Design of Highly Selective Alkyne Hydrothiolation Rh(I)-NHC Catalysts: Carbonyl-Triggered Non-Oxidative Mechanism

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ABSTRACT: New Rh^I-IPr {IPr = 1,3-bis-(2,6-diisopropylphenyl)imidazolin-2-carbene} complexes bearing a N,O-pyridine-2-methanolato (N-O) bidentate ligand have been prepared. The carbonyl complex Rh(N-O)(IPr)(CO) efficiently catalyzes the hydrothiolation of a range of alkynes with high selectivity to α -vinyl sulfides. Reactivity studies and DFT calculations have revealed a new non-oxidative catalytic pathway, passing through Rh^I catalytic intermediates, which is driven by the interplay between the pyridine-2-methanolato and carbonyl ligands. The basic alkoxo ligand promotes the deprotonation of the thiol to generate the Rh^I active species, whereas the π -acceptor character of carbonyl ligand hinders the oxidative addition process. In addition, the stereochemistry of the key thiolate- π -alkyne intermediate, which is determined by the electronic preference of the carbonyl ligand to coordinate *cis* to IPr, facilitates the rate-limiting alkyne thiometallation step.

INTRODUCTION

Vinyl sulfides constitute an interesting group of organic molecules with valuable biological applications¹ and remarkable versatility as synthetic intermediates.² Although several approaches have been described,³ one of the more straightforward and atom economic preparative methods consists in the addition of a S-H bond of a thiol across a C-C triple bond, known as alkyne hydrothiolation.⁴ While this process can be initiated by radical,⁵ and basic⁶ or acid⁷ promoters, transition metal catalysis represents a more flexible approach to control the regioselectivity.⁸ Particularly, rhodium catalysts behave as chameleonic species, since subtle tuning of the ancillary ligands strongly influences the catalytic outcome.⁹ It becomes evident that, in order to obtain the desired product, the in-depth understanding of the mode of action of the catalyst is essential. In this context, the more common mechanism for rhodium-based catalysts starts with the oxidation of the Rh^I metal precursor to Rh^{III} by addition of the S-H bond of the thiol (Scheme 1). Subsequent 1,2 or 2,1 alkyne insertion into Rh-H or Rh-S bonds generates four pathways which, followed by reductive elimination, affords α - or β -*E*-vinyl sulfides. As a viable alternative, the non-oxidative route consists on the deprotonation of the thiol by an internal base present in the catalytic precursor to generate a Rh-thiolate species. Then, alkyne insertion and protonolysis by an external thiol or a protonated hemilabile ligand affords preferentially the branched vinyl sulfides and regenerates Rh^I-SR active species.^{9m} Vinylidene intermediates or external attack of thiol to a coordinated alkyne are less prevalent in rhodium systems. The

complexity of the process entails a rational design of the catalytic precursors to channel the reactive intermediates through the desired reaction pathway.

Scheme 1. Rhodium-Based Alkyne Hydrothiolation Mechanisms.

Our group has recently disclosed that rhodium(I)-N-heterocyclic carbene (NHC) catalysts efficiently perform alkyne hydrothiolation under mild conditions (Scheme 2).^{9f} Addition of pyridine remarkably increased the selectivity towards the more valuable Markovnikov-type adducts.^{2b} A complex interplay between carbene, pyridine and hydride ligands within the active species accounts for 1,2-insertion of the alkyne into a Rh-S bond as rate-limiting and selectivity determining step. In the quest for an improvement of Markovnikov-selectivity, we hypothesized that introduction of an internal base in the catalyst precursor should prevent the formation of hydride species, thereby suppressing the hydrometallation pathways.^{9h} However, the resulting thiolate-Rh^I intermediates are inactive and undergo a subsequent thiol addition to generate hydride-bisthiolate-Rh^{III} species that show similar selectivity than its chloride counterparts. As an alternative approach, we envisaged the shift of the dinuclear–mononuclear equilibrium by the anchorage of the pyridine moiety through a bidentate quinolinolate ligand.⁹ⁱ Interestingly, the reaction proceeds through a hydrometallation mechanism with the reductive elimination as the rate-limiting step. In addition, the selectivity was increased up to 97% after addition of pyridine. It has been determined that stabilization gained by pyridine coordination into linear rhodium-alkenyl intermediates increase the reductive elimination energy barrier, which is not operative for the branched alkenyl isomer, thus resulting in high Markovnikov selectivity.

Despite the success attained in the design of Rh-NHC based hydrothiolation catalysts, further improvements are still desirable. We now revisit our idea that Rh^I-thiolate species could be potential Markovnikov-selective alkyne hydrothiolation catalysts.^{9h} In view of the experience gained in catalyst design, the new catalysts must fulfill several requirements: *i*) a bulky and powerful electron-donor NHC ligand provides stability to active species as well as control over the coordination position of the labile ligands and substrates, and hence over selectivity outcome;¹⁰ *ii*) the catalyst precursor must contain an internal base to deprotonate the thiol and generate a thiolate ligand without change in the oxidation state of the metal; *iii*) the presence of a chelate ligand should control the potential equilibrium between mononuclear–dinuclear species. Indeed, we have observed that a pyridine moiety provides stability and flexibility to the catalytic system; and *iv*) the introduction of a π -acceptor ligand would disfavor the oxidative addition to Rh^I-thiolate intermediates. With these prerequisites established, we envisage the potential of the pyridine-2-methanolato ligand due to the presence of the basic alkoxo group and the pyridine moiety that enable a chelate coordination.¹¹ In addition, a carbonyl ligand may play the role of a π -acceptor ligand.

Herein, we report on the synthesis of Rh-NHC-CO complexes bearing a chelate pyridine-2-methanolato ligand as efficient catalysts for Markovnikov-selective alkyne hydrothiolation. Stoichiometric studies supported by DFT calculations suggest a non-oxidative mechanism pathway thus confirming our previous expectations.

Scheme 2. The Quest for Improved Markovnikov-Selective Rh-NHC Based Catalysts.

RESULTS AND DISCUSSION

Synthesis of Catalysts. We have previously observed that the dinuclear derivative $[\text{Rh}(\mu\text{-OH})(\text{IPr})(\eta^2\text{-coe})_2]$ (**1**) {IPr = 1,3-bis-(2,6-diisopropylphenyl)imidazolin-2-carbene; coe = cyclooctene} is a suitable precursor for the preparation of alkoxo complexes by deprotonation of the corresponding alcohol by the basic hydroxo ligand. Thus, reaction of **1** with 2-hydroxymethylpyridine at 40 °C for 2 h resulted in the formation of $\text{Rh}\{\kappa^2\text{-O,N-[2-(OCH}_2\text{)py]}\}(\text{IPr})(\eta^2\text{-coe})$ (**2**), which was isolated as yellow solid in 70% yield. Alternatively, the olefin-alkoxo derivative **2** can be prepared in 74% yield from the chloride-bridge dinuclear complex $[\text{Rh}(\mu\text{-Cl})(\text{IPr})(\eta^2\text{-coe})_2]$ (**3**), precursor of **1**, by treatment with the potassium salt of pyridine-2-methanolato. In contrast to the similar 8-quinolinolate-coe complex $\text{Rh}\{\kappa^2\text{-O,N-(C}_9\text{H}_6\text{NO)}\}(\eta^2\text{-coe})(\text{IPr})$,⁹ⁱ only one structural isomer having the pyridine moiety *trans* to IPr was observed for the pyridine-2-methanolato compound, as inferred from selective 1D-NOESY ¹H NMR experiments and DFT calculations (see SI). Complex **2** is highly air-sensitive. In fact, the dioxygen adduct $\text{Rh}\{\kappa^2\text{-O,N-[2-(OCH}_2\text{)py]}\}(\text{IPr})(\text{O}_2)$ (**4**) was obtained as a violet solid in 85% after bubbling air through a solution of **2**. Interestingly, the carbonyl complex $\text{Rh}\{\kappa^2\text{-O,N-[2-(OCH}_2\text{)py]}\}(\text{IPr})(\text{CO})$ (**5**) was prepared by treatment of **1** with two equiv of 2-hydroxymethylpyridine for 4 h at 80 °C and isolated in 76% yield. Likely, the carbonyl ligand of **5** arise from decarbonylation of the alkoxypyridine via a rhodium-hydride-piconylaldehyde intermediate that release pyridine and molecular hydrogen (see SI for the proposed mechanism).¹² In fact, pyridine was detected by GC-MS in the mother liquor, which supports the proposed mechanism. As it could be expected, bubbling of carbon monoxide through a solution of **2** or **4** also affords **5**.

Scheme 3. Formation of Alkoxypyridine-Rhodium Complexes.

Complex **2** presents a fluxional behavior in the ^1H NMR spectrum at room temperature due to rotation of IPr, which is resolved at -40°C . The spectrum displays the typical set of resonances for a substituted pyridine ring. The H_6 proton adjacent to the nitrogen atom appears at δ 8.36 ppm as a small doublet (5.5 Hz), whereas the resonances corresponding to the remaining pyridinic protons appeared between 6.60 and 6.07 ppm. The methylene group shows a singlet at 5.67 ppm. Coordination of coe is confirmed by the presence of a resonance at 2.68 ppm. The more representative signals in the $^{13}\text{C}\{^1\text{H}\}$ -APT NMR spectrum of **2** are two doublets at δ 185.9 ($J_{\text{C-Rh}} = 61.2$ Hz) and 51.2 ppm ($J_{\text{C-Rh}} = 12.9$ Hz), corresponding to the carbene and the coordinated olefin, respectively. Complex **4** also displays rotation of IPr ligand but faster than **2**, as previously presented for similar complexes $\text{RhCl}(\text{IPr})(\text{py})\text{L}$.^{13h} Carbene carbon atom resonates in the $^{13}\text{C}\{^1\text{H}\}$ -APT NMR spectrum at δ 179.7 as doublet with $J_{\text{C-Rh}} = 58.4$ Hz.

Regarding **5**, the ^1H NMR spectrum displays the typical signals for IPr and pyridine-2-methanolato ligands. The presence of a CO ligand in **5** is corroborated by a doublet at δ 193.0 ppm ($J_{\text{C-Rh}} = 70.3$ Hz) in the $^{13}\text{C}\{^1\text{H}\}$ -APT NMR spectrum, whereas the carbene carbon atom of IPr appears at 186.1 ppm as a doublet with a $J_{\text{C-Rh}}$ of 57.3 Hz. The ^1H - ^{15}N HMBC spectrum is indicative of coordination of nitrogen atom since a cross peak appears at 257.3 ppm, significantly more shielded than the signal corresponding to free 2-hydroxymethylpyridine at 301.2 ppm. In addition, the IR spectrum shows a strong carbonyl stretching absorption band at 1909 cm^{-1} . This low frequency value is indicative of the high electron richness of the Rh^{I} center that bears IPr, pyridine and alkoxo as strong electron-releasing ligands.

The structures of **4** and **5**, in the solid state, have been determined by two single crystal X-ray diffraction analyses (Figure 1). Single crystals were grown by slow diffusion of *n*-hexane into toluene (**4**) or C_6D_6 (**5**) solutions of the complexes. Both compounds exhibit a crystallographically imposed planar symmetry making independent just half of the molecule; the symmetry plane contains the rhodium, the whole pyridine-2-methanolato ligand and, in **5**, the carbonyl group. In **4**, a minor static disorder in the metal coordination sphere was identified, implying a positional exchange of the methoxo and dioxygen moieties (see experimental part).

Figure 1. X-ray structures of **4** and **5**. Selected bond lengths (Å) and angles ($^\circ$). For complex **4**, only the most abundant disordered complex {0.874(3) occupancy} is represented and geometrical data refer only to this specimen. **4**: Rh-C(1) 1.977(5), Rh-N(2) 2.078(4), Rh-O(1) 1.922(4), Rh-O(2) 1.973(3), O(2)-O(2') 1.375(7); C(1)-Rh-N(2) 174.1(2), C(1)-Rh-O(1) 91.53(19), C(1)-Rh-O(2) 92.17(16), N(2)-Rh-O(1) 82.57(18), N(2)-Rh-O(2) 93.36(14), O(1)-Rh-O(2) 159.25(10). **5**: Rh-C(8) 1.996(5), Rh-N(1) 2.089(4), Rh-O(1) 2.017(4), Rh-C(7) 1.826(6); C(8)-Rh-N(1) 170.84(18), C(8)-Rh-O(1) 89.95(18), C(8)-Rh-C(7) = 92.0(2), N(1)-Rh-O(1) = 80.89(16), N(1)-Rh-C(7) = 97.1(2), O(1)-Rh-C(7) = 178.03(19).

Both complexes present a slightly distorted square-planar environment around the rhodium atom. The distortions fundamentally arise from the chelate coordination of the *N,O*-bidentate ligand {82.57(18) $^\circ$ in **4** vs. 80.89(16) $^\circ$ in **5**}. A *trans* relative situation of the pyridinic nitrogen atom to the IPr ligand has been also observed {174.1(2) $^\circ$ (**4**) vs. 170.84(18) $^\circ$ (**5**)}. The rhodium-carbene separations {1.977(5) (**4**) and 1.996(5) Å (**5**)} lay in the typical range for a Rh-IPr single bond.¹³ The O-O separation of the coordinated molecular oxygen fits well with the description of a $\{\text{O}_2\}$ ligand {O(2)-O(2') 1.383.5 Å}.^{13h} The higher *trans* influence of carbonyl group compared to that of the $\eta^2\text{-O}_2$ dioxygen ligand is reflected in the longer Rh-O bond distance observed in **5**, 2.017(4) Å, if compared to that significantly shorter determined in **4**, 1.922(4) Å. Similarly to previous described Rh^{I} -NHC complexes, the wingtips of the carbene adopt an out-of-plane disposition from the square-planar metal environment.

Catalytic Activity in Alkyne Hydrothiolation. The catalytic activity of pyridine-2-methanolato complexes for alkyne hydrothiolation was evaluated. The addition of thiophenol to phenylacetylene in 1:1 ratio was chosen as benchmark reaction. Catalytic reactions were monitored in NMR tubes containing 0.5 mL of C_6D_6 and 2 mol% of catalyst loading. Catalytic results are compiled in Table 1. The catalytic activity of complex **2** in alkyne hydrothiolation is similar to related Rh-quinolinolate-coe catalysts.⁹ⁱ Formation of α -vinyl sulfide is favoured but the selectivity is not very high (entry 1). The $\eta^2\text{-O}_2$ derivative **4** is also active, reaching 92 % conversion after 26 h at r.t. with 73% selectivity to Markonikov-type product (entry 2). The catalytic activity in alkyne hydrothiolation of a rhodium- $\eta^2\text{-O}_2$ complex has been previously reported.^{9j} Gratifyingly, complex **5** is much more efficient. Selectivity towards α -vinyl sulfide reaches 97 % at room temperature, with a 80 % conversion after 15 h (entry 3). In this case, addition of pyridine is not essential for the control of the selectivity, although an increase of the Markovnikov product up to 99 % was observed, albeit with a reduction of the activity (entry 4). In order to disclose the effect of the carbonyl ligand over catalytic activity,^{9g,m} the performances of the known complexes $\text{RhCl}(\text{IPr})(\text{CO})(\text{py})$ ^{13h} (**6**) and $\text{RhCl}(\text{IPr})(\text{CO})_2$ ^{13d} (**7**) was studied. Catalyst **6**, containing CO and pyridine ligands, shows activity but is less active and selective than **5** (entry 5). In

contrast, complex **7** is not effective as alkyne hydrothiolation catalyst since only poly(phenylacetylene) was recovered (entry 6).

Table 1. Phenylacetylene Hydrothiolation with Thiophenol.^a

Entry	Catalyst	Additive ^b	time(h)	Conversion % ^c	α/β -E
1	2	--	24	83	69/31
2	4	--	26	92	73/27
3	5	--	15	80	97/3
4	5	pyridine	12	25	99/1
5	6	--	13	30	75/25
6	7	--	21	-- ^d	--

^a0.5 mL of C₆D₆ with 2 mol % of catalyst, [alkyne] = [thiol] = 1.0 M at 25 °C. ^b10 equivalents. ^cRelative to phenylacetylene. Calculated by NMR integration. ^dPoly(phenylacetylene) was formed.

The scope of catalyst **5** was studied for a set of thiols and alkynes. Table 2 shows the results of catalytic alkyne hydrothiolation of phenylacetylene with different thiols. The reactions were performed at 50 °C with 2 mol% catalyst loading. As a general trend, high selectivity to α -vinyl sulfides was attained, over 87 % for all cases. Interestingly, the reaction with 1-butanethiol proceeded faster, although with slightly lower selectivity than thiophenol (entry 2). Other aliphatic thiols such as benzylthiol or a doubly protected cysteine, N-tert-butoxycarbonyl (Boc) and methylester, reacted more slowly but with excellent regioselectivity up to 96 % in the second example (entries 3 and 4). The terminal bis-mercaptane 1,6-hexanedithiol reacts with two molecules of alkyne to form a bis-vinyl sulfide (entry 5), whereas 2-thiopyridine is not efficient as hydrothiolation partner (entry 6).

Table 2. Phenylacetylene hydrothiolation with Several Thiols Catalyzed by **5.^a**

Entry	Thiol	time(h)	Conversion % ^b	α/β -E
1		8	95	96/4
2		5	97	87/13
3		22	64	87/13
4		22	89	96/4
5 ^c		24	94	90/10 ^d
6		24	--	--

^a0.5 mL of C₆D₆ with 2 mol % of catalyst, [alkyne] = [thiol] = 1.0 M at 50 °C. ^bRelative to phenylacetylene. Calculated by NMR integration. ^c1:2 thiol: alkyne ratio. ^dRatio between α/α and β -E/ α .

Table 3 shows the results of the hydrothiolation of a range of alkynes with thiophenol. In all cases selectivity to α -vinyl sulfides is higher than that previously obtained for related Rh-NHC catalysts.^{9f,h} Aliphatic alkynes such as 1-hexyne and propargyl methyl ether required 21–24 h for achieving a conversion of 99 % with excellent selectivity (entries 1 and 2). The enyne 1-ethynylcyclohex-1-ene reacted preferentially by the triple bond reaching a 97 % selectivity (entry 3). In contrast, 2-ethynylpyridine displayed a totally different behaviour, since 70/30 ratio of β -Z/ β -E vinyl sulfides was observed (entry 4). Coordination of

the pyridine fragment of the substrate must play an important role in this case. Finally, the internal alkyne 3-hexyne gave the β -E-vinyl sulfide as a result of a *syn* addition of the thiol over the alkyne.

Table 3. Thiophenol Addition to Several Alkynes Catalyzed by **5.^a**

Entry	Alkyne	time(h)	Conversion %	α/β -E
1		24	99	97/3
2		21	99	97/3
3		21	88	97/3
4		22	99	0/70/30 ^c
5		48	75	0/100

^a0.5 mL of C₆D₆ with 2 mol % of catalyst, [alkyne] = [thiol] = 1.0 M at 50 °C. ^bRelative to the corresponding alkyne. Calculated by NMR integration. ^c β -Z vinyl sulfide.

Mechanistic Studies. With the aim of shedding light into the operative mechanism for alkyne hydrothiolation and the role played by the pyridine-2-methanolato and carbonyl ligands, several stoichiometric reactions were carried out. Complex **5** did not react with phenylacetylene after one night at 50° C. However, addition of one equivalent of benzylthiol to a toluene-*d*₈ solution of **5** in an NMR tube at -30 °C cleanly afforded the Rh^I-thiolate complex Rh(SCH₂Ph){ η^1 -N-[2-(HOCH₂)py]}(IPr)(CO) (**8**) (Scheme 4). Formation of **8** results from the protonation of the alkoxo ligand of **5** by the thiol and coordination of the resulting thiolate. However, alternative mechanisms such as oxidative addition of thiol to the Rh^I center to form a rhodium-hydride-thiolate intermediate and subsequent hydride-alkoxo reductive elimination or a σ -bond metathesis process should not be discarded. In this regard, it is worth to note that no hydride resonances could be detected. Attempts for isolation of **8** in the solid stated failed.

Scheme 4. Formation of Rhodium-thiolate Complex **8.**

The NMR spectra of **8** are in accordance with the proposed structure. A set of three signals at δ 6.17, 5.44, and 4.18 ppm in the ¹H NMR spectrum at -30 °C related by ¹H-¹H COSY cross peaks are ascribed to the protons of the hydroxymethyl group (Figure 2). The absence of a correlation peak for the signal at 6.17 ppm in the ¹³C-¹H HSQC experiment, in addition to an interaction between the resonances at 5.44 and 4.18 ppm with the same carbon atom at 60.0 ppm, confirms that the more deshielded doublet correspond to the -OH proton. Moreover, this signal shifts to 6.38 ppm at -60 °C. Coordination of sulphur atom to rhodium results in diastereotopic methylene protons appearing at 2.77 and 2.51 ppm, displaying a scalar coupling of 12.5 Hz. The more relevant signals of the ¹³C{¹H}-APT spectrum are two doublets at δ 188.6 (*J*_{C-Rh} = 72.1 Hz) and 184.1 ppm (*J*_{C-Rh} = 53.6

Hz) corresponding to CO and IPr ligands, respectively. The nitrogen atom of the η^1 -N 2-hydroxypyridine ligand resonates at δ 254.0 ppm.

Figure 2. ^1H NMR spectra of **8** at $-30\text{ }^\circ\text{C}$ (up) and $-60\text{ }^\circ\text{C}$ (down).

Thereafter, the reactivity of **8** towards alkynes was studied. Thus, treatment of a freshly prepared sample of **8** with phenylacetylene at $-30\text{ }^\circ\text{C}$ showed no reaction. However, heating the sample at room temperature gave rise to the formation of the α -vinyl sulfide product resulting from hydrothiolation and a mixture of unidentified rhodium species. In addition, no reaction was observed after treatment of **8** with a second equivalent of benzylthiol at low temperature although the sample slowly decomposed at room temperature.

A competitive hydrothiolation experiment between phenylacetylene and phenylacetylene- d_1 was performed in order to evaluate the kinetic isotope effect $k_{\text{H}}/k_{\text{D}}$ (Scheme 5).¹⁴ A *syn* addition of the thiol across the triple bond is confirmed since only *E*-deuterostyrene was obtained. A secondary KIE value of 1.28 ± 0.03 is calculated, which indicates that a C-D bond is not breaking in the rate-determining step and agrees with a turn-over limiting alkyne migratory insertion mechanism.¹⁵

Scheme 5. KIE measurement for hydrothiolation reaction.

Scheme 6. Mechanistic Proposal for Alkyne Hydrothiolation Mediated by **5**.

In view of these results a mechanistic proposal is presented in Scheme 6. In the first step, the activation of a thiol molecule by **5** gives rise to the formation of a thiolate- η^1 -N-hydroxypyridine intermediate **I** similar to **8**. From this point, two plausible pathways are conceivable: *i*) activation of the alkyne in a Rh^{I} intermediate or *ii*) oxidative addition of the thiol. In the first case, the

non-oxidative cycle starts by exchange of alkyne and pyridine ligands to form **II**. In this intermediate 1,2-thiolate insertion is more likely to afford the thioalkenyl unsaturated species **III** in which a molecule of thiol can coordinate to form **IV**. Subsequent sequential thiol oxidative addition-reductive elimination or protonolysis and addition of the pyridine ligand regenerates **I**.

The second cycle (Scheme 6, left) starts by the oxidative addition of a thiol molecule to form the bithiolate-hydride-Rh^{III} intermediate **V**. Oxidative addition of the alkyne on **I** is possible but unlikely since thiol is more acidic. Next step is alkyne coordination to the vacant site of **V** located *trans* to the higher *trans*-influence hydride ligand to yield **VI**, and therefore 1,2-thiolate insertion results in the formation of **VII**. Subsequent hydride-thioalkenyl reductive elimination give rise to the branched vinyl sulfide, thus regenerating the catalytically active species by oxidative addition of thiol on the resulting unsaturated species. The above described stoichiometric results points to the non-oxidative mechanism to be operative. It seems reasonable that the oxidative addition of thiol in **I** is hampered by the presence of a π -acceptor carbonyl ligand, which contrasts with the reactivity previously observed for the intermediate Rh(SR)(IPr)(η^2 -coe)(py) lacking of such a strong electron-acceptor ligand.^{9h}

Theoretical Calculations on the Mechanism. A detailed DFT computational analysis on the mechanism of alkyne hydrothiolation promoted by **5** has been carried out. The B3LYP method including dispersion correction has been used throughout the study. Full IPr, pyridine-2-methanolato, thiophenol and phenylacetylene have been explicitly considered. All the energies are relative to the starting point **A** (compound **5**) and the corresponding reactants. The first process studied is the deprotonation of the thiol by the alkoxo ligand (Figure 3). Approximation of a thiol molecule to **A** by formation of a hydrogen bond stabilizes the complex 8.3 kcal mol⁻¹ (**A'**). From this point, protonation of the alkoxo group by the external thiol takes place via **B-TS** to generate **C** which is 13.7 kcal mol⁻¹ more stable than **A**. An alternative pathway via oxidative addition of thiol to **A** is unfeasible as the resulting hydride-thiolate-Rh^{III} **C'** is located at 0.3 kcal mol⁻¹.

Figure 3. Computed energies (ΔG in kcal mol⁻¹) for the protonation of the alkoxo ligand by the external thiol.

Compound **C** may evolve by the two pathways described in Scheme 6. Both routes were computed and presented in Figures 4-7. The first step in the non-oxidative pathway is the pyridine-alkyne exchange to yield the Rh^I- π -alkyne intermediate **D** which is 8.2 kcal mol⁻¹ less stable than **C**, which reflects the affinity of the catalytic system for pyridine ligands. Due to the two possible orientations for the coordinated alkyne to the metallic center, the route bifurcates to yield α -vinyl sulfides (**E-G**, red line) via 1,2-thiolate insertion or β -*E*-vinyl sulfides via 2,1-thiolate insertion (**E'-G'**, blue line). The Markovnikov-type addition pathway is less energetically demanding, showing a barrier of 30.2 kcal mol⁻¹ via **E-TS**, in contrast to 31.6 kcal mol⁻¹ computed for the lineal vinyl sulfide via **E'-TS**. These transition states evolve to thio-metallacyclobutane intermediates **F** and **F'** in which, after an isomerization process, the sulfur atom is located *trans* to IPr. Subsequent decooordination of the sulfur atom allows the free access to a new molecule of thiol to generate **G** and **G'**.

Figure 4. DFT calculated (ΔG in kcal mol⁻¹) along the energy surface for the formation of vinyl sulfides through a non-oxidative process. Structures **E** to **G** correspond to α -vinyl sulfide formation ($R^1 = \text{Ph}$, $R^2 = \text{H}$, red line) and structures **E'** to **G'** lead to β -*E*-vinyl sulfides ($R^1 = \text{H}$, $R^2 = \text{Ph}$, blue line).

The next step of the non-oxidative pathway is the release of vinyl sulfide from **G** and **G'**. Two possibilities have been computed (Figure 5). In the first one, oxidative addition of a molecule of thiol on **G** and **G'** generates hydride-thiolate-Rh^{III} intermediates **I** and **I'** via **H-TS** and **H'-TS**. Subsequent reductive elimination through **J-TS** and **J'-TS** yields **K** and **K'**, respectively. The second pathway consists in the direct formation of **K** and **K'** by protonolysis within **G** and **G'** via **L-TS** and **L'-TS**. Both pathways show very similar energetic barriers. In fact, oxidative addition-reductive elimination is the preferred pathway for the formation of α -vinyl sulfide (3.3 vs 5.4 kcal mol⁻¹), whereas protonolysis is more favourable for the formation of β -*E*-vinyl sulfide (8.2 vs 8.7 kcal mol⁻¹). Nevertheless, in both cases lower energetic barriers related to those found in the migratory insertion step have been computed.

Figure 5. DFT calculated (ΔG in kcal mol⁻¹) along the energy surface for the formation of vinyl sulfides through oxidative addition – reductive elimination (**H-TS** to **K**) or protonolysis (**L-TS**). Structures **G** to **K** correspond to α -vinyl sulfide formation ($R^1 = \text{Ph}$, $R^2 = \text{H}$, red line) and structures **G'** to **K'** lead to β -*E*-vinyl sulfides ($R^1 = \text{H}$, $R^2 = \text{Ph}$, blue line).

In the other hand, the first step in the process that implies oxidation of the metallic center is the oxidative addition of the thiol (Figure 6). The thiol replaces 2-hydroxymethylpyridine to form **M** which is destabilized 10.4 kcal mol⁻¹ with regard to **C**. From this intermediate activation of S-H bond takes place via **N-TS** located at 10.1 kcal mol⁻¹ relative to **A**, to form the hydride-bis-

thiolate compound **O'**, which isomerizes to the more stable complex **O** with both thiolated ligand disposed mutually *trans* and the carbonyl moiety located *trans* to IPr.

Figure 6. DFT calculations (ΔG in kcal mol⁻¹) for the oxidative addition of thiol to intermediate **C**.

After formation of **O** the catalytic cycle may follow the hydrometallation or thiometallation pathways (Figure 7). Coordination of the alkyne in the vacant site of **O** generates **P**, which is destabilized by 1.0 kcal mol⁻¹. Then insertion of the alkyne into Rh-S bond takes place via **Q-TS** and **Q'-TS**. Taking into account that we are under Curtin-Hammett conditions (see Figure 6), the energetic barrier from **C** to the transition states is 31.6 and 35.2 kcal mol⁻¹, respectively, both higher than that computed for the rate-limiting step in the non-oxidative cycle, making impractical further analysis of that pathway. In contrast to thiometallation, an isomerization after coordination of alkyne is necessary in order to hydrometallation process to be operative as hydride and π -alkyne ligands have to be disposed mutually *cis*. Intermediates **R** and **R'** are 17.7 and 17.5 kcal mol⁻¹ higher in energy than **O**, respectively. After this point, insertion of alkyne into Rh-H bond goes through transition states **S-TS** and **S'-TS** with energetic barrier from **C** of 33.9 and 37.0 kcal mol⁻¹, respectively.

Figure 7. DFT calculated (ΔG in kcal mol⁻¹) along the energy surface for the formation of vinyl sulfides through hydrometallation and thiometallation processes. Structures **P** to **S** correspond to α -vinyl sulfide formation ($R^1 = \text{Ph}$, $R^2 = \text{H}$, red line) and structures **P'** to **S'** lead to β -E-vinyl sulfides ($R^1 = \text{H}$, $R^2 = \text{Ph}$, blue line).

In all pathways studied the migratory insertion is the rate-limiting step. The lower barrier is found for the non-oxidative process (30.2 kcal mol⁻¹), whereas the routes that involve Rh^{III} intermediates show 31.6 and 33.9 kcal mol⁻¹ for the thiometallation and hydrometallation pathways, respectively. These results are

in agreement with the calculated KIE and the low activity observed at room temperature. However, catalyst **5** displays higher selectivity than the previously reported Rh-NHC catalysts, without the need of addition of pyridine. It is worth mentioning that the operative mechanism for catalyst precursor **5**, which proceeds through Rh^I catalytic intermediates, is markedly different to that observed for related Rh-NHC catalytic systems that involve Rh^{III} active species. The key point is the presence of an internal base such as the alkoxo ligand. This requisite was already present in Rh(μ -OH)(IPr)(η^2 -olefin)/py catalytic systems. However, the carbonyl ligand in **5** plays an important role. Theoretical studies over Rh-NHC square planar systems have revealed that pyridine has a tendency to coordinate *trans* to IPr, whereas π -acceptor ligands are prone to bind *cis* to IPr.^{13h} This coordination affinity results in a mutually *trans* disposition of thiolate and alkyne in the key intermediate species for the pyridine-based catalysts, whereas these ligands are mutually *cis* in the CO-based systems, facilitating the rate-limiting alkyne thiometallation step.

CONCLUSIONS

In summary, the new Rh^I-NHC-CO complex bearing a pyridine-2-methanolato ligand is an efficient catalyst for alkyne hydrothiolation with high selectivity towards the Markovnikov product. The rational catalyst design has resulted in an improvement of the selectivity with regard to previously reported Rh-NHC systems without the need of addition of pyridine. Reactivity studies and DFT calculations have revealed a new non-oxidative catalytic pathway passing through Rh^I catalytic intermediates. The basic alkoxo ligand assists the deprotonation of the incoming thiol to generate the Rh^I active species. On the other hand, the carbonyl ligand plays an essential role as its π -acceptor capacity hampers the oxidative addition processes. Indeed, its affinity to coordinate *cis* to the IPr ligand opens the way for a *cis* thiolate- π -alkyne intermediate, which favors the rate-limiting migratory insertion step. These results prompt us to apply the underlying principles to the design of improved catalysts for C-C and C-Heteroatom forming catalytic reactions.

EXPERIMENTAL SECTION

General Considerations. All reactions were carried out with rigorous exclusion of air using Schlenk-tube techniques. The reagents were purchased from commercial sources and used as received, except for phenylacetylene that was distilled and stored over molecular sieves. Organic solvents were dried by standard procedures and distilled under argon prior to use or obtained oxygen- and water-free from a Solvent Purification System (Innovative Technologies). The organometallic precursors **1**^{9h} and **3**^{13a} were prepared as previously described. Chemical shifts (expressed in parts per million) are referenced to residual solvent peaks (¹H, ¹³C{¹H}) or liquid NH₃ (¹⁵N). Coupling constants, *J*, are given in hertz. Spectral assignments were achieved by combination of ¹H-¹H COSY, ¹³C{¹H}-APT and ¹H-¹³C HSQC/HMBC experiments. H, C and N analysis were carried out in a Perkin-Elmer 2400 CHNS/O analyzer. GC-MS analysis were recorder on an Agilent 5973 mass selective detector interfaced to an Agilent 6890 series gas chromatograph system, using a HP-5MS 5% phenyl methyl siloxane column (30 m x 250 mm with a 0.25 mm film thickness). The organic products were identified by comparison with the previously reported data: phenyl (1-phenylvinyl) sulfide,^{3g} butyl (1-phenylvinyl) sulfide,¹⁶ benzyl (1-phenylvinyl) sulfide,^{9c} phenyl S-(1-phenylvinyl)-N-Boc-L-

cysteine-methylester,^{9f} 1,6-Bis((1-phenylvinyl)thio)hexane,^{9f} phenyl (hex-1-en-2-yl) sulfide,¹⁷ phenyl (3-methoxyprop-1-en-2-yl) sulfide,^{8b} phenyl 1-(cyclohex-1-en-1-yl)vinyl sulfide,^{9c} 2-(2-(phenylthio)vinyl)pyridine,^{8b} (*E*)-3-(phenylthio)hex-3-ene.^{5b}

Preparation of Rh{ κ^2 -O,N-[2-(OCH₂)py]}(IPr)(η^2 -coe) (2).

Method a: A yellow solution of **1** (100 mg, 0.08 mmol) in 10 mL of toluene was treated with 2-hydroxymethylpyridine (15 μ L, 0.16 mmol) and stirred at 313 K for 2 h. Then, the solution was concentrated to ca. 1 mL and *n*-hexane added to induce the precipitation of a yellow solid, which was washed with *n*-hexane (3 x 3 mL) and dried in vacuo. Yield: 78.3 mg (70 %). **Method b:** A solution of 2-hydroxymethylpyridine (35 μ L, 0.36 mmol) in 5 mL of THF was treated with potassium tert-butoxide (42 mg, 0.37 mmol) and stirred at r.t. for 30 min. Then, this solution was poured over a solution of **3** (215 mg, 0.17 mmol) in 5 mL of THF and stirred at r.t. for 1.5 h. Afterwards, the solution was concentrated to ca. 1 mL and *n*-hexane was added to induce the precipitation of a yellow solid, which was washed with *n*-hexane (3 x 1 mL) and dried in vacuo. Yield: 178 mg (74 %). Satisfactory elemental analysis could not be obtained. ¹H NMR (500 MHz, toluene-*d*₈, 233 K): δ 8.36 (d, $J_{\text{H-H}} = 5.5$, 1H, H_{6-py}), 7.5-7.0 (m, 6H, H_{Ph-IPr}), 6.60 (m, 2H, H_{4-py}, H_{3-py}), 6.50 (s, 2H, =CHN), 6.07 (dd, $J_{\text{H-H}} = 6.8$, 5.5, 1H, H_{5-py}), 5.67 (s, 2H, CH₂O), 4.61 and 2.52 (both sept, $J_{\text{H-H}} = 6.8$, 4H, CHMeIPr), 2.68 (m, 2H, =CH_{coe}), 1.9-1.0 (m, 12H, CH_{2coe}), 1.62, 1.46, 1.14, and 1.04 (all d, $J_{\text{H-H}} = 6.8$, 24H, CHMeIPr). ¹³C{¹H}-APT NMR (75.1 MHz, toluene-*d*₈, 233 K): δ 185.9 (d, $J_{\text{C-Rh}} = 61.2$, Rh-CIPr), 175.0 (s, C_{2-py}), 150.5 (s, C_{6-py}), 148.0 and 145.4 (both s, C_{q-IPr}), 137.6 (s, C_{qN}), 133.0 (s, C_{4-py}), 129.2, 124.3, and 122.5 (all s, CH_{Ph-IPr}), 123.6 (s, =CHN), 119.4 (s, C_{5-py}), 117.8 (s, C_{3-py}), 79.2 (s, CH₂O), 51.2 (d, $J_{\text{C-Rh}} = 12.9$, =CH_{coe}), 30.7, 30.6, and 26.4 (all s, CH_{2coe}), 28.7 and 28.5 (both s, CHMeIPr), 26.6, 26.4, 23.5, and 22.7 (all s, CHMeIPr).

Preparation of Rh{ κ^2 -O,N-[2-(OCH₂)py]}(IPr)(O₂) (4). Air was bubbled through a toluene solution (10 mL) of **2** (100 mg, 0.141 mmol) for 15 min at r.t. Then, the solvent was evaporated to dryness and the residue stirred with *n*-hexane to give a violet solid which was washed with *n*-hexane (4 x 2 mL) and dried in vacuo. Yield: 76 mg (85%). Anal. Calcd. for C₃₃H₄₂N₃O₃Rh: C, 62.75; H, 6.70; N, 6.65. Found: C, 62.51; H, 6.72; N, 6.48. ¹H NMR (400 MHz, C₆D₆, 298 K): δ 7.64 (dd, $J_{\text{H-H}} = 5.4$, 1H, H_{6-py}), 7.2-7.3 (m, 6H, H_{Ph}), 6.73 (s, 2H, =CHN), 6.52 (vt, $N_{\text{H-H}} = 15.4$, 1H, H_{4-py}), 6.23 (dd, $J_{\text{H-H}} = 7.7$, 5.4, 1H, H_{5-py}), 6.20 (d, $J_{\text{H-H}} = 7.5$, 1H, H_{3-py}), 4.81 (s, 2H, CH₂O), 3.28 (sept, $J_{\text{H-H}} = 6.7$, 4H, CHMeIPr), 1.58 and 1.17 (d, $J_{\text{H-H}} = 6.7$, 12H, CHMeIPr). ¹³C{¹H}-APT NMR (100.6 MHz, C₆D₆, 298K): δ 179.7 (d, $J_{\text{C-Rh}} = 58.4$, Rh-CIPr), 169.1 (d, $J_{\text{C-Rh}} = 3$, C_{2-py}), 147.2 (s, C_{6-py}), 147.1 (s, C_{q-IPr}), 136.7 (s, C_{qN}), 134.8 (s, C_{4-py}), 129.5 and 123.5 (s, CH_{m-p-IPr}), 124.0 (s, =CHN), 120.9 (s, C_{5-py}), 116.2 (s, C_{3-py}), 81.8 (s, CH₂O), 28.9 (s, CHMeIPr), 25.9 and 23.2 (s, CHMeIPr).

Preparation of Rh{ κ^2 -O,N-[2-(OCH₂)py]}(IPr)(CO) (5). A yellow solution of **1** (100 mg, 0.08 mmol) in 10 mL of toluene was treated with 2-hydroxymethylpyridine (30 μ L, 0.32 mmol) and stirred at 353 K for 4 h. Then, the solution was concentrated to ca. 1 mL and *n*-hexane added to induce the precipitation of a yellow solid, which was washed with *n*-hexane (3 x 3 mL) and dried in vacuo. Yield: 75.4 mg (76 %). Anal. Calcd. for C₃₄H₄₂N₃O₂Rh: C, 65.07; H, 6.75; N, 6.70. Found: C, 64.92; H, 6.92; N, 6.62. ¹H NMR (300 MHz, C₆D₆, 298 K): δ 8.22 (d, $J_{\text{H-H}} = 4.0$, 1H, H_{6-py}), 7.3-7.0 (m, 6H, H_{Ph-IPr}), 6.81 (s, 2H, =CHN), 6.57 (vt, $N_{\text{H-H}} = 14.6$, 1H, H_{4-py}), 6.42 (d, $J_{\text{H-H}} = 7.8$, 1H, H_{3-py}), 5.98 (t, $J_{\text{H-H}} = 5.9$, 1H, H_{5-py}), 5.37 (s, 2H, CH₂O), 3.52 (sept, $J_{\text{H-H}} = 6.7$, 4H, CHMeIPr), 1.73 and 1.27 (both d, $J_{\text{H-H}} = 6.5$, 24H, CHMeIPr). ¹³C{¹H}-APT NMR (75.1 MHz, C₆D₆, 298 K): δ

193.0 (d, $J_{\text{C-Rh}} = 70.3$, CO), 186.1 (d, $J_{\text{C-Rh}} = 57.3$, Rh-CIPr), 174.1 (s, C_{2-py}), 149.7 (s, C_{6-py}), 146.7 (s, C_{q-IPr}), 137.1 (s, C_{qN}), 133.7 (s, C_{4-py}), 129.6 and 123.7 (both s, C_{Ph-IPr}), 123.6 (s, =CHN), 120.3 (s, C_{5-py}), 117.8 (s, C_{3-py}), 78.1 (s, CH₂O), 28.9 (s, CHMeIPr), 25.9 and 23.0 (both s, CHMeIPr). ¹H-¹⁵N NMR HMBC (40.1 MHz, toluene-*d*₈, 243 K): δ 257.3 (N_{py}), 192.0 (N_{IPr}).

In situ formation Rh(SCH₂Ph){ η^1 -N[2-(HOCH₂)py]}(IPr)(CO) (8). A toluene-*d*₈ solution of **3** (20 mg, 0.032 mmol) in an NMR tube at 243 K was treated with benzylthiol (3.8 μ L, 0.032 mmol). NMR spectra were recorded immediately at 243 K. ¹H NMR (400 MHz, toluene-*d*₈, 243 K): δ 8.17 (d, $J_{\text{H-H}} = 5.2$, 1H, H_{6-OPY}), 7.5-7.1 (m, 11H, H_{Ph}), 6.68 (s, 2H, =CHN), 6.48 (br, 2H, H_{3-py} and H_{4-py}), 6.17 (d, $J_{\text{H-H}} = 10.0$, 1H, HOCH₂py), 5.96 (dd, $J_{\text{H-H}} = 8.7$, 5.2, 1H, H_{5-py}), 5.44 (d, $J_{\text{H-H}} = 10.7$, 1H, HOCH₂py), 4.18 (dd, $J_{\text{H-H}} = 10.7$, 10.0, 1H, HOCH₂py), 3.41 and 3.29 (both br, 4H, CHMeIPr), 2.77 and 2.51 (both d, $J_{\text{H-H}} = 12.5$, 2H, PhCH₂S), 1.66, 1.60, 1.13, and 1.11 (all br, 24H, CHMeIPr). ¹³C{¹H}-APT NMR (100.6 MHz, toluene-*d*₈, 243 K): δ 188.6 (d, $J_{\text{C-Rh}} = 72.1$, CO), 184.1 (d, $J_{\text{C-Rh}} = 53.6$, Rh-CIPr), 162.9 (s, C_{2-py}), 152.8 (s, C_{6-py}), 145.4 (s, C_qCH₂S), 137.2 (s, C_{qN}), 136.1 (s, C_{4-py}), 129.9, 128.9, 128.6, 127.6, and 125.5 (all s, CH_{Ph}), 124.0 (s, C_{3-py}), 121.9 (s, C_{5-py}), 121.7 (s, =CHN), 60.0 (s, HOCH₂py), 30.7 (s, PhCH₂S), 28.4 and 28.2 (both s, CHMeIPr), 26.7, 26.3, and 22.6 (all s, CHMeIPr). ¹H-¹⁵N NMR HMBC (40.1 MHz, toluene-*d*₈, 243 K): δ 254.0 (N_{py}), 192.0 (N_{IPr}).

Standard conditions for catalytic hydrothiolation of alkynes. A NMR tube containing a solution of 0.01 mmol of catalyst in 0.5 mL of C₆D₆ was treated with 0.5 mmol of thiol and 0.5 mmol of alkyne. The reaction was monitored by ¹H NMR at the required temperature and the conversion was determined by integration of the corresponding resonances of the alkyne and the products. The final reaction products was analysed by GC-MS techniques.

KIE determination. A NMR tube containing a solution of 0.01 mmol of catalyst in 0.5 mL of C₆D₆ was treated with 0.5 mmol of thiophenol, 0.25 mmol of phenylacetylene, and 0.25 mmol of phenylacetylene-*d*₁. The reaction was monitored by ¹H NMR (500 MHz) at 298K and the conversion was determined by integration of the corresponding resonances of the thiol and the products.

Crystal Structure Determinations. Single crystals for the X-ray diffraction studies were grown by slow diffusion of *n*-hexane into toluene (**4**) or C₆D₆ (**5**) solutions of the complexes. X-ray diffraction data were collected at 100(2) K on a Bruker APEX Duo CCD diffractometer with graphite-monochromated Mo-K α radiation ($\lambda = 0.71073$ Å) using narrow ω rotations (0.3°). Intensities were integrated and corrected for absorption effects with SAINT-PLUS,¹⁸ and SADABS¹⁹ programs, both included in APEX2 package. The structures were solved by Patterson methods with SHELXS-97²⁰ and refined, by full matrix least-squares on F^2 , with SHELXL-2014.²¹ In both cases, the crystallographic imposed symmetry makes only half of the complex to be asymmetric, having the metal, the carbene carbon atom and the pyridine-2-methanolato ligand on the symmetry plane. Both structures were refined first with isotropic and later with anisotropic displacement parameters for non-disordered non-H atoms. Specific relevant details on each structure are described below.

Crystal data for **4**: C₃₃H₄₂N₃O₃Rh; $M = 631.60$; brown prism 0.114 x 0.126 x 0.131 mm³; orthorhombic, $Pnma$; $a = 17.597(4)$, $b = 17.206(4)$, $c = 9.999(2)$ Å; $Z = 4$; $V = 3027.5(11)$ Å³; $D_c = 1.386$ g·cm⁻³; $\mu = 0.601$ mm⁻¹; min. and max. absorption correction factors 0.855 and 0.946; $2\theta_{\text{max}} = 50.05^\circ$; 22854 reflections

collected, 2768 unique ($R_{\text{int}} = 0.0462$); number of data/restraints/parameters 2768/17/247; final GOF 1.119; $R_1 = 0.0345$ (2159 reflections, $I > 2\sigma(I)$); $wR(F^2) = 0.0967$ for all data. After anisotropic refinement of all non-hydrogen atoms, an anomalous very intense residual was present in close proximity of the metal; at the same time some hydrogen atoms of the carbene ligand became clearly apparent at the difference Fourier maps. Detailed inspection of the electron density around the metal-coordinated atoms also showed weak residuals in the proximity of both independent oxygen atoms: methoxy group and dioxygen ligand. All these residuals have been interpreted assuming a minor disorder of these two ligands being interchanged at both sides of the metal. The second disordered coordination of the methoxy/dioxygen moieties is present in the crystal in a very small fraction {relative occupancy of 0.126 vs. 0.874(3)}, being this the reason to observe only one significant residual close to the metal atom. Hydrogens have been included only for those non-disordered atoms, in some cases (when clearly observed) as free isotropic atoms, and in other cases (for terminal methyl groups) in calculated positions. Final residuals were all well under $1 \text{ e}/\text{\AA}^3$.

Crystal data for **5**: $\text{C}_{34}\text{H}_{42}\text{N}_3\text{O}_2\text{Rh} \cdot 2 \text{C}_6\text{D}_6$; $M = 783.86$; orange prism $0.195 \times 0.185 \times 0.082 \text{ mm}^3$; orthorhombic, $Pnma$; $a = 17.857(5)$, $b = 21.917(6)$, $c = 10.326(3) \text{ \AA}$; $Z = 4$; $V = 4041.3(18) \text{ \AA}^3$; $D_c = 1.288 \text{ g cm}^{-3}$; $\mu = 0.463 \text{ mm}^{-1}$; min. and max. absorption correction factors 0.845 and 0.948; $2\theta_{\text{max}} = 54.20^\circ$; 45624 reflections collected, 4570 unique ($R_{\text{int}} = 0.0640$); number of data/restraints/parameters 4570/0/320; final GOF 1.105; $R_1 = 0.0568$ (3914 reflections, $I > 2\sigma(I)$); $wR(F^2) = 0.1162$ for all data. A benzene solvent molecule was observed in the crystal structure. Hydrogens were observed from difference Fourier maps, and refined as free isotropic atoms, except those bonded to the terminal methyl groups. Two residual peaks slightly above $1 \text{ e}/\text{\AA}^3$ were observed in the final difference map, but they have no chemical sense.

Computational details. All DFT theoretical calculations have been carried out using the Gaussian program package.²² The B3LYP method²³ has been employed, including the D3 dispersion correction scheme developed by Grimme²⁴ for both energies and gradient calculations and the “ultrafine” grid. The def2-SVP basis set²⁵ has been selected for all atoms. The nature of the stationary points has been confirmed by analytical frequency analysis. We have reported in the SI the computational results including the cartesian coordinates (in $\text{\AA}$), absolute energy (in a.u) and graphical representation.

ASSOCIATED CONTENT

X-ray crystallographic information files containing full details of the structural analysis of complexes **4** and **5** (CIF format). Cartesian coordinates for theoretical calculations (xyz format). Experimental procedures, KIE determination, and NMR spectra for complexes. This material is available free of charge via the Internet at <http://pubs.acs.org>

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Notes

The authors declare no competing financial interest

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REFERENCES

- (1) (a) Brooks, G.; Coleman, K.; Davies, J. S.; Hunter, P. A. *J. Anti-biot.* **1988**, *41*, 892. (b) Johannesson, P.; Lindeberg, G.; Johansson, A.; Nikiforovich, G. V.; Gogoll, A.; Synnergren, B.; LeGrèves, M.; Nyberg, F.; Karlén, A.; Hallberg, A. *J. Med. Chem.* **2002**, *45*, 1767. (c) Sader, H. S.; Johnson, D. M.; Jones, R. N. *Antimicrob. Agents. Chemoter.* **2004**, *48*, 53. (d) Tian, Y.; Li, J.; Zeng, X.; Wang, D.; Liu, Q.; Niu, X.; Huang, X.; Xu, N.; Li, Z. *Chem. Sci.* **2016**, *7*, 3325.
- (2) (a) Trost, B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075. (b) Schaumann, E. *Top. Curr. Chem.* **2007**, *274*, 1. (c) Liu, T.; Zhao, X.; Lu, L.; Cohen, T. *Org. Lett.* **2009**, *11*, 4576. (d) Quinet, C.; Sampoux, L.; Markó, I. E. *Eur. J. Org. Chem.* **2009**, 1806. (e) Cui, Y.; Floreancing, P. E. *Org. Lett.* **2012**, *14*, 1720. (f) Kiemele, E. R.; Watier, M.; Bichler, P.; Love, J. A. *Org. Lett.* **2016**, *18*, 492.
- (3) (a) Rusell, G. A.; Ngoviwatchai, P.; Tashtoush, H. I.; Pla-Dalmau, A.; Khanna, R. K. *J. Am. Chem. Soc.* **1988**, *110*, 3530. (b) Han, L.-B.; Tanaka, M. *J. Am. Chem. Soc.* **1998**, *120*, 8249. (c) Kuniyasu, H.; Yamashita, F.; Hirai, T.; Ye, J.-H.; Fujiwara, S.-i.; Kambe, N. *Organometallics* **2006**, *25*, 566. (d) Silveira, C. C.; Santos, P. C. S.; Mendes, S. R.; Braga, A. R. *J. Organomet. Chem.* **2008**, *693*, 3787. (e) Hooper, J. F.; Chaplin, A. B.; González-Rodríguez, C.; Thompson, A. L.; Weller, A. S.; Willis, M. C. *J. Am. Chem. Soc.* **2012**, *134*, 2906. (f) Feng, J.; Lu, G.; Lv, M.; Cai, C. *Asian. J. Org. Chem.* **2014**, *3*, 77.
- (4) (a) Bichler, P.; Love, J. A. in *Topics of Organometallic Chemistry*, Vol. 31 (Ed.: A. Vigalok), Springer, Heidelberg, **2010**, pp. 36. (b) Beletskaya, I. P.; Ananikov, V. P. *Chem. Rev.* **2011**, *111*, 1596. (c) Castarlenas, R.; Di Giuseppe, A.; Pérez-Torrente, J. J.; Oro, L. A. *Angew. Chem. Int. Ed.* **2013**, *52*, 211. (d) Ogawa, A. in *Topics of Organometallic Chemistry*, Vol. 43 (Eds.: V. P. Ananikov, M. Tanaka), Springer, Heidelberg, **2013**, pp. 325. (e) Dondoni, A.; Marra, A. *Eur. J. Org. Chem.* **2014**, 3955. (f) Orlov, N. V. *ChemistryOpen* **2015**, *4*, 682. (g) Di Giuseppe, A.; Castarlenas, R.; Oro, L. A. in *Topics of Organometallic Chemistry*, Springer, Heidelberg, ASAP, DOI: 10.1007/3418_2016_171.
- (5) (a) Griesbaum, K. *Angew. Chem. Int. Ed.* **1970**, *9*, 273. (b) Benati, L.; Montevecchi, P. C.; Spagnolo P. *J. Chem. Soc., Perkin Trans.* **1991**, 2103. (c) Lo Conte, M.; Pacifico, S.; Chambery, A.; Marra, A.; Dondoni, A. *J. Org. Chem.* **2010**, *75*, 4644. (d) Chun, S.; Chung, J.; Park, J. E.; Chung, Y. K. *ChemCatChem* **2016**, *8*, 2476. (e) Wang, H.; Lu, Q.; Chiang, C.-W.; Luo, Y.; Zhou, J.; Wang, G.; Lei, A. *Angew. Chem. Int. Ed.* **2017**, *56*, 595.
- (6) (a) Ipatieff, V. N.; Pines, H.; Friedman, B. S. *J. Am. Chem. Soc.* **1938**, *60*, 2731. (b) Screttas, C. G.; Michal-Screttas, M. *J. Org. Chem.* **1979**, *44*, 713. (c) Weiwer, M.; Coulombel, L.; Duñach, E. *Chem. Commun.* **2006**, 332. (d) Kuciński, K.; Pawluć, P.; Marciniak, B.; Hreczycho, G. *Chem. Eur. J.* **2015**, *21*, 4940.
- (7) (a) Truce, W. E.; Simms, J. A.; Boudakian, M. M. *J. Am. Chem. Soc.* **1956**, *78*, 695. (b) Kondoh, A.; Takami, K.; Yorimitsu, H.; Oshima, K. *J. Org. Chem.* **2005**, *70*, 6468. (c) Truong, V. X.; Dove, A. P. *Angew. Chem. Int. Ed.* **2013**, *52*, 4132. (d) Kumar, R.; Saima; Sharda, A.; Andhare, N. H.; Richa; Sinha, A. K. *Angew. Chem. Int. Ed.* **2015**, *54*, 828.
- (8) (a) Kuniyasu, H.; Ogawa, A.; Sato, K.-I.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 5902. (b) Ananikov, V. P.; Malyshev, D. A.; Beletskaya, I. P.; Aleksandrov, G. G.; Eremenko, I. L. *Adv. Synth. Catal.* **2005**, *347*, 1993. (c) Kondoh, A.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2007**, *9*, 1383. (d) Munro-Leighton, C.; Delp, S. A.; Alsop, N. M.; Blue, E. D.; Gunnoe, T. B. *Chem. Commun.* **2008**, 111. (e) Weiss, C. J.; Wobser, S. D.; Marks, T. J. *J. Am. Chem. Soc.* **2009**, *131*, 2062. (f) Ananikov, V. P.; Gayduck, K. A.; Orlov, N. V.; Beletskaya, I. P.; Khrustalev, V. N.; Antipin, M. Y. *Chem. Eur.* **2010**, *16*, 2063. (g) Weiss, C. J.; Marks, T. J. *J. Am. Chem. Soc.* **2010**, *132*, 10533. (h) Gerber, R.; Frech C. M. *Chem. Eur. J.* **2012**, *18*, 8901. (i) Cabrero-Antonino, J. R.; Leyva-Pérez, A.; Corma, A. *Adv. Synth. Catal.* **2012**, *354*, 678. (j) Yang, Y.; Rioux, R. M. *Green Chem.* **2014**, *16*, 3916. (k) Cadu, A.; Watile, R. A.; Biswas, S.; Orthaber, A.; Sjöber, P. J. R.;

- Samec, J. S. M. *Org. Lett.* **2014**, *16*, 5556. (l) Degtyareva, E. S.; Burykina, J. V.; Fakhruddinov, A. N.; Gordeev, E. G.; Khrustalev, V. N.; Ananikov, V. P. *ACS Catal.* **2015**, *5*, 7208. (m) Modem, S.; Kankala, S.; Balaboina, R.; Thirukovela, N. S.; Jonnalagadda, S. B.; Vadde, R.; Vasam, C. S. *Eur. J. Org. Chem.* **2016**, 4635.
- (9) See for example: (a) Ogawa, A.; Ikeda, T.; Kimura, K.; Hirao, J. *J. Am. Chem. Soc.* **1999**, *121*, 5108. (b) Burling, S.; Field, L. D.; Messerle, B. A.; Vuong, K. Q.; Turner, P. *Dalton Trans.* **2003**, 4181. (c) Cao, C.; Fraser, L. R.; Love, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 17614. (d) Misumi, Y.; Seino, H.; Mizobe, Y. *J. Organomet. Chem.* **2006**, *691*, 3157. (e) Shuai, S.; Bichler, P.; Kang, B.; Buckley, H.; Love, J. A. *Organometallics* **2007**, *26*, 5778. (f) Di Giuseppe, A.; Castarlenas, R.; Pérez-Torrente, J. J.; Crucianelli, M.; Polo, V.; Sancho, R.; Lahoz, F. J.; Oro, L. A. *J. Am. Chem. Soc.* **2012**, *134*, 8171. (g) Kankala, S.; Nerella, S.; Vadde, R.; Vasam, C. S. *RSC Adv.* **2013**, *3*, 23582. (h) Palacios, L.; Artigas, M. J.; Polo, V.; Lahoz, F. J.; Castarlenas, R.; Pérez-Torrente, J. J.; Oro, L. A. *ACS Catal.* **2013**, *3*, 2910. (i) Pritzus, A. B.; Breit, B. *Angew. Chem. Int. Ed.* **2015**, *54*, 3121. (j) Kleinhans, G.; Guisado-Barrios, G.; Liles, D. C.; Bertrand, G.; Bezuidenhout, D. I. *Chem. Commun.* **2016**, *52*, 3504. (k) Kennemur, J. L.; Kortman, G. D.; Hull, K. L. *J. Am. Chem. Soc.* **2016**, *138*, 11914. (l) Palacios, L.; Di Giuseppe, A.; Artigas, M. J.; Polo, V.; Lahoz, F. J.; Castarlenas, R.; Pérez-Torrente, J. J.; Oro, L. A. *Catal. Sci. Technol.* **2016**, *6*, 8548. (m) Strydom, I.; Guisado-Barrios, G.; Fernández, L.; Liles, D. C.; Peris, E.; Bezuidenhout, D. I. *Chem. Eur. J.* **2017**, *23*, 1393.
- (10) (a) Hermann, W. *Angew. Chem. Int. Ed.* **2002**, *41*, 1290. (b) Lapert, M. F. *Coord. Chem. Rev.* **2005**, *690*, 5467. (c) Díez-González, S.; Marion, N.; Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3612. (d) Arduengo, III, A. J.; Iconaru, L. I. *Dalton Trans.* **2009**, 6903. (e) Hopkinson, M. N.; Richter, C.; Schedler, M.; F. Glorius, F. *Nature*, **2014**, *510*, 485. (f) Mata, J. A.; Hahn, F. E.; Peris, E. *Chem. Sci.*, **2014**, *5*, 1723.
- (11) (a) Canovese, L.; Cattalini, L.; Marangoni, G.; Tobe, M. *J. Chem. Soc. Dalton Trans.* **1985**, 731. (b) Cooper, D. A.; Rettig, S. J.; Storr, A. *Can. J. Chem.* **1986**, *64*, 566. (c) Darensbourg, D. J.; Fontal, B.; Chojnacki, S. S.; Klausmeyer, K. K.; Reibenspies, J. H. *Inorg. Chem.* **1994**, *33*, 3526. (d) Martos-Calvente, R.; de la Peña O'Shea, V. A.; Campos-Martin, J. M.; Fierro, J. L. G.; Gutiérrez-Puebla, E. *J. Mol. Cat. A: Chem.* **2004**, *214*, 269. (e) Telfer, S. G.; Parker, N. D.; Kuroda, R.; Harada, T.; Lefebvre, J.; Leznoff, D. B. *Inorg. Chem.* **2008**, *47*, 209. (f) Fandos, R.; Gallego, B.; López-Solera, M. I.; Otero, A.; Rodríguez, A.; Ruiz, M. J.; Terreros, P.; van Mourik, T. *Organometallics* **2009**, *28*, 1329. (g) Icsel, C.; Yilmaz, V. T.; Golcu, A.; Ulukaya, E.; Buyukgungor, O. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 2117. (h) Carmona, D.; Lamata, P.; Sánchez, A.; Pardo, P.; Rodríguez, R.; Ramírez, P.; Lahoz, F. J.; García-Orduña, P.; Oro, L. A. *Organometallics* **2014**, *33*, 4016. (i) Monakhov, K. Y.; López, X.; Speldrich, M.; van Leusen, J.; Kögerler, P.; Braunstein, P.; Poblet, J. M. *Chem. Eur. J.* **2014**, *20*, 3769.
- (12) Vaska, L.; DiLuzio, J. W. *J. Am. Chem. Soc.* **1961**, *83*, 2784-2785.
- (13) (a) Yu, X.-Y.; Patrick, B. O.; James, B. R. *Organometallics* **2006**, *25*, 4870. (b) Gois, P. M. P.; Trindade, A. F.; Veiros, L. F.; André, V.; Duarte, M. T.; Afonso, C. A. M.; Caddick, S.; Cloke, G. N. *Angew. Chem. Int. Ed.* **2007**, *46*, 5750. (c) Praetorius, J. M.; Wang, R.; Crudden, C. M. *Eur. J. Inorg. Chem.* **2009**, 1746. (d) Zenkina, O. V.; Keske, E. C.; Kochhar, G. S.; Wang, R.; Crudden, C. M. *Dalton Trans.* **2013**, *42*, 2282. (e) Palacios, L.; Di Giuseppe, A.; Opalinska, A.; Castarlenas, R.; Pérez-Torrente, J. J.; Lahoz, F. J.; Oro, L. A. *Organometallics* **2013**, *32*, 2768. (f) Azpiroz, R.; Rubio-Pérez, L.; Di Giuseppe, A.; Passarelli, V.; Lahoz, F. J.; Castarlenas, R.; Pérez-Torrente, J. J.; Oro, L. A. *ACS Catal.* **2014**, *4*, 4244. (g) Keske, E. C.; Moore, B. D.; Zenkina, O. V.; Wang, R.; Schatte, G.; Crudden, C. M. *Chem. Commun.* **2014**, *50*, 9883. (h) Palacios, L.; Di Giuseppe, A.; Castarlenas, R.; Lahoz, F. J.; Pérez-Torrente, J. J.; Oro, L. A. *Dalton Trans.* **2015**, *44*, 5777. (i) Buhl, H.; Ganter, C. *J. Organomet. Chem.* **2016**, *809*, 74.
- (14) Gómez-Gallego, M.; Sierra, M. A. *Chem. Rev.* **2011**, *111*, 4857.
- (15) Weiss, C. J.; Wobser, S. D.; Marks, T. J. *Organometallics* **2010**, *29*, 6308.
- (16) Ikehira, H.; Tanimoto, S.; Oida, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2537.
- (17) Fiandese, V.; Marchese, G.; Naso, F.; Ronzini, L. *Synthesis* **1987**, 1034.
- (18) SAINT+, version 6.01: Area-Detector Integration Software, Bruker AXS, Madison, WI, USA, 2001.
- (19) Sheldrick, G. M. *SADABS program*, University of Göttingen, Göttingen, Germany, 1999.
- (20) Sheldrick, G. M. *Acta Crystallogr. Sect. A*, **1990**, *46*, 467.
- (21) Sheldrick, G. M. *Acta Crystallogr.* **2015**, *C71*, 3.
- (22) Firsch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, revision A.1; Gaussian, Inc.: Wallingford, CT, 2004.
- (23) (a) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B: Condens. Matter Mater. Phys.* **1988**, *37*, 785. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372. (c) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.
- (24) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. *J. Chem. Phys.* **2010**, *132*, 154104.
- (25) Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297.