

A Simple Preparation of Pyridine-Derived N-Heterocyclic Carbenes and Their Transformation into Bridging Ligands by Orthometalation**

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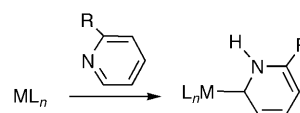
In memory of Lorenzo Pueyo

A plethora of transition-metal complexes containing N-heterocyclic carbene (NHC) ligands have been prepared over the past decade,^[1] particularly because many of them are among the most active catalysts for important organic reactions, such as olefin metathesis and various C–C bond-forming processes.^[2] The great majority of the NHC ligands of these complexes are two-nitrogen, five-membered, heterocyclic carbenes.

Metal complexes containing one-nitrogen, six-membered, heterocyclic carbene ligands are far less common.^[3–12] Cationic nickel(II) or palladium(II) complexes that have been prepared in the laboratories of Raubenheimer, Herrmann, or Frenking by oxidative addition (or oxidative substitution) of the C–X (X = halogen) bond of N-alkyl (or N-aryl) halopyridinium (or haloquinolinium, haloacridinium, etc.) salts to appropriate metal(0) precursors.^[3] This synthetic method is restricted to metal complexes that can undergo easy oxidative addition reactions. It can provide not only complexes with normal pyrid-2-ylidene-type ligands, in which the metal is bound to a C atom away from the N atom of the heterocyclic ligand (**A** in Scheme 1, for example), but also complexes with

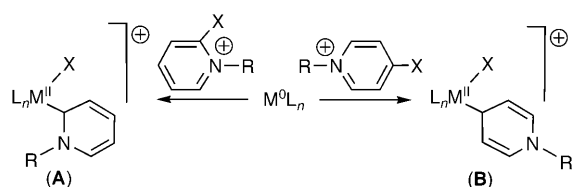
remote pyrid-4-ylidene-type ligands, in which the metal is bound to a C atom *para* to the N atom (**B** in Scheme 1, for example). These complexes are also active as catalysts for C–C coupling reactions.^[3,5] Some pyridine-derived NHC ligands have also been prepared by oxidative addition of pyridinium C–H bonds,^[6] N-alkylation of coordinated pyridyl ligands,^[7] and deprotonation of isoquinolinium cations.^[8]

Recent studies by the groups of Bergman,^[9] Carmona,^[10] Esteruelas,^[11] and Li^[12] have shown that some pyridines can undergo metal-induced rearrangements to form NHC ligands. These reactions, which are restricted to a few metal systems, generally involve tautomerization processes (such as that shown in Scheme 2 for 2-substituted pyridines).



Scheme 2. Metal-induced tautomerization of substituted pyridines.

Herein, we report that simple pyrid-2-ylidenes can also be prepared by deprotonation of N-substituted pyridinium cations (Scheme 3) and that they can be trapped in solution by metal complexes, such as $[\text{Ru}_3(\text{CO})_{12}]$. Interestingly, the great basicity of this type of NHC^[3,6] and the polynuclear character of the ruthenium cluster trigger the room-temperature transformation of the initial $\kappa^1\text{-C}^2$ -pyrid-2-ylidene ligands into unprecedented face-capping $\mu_3\text{-}\kappa^2\text{-C}^2, \text{C}^3$ -pyrid-3-yl-2-ylidene ligands by orthometalation. The mechanism of this process, modeled by density functional (DFT) calculations, is also reported.



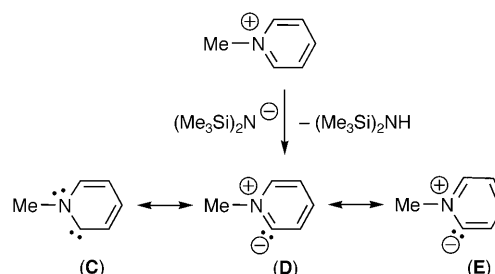
Scheme 1. Syntheses of complexes containing “normal” (**A**) and “remote” (**B**) pyridylidene ligands derived from halopyridinium cations.

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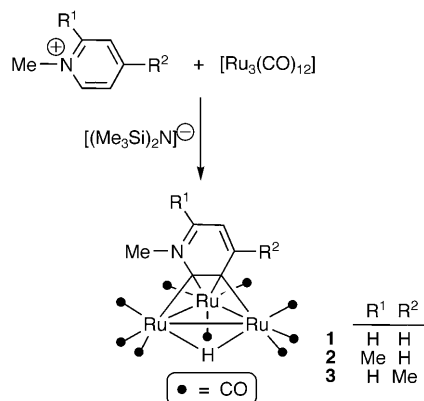
[**] This work has been supported by the Spanish Ministerio de Ciencia e Innovación (projects CTQ2007-60865 and MAT2006-1997). Fellowships from the University of Carabobo (Venezuela, to M.G.S.-V.) and Xunta de Galicia (Spain, to D.V.-G.) are also acknowledged.

Supporting Information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.200804945>.



Scheme 3. Deprotonation of N-methylpyridinium to give N-methylpyrid-2-ylidene. The carbene (**C**) and ylidic (**D** and **E**) resonance structures of this NHC are also shown.

Treatment of a THF solution containing equimolar amounts of $[\text{Ru}_3(\text{CO})_{12}]$ and *N*-methylpyridinium triflate with potassium bis(trimethylsilyl)amide at room temperature allowed the isolation of the trinuclear cluster $[\text{Ru}_3(\mu\text{-H})(\mu_3\text{-}\kappa^2\text{-C}^2, \text{C}^3\text{-L})(\text{CO})_9]$ ($\text{L} = N\text{-methylpyrid-3-yl-2-ylidene}$, **1**). Analogous clusters ($\text{L} = N\text{-methyl-2-picolin-5-yl-6-ylidene}$, **2**; $\text{L} = N\text{-methyl-4-picolin-3-yl-2-ylidene}$, **3**) were obtained from reactions using *N*-methyl-2-picolinium or *N*-methyl-4-picolinium triflates as carbene precursors (Scheme 4).^[13] The



Scheme 4. Synthesis of complexes **1–3**.

IR spectra of compounds **1–3** contain a nearly identical $\tilde{\nu}(\text{CO})$ stretching region, indicating that they have analogous structures. The ^1H NMR spectra of these complexes confirm the presence of a hydride and the corresponding organic ligand (**L**).^[14]

The X-ray structure of compound **3** (Figure 1)^[15] shows the organic ligand to be bound to all three Ru atoms in such a way that the C1 carbon atom bridges the Ru1–Ru3 edge and the C2 carbon atom bridges the Ru2–Ru3 edge, the C1–C2 and Ru1–Ru2 bonds being parallel. An analysis of the Ru–C

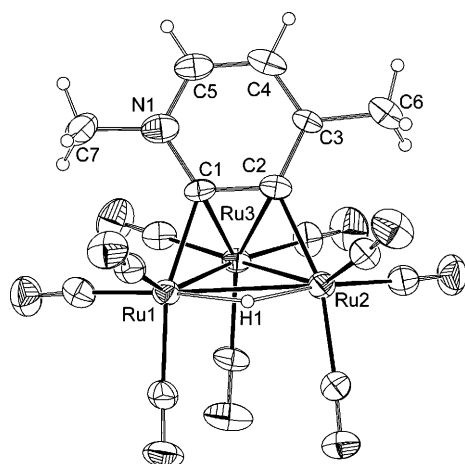


Figure 1. Molecular structure of compound **3**. Thermal ellipsoids are set at 30% probability. Selected bond lengths [Å]: Ru1–C1 2.112(8), Ru2–C2 2.093(9), Ru3–C1 2.292(9), Ru3–C2 2.298(9), C1–C2 1.43(1), C2–C3 1.41(1), C3–C4 1.37(2), C3–C6 1.49(2), C4–C5 1.39(2), N1–C1 1.39(1), N1–C5 1.35(2), N1–C7 1.48(2).

bond lengths reveals that Ru1–C1 and Ru2–C2 are approximately 0.2 Å shorter than Ru3–C1 and Ru3–C2. There is a dihedral angle of 65.5(2)° between the planes that contain the pyridine ring and the Ru_3 triangle. These data indicate that the organic ligand behaves as a 5-electron donor that can be adequately described by the ylidic resonance form **E** (Scheme 3), with C1 attached to Ru1, C2 to Ru2, and the C1=C2 double bond π -coordinated to Ru3. The cluster shell is completed by a hydride, H1, which bridges the Ru1–Ru2 edge, and nine carbonyl ligands.

This structure is related to those reported by Whittlesey and co-workers for two trinuclear clusters of general formula $[\text{Ru}_3(\mu\text{-H})(\mu_3\text{-L}')(\text{CO})_9]$, in which the capping L' ligands arise from the metalation on C^5 of abnormally bound imidazol-4-ylidenes having very bulky groups, adamantyl^[16a] or *tert*-butyl^[16b] on the nitrogen atoms. It seems that, in trinuclear cluster chemistry, structures with face-capping NHC ligands are particularly favored with original NHC ligands that contain a CH group adjacent to the carbene carbon atom.

Recent studies by our group^[17] and also by those of Whittlesey^[16] and Cole^[18] have revealed that some imidazole-derived NHCs can be incorporated into triruthenium carbonyl clusters, when the NHCs are not used in excess,^[16c,18] to give isolable derivatives of the type $[\text{Ru}_3(\text{CO})_{11}(\text{NHC})]$. These clusters are prone to undergo intramolecular $\text{C}(\text{sp}^2)\text{-H}$,^[16a,b] $\text{C}(\text{sp}^3)\text{-H}$,^[17a,c-e] and/or $\text{C}(\text{sp}^2)\text{-N}$ ^[17d] bond-activation processes, but only the double C–H activation of a methyl group in $[\text{Ru}_3(\text{CO})_{11}(\text{Me}_2\text{Im})]$ ($\text{Me}_2\text{Im} = 1,3\text{-dimethylimidazol-2-ylidene}$) has been mechanistically studied.^[17a]

The mechanism of the reaction that leads to compound **1** from $[\text{Ru}_3(\text{CO})_{12}]$ and *N*-methylpyrid-2-ylidene has been modeled by DFT calculations at the B3LYP/LanL2DZ/6-31G(d,p) level (Figures 2 and 3).^[19] The initial intermediate **i1**, which is proposed to contain the intact carbene ligand in an equatorial position, as has been demonstrated for other $[\text{Ru}_3(\text{CO})_{11}(\text{NHC})]$ clusters,^[17b] undergoes a ligand rearrangement that places the carbene ligand in an axial position (**i2**).

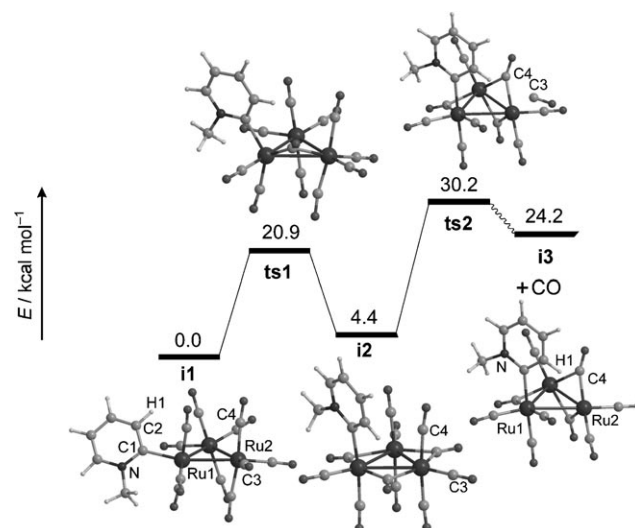


Figure 2. DFT-optimized structures and relative energy profile of the stationary points involved in the transformation of $[\text{Ru}_3(\text{CO})_{11}\text{L}]$ ($\text{L} = N\text{-methylpyrid-2-ylidene}$; **i1**) into **i3** + CO.

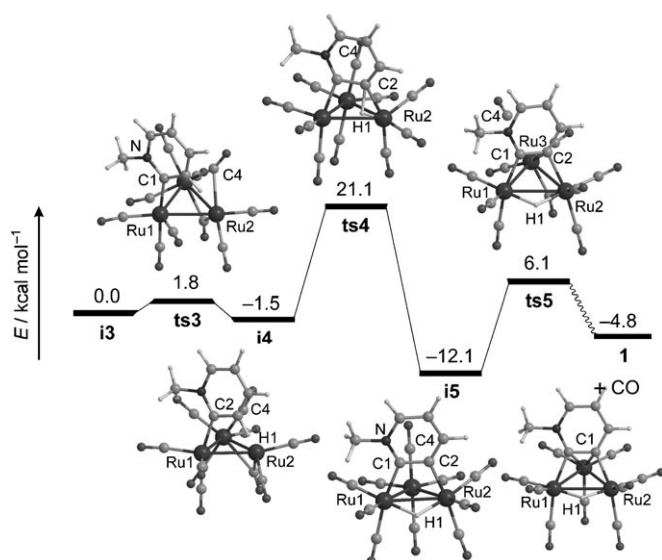


Figure 3. DFT-optimized structures and relative energy profile of the stationary points involved in the transformation of **i3** into **1** + CO.

The next step (**i2** to **i3**) is the rate-limiting step of the overall transformation (energy barrier = 30.2 kcal mol⁻¹). Such a high energy barrier is responsible for the slow rate of the reaction.^[13] This step is a CO-elimination process in which a CO ligand of Ru2 is released (C3–Ru2 3.093 Å in **ts2**) at the same time that the H1 hydrogen atom approaches Ru2 (H1–Ru2 3.389 Å in **ts2**). The rearrangement of the CO ligands of **i3** leads to the unsaturation of Ru2, which is alleviated by a short contact between H1 and Ru2 (H1–Ru2 2.446 Å in **i4**). Such an interaction in **i4**, which is also favored by the opposing atomic charges of these atoms (+0.258 for H1 and –0.222 for Ru2), evolves through **ts4** toward the oxidative addition of the C2–H1 bond to the Ru2 atom, in such a way that, in **i5**, H1 bridges the Ru1–Ru2 edge (H1–Ru1 1.813 Å, H1–Ru2 1.804 Å) and C2 is bonded to Ru2 (C2–Ru2 2.127 Å). In the final step (**i5** to **1**), the coordination of the ring C1=C2 bond to Ru3 is accompanied by the elimination of an axial CO ligand from Ru3. The low energy barrier of **ts5** and the irreversibility of this step, owing to the release of CO gas, drive the reaction.

In summary, we have demonstrated that pyrid-2-ylidenes can be prepared by simple deprotonation of readily available *N*-methylpyridinium cations and that they can be trapped by [Ru₃(CO)₁₂]. This synthetic strategy will have important implications in the synthesis, reactivity, and catalytic activity of pyrid-2-ylidene derivatives of other transition metals. In their reactions with [Ru₃(CO)₁₂], the high basicity of pyrid-2-ylidenes,^[3,6] which enhances the negative charges of the metal atoms, the close proximity of a metal atom in a trinuclear cluster to the ligand *ortho*-C–H bond, and the irreversibility of the CO elimination steps trigger the orthometalation of pyrid-2-ylidenes and the subsequent face-capping coordination of the resulting metalated ligands. This mechanistic model not only explains the formation of clusters **1–3**, but also that of any trinuclear cluster having a face-capping ligand derived from a NHC that contains a CH group adjacent to the

carbene carbon atom, such as those unexpectedly obtained by Whittlesey and co-workers with imidazol-4-ylidenes.^[16a,b]

Received: October 9, 2008

Keywords: C–H activation · carbenes · cluster compounds · nitrogen heterocycles · ruthenium

- [1] For recent general reviews, see: a) F. E. Hahn, M. C. Jahnke, *Angew. Chem.* **2008**, *120*, 3166–3216; *Angew. Chem. Int. Ed.* **2008**, *47*, 3122–3172; b) H. Clavier, K. Grela, A. Kirschning, M. Mauduit, S. P. Nolan, *Angew. Chem.* **2007**, *119*, 6906–6922; *Angew. Chem. Int. Ed.* **2007**, *46*, 6786–6801.
- [2] For recent reviews, see: a) F. A. Glorius, *Top. Organomet. Chem.* **2007**, *21*, 1–20; b) *N-Heterocyclic Carbenes in Synthesis* (Ed.: S. P. Nolan), Wiley-VCH, Weinheim, **2006**; c) F. E. Hahn, *Angew. Chem.* **2006**, *118*, 1374–1378; *Angew. Chem. Int. Ed.* **2006**, *45*, 1348–1352.
- [3] For a review of one-N, six-membered, heterocyclic carbene complexes, see: H. G. Raubenheimer, S. Cronje, *Dalton Trans.* **2008**, 1265–1272.
- [4] a) C. P. Newman, G. J. Clarkson, N. W. Alcock, J. P. Rourke, *Dalton Trans.* **2006**, 3321–3325; b) W. H. Meyer, M. Deetlefs, M. Pohlmann, R. Scholz, M. W. Esterhuysen, G. R. Julius, H. G. Raubenheimer, *Dalton Trans.* **2004**, 413–420; c) G. W. V. Cave, A. J. Hallett, W. Errington, J. P. Rourke, *Angew. Chem.* **1998**, *110*, 3466–3468; *Angew. Chem. Int. Ed.* **1998**, *37*, 3270–3272; d) H. G. Raubenheimer, J. G. Toerien, G. J. Kruger, R. Otte, W. van Zyl, P. Olivier, *J. Organomet. Chem.* **1994**, *466*, 291–295; e) R. Aumann, P. Hinterding, *Chem. Ber.* **1992**, *125*, 2765–2772; f) B. Crociani, F. Di Bianca, A. Giovenco, A. Scrivanti, *J. Organomet. Chem.* **1983**, *251*, 393–411; g) P. J. Fraser, W. R. Roper, F. G. A. Stone, *J. Chem. Soc. Dalton Trans.* **1974**, 760–764.
- [5] a) M. Albrecht, H. Stoeckli-Evans, *Chem. Commun.* **2005**, 4705–4707; b) S. K. Schneider, P. Roembke, G. R. Julius, C. Loschen, H. G. Raubenheimer, G. Frenking, W. A. Herrmann, *Eur. J. Inorg. Chem.* **2005**, 2973–2977.
- [6] J. S. Owen, J. A. Labinger, J. E. Bercaw, *J. Am. Chem. Soc.* **2004**, *126*, 8247–8255.
- [7] F. P. Fanizzi, G. J. Sunley, J. A. Wheeler, H. Adams, N. A. Bailey, P. M. Maitlis, *Organometallics* **1990**, *9*, 131–136.
- [8] S. Gómez-Bujedo, M. Alcarazo, C. Pichon, E. Alvarez, R. Fernández, J. M. Lassaletta, *Chem. Commun.* **2007**, 1180–1182.
- [9] S. H. Wiedemann, J. C. Lewis, J. A. Ellman, R. G. Bergman, *J. Am. Chem. Soc.* **2006**, *128*, 2452–2462.
- [10] a) S. Conejero, P. Lara, M. Paneque, A. Petronilho, M. L. Poveda, O. Serrano, F. Batiré, E. Alvarez, C. Moya, V. Salazar, E. Carmona, *Angew. Chem.* **2008**, *120*, 4452–4455; *Angew. Chem. Int. Ed.* **2008**, *47*, 4380–4383; b) E. Alvarez, S. Conejero, P. Lara, J. A. López, M. Paneque, A. Petronilho, M. L. Poveda, D. del Río, O. Serrano, E. Carmona, *J. Am. Chem. Soc.* **2007**, *129*, 14130–14131; c) E. Alvarez, S. Conejero, M. Paneque, A. Petronilho, M. L. Poveda, O. Serrano, E. Carmona, *J. Am. Chem. Soc.* **2006**, *128*, 13060–13061.
- [11] a) M. L. Buil, M. A. Esteruelas, K. Garcés, M. Oliván, E. Oñate, *J. Am. Chem. Soc.* **2007**, *129*, 10998–10999; b) M. A. Esteruelas, F. J. Fernández-Alvarez, E. Oñate, *Organometallics* **2007**, *26*, 5239–5245; c) M. A. Esteruelas, F. J. Fernández-Alvarez, E. Oñate, *J. Am. Chem. Soc.* **2006**, *128*, 13044–13045.
- [12] G. Song, Y. Li, S. Chen, X. Li, *Chem. Commun.* **2008**, 3558–3560.
- [13] A toluene solution of K[(Me₃Si)₂N] (315 μL, 0.5 M, 0.156 mmol) was added to a mixture of [Ru₃(CO)₁₂] (100 mg, 0.156 mmol) and *N*-methylpyridinium triflate (38 mg, 0.156 mmol) in THF

(20 mL). The mixture was stirred at room temperature until the consumption of the starting ruthenium complex was confirmed by IR spectroscopy (10 h). The solvent was removed under reduced pressure and the residue was extracted into toluene (20 mL) to give a red solution and a brown solid. The solution was concentrated and purified by preparative thin-layer chromatography (silica gel). Elution with dichloromethane/hexane (1:4) afforded compound **1** (10 mg, 10%) as a red-orange band. A dark brown residue remained uneluted on the plate baseline. Compounds **2** and **3** were prepared in similar yields from the respective appropriate *N*-methylpicolinium triflate.

- [14] Spectroscopic data: a) **1**: ^1H NMR (CDCl_3): δ = 8.28 (d, J = 6.5 Hz, 1H), 7.99 (d, J = 6.5 Hz, 1H), 6.82 (t, J = 6.5 Hz, 1H), 4.09 (s, 3H), –18.08 ppm (s, 1H); IR (CH_2Cl_2): $\tilde{\nu}(\text{CO})$ = 2079 (m), 2052 (s), 2013 (vs), 1981 (m, sh), 1950 cm^{-1} (w, sh); b) **2**: ^1H NMR (CDCl_3): δ = 8.18 (d, J = 7.5 Hz, 1H), 6.69 (d, J = 7.5 Hz, 1H), 4.07 (s, 3H), 3.68 (s, 3H), –17.95 ppm (s, 1H); IR (CH_2Cl_2): $\tilde{\nu}(\text{CO})$ = 2078 (m), 2049 (s), 2013 (vs), 1981 (m, sh), 1949 cm^{-1} (w, sh); c) **3**: ^1H NMR (CDCl_3): δ = 7.95 (d, J = 6.0 Hz, 1H), 6.84 (d, J = 6.0 Hz, 1H), 4.05 (s, 3H), 2.54 (s, 3H), –17.76 ppm (s, 1H); ^{13}C NMR (DEPT, CDCl_3): δ = 177.7 (C), 174.5 (C), 146.5 (C), 143.1 (CH), 115.8 (CH), 50.7 (CH_3), 26.8 ppm (CH_3); IR (CH_2Cl_2): $\tilde{\nu}(\text{CO})$ = 2077 (m), 2048 (s), 2013 (vs), 1986 (m, sh), 1945 cm^{-1} (w, sh).
- [15] Crystal data for **3**·(hexane) $_{0.25}$: $\text{C}_{16}\text{H}_{19}\text{NO}_9\text{Ru}_3 \cdot 0.25(\text{C}_6\text{H}_{14})$; M_r = 680.46; crystal size 0.12 × 0.07 × 0.02 mm; triclinic; space group $P\bar{1}$; a = 9.630(2), b = 9.910(2), c = 12.358(3) Å; α = 80.472(1), β = 71.785(1), γ = 79.735(1)°; V = 1094.7(4) Å³; Z = 2; ρ_{calcd} = 2.064 g cm^{-3} ; $F(000)$ = 650; μ = 2.090 mm^{-1} ; 10 691 reflections measured, 3640 independent reflections; R_1 = 0.0609 and wR_2 = 0.1996 (all data). CCDC 703646 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- [16] a) M. R. Crittall, C. E. Ellul, M. F. Mahon, O. Saker, M. K. Whittlesey, *Dalton Trans.* **2008**, 4209–4211; b) C. E. Ellul, M. F. Mahon, O. Saker, M. K. Whittlesey, *Angew. Chem.* **2007**, *119*, 6459–6461; *Angew. Chem. Int. Ed.* **2007**, *46*, 6343–6345; c) C. E. Ellul, O. Saker, M. F. Mahon, D. C. Apperley, M. K. Whittlesey, *Organometallics* **2008**, *27*, 100–108.
- [17] a) J. A. Cabeza, E. Pérez-Carreño, *Organometallics* **2008**, *27*, 4697–4702; b) J. A. Cabeza, I. del Río, D. Miguel, E. Pérez-Carreño, M. G. Sánchez-Vega, *Organometallics* **2008**, *27*, 211–217; c) J. A. Cabeza, I. del Río, D. Miguel, E. Pérez-Carreño, M. G. Sánchez-Vega, *Dalton Trans.* **2008**, 1937–1942; d) J. A. Cabeza, I. del Río, D. Miguel, M. G. Sánchez-Vega, *Angew. Chem.* **2008**, *120*, 1946–1948; *Angew. Chem. Int. Ed.* **2008**, *47*, 1920–1922; e) J. A. Cabeza, I. del Río, D. Miguel, M. G. Sánchez-Vega, *Chem. Commun.* **2005**, 3956–3958.
- [18] M. I. Bruce, M. L. Cole, R. S. C. Fung, C. M. Forsyth, M. Hilder, P. C. Junk, K. Konstantas, *Dalton Trans.* **2008**, 4118–4128.
- [19] The experimental details of the DFT calculations, as well as tables containing computed interatomic distances, NPA atomic charges, and Cartesian atomic coordinates for all optimized stationary points are contained in the Supporting Information.