 7.23 (ddd, 1H, $^3J = 7.4$, $^3J = 5.8$, $^4J = 1.4$, H5′), 6.79 (s, 1H, H3), 3.82 (d, 1H, $^2J = 13.2$, CH_2), 3.23 (d, 1H, $^2J = 13.2$, CH_2), 2.44 (s, 3H, NCMe), 2.32 (s, 3H, Me), 2.23 (s, 3H, Me), 2.15 (s, 3H, NMe_2), 2.07 (s, 3H, NCMe), 1.34 (s, 3H, NMe_2). ^{13}C NMR: 176.72, 159.58, 155.85, 153.31, 150.56, 139.21, 138.63, 135.98, 135.06, 132.81, 126.81, 125.68, 122.92, 122.68, 120.69, 118.31, 72.80 (CH_2), 52.15 (NMe_2), 50.46 (NMe_2), 19.31 (Me), 18.76 (Me), 4.01 (NC*Me*), 3.39 (NC*Me*).

2.2.3.4. Complex ***3d***. Yield: 49%. MS: 649(5) $[M^+ + PF_6^-]$, 504(23) $[M^+]$, 463(10) $[M^+ - NCMe]$, 422(25) $[M^+ - 2NCMe]$. IR: 2252 (m, NCMe), 841 (s, PF_6^-). ^{1}H NMR: 9.34 (dd, 1H, $^3J = 5.2$, $^4J = 0.8$, H6″), 8.65 (dd, 1H, $^3J = 5.4$, $^4J = 0.8$, H6′), 8.39 (d, 1H, $^3J = 8.2$, H3″), 8.26 (d, 1H, $^3J = 8.0$, H3′), 8.06 (td, 1H, $^3J = 7.8$, $^4J = 1.6$, H4″), 7.80 (td, 1H, $^3J = 7.8$, $^4J = 1.6$, H4′), 7.72 (ddd, 1H, $^3J = 7.4$, $^3J = 5.5$, $^4J = 1.1$, H5″), 7.56 (d, 1H, $^4J = 1.2$, H6), 7.24 (ddd, 1H, $^3J = 7.4$, $^3J = 5.8$, $^4J = 1.4$, H5′), 6.80 (d, 1H, $^3J = 7.4$, H3), 6.41 (dd, 1H, $^3J = 7.4$, $^4J = 1.2$, H4), 3.83 (broad, 4H, MeO+CH_2), 3.26 (d, 1H, $^2J = 13.2$,

CH_2), 2.45 (s, 3H, NCMe), 2.16 (s, 3H, NMe_2), 2.07 (s, 3H, NCMe), 1.35 (s, 3H, NMe_2). ^{13}C NMR: 176.57, 159.44, 157.52, 155.80, 153.39, 150.64, 140.38, 135.97, 134.96, 126.49, 125.46, 122.95, 122.59, 121.12, 118.08, 105.05, 72.42 (CH_2), 54.37 (MeO), 51.96 (NMe_2), 50.27 (NMe_2), 3.98 (NC*Me*), 3.17 (NC*Me*).

*2.2.3.5. Complexes **3e** and **3′e** (1:1 mixture).* Yield: 48%. MS: 649(5) $[M^+ + PF_6^-]$, 504(15) $[M^+]$, 463(4) $[M^+ - NCMe]$, 422(28) $[M^+ - 2NCMe]$. IR: 841 (s, PF_6^-), 2252 (m, NCMe). ^1H NMR: 9.34 (d, 1H, $^2J = 5.5$, H6″), 9.30 (d, 1H, $^2J = 5.5$, H6″), 8.65 (d, 1H, $^3J = 4.7$, H6′), 8.60 (d, 1H, $^3J = 4.7$, H6′), 8.40 (d, 1H, $^3J = 7.7$, H3″), 8.38 (d, 1H, $^3J = 8.2$, H3″), 8.22 (m, 2H, H′3′+H3′), 8.12 (td, 1H, $^3J = 8.0$, $^4J = 1.3$, H4″), 8.04 (td, 1H, $^3J = 8.2$, $^4J = 1.6$, H4″), 7.82 (m, 2H, H4′+H6), 7.75 (m, 2H, H5″+H4′), 7.43 (td, 1H, $^3J = 7.2$, $^4J = 1.4$, H5″), 7.24 (ddd, 1H, $^3J = 7.5$, $^3J = 5.7$, $^4J = 1.3$, H5′), 7.05 (ddd, 1H, $^3J = 7.2$, $^3J = 6.0$, $^4J = 1.1$, H5′), 6.91 (t, 1H, $^3J = 7.4$, H′4), 6.72 (d, 1H, $^3J = 8.2$, H5), 6.70 (d, 1H, $^3J = 7.4$, H′3 or H′5), 6.68 (d, 1H, $^3J = 7.4$, H′3 or H′5), 6.66 (s, 1H, H3), 4.00 (d, 1H, $^2J = 13.5$, CH_2), 3.85 (d, 1H, $^2J = 13.5$, CH_2), 3.76 (s, 6H, MeO), 3.28 (d, 1H, $^2J = 13.5$, CH_2), 3.26 (d, 1H, $^2J = 13.5$, CH_2), 2.47 (s, 3H, NCMe), 2.45 (s, 3H, NCMe), 2.18 (s, 3H, NMe_2), 2.14 (s, 3H, NMe_2), 2.06 (s, 3H, NCMe), 1.99 (s, 3H, NCMe), 1.36 (broad, 6H, NMe_2). ^{13}C NMR: 168.41, 163.70, 159.60, 159.43, 156.31, 156.00, 155.11, 153.29, 150.77, 149.36, 148.25, 137.33, 135.92, 135.82, 134.82, 127.20, 125.40, 125.31, 122.76, 122.59, 122.08, 118.03, 115.24, 111.46, 108.15, 107.66, 73.50 (CH_2), 73.04 (CH_2), 55.07 (MeO), 54.74 (MeO), 52.00 (NMe_2), 51.79 (NMe_2), 50.50 (NMe_2), 50.22 (NMe_2), 4.07 (NC*Me*), 3.99 (NC*Me*), 3.16 (NC*Me*), 2.81 (NC*Me*).

*2.2.3.6. Complex **3f**.* Yield: 50%. MS: 679(5) $[M^+ + PF_6^-]$, 534(19) $[M^+]$, 493(4) $[M^+ - NCMe]$, 452(46) $[M^+ - 2NCMe]$. IR: 2259 (m, NCMe), 841 (s, PF_6^-). ^1H NMR: 9.34 (d, 1H, $^3J = 4.7$, H6″), 8.66 (d, 1H, $^3J = 5.0$, H6′), 8.40 (d, 1H, $^3J = 8.2$, H3″), 8.28 (d, 1H, $^3J = 8.0$, H3′), 8.06 (td, 1H, $^3J = 7.7$, $^4J = 1.2$, H4″), 7.80 (td, 1H, $^3J = 7.8$, $^4J = 1.1$, H4′), 7.72 (ddd, 1H, $^3J = 7.4$, $^3J = 5.2$, $^4J = 1.1$, H5″), 7.35 (s, 1H, H6), 7.25 (ddd, 1H, $^3J = 7.4$, $^3J = 5.8$, $^4J = 1.4$, H5′), 6.76 (d, 1H, $^3J = 7.4$, H3), 3.91 (s, 3H, MeO), 3.76 (broad, 4H, MeO+CH_2), 3.25 (d, 1H, $^2J = 12.1$, CH_2), 2.47 (s, 3H, NCMe), 2.17 (s, 3H, NMe_2), 2.08 (s, 3H, NCMe), 1.35 (s, 3H, NMe_2). ^{13}C NMR: 170.78, 159.54, 156.00, 153.56, 150.72, 135.85, 134.85, 126.49, 125.46, 122.73, 122.58, 120.95, 120.87, 118.09, 106.50, 72.71 (CH_2), 56.08 (MeO), 55.66 (MeO), 51.91 (NMe_2), 50.33 (NMe_2), 4.00 (NC*Me*), 3.14 (NC*Me*).

*2.2.3.7. Complex **3g**.* Yield: 52%. MS: 679(2) $[M^+ + PF_6^-]$, 534(4) $[M^+]$, 493(2) $[M^+ - NCMe]$, 452(10) $[M^+ - 2NCMe]$. IR: 2263 (m, NCMe), 840 (s, PF_6^-). ^1H NMR: 9.29 (dd, 1H, $^3J = 5.5$, $^4J = 0.8$, H6″), 8.62 (dd, 1H, $^3J = 5.8$, $^4J = 0.8$, H6′), 8.38 (d, 1H, $^3J = 8.2$, H3″), 8.25 (d, 1H, $^3J = 8.2$, H3′), 8.04 (td, 1H, $^3J = 8.2$, $^4J = 1.6$, H4″), 7.80 (ddd, 1H, $^3J = 8.2$, $^3J = 7.4$, $^4J = 1.4$, H4′), 7.70 (ddd, 1H, $^3J = 7.4$, $^3J = 5.4$, $^4J = 1.1$, H5″), 7.24 (ddd, 1H, $^3J = 7.5$, $^3J = 5.7$, $^4J = 1.3$, H5′), 6.42 (d, 1H, $^4J = 1.1$, H3 or H5), 6.37 (d, 1H, $^4J = 1.1$, H3 or H5), 3.95 (d, 1H, $^2J = 13.5$, CH_2), 3.76 (s, 6H, 2MeO), 3.22 (d, 1H, $^2J = 13.5$, CH_2), 2.47 (s, 3H, NCMe), 2.17 (s, 3H, NMe_2), 1.99 (s, 3H, NCMe), 1.35 (s, 3H, NMe_2). ^{13}C NMR: 168.62, 159.51, 156.49, 155.19 (C6′), 150.82 (C6″), 135.78 (C4″), 134.70 (C4′), 126.48 (C5″), 125.30 (C5′), 122.57, 120.90 (C3″+C3′), 118.29, 100.73 (C3 or C5), 96.15 (C3 or C5), 73.75 (CH_2), 55.04 (MeO), 54.77 (MeO), 51.73 (NMe_2), 50.27 (NMe_2), 4.07 (NC*Me*), 2.81 (NC*Me*).

*2.2.3.8. Complex **3h**.* Yield: 50%. MS: 709(4) $[M^+ + PF_6^-]$, 564(19) $[M^+]$, 523(4) $[M^+ - NCMe]$, 482(51) $[M^+ - 2NCMe]$. IR: 2259 (m, NCMe), 841 (s, PF_6^-). ^1H NMR: 9.33 (dd, 1H, $^3J = 5.2$, $^4J = 0.8$, H6″), 8.68 (dd, 1H, $^3J = 5.7$, $^4J = 0.8$, H6′), 8.40 (d, 1H, $^3J = 8.2$, H3″), 8.28 (d, 1H, $^3J = 8.0$, H3′), 8.06 (td, 1H, $^3J = 8.0$, $^4J = 1.6$, H4″), 7.81 (td, 1H, $^3J = 8.0$, $^4J = 1.6$, H4′), 7.72 (ddd, 1H, $^3J = 7.4$, $^3J = 5.2$, $^4J = 1.6$, H5″), 7.28 (td, 1H, $^3J = 5.8$, $^4J = 1.4$, H5′), 7.20 (s, 1H, H6), 3.93 (s, 3H, MeO), 3.79 (broad, 4H, MeO+CH_2), 3.74 (s, 3H, MeO), 3.44 (d, 1H, $^2J = 13.7$, CH_2), 2.47 (s, 3H, NCMe), 2.18 (s, 3H, NMe_2), 2.07 (s, 3H, NCMe), 1.37 (s, 3H, NMe_2). ^{13}C NMR: 176.56, 159.43, 155.91, 153.63 (C6′), 151.24, 150.66 (C6″), 135.93 (C4″), 134.94 (C4′), 127.22, 126.48 (C5″), 125.49 (C5′), 122.75 (C3′), 122.59 (C3″), 118.27, 116.28 (C6), 68.24 (CH_2), 60.21 (2MeO), 55.69 (MeO), 52.08 (NMe_2), 50.60 (NMe_2), 4.05 (NC*Me*), 3.11 (NC*Me*).

*2.2.3.9. Complex **3i**.* Yield: 49%. MS: 709(3) $[M^+ + PF_6^-]$, 564(15) $[M^+]$, 523(5) $[M^+ - NCMe]$, 482(42) $[M^+ - NCMe - NCMe]$. IR: 2260 (m, NCMe), 841 (s, PF_6^-). ^1H NMR: 9.21 (d, 1H, $^3J = 5.2$, $^4J = 0.8$, H6″), 8.65 (dd, 1H, $^3J = 5.5$, $^4J = 0.8$, H6′), 8.30 (d, 1H, $^3J = 8.2$, H3″), 8.18 (d, 1H, $^3J = 8.0$, H3′), 7.96 (td, 1H, $^3J = 7.7$, $^4J = 1.6$, H4″), 7.71 (td, 1H, $^3J = 7.7$, $^4J = 1.1$, H4′), 7.61 (ddd, 1H, $^3J = 7.4$, $^3J = 5.3$, $^4J = 1.1$, H5″), 7.15 (ddd, 1H, $^3J = 7.4$, $^3J = 6.0$, $^4J = 1.4$, H5′), 6.56 (s, 1H, H3), 3.78 (broad, 4H, MeO+CH_2), 3.67 (s, 3H, MeO), 3.62 (s, 3H, MeO), 3.16 (d, 1H, $^2J = 13.2$, CH_2), 2.39 (s, 3H, NCMe), 2.07 (s, 3H, NMe_2), 1.91 (s, 3H, NCMe), 1.25 (s, 3H, NMe_2). ^{13}C NMR: 161.65, 159.55, 156.45, 154.75 (C6′), 150.79 (C6″), 135.98 (C4″), 134.96 (C4′), 126.56 (C5″), 125.38 (C5′), 122.72 (C3′), 122.66 (C3″), 118.04, 112.47 (C3), 104.42, 73.23 (CH_2), 60.21 (MeO), 59.98

(MeO), 56.00 (MeO), 52.17 (NMe_2), 50.10 (NMe_2), 4.01 (NC*Me*), 3.12 (NC*Me*).

2.2.3.10. Complex ***3j***. Yield: 47%. MS: 637(1) $[M^+ + PF_6^-]$, 492(14) $[M^+]$, 451(3) $[M^+ - NCMe]$, 410(19) $[M^+ - 2NCMe]$, 367(4), 257(2). IR: 2269 (m, NCMe), 840 (s, PF_6^-). ^1H NMR: 9.30 (dd, 1H, $^3J = 5.5$, $^4J = 0.8$, H6″), 8.56 (dd, 1H, $^3J = 5.7$, $^4J = 0.8$, H6′), 8.42 (d, 1H, $^3J = 8.2$, H3″), 8.29 (d, 1H, $^3J = 8.0$, H3′), 8.08 (td, 1H, $^3J = 7.4$, $^4J = 1.6$, H4″), 7.82 (td, 1H, $^3J = 7.5$, $^4J = 1.6$, H4′), 7.73 (ddd, 1H, $^3J = 7.5$, $^3J = 5.5$, $^4J = 1.1$, H5″), 7.52 (dd, 1H, $^3J_{FH}$ 9.7, $^4J = 2.5$, H6), 7.25 (ddd, 1H, $^3J = 7.5$, $^3J = 5.5$, $^4J = 1.5$, H5′), 7.00 (dd, 1H, $^3J = 8.0$, $^4J_{FH}$ 5.8, H3), 6.55 (ddd, 1H, $^3J_{FH}$ 9.9, $^3J = 8.0$, $^4J = 2.7$, H5), 3.82 (d, 1H, $^2J = 13.5$, CH_2), 3.32 (d, 1H, $^2J = 13.5$, CH_2), 2.44 (s, 3H, NCMe), 2.18 (s, 3H, NMe_2), 2.07 (s, 3H, NCMe), 1.37 (s, 3H, NMe_2). ^{13}C NMR: 157.55 (d, $^1J = 269.8$, CF), 153.32 (C6′), 150.72 (C6″), 143.76, 136.17 (C4″), 135.24 (C4′), 127.23 (C5″), 126.53 (C5′), 125.62 (C3′), 122.88 (C3″), 122.77 (d, $^2J = 16.6$, C6), 121.51 (d, $^3J = 7.5$, C3), 118.35, 106.17 (d, $^2J = 22.5$, C4), 72.31 (CH_2), 52.07 (NMe_2), 50.35 (NMe_2), 4.08 (NC*Me*), 3.05 (NC*Me*).

2.2.3.11. Complex ***3k***. Yield: 43%. MS: 542(3) $[M^+]$, 501(1) $[M^+ - NCMe]$, 460(6) $[M^+ - 2NCMe]$. IR: 2270 (m, NCMe), 1326 (m, CF_3), 1114 (m, CF_3), 839 (s, PF_6). ^1H NMR: 9.27 (d, 1H, $^3J = 5.5$, H6″), 8.72 (d, 1H, $^3J = 5.5$, H6′), 8.45 (d, 1H, $^3J = 7.7$, H3″), 8.20 (d, 1H, $^3J = 8.0$, H3′), 8.14 (td, 1H, $^3J = 8.0$, $^4J = 1.3$, H4″), 7.95 (d, 1H, $^3J = 8.0$, H6), 7.60 (ddd, 1H, $^3J = 7.4$, $^3J = 5.8$, $^4J = 1.6$, H4′), 7.43 (td, 1H, $^3J = 7.2$, $^4J = 1.4$, H5″), 7.05 (ddd, 1H, $^3J = 7.2$, $^3J = 6.0$, $^4J = 1.1$, H5′), 6.96 (d, 1H, $^3J = 7.7$, H3), 6.37 (d, 1H, $^3J = 7.4$, H5), 3.92 (d, 1H, $^2J = 13.7$, CH_2), 3.50 (d, 1H, $^2J = 13.7$, CH_2), 2.44 (s, 3H, NCMe), 2.20 (s, 3H, NMe_2), 2.07 (s, 3H, NCMe), 1.38 (s, 3H, NMe_2). ^{13}C NMR: 159.10, 153.11, 150.74, 150.19, 136.07, 135.51, 134.78, 132.81, 127.07, 125.48, 123.92, 123.24, 123.04, 122.81, 118.39, 73.41 (CH_2), 53.59 (NMe_2), 51.11 (NMe_2), 4.10 (NC*Me*), 3.19 (NC*Me*).

2.2.3.12. Complex ***3l***. Yield: 44%. MS: 687(5) $[M^+ + PF_6^-]$, 542(57) $[M^+]$, 501(12) $[M^+ - NCMe]$, 460(100) $[M^+ - 2NCMe]$. IR: 2270 (m, NCMe), 1314 (m, CF_3), 1114 (m, CF_3), 840 (s, PF_6^-). ^1H NMR: 9.34 (d, 1H, $^3J = 5.2$, H6″), 8.48 (d, 1H, $^3J = 5.7$, H6′), 8.43 (d, 1H, $^3J = 7.4$, H3″), 8.30 (d, 1H, $^3J = 8.2$, H3′), 8.10 (m, 2H, H4″+H6), 7.83 (td, 1H, $^3J = 7.7$, $^4J = 1.1$, H4′), 7.74 (td, 1H, $^3J = 5.5$, $^3J = 5.5$, $^4J = 1.1$, H5″), 7.24 (td, 1H, $^3J = 5.8$, $^4J = 1.2$, H5′), 7.15 (m, 2H, H3+H4), 3.89 (d, 1H, $^2J = 13.7$, CH_2), 3.40 (d, 1H, $^2J = 13.7$, CH_2), 2.44 (s, 3H, NCMe), 2.20 (s, 3H, NMe_2), 2.06 (s, 3H, NCMe), 1.38 (s, 3H, NMe_2). ^{13}C NMR: 184.18, 158.95, 155.35, 152.71, 152.46, 150.38, 135.92, 135.03, 132.54, 126.21, 125.30, 122.60, 122.34, 120.05, 118.44, 72.30 (CH_2), 51.82 (NMe_2), 50.23 (NMe_2), 3.61 (NC*Me*), 2.79 (NC*Me*).

2.2.3.13. Complex ***3n***. Yield: 23%. MS: 662(2) $[M^+ + PF_6^-]$, 517(12) $[M^+]$, 476(12) $[M^+ - NCMe]$, 435(25) $[M^+ - 2NCMe]$. IR: 2252 (m, NCMe), 841 (s, PF_6^-). ^1H NMR: 9.33 (dd, 1H, $^3J = 5.7$, $^4J = 0.8$, H6″), 8.73 (dd, 1H, $^3J = 5.8$, $^4J = 0.8$, H6′), 8.41 (d, 1H, $^3J = 8.0$, H3″), 8.27 (d, 1H, $^3J = 8.2$, H3′), 8.06 (td, 1H, $^3J = 8.0$, $^4J = 1.6$, H4″), 7.79 (td, 1H, $^3J = 8.0$, $^4J = 1.6$, H4′), 7.72 (ddd, 1H, $^3J = 7.1$, $^3J = 5.8$, $^4J = 0.8$, H5″), 7.33 (d, 1H, $^4J = 2.8$, H6), 7.25 (ddd, 1H, $^3J = 7.4$, $^3J = 6.0$, $^4J = 1.0$, H5′), 6.87 (d, 1H, $^3J = 8.0$, H3), 6.34 (dd, 1H, $^3J = 8.0$, $^4J = 2.8$, H4), 3.79 (d, 1H, $^2J = 13.2$, CH_2), 3.21 (d, 1H, $^2J = 13.2$, CH_2), 2.95 (s, 6H, NMe_2), 2.45 (s, 3H, NCMe), 2.16 (s, 3H, NMe_2), 2.07 (s, 3H, NCMe), 1.34 (s, 3H, NMe_2). ^{13}C NMR: 182.06, 159.53, 155.82, 153.45 (C6′), 150.59 (C6″), 149.21, 137.17, 135.83 (C4″), 134.78 (C4′), 126.47 (C5″), 125.34 (C5′), 122.73 (C3″), 122.60 (C6+C3′), 120.88 (C3), 118.36, 106.27 (C4), 72.53 (CH_2), 51.85 (NMe_2), 50.21 (NMe_2), 40.79 (NMe_2), 4.01 (NC*Me*), 3.11 (NC*Me*).

2.2.3.14. Complex ***3o***. Yield: 11%. MS: 664(3) $[M^+ + PF_6^-]$, 519(27) $[M^+]$, 478(7) $[M^+ - NCMe]$, 437(39) $[M^+ - 2NCMe]$. IR: 2262 (m, NCMe), 1503 (m, NO_2), 1333 (m, NO_2), 842 (s, PF_6^-). ^1H NMR: 9.34 (dd, 1H, $^3J = 5.4$, $^4J = 0.8$, H6″), 8.56 (d, 1H, $^4J = 2.5$, H6), 8.50 (dd, 1H, $^3J = 5.0$, $^4J = 0.8$, H6′), 8.43 (d, 1H, $^3J = 8.0$, H3″), 8.31 (d, 1H, $^3J = 8.2$, H3′), 8.10 (td, 1H, $^3J = 8.2$, $^4J = 1.6$, H4″), 7.84 (td, 1H, $^3J = 8.2$, $^4J = 1.6$, H4′), 7.75 (ddd, 1H, $^3J = 7.4$, $^3J = 5.2$, $^4J = 1.1$, H5″), 7.73 (dd, 1H, $^3J = 8.2$, $^4J = 2.5$, H4), 7.23 (ddd, 1H, $^3J = 7.4$, $^3J = 5.8$, $^4J = 1.4$, H5′), 7.18 (d, 1H, $^3J = 8.2$, H3), 3.92 (d, 1H, $^2J = 14.3$, CH_2), 3.45 (d, 1H, $^2J = 14.3$, CH_2), 2.44 (s, 3H, NCMe), 2.22 (s, 3H, NMe_2), 2.10 (s, 3H, NCMe), 1.40 (s, 3H, NMe_2). ^{13}C NMR: 159.20, 156.54, 155.70, 153.06, 146.38, 135.38, 130.37, 126.36, 122.89, 121.17, 118.31, 116.09, 115.53, 72.68 (CH_2), 51.95 (NMe_2), 50.88 (NMe_2), 3.47 (NC*Me*), 3.05 (NC*Me*).

2.2.3.15. Complex ***3p***. Yield: 14%. MS: 644(3) $[M^+ + PF_6^-]$, 499(17) $[M^+]$, 458(10) $[M^+ - NCMe]$, 417(45) $[M^+ - 2NCMe]$. IR: 2267 (m, CN), 2270 (m, CN), 842 (s, PF_6^-). ^1H NMR: 9.35 (dd, 1H, $^3J = 5.3$, $^4J = 0.8$, H6″), 8.55 (dd, 1H, $^3J = 5.1$, $^4J = 0.8$, H6′), 8.42 (d, 1H, $^3J = 8.1$, H3″), 8.29 (d, 1H, $^3J = 8.2$, H3′), 8.19 (d, 1H, $^4J = 2.4$, H6), 8.09 (td, 1H, $^3J = 8.2$, $^4J = 1.6$, H4″), 7.83 (td, 1H, $^3J = 8.2$, $^4J = 1.6$, H4′), 7.75 (ddd, 1H, $^3J = 7.4$, $^3J = 5.2$, $^4J = 1.1$, H5″), 7.28 (dd, 1H, $^3J = 8.2$, $^4J = 2.4$, H4), 7.24 (ddd, 1H, $^3J = 7.4$, $^3J = 5.8$, $^4J = 1.4$, H5′), 7.16 (d, 1H, $^3J = 8.2$, H3), 3.93 (d, 1H, $^2J = 14.3$, CH_2), 3.46 (d, 1H,

^2J = 14.3, CH_2), 2.44 (s, 3H, NCMe), 2.23 (s, 3H, NMe_2), 2.11 (s, 3H, NCMe), 1.41 (s, 3H, NMe_2). ^{13}C NMR: 162.3, 159.36, 155.54, 154.80, 153.86, 147.38, 134.48, 130.37, 127.23, 122.89, 121.17, 118.57, 118.31, 116.19, 116.02, 72.70 (CH_2), 51.97 (NMe_2), 51.00 (NMe_2), 3.46 (NC*Me*), 3.05 (NC*Me*).

2.2.4. Complex *4a*

The same procedure as for complexes **3** was applied using pivalonitrile instead of acetonitrile. Yield: 53%. MS: 703(1) $[M^+ + PF_6^-]$, 558(47) $[M^+]$, 475(8) $[M^+ - NC^tBu]$, 392(100) $[M^+ - 2NC^tBu]$. IR: 2232 (m, NCMe), 841 (s, PF_6^-). ^1H NMR: 9.20 (dd, 1H, ^3J = 5.5, ^4J = 0.8, H6″), 8.52 (dd, 1H, ^3J = 5.5, ^4J = 0.8, H6′), 8.44 (d, 1H, ^3J = 8.0, H3″), 8.29 (d, 1H, ^3J = 8.2, H3′), 8.08 (ddd, 1H, ^3J = 8.0, ^3J = 7.7, ^4J = 1.4, H4″), 7.84–7.74 (m, 3H, H6+H4′+H5″), 7.23 (ddd, 1H, ^3J = 7.7, ^3J = 5.5, ^4J = 1.4, H5′), 7.11 (td, 1H, ^3J = 7.2, ^4J = 0.8, H5), 7.03 (d, 1H, ^3J = 7.2, H3), 6.88 (td, 1H, ^3J = 7.2, ^4J = 1.4, H4) 3.72 (d, 1H, ^2J = 13.5, CH_2), 3.36 (d, 1H, ^2J = 13.5, CH_2), 2.20 (s, 3H, NMe_2), 1.42 (s, 3H, NMe_2), 1.40 (s, 9H, ^{t}Bu), 1.10 (s, 9H, ^{t}Bu). ^{13}C NMR: 159.26, 155.72, 153.06, 150.14, 147.65, 137.04, 136.11, 135.16, 126.78, 125.55, 125.38, 122.88, 122.74, 121.03, 120.37, 118.40, 72.90 (CH_2), 52.26 (NMe_2), 50.32 (NMe_2), 30.60, 29.93, 27.76 (^{t}Bu), 27.73 (^{t}Bu).

2.3. Crystal structure determination

Complexes **1a** and **3f** data were collected on a Bruker SMART APEX CCD area diffractometer by the ω-scan method [22], while complex **3d** data were collected on a Siemens P4 four-circle/single-counter diffractometer data [23]. In all cases Mo Kα radiation (λ = 0.71073 Å) was used and no significant decay was observed during data collection. Crystal data and other experimental information are given in Table 1 with further details in Supporting Information. For only compound **1a** an analytical absorption correction was applied. The structures were solved by direct methods and refined by full-matrix least-squares on all unique F^2 values [24]. Hexafluorophosphate fluorine atoms were modeled as disordered over two sets of sites, occupancies refined to 0.51(1), 0.64(2) and 0.54(2) and the complements for complexes **1a**, **3d** and **3f**, respectively. Anisotropic displacement parameters were assigned to all the non-hydrogen atoms. Hydrogen atoms were placed in idealized positions and allowed to ride on their respective parent atoms. The complexes **3d** and **3f** are CH_2Cl_2 solvates; the solvent molecules are statistical and/or orientationally disordered. The largest peaks in final difference syntheses lie close to solvent and disordered atoms.

Table 1
Crystallographic data for compounds **1a**, **3d**, and **3f**

Complex	**1a**	**3d**	**3f**
Empirical formula	$C_{17}H_{21}F_6N_2PRu$	$C_{24}H_{28}N_5ORuPF_6 \cdot 1/4\ CH_2Cl_2$	$C_{25}H_{29}N_5O_2RuPF_6 \cdot 1/2CH_2Cl_2$
Formula weight	499.40	669.79	720.03
T (K)	293(2)	293(2)	293(2)
λ (Å)	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic	Monoclinic
Crystal size (mm)	$0.362 \times 0.232 \times 0.202$	$0.32 \times 0.16 \times 0.10$	$0.262 \times 0.218 \times 0.176$
Color, habit	Orange, prism	Deep red, parallelepiped	Deep red, parallelepiped
Space group	$P2_1/n$	$P2_1/c$	$P2_1/c$
a (Å)	10.805 (1)	14.203(2)	14.785(1)
b (Å)	12.762(1)	12.364(2)	12.384(1)
c (Å)	14.064 (1)	17.888(2)	17.976(1)
α (°)	90	90	90
β (°)	94.795(1)	92.72(1)	90.201(1)
γ (°)	90	90	90
V (Å^3)	1932.5(3)	3137.7(6)	3291.1(3)
Z	4	4	4
Absorption coefficient (mm^{-1})	0.954	0.653	0.670
θ Range (°)	2.16–27.54	3.00–25.00	2.00–25.00
Index range	$-14 \leqslant h \leqslant 14$, $-16 \leqslant k \leqslant 16$, $-18 \leqslant l \leqslant 17$	$0 \leqslant h \leqslant 16$, $0 \leqslant k \leqslant 14$, $-21 \leqslant l \leqslant 21$	$-17 \leqslant h \leqslant 17$, $-14 \leqslant k \leqslant 14$, $-21 \leqslant l \leqslant 21$
Reflections collected	19003	5752	26256
Independent reflections (R_{int})	4447 (0.0398)	5517 (0.0631)	5787 (0.1084)
Data/restraints/parameters	4447/0/302	5517/1/355	5787/0/390
Goodness-of-fit on F^2	0.966	1.000	0.980
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0341, wR_2 = 0.0737	R_1 = 0.0846, wR_2 = 0.1998	R_1 = 0.0717, wR_2 = 0.1727
R indices (all data)	R_1 = 0.0463, wR_2 = 0.0779	R_1 = 0.1689, wR_2 = 0.2636	R_1 = 0.1261, wR_2 = 0.1954
Largest difference peak and hole (e Å^{-3})	0.557 and −0.333	1.401 and −0.611	0.990 and −0.476

3. Results and discussion

3.1. Synthesis of $[(\eta^6\text{-}C_6H_6)Ru(C_6HR^1R^2R^3\text{-}o\text{-}CH_2NMe_2)(RCN)]PF_6$ complexes

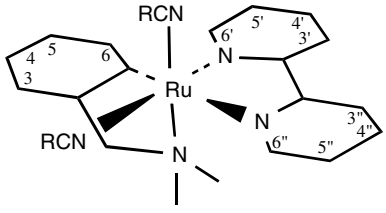
The cycloruthenation of substituted *N*,*N*-dimethylbenzylamines in Chart 1 by $[(\eta^6\text{-}C_6H_6)RuCl(\mu\text{-}Cl)]_2$ in acetonitrile in the presence of NaOH and KPF_6, which leads to the formation of corresponding cycloruthenated complexes **1a**–**p** (Scheme 3) in good to moderate yields, has been performed as described elsewhere [19]. Closely related neutral compounds $[(\eta^6\text{-}C_6H_6)Ru(C_6HR^1R^2R^3\text{-}o\text{-}CH_2NMe_2)Cl]$ with the ligands **b**, **f** and **j** have been synthesised earlier using, however, a different strategy via a transmetalation reaction using mercury derivatives of *N*,*N*-dimethylbenzylamines [25]. Yellow complexes **1a**–**p** are stable in the solid state under inert atmosphere but decompose readily when dissolved in acetonitrile or dichloromethane. The solubility in CH_2Cl_2 is low but the yellow solution of the dissolved material turns green rapidly.

In principle, the cycloruthenation of 3-substituted and 3,4-disubstituted *N*,*N*-dimethylbenzylamines (**c**, **e**, **f** and **k**) could afford two positional isomers as a result of the Ru^{II} attack at the C2 or C6 aromatic carbons as shown in Scheme 4. Interestingly, both isomers have only been observed for 3-methoxy-*N*,*N*-dimethylbenzylamine (**e**) and a mixture of regioisomers **1e** and **1′e** has been isolated. The integration of resonances in the ^1H NMR spectra indicated a 1:1 ratio for **1e** and **1′e**. No attempts of separating the isomers have, however, been made. The cycloruthenation of other asymmetrically substituted amines (**c**, **f**, and **k**) occurs regioselectively and the 6-metalation is the only pathway observed. Usually, the cyclometalation at C2 is sterically restricted as compared to the 6-metalation unless 3-substituent has a donor atom, as oxygen in this case, that enforces the 2-metalation by coordinating to a metal center (Scheme 4) [26,27]. The absence of 2-metalated product for 3,4-dimethoxy substituted *N*,*N*-dimethylbenzylamine (**f**) suggests that the cycloruthenation takes place as an electrophilic substitution by Ru^{II}. In fact, the C6 site of **f** is activated by the *para* methoxy group to a such degree that its ''orienting'' effect responsible for the metalation at C2 becomes frozen. The electrophilic nature of Ru^{II} in this reaction is additionally supported by the necessity of using a strong base, i.e. NaOH, for the C–H bond cleavage. Such behavior is a general feature for the electrophilic cyclometalation encountered in numerous cyclopalladation reactions [27]. Lower yields of complexes **1o**,**p** with strong electron-withdrawing substituents NO_2 and CN are also in accordance with an electrophilic nature of the cycloruthenation by $[(\eta^6\text{-}C_6H_6)RuCl(\mu\text{-}Cl)]_2$. It is worth noting that no reaction has previously been observed between nitro-substituted *N*,*N*-dimethylbenzylamine (**o**) and $[(\eta^6\text{-}C_6H_6)RuCl(\mu\text{-}Cl)]_2$ under similar conditions [19]. This difference in reactivity is tentatively due to the fact that this time the reactions were performed at lower temperature than in the previous work for which the cycloruthenation reactions were run at 45 °C. Some of us have indeed found recently that the yield of the cycloruthenation reactions of nitrogen-containing ligands can be markedly improved by conducting these reactions at 20 °C instead of 45 °C using, however, a longer reaction time [25].

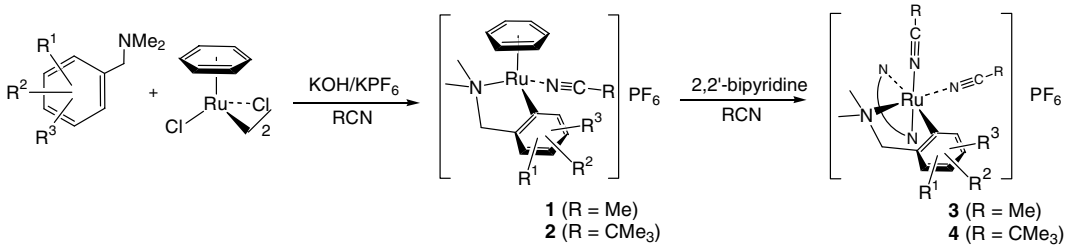
The cycloruthenation by $[(\eta^6\text{-}C_6H_6)RuCl(\mu\text{-}Cl)]_2$ occurs also, if acetonitrile solvent is replaced by more bulky pivalonitrile. Provided other conditions are kept the same, complex **2a** could be isolated in a 35% yield, which is slightly lower as compared with its acetonitrile analog **1a** [12].

3.2. Preparation of $[Ru(C_6HR^1R^2R^3\text{-}o\text{-}CH_2NMe_2)(bpy)(RCN)_2]PF_6$ complexes

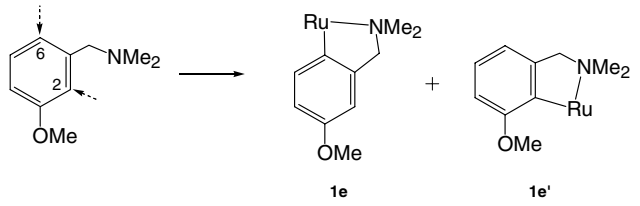
Complexes **1a**–**p** react with one equivalent of 2,2′-bipyridine in acetonitrile at room temperature to give purple crystalline complexes $[Ru(C_6HR^1R^2R^3\text{-}o\text{-}CH_2NMe_2)(bpy)(RCN)_2]PF_6$ (**3a**–**p**) in moderate yields



Scheme 2. Numbering scheme used for the chemical shift assignment.



Scheme 3. Principal synthetic procedures used in this work.



Scheme 4. Regio options for ruthenation of 3-methoxy-*N*,*N*-dimethylbenzylamine.

(~50%) (Scheme 2). It is noteworthy that the product from complex **1m** bearing the tertiary butyl ring substituent could not be isolated as a pure solid. The purple solution obtained after reacting **1m** with bpy turns black readily upon chromatographic purification on alumina due to decomposition. When a 1:1 mixture of **1e** and **1′e** was reacted under these conditions, a 1:1 mixture of **3e** and **3′e** was obtained (based on the integration of the ^{1}H NMR signals). Complex **4a** was similarly prepared from **2a** under the same conditions but using pivalonitrile as the reaction medium.

3.3. X-ray structural investigations

The crystal structure of complex **1a** shown in Fig. 1 could be compared with the structure of **3a**, which has previously been reported [12]. The presence of η^6-bound benzene has no effect on geometrical characteristics of the cycloruthenated *N*,*N*-dimethylbenzylamine. The Ru–C and Ru–N2 bond distances of **1a** are insignificantly longer. An objective of X-ray diffraction study of compounds **3d** and **3f** has been in finding evidence that strong electron-donating methoxy substituents in the *N*,*N*-dimethylbenzylamine ring do not affect electronic properties of complexes **3a**–**p** to a such extent that

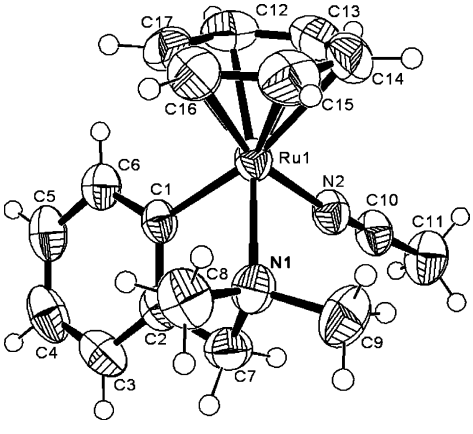


Fig. 1. ORTEP diagram of complex **1a**. Selected bond distances (Å) and bond angles (°): Ru–C(1) 2.069(2), Ru–N(1) 2.170(2), Ru–N(2) 2.058(2), Ru–C(12) 2.183(3), Ru–C(13) 2.180(3), Ru–C(14) 2.273(3), Ru–C(15) 2.240(3), Ru–C(16) 2.184(3), Ru–C(17) 2.178(3), C(1)–Ru–N(1) 78.10(10), C(1)–Ru–N(2) 85.98(9), N(1)–Ru–N(2) 86.65(9).

this changes a mutual ligand arrangement. The structures of both **3d** and **3f** shown in Fig. 2 indicate the same geometry as for **3a**. The acetonitrile ligands are mutually *cis* and the σ-bound carbon is *trans* to one of the nitrogen atoms of 2,2′-bipyridine. There are two kinds of Ru–N bonds in complexes **3d**, **f**, viz. the shorter (2.003, 2.016, and 2.067 Å for **3d**; 2.005, 2.045, and 2.062 Å for **3f**) and the longer ones (2.176 and 2.153 Å for **3d**; 2.137 and 2.186 Å for **3f**). The bond length difference can be explained by the nature of the nitrogen ligands bound to the metal. Due to the back-bonding effects, pyridines and particularly nitriles are more strongerly bound to Ru^{II} than tertiary amines and the corresponding metal-nitrogen bonds are thus shorter. The trans influence of the σ-bound carbon of the metalated phenyl ring of substituted *N*,*N*-dimethylbenzylamine is manifested in an elongation of the Ru–N(7) bond in both complexes.

3.4. Electrochemical studies

Electrochemical properties of complexes **3a**–**p** and **4a** have been investigated by cyclic voltammetry in methanol solution. They all are sparingly soluble in this solvent, the properties of which mimic water. Since we are primarily interested in bioapplications of complexes such as **3** and **4** and in their interactions with oxidizing enzymes, in particular, the study has been focused on oxidizing capabilities of the complexes. Typical cyclic voltammograms of complexes **3** shown in Fig. 3 reflect a $Ru^{II/III}$ transition, which is quasi-reversible under these conditions (see Fig. 3 for conditions), the peak separations are in the range 70–130 mV at a 100 mV s^{-1} scan rate. As seen in Fig. 3, the redox potentials for a $Ru^{II/III}$ feature depend notably on the nature of ring-substituents. It is interesting to note that cyclic voltammograms for the mono methoxy-substituted complexes are very similar to those in Fig. 2. However, the di- and trimethoxy species **3f**–**i** are characterized by an extra irreversible oxidation wave at higher potentials (Fig. 4). The irreversible feature is presumably due to a ligand-centered oxidation, since it is only observed for poly-methoxy substituted *N*,*N*-dimethylbenzylamine complexes.

The dependence of the $Ru^{II/III}$ redox potentials on the nature of the ring substituents has been parametrized in terms of the Hammett formalism [28]. The best linear correlation is achieved when the potentials are plotted against the sum of the Hammett constants σ_p^+ and σ_m (Fig. 5). The corresponding analytical expression is given by the following equation:

$$E^{0\prime}(\mathrm{mV}) = (520 \pm 10) + (120 \pm 10) \times (\sigma_p^+ + \sigma_m). \quad (1)$$

Eq. (1) suggests that the electronic effect from ring substituents is delivered at Ru^{II} via two channels, i.e. the

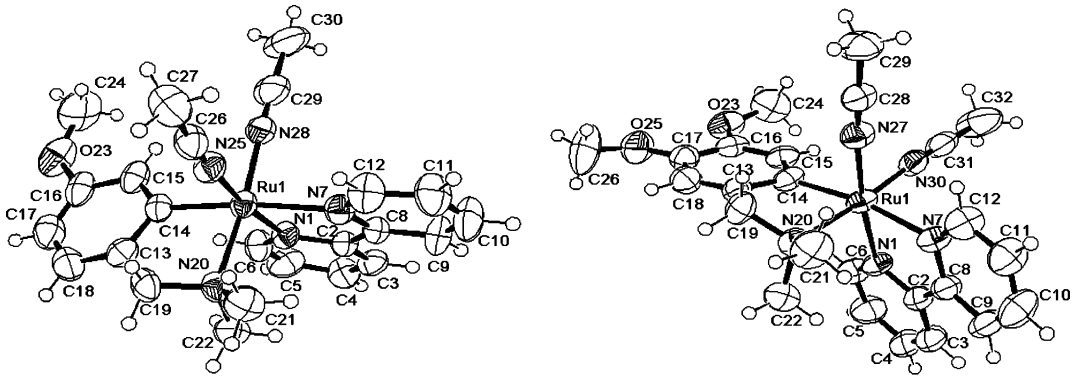


Fig. 2. ORTEP diagrams of complexes **3d** and **3f**. Selected bond distances (Å) and bond angles (°). **3d**: Ru–N(25) 2.016(10), Ru–N(28) 2.003(11), Ru–N(1) 2.067(8), Ru–N(20) 2.176(11), Ru–N(7) 2.153(9), Ru–C(14) 2.034(10), N(28)–Ru–N(25) 89.0(4); N(28)–Ru–C(14) 94.6(4); N(25)–Ru–C(14) 90.3(4); N(28)–Ru–N(1) 88.0(4); C(14)–Ru–N(1) 96.2(4); N(28)–Ru–N(7) 88.9(4); N(25)–Ru–N(7) 95.9(4); N(25)–Ru–N(20) 89.6(4); C(14)–Ru–N(20) 81.3(4); N(1)–Ru–N(20) 93.9(4); N(7)–Ru–N(20) 95.3(4). **3f**: Ru–N(27) 2.045(7); Ru–N(30) 2.005(7); Ru–N(1) 2.062(6); Ru–N(20) 2.186(6); Ru–N(7) 2.137(7); Ru–C(14) 2.058(7); N(30)–Ru–N(27) 89.9(3); N(30)–Ru–N(1) 86.9(2); N(30)–Ru–C(14) 95.4(3); N(27)–Ru–C(14) 90.6(3); N(1)–Ru–C(14) 96.7(3); N(30)–Ru–N(7) 92.7(2); N(27)–Ru–N(7) 95.5(2); N(1)–Ru–N(7) 77.6(2); N(27)–Ru–N(20) 89.8(2); N(1)–Ru–N(20) 94.0(2); C(14)–Ru–N(20) 79.8(3); N(7)–Ru–N(20) 92.1(2).

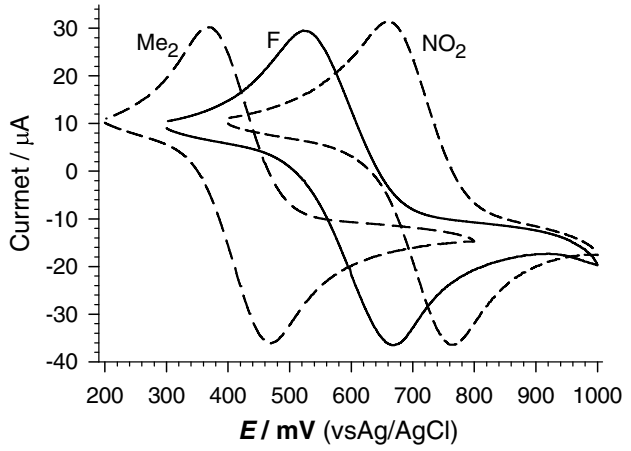


Fig. 3. Cyclic voltamograms of complexes **3c**, **3j**, and **3o** obtained in MeOH, 0.1 M n-Bu_4NClO_4, scan rate 100 mV s^{-1}, glassy carbon electrode.

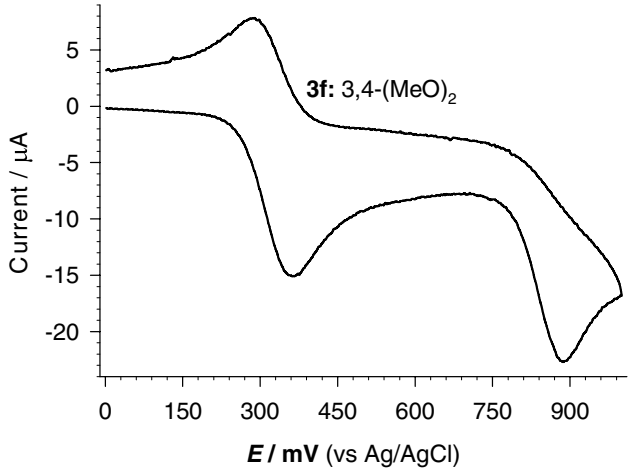


Fig. 4. Cyclic voltamogram of complex **3f** showing the existence of the irreversible oxidation feature around 0.88 V. For conditions, see the legend to Fig. 3.

metal–carbon bond and the tertiary amine chelate arm. It is shown in Fig. 5 that the redox potentials vary in an almost 400 mV range and an exact potential can be adjusted by using the parameters of Eq. (1). It is worth mentioning that our attempts to further decrease $E^{0\prime}$ by using tri-methoxy substituted species have not been successful. For example, the redox potential of **3h**, which equals 440 mV, is significantly shifted anodically as compared with di-substituted complex **3f** (324 mV). This is presumably due to an increase in the bulkiness of **3h** on addition of an extra substituent. Similar effect has been reported for mono alkyl substituted ferrocenes – an increase in the length of the alkyl radical results in a gradual anodic shift of redox potentials [29]. The same effect is obviously responsible for a higher redox potential of pivalonitrile complex **4a** (535 mV) compared with its acetonitrile analog **2a** (498 mV).

*3.5. Oxidation of PQQ-dependent glucose dehydrogenase by complexes **3***

Glucose dehydrogenase (GDH) belongs to a family of PQQ-dependent oxidizing biocatalysts, which has been discovered about two decades ago [30, 31]. The significance of these enzymes is due to the fact that electron acceptors other than dioxygen perform their reoxidation. Cytochromes *c*, small blue-copper proteins, or an internal heme *c* group can function as natural electron acceptors [30,31]. Correspondingly, transition metal acceptors such as Ru^{II} complexes reported here are

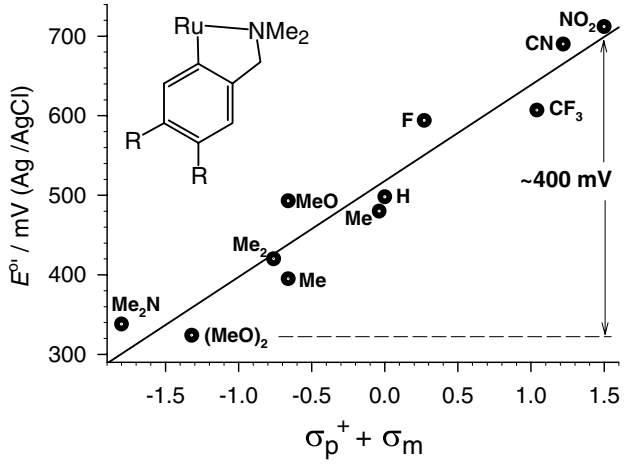


Fig. 5. The Hammett plot showing that the observed redox potentials of complexes **3** in MeOH is a linear function of the sum of the σ_p^+ and σ_m parameters. See text for explanations and details.

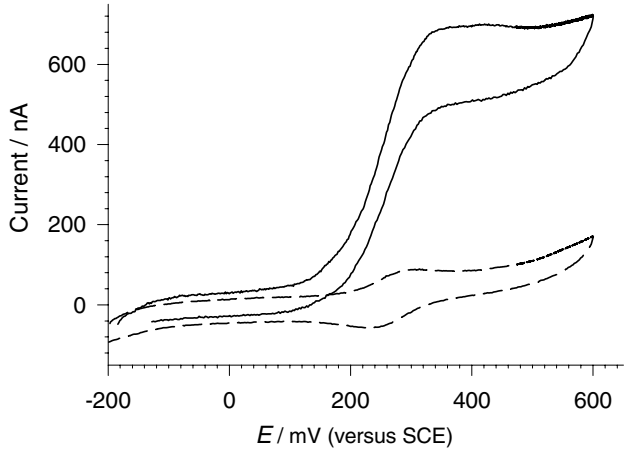


Fig. 6. Cyclic voltamogram of complex **3a** in aqueous solution at pH 7.0 in the presence of 0.1 M D-glucose (dash line) and the same in the presence of 1×10^{-4} M GDH (solid line). Scan rate 2 mV s^{-1}, 0.01 M phosphate, 25 °C.

expected substitutes of the natural ones in electrocatalysis by PQQ-dependent enzymes such as glucose dehydrogenase. GDH is an heme free protein and therefore it has a low tendency to exchange electrons directly with an electrode. Therefore, a search for efficient mediators capable of functioning as shown in Scheme 1 is urgent. Previously, we have introduced several ferrocene derivatives as mediators of PQQ-dependent alcohol and glucose dehydrogenases [32,33]. Here, we show that complexes such as **3** seem promising as soluble mediators of GDH.

The cyclic voltammogram of complex **3a** in a buffered aqueous solution is a dash line in Fig. 6. It is unaffected in the presence of D-glucose but a solid line illustrates a spectacular current increase in the presence of GDH. This electrobiocatalytic effect is customarily accounted for in terms Eqs. (2)–(4) [17]. The first is the enzyme-catalyzed oxidation of D-glucose. Eq. (3) describes the oxidation of reduced GDH by electrochemically generated Ru^{III}, which is followed by an electrode process (Eq. (4)). The data such as in Fig. 6 analyzed using the formalism of Bourdillon, et al. [34], allowed to calculate the second-order rate constant $k = 4.8 \times 10^7$ M^{-1} s^{-1} at 25 °C and pH 7.0. This is in fact a very high rate of oxidation of glucose-converting enzymes by a transition-metal based mediator [17].

$$\mathrm{GDH(ox)} + \text{d-glucose} \rightarrow \mathrm{GDH(red)} + \delta\text{-d-gluconolactone} + 2\mathrm{H^+} \quad (2)$$

$$\mathrm{GDH(red)} + 2\mathrm{Ru^{III}} \xrightarrow{k} \mathrm{GDH(ox)} + 2\mathrm{Ru^{II}} \quad (3)$$

$$\mathrm{Ru^{II}} \rightarrow \mathrm{Ru^{III}(electrode)} \quad (4)$$

Thus, the reaction between M(ox) and E(red) in Scheme 1 occurs fast for this particular enzyme and the cycloruthenated complex. Rather surprisingly, ring-substituted complexes **3**, both with electron-donating (**3n**) and -withdrawing (**3p**) groups oxidize GDH(red) with still high but lower rates under the same conditions (2.0×10^5 and 1.1×10^6 M^{-1} s^{-1}, respectively). The simplest rationalization of this rate drop is the steric effect brought about by the ring substituents but obviously more work is needed for proving this statement. This study is currently underway.

4. Conclusion

We have described the uncomplicated synthesis and properties of cycloruthenated complexes $[Ru(C_6H\text{-}R^1R^2R^3\text{-}o\text{-}CH_2NMe_2)(bpy)(RCN)_2]PF_6$ (R = Me and CMe_3). Two labile *cis*-nitrile ligands in the coordination sphere of the cyclometalated *N*,*N*-dimethylbenzylamine complexes make them convenient precursors for further modifications. Electronic properties of the complexes are fairly sensitive to substituents in the aromatic ring of cyclometalated ligand and the redox potentials vary in a 400 mV range. A significant bioelectrochemical potential of the complexes reported has been demonstrated by showing that they reoxidize readily the reduced active site of PQQ-dependent enzyme glucose dehydrogenase.

5. Supporting information

Crystallographic data for **1a**, **3d** and **3f** have been deposited at the Cambridge Crystallographic Data Centre with deposition numbers CCDC No. 247141 for **1a**, CCDC No. 247142 for **3d** and CCDC No. 247143 for **3f**, respectively. Copies of the information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223

336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Acknowledgement

Financial support from CONACyT (Project No. 34293-E) is gratefully acknowledged.

References

[1] A.C. Cope, R.W. Siekman, J. Am. Chem. Soc. 87 (1965) 7272.
[2] A.D. Ryabov, Synthesis (1985) 233.
[3] M. Pfeffer, Recl. Trav. Chim. Pays-Bas 109 (1990) 567.
[4] J. Spencer, M. Pfeffer, Adv. Met. Org. Chem. 6 (1998) 103.
[5] V. Ritleng, C. Sirlin, M. Pfeffer, Chem. Rev. 102 (2002) 1731.
[6] W.A. Herrmann, V.P.W. Böhm, C. Reisinger, J. Organomet. Chem. 576 (1999) 23.
[7] I.P. Beletskaya, A.V. Cheprakov, Chem. Rev. 100 (2000) 3009.
[8] M. Albrecht, G. van Koten, Angew. Chem., Int. Ed. 40 (2001) 3750.
[9] J. Dupont, M. Pfeffer, J. Spencer, Eur. J. Inorg. Chem. (2001) 1917.
[10] E.V. Krooglyak, G.M. Kazankov, S.A. Kurzeev, V.A. Polyakov, A.N. Semenov, A.D. Ryabov, Inorg. Chem. 35 (1996) 4804.
[11] G.M. Kazankov, V.S. Sergeeva, E.N. Efremenko, L. Alexandrova, S.D. Varfolomeev, A.D. Ryabov, Angew. Chem., Int. Ed. Engl. 39 (2000) 3117.
[12] A.D. Ryabov, V.S. Sukharev, L. Alexandrova, R. Le Lagadec, M. Pfeffer, Inorg. Chem. 30 (2001) 6529.
[13] V.S. Soukharev, A.D. Ryabov, E. Csöregi, J. Organomet. Chem. 668 (2003) 75.
[14] I.S. Alpeeva, V.S. Soukharev, L. Alexandrova, N.V. Shilova, N.V. Bovin, E. Csöregi, A.D. Ryabov, I.Y. Sakharov, J. Biol. Inorg. Chem. 8 (2003) 683.
[15] A.D. Ryabov, V.S. Soukharev, L. Alexandrova, R. Le Lagadec, M. Pfeffer, Inorg. Chem. 42 (2003) 6598.
[16] J. Castillo, S. Gáspár, S. Leth, M. Niculescu, A. Mortari, I. Bontidean, V. Soukharev, S.A. Dorneanu, A.D. Ryabov, E. Csöregi, Sensors Actuators B 102 (2004) 179.
[17] A.D. Ryabov, Adv. Inorg. Chem. 55 (2004) 201.
[18] R.A. Zelonka, M.C. Baird, Can. J. Chem. 50 (1972) 3063.
[19] S. Fernandez, M. Pfeffer, V. Ritleng, C. Sirlin, Organometallics 18 (1999) 2390.
[20] S. Bhattacharyya, J. Org. Chem. 60 (1995) 4928.
[21] L. Marcinkeviciene, I. Bachmatova, R. Semenaite, R. Rudomanskis, G. Brazenas, R. Meskiene, R. Meskys, Biotechnol. Lett. (1999) 187.
[22] Bruker SMART (Version 5.625 control), SAINT-Plus (Version 6.23C integration). Bruker AXS Inc., Madison, WI, USA, 2000.
[23] XSCANS (Version 2.1). Siemens Analytical X-ray Instruments Inc., Madison, WI, USA, 1993.
[24] G.M. Sheldrick, SHELXTL (Version 6.12), Bruker AXS Inc., Madison, WI, USA, 2000.
[25] M. Pfeffer, J.P. Sutter, E. Urriolabeitia, Inorg. Chim. Acta 249 (1996) 63.
[26] I. Omae, Organometallic Intramolecular-coordination Compounds, Elsevier, Amsterdam, 1986.
[27] A.D. Ryabov, Chem. Rev. 90 (1990) 403.
[28] C. Hansch, A. Leo, R.W. Taft, Chem. Rev. 91 (1991) 165.
[29] M.A. Bazhenova, S.S. Bogoush, A.G. Herbst, T.V. Demeschik, Y.G. Komarovskya, V.S. Kurova, M.D. Reshetova, A.D. Ryabov, E.S. Ryabova, Y.N. Firsova, Izv. RAN. Ser. Khim. (1996) 2575.
[30] J.A. Duine, J. Biosci. Bioeng. 88 (1999) 231.
[31] J.A. Duine, in: J. Reedijk, E. Bouwman (Eds.), Bioinorganic Catalysis, 2nd ed., Marcel Dekker, New York, 1999, pp. 563–585.
[32] J. Razumiene, R. Meskys, V. Gureviciene, V. Laurinavicius, M.D. Reshetova, A.D. Ryabov, Electrochem. Commun. 2 (2000) 307.
[33] J. Razumiene, A. Vilkanauskyte, V. Gureviciene, V. Laurinavicius, N.V. Roznyatovskaya, Y.V. Ageeva, M.D. Reshetova, A.D. Ryabov, J. Organomet. Chem. 668 (2003) 83.
[34] C. Bourdillon, C. Demaille, J. Moiroux, J.-M. Savéant, J. Am. Chem. Soc. 115 (1993) 2.