Selective C–H Bond Functionalization of 2-(2-Thienyl)pyridine by a Rh-NHC Catalyst


Dedication (optional)

Complex [Rh(µ-Cl)(H)2(IPr)]2 efficiently catalyzes the selective functionalization of 2-(2-thienyl)pyridine with a range of alkenes and internal alkynes. A catalytic cycle is proposed based on the identification of key reaction intermediates and the study of their reactivity by NMR. Theoretical calculations at the DFT level support that the reaction proceeds by initial N coordination of 2-(2-thienyl)pyridine followed by loss of molecular hydrogen to afford the active catalyst. Subsequently, cyclometallation of 2-(2-thienyl)pyridine takes place, followed by coordination of the unsaturated substrate (alkyne or alkene) at the vacant position trans to the hydride, and reductive elimination of the thiophene moiety. Finally, cyclometallation of the thiophene moiety renders the hydride cis to the unsaturated substrate, which leads to migratory insertion into the Rh–H bond and subsequent reductive elimination of the functionalized product.

Introduction

Thiophene moieties are present in a great number of naturally-occurring and synthetic organic molecules, including pharmacologically active heterocyclic compounds[1] and thiophene-based materials.[2] Methods for the preparation of thiophene derivatives mainly rely on the formation of the heterocyclic ring from organic condensations.[3]

The functionalization of thiophenic rings by cross-coupling reactions (e.g. Suzuki-Miyaura, Stille, Heck or Sonogashira) requires prefunctionalization of the desired C–H bond in the thiophene moiety by halogenation.[2b, 4] An atom economic and more sustainable alternative to cross-coupling reactions is the directed functionalization via C–H bond activation, which circumvents the need for prefunctionalization and minimizes selectivity issues.[5] The design of the catalytic system is of paramount importance to allow for C–H bond activation under relatively mild conditions and, ultimately, control the selectivity of the reaction. In this regard, a better understanding of the mechanisms involved in the functionalization of C–H bonds would be a stepping stone towards the preparation of more efficient catalysts. In the particular case of a model substrate such as 2-(2-thienyl)pyridine, the literature presents a variety of C–H functionalization reactions,[6] including several examples of hydroarylation reactions;[7] however, their reaction mechanisms have been barely studied.

N-Heterocyclic carbenes are strong donor ligands, which render highly electron-rich metal centers. Consequently, they facilitate oxidative addition reactions by increasing π-backdonation to the σ* orbital of the C–H bond and by making high oxidation states of the
metal more accessible.[8] In the particular case of Rh-NHC complexes, remarkable examples that illustrate the capacity of these complexes to undergo formation of cyclometalated species and, eventually, C–H bond functionalization, have been described in the literature.[9,7b]

Complex \([\text{Rh}(\mu-\text{Cl})(\text{H})_2(\text{IPr})]_2\)\[10\] (IPr = 1,3-bis-(2,6-diisopropylphenyl)imidazol-2-ylidene) shows promise as a catalyst in C–H bond functionalization reactions. Its parent complex, \([\text{Rh}(\mu-\text{Cl})(\text{COE})(\text{IPr})]_2,\[11\] has proved an efficient catalyst for this type of reaction;\[9a-b\] however, two main advantages can be conceived from the use of \([\text{Rh}(\mu-\text{Cl})(\text{H})_2(\text{IPr})]_2\) as catalyst: (i) the absence of olefin should render a more electron-rich metal center, and (ii) loss of molecular hydrogen from the complex would afford an unsaturated species that facilitates the coordination of the substrate.[12] However, to our best knowledge, no examples of C–H functionalization or activation have been hitherto reported with this complex.

Herein, we studied the reactivity of Rh(III) N-Heterocyclic carbene (NHC) complex \([\text{Rh}(\mu-\text{Cl})(\text{H})_2(\text{IPr})]_2\) with 2-(2-thienyl)pyridine. Moreover, selective functionalization of the C–H bond of the thiophene ring was achieved by hydroarylation of alkynes and alkenes. Key intermediate species of the reaction have been identified and a reaction mechanism proposed based on their reactivity and DFT calculations.

Results and Discussion

The ability of complex \([\text{Rh}(\mu-\text{Cl})(\text{H})_2(\text{IPr})]_2\) (1) to undergo C–H bond activation of the thiophene moiety in 2-(2-thienyl)pyridine was studied by NMR. Complex \([\text{Rh}(\text{Cl})(\text{H})(\text{IPr})(\text{N-PyTh})]_2\) (2) (PyTh = 2-(2-thienyl)pyridine) was obtained by reaction of 1 with two equivalents of 2-(2-thienyl)pyridine at –78 ºC. The temperature was increased stepwise in an NMR spectrometer from 203 K in order to study the structure and stability of the complex. At temperatures above 263 K, 2 evolves to give \([\text{Rh}(\text{Cl})(\text{H})(\text{IPr})(\kappa^2\text{N,C-PyTh})])_2\) (4), probably through loss of molecular hydrogen, as suggested by James et. al. for similar complexes,[11] followed by selective oxidative addition of the C8–H bond (Scheme 1; For numbering see Experimental Section). The low stability of 2 at room temperature precluded its isolation; however, full NMR characterization was possible at low temperature.

Scheme 1. Proposed mechanism for the formation of 4 from reaction of complex 1 with 2-(2-thienyl)pyridine.
1H NMR spectra of 2 in toluene-d8 at 263 K show the resonance corresponding to the two hydride protons as a doublet at $\delta = -18.4$ ppm, with a coupling constant of 39.6 Hz to the 103Rh nucleus. A dihydrogen complex can be discarded as the $T1(\text{min})$ value measured by the standard inversion-recovery method for the high-field signal is 391 ms at 500 MHz and 273 K. Significant 1H NMR signals at 263 K for 2 are also those belonging to the IPr ligand, which features a singlet at $\delta = 6.56$ ppm for the NCH protons, a septet at $\delta = 3.40$ ppm for the equivalent methines of the isopropyl groups and two doublets for the methyl protons at $\delta = 1.49$ and 1.15 ppm, indicating free rotation around the Rh–C bond and the existence of a symmetry plane that contains the NHC ligand. In the 13C{1H} NMR spectra of 2 in toluene-d8 at 263 K the most significant signal is that corresponding to the carbene carbon, which appears at $\delta = 185.0$ ppm as a doublet, with a JC-Rh of 53.2 Hz. Only one singlet is observed either for the two NCH carbon atoms of the imidazole ring or the four CH’s of the isopropyl groups of the IPr ligand at $\delta = 123.3$ and 28.4 ppm respectively. The eight methyl groups show two singlets at $\delta = 25.3$ and 23.2 ppm.

The symmetry of the IPr ligand at 263 K can be rationalized by invoking free rotation of the ligand about the C–Rh bond together with a fast exchange between species 2 and 2’. At temperatures below 223 K the CH’s of the isopropyl groups and the two hydrides become non-equivalent due to slow interconversion between the two conformations of 2 in the NMR time scale. The two hydrides appear at 203 K as two doublets at $\delta = -17.20$ and $-18.50$ ppm with coupling constants of 29.8 and 47.7 Hz respectively (Figure 1). According to literature data, values of coupling constants ca. 50 Hz suggest a complex with a vacant coordination site trans to the hydride, where the thiophene moiety is not coordinated (Scheme 1).[13] On the other hand, the similar chemical shifts of the hydrides, separated by scarcely more than 1 ppm, suggest that a κ2N,S coordination mode, with a weak Rh–S interaction, cannot be entirely excluded. The NMR studies above presented suggest the presence of two simultaneous dynamic processes: i) interconversion $2\leftrightarrow 2'$ and ii) rotation about the CNHC–Rh bond.

![Figure 1. High-field 1H NMR spectra of 2 in toluene-d8 at various temperatures.](image-url)
Formation of a dihydrogen complex through which molecular hydrogen could be eliminated at temperatures above 263 K would explain formation of the proposed reaction intermediate 3. However, in spite of our attempts to identify 3 in solution by fine tuning of the temperature, this could neither be characterized nor observed by NMR measurements.

Complex 4 was prepared selectively by reaction of 1 with 2 equivalents of 2-(2-thienyl)pyridine under argon for 1 h at 60 °C in toluene. The 1H NMR spectra of 4 shows as most representative resonance that corresponding to the hydride proton at δ = –26.9 ppm, which appears as a doublet (50.0 Hz) due to scalar coupling to the 103Rh nucleus. A coupling constant of 50.0 Hz is reminiscent of similar complexes reported in the literature where the hydride is trans to a vacant coordination site.[11] In the 13C{1H} NMR spectra the most significant signal is that corresponding to the NCN carbon, which appears as a doublet at δ = 183.9 ppm with a coupling constant of 55.1 Hz to the Rh nucleus, and the doublet resonance at δ = 162.3 ppm that corresponds to the carbon atom of the newly formed C–Rh bond (JC–Rh = 35.3 Hz). The 1H NMR spectra of the IPr ligand in 4 shows a loss of symmetry compared to that in 2. The NCH protons appear as two doublets at δ = 6.79 and 6.74 ppm with a coupling constant of 2.0 Hz. The methines of the isopropyl groups show four septets at δ = 3.90, 3.59, 3.13, and 3.09 ppm and the methyl protons eight doublets at δ = 1.85, 1.64, 1.19, 1.12, 1.08, 1.02, 1.00, and 0.78 ppm, all of them with coupling constants of 6.8 Hz. The three resonances that belong to the thiophene ring in 2 (two doublets at δ = 6.88 and 6.17 ppm and a doublet of doublets at δ = 6.60) disappear to give two new resonances in 4, which emerge as two doublets at δ = 7.07 and 6.86 ppm with a coupling constant of 5.0 Hz. This confirms the selective activation of the C8–H bond. The selective cyclometallation of the thiophene versus the pyridine ring can be explained in terms of the stronger Rh–N bond compared to the Rh–S bond, which leads κ1N coordination of the substrate and subsequent C–H bond activation of the thiophene ring.

1H-1H NOE NMR experiments show NOE between the CH3 protons of the isopropyl groups and the thiophene aromatic protons, which seems to confirm that the pyridine moiety is trans to the NHC ligand (supporting information), in agreement with previous literature examples.[13, 14]

The assumption that formation of 4 occurs via 3 is supported by DFT (B3LYP) methods (Figure 2). The possibility of σ-bond metathesis or concerted pathways was discarded due to the high energy barriers found for these processes compared to that obtained via loss of molecular hydrogen (ΔG = 40.5, 33.2 and 9.3 kcal mol–1 respectively). Formation of 3 occurs by barrierless elimination of molecular hydrogen from 2,[15, 16] which then undergoes side-on coordination of the C–H bond to give TS3/4. Noteworthy, a Rh⋯S distance of 2.26 Å was found for intermediate 3, which is in the range of reported Rh⋯S bond distances.[17] This contrasts with the significantly longer Rh⋯S distance calculated for 2 (2.69 Å), which is probably a consequence of the strong trans effect of the hydrido ligand, what would be in agreement with the NMR data presented above. The slightly endergonic overall process for the formation of 4 from 2 is driven by loss of molecular hydrogen from the reaction mixture.

The concerted pathway and the σ-bond metathesis mechanism proposed in Figure 2 require an approach of the C–H bond to the metal center that takes places by rotation of the C–C bond
that links the pyridine and the thiophene rings in order to allow the side-on interaction of the C–H bond with the rhodium center. The resulting conformation (2r) is 2.7 Kcal mol–1 less stable than 2, where the sulfur atom was pointing towards the rhodium center. Subsequently, the two transition states, TS2/4m and TS2/4c, are formed. The former comes about according to a σ-bond metathesis mechanism, i.e., the activation of the C–H bond is assisted by one of the hydrido ligands, which interacts with the proton of the C–H bond. However, the latter forms by a concerted mechanism where the H2 molecule is formed from the two hydrido ligands, with concomitant side-on coordination of the C–H bond. Finally, in both cases, elimination of molecular hydrogen and concomitant cyclometallation of the 2-(2-thienyl)pyridine ligand would afford 4.

Figure 2. DFT calculated relative energy [ΔG in kcal·mol–1] profiles for the formation of 4 from 2.

Alkene hydroarylation

Addition of styrene to 4 leads to coordination of the olefin and concomitant reductive elimination of the thiophene moiety and the hydrido ligand to give [Rh(Cl)(IPr)(η2-PhCH=CH2)(N-PyTh)] (5) (Scheme 2). 1H NMR shows as most representative resonances those belonging to the coordinated styrene at δ 4.60, 2.42 and 1.82 ppm, and the three protons of the thiophene moiety at δ 7.61, 7.13 and 7.6 ppm. In the 13C{1H} NMR spectra, the doublet corresponding to the cyclometallated carbon atom at δ 129.8 ppm disappears and two new doublets assignable to the coordinated olefin emerge at δ 54.5 and 32.8 ppm with coupling constants of 17.3 and 15.9 Hz respectively. 1H-1H NOE NMR experiments show NOE between the methinic proton of the isopropyl groups and the olefinic protons, which supports that the olefin is coordinated cis to the NHC ligand (supporting information).

Formation of intermediate 5 by coordination of the unsaturated substrate and concomitant reductive elimination of the thiophene moiety occurs instead of migratory insertion of the
alkene into the Rh–H bond. A plausible explanation for this reactivity may be the fact that coordination of the unsaturated substrate occurs at the vacant position trans to the hydrido ligand, which prevents migratory insertion into the Rh–H bond. Based on these results, complex 1 may be able to catalyze the hydroarylation of alkenes by a reaction mechanism that entails: (i) cyclometallation of the thiophene ring to give complex 4; (ii) coordination of the unsaturated reagent followed by reductive elimination of the thiophene moiety and the hydrido ligand to give 5; (iii) second cyclometallation of the thiophene ring; (iv) migratory insertion of the olefin into the C–H bond; (v) reductive elimination to give the functionalized organic product and, finally, (vi) substitution of the functionalized product by 2-(thiophen-2-yl)pyridine to regenerate the active species.

Scheme 2. Proposed catalytic cycle for the hydroarylation of terminal alkenes.

The above described reactivity of 1 prompted us to test its activity in the directed C–H functionalization of 2-(2-thienyl)pyridine. The hydroarylation of 3,3-dimethylbut-1-ene with 2-(2-thienyl)pyridine was performed in benzene at 80 ºC, employing equimolar amounts of the reagents and a 5 mol% loading of pre-catalyst 1 (Scheme 3).
Scheme 3. Hydroarylation reaction of terminal alkenes with 2-(2-thienyl)pyridine. [a] Reaction conditions: 2-(thiophen-2-yl)pyridine (0.23 mmol), olefin derivative (0.23 mmol), catalyst 1 (5 mol%) in C₆D₆ (0.4 mL) at 80 ºC. [b] The reaction was carried out at 120 ºC using toluene-d₈ as solvent.

The linear product Iₐ[7b] was obtained selectively in good yields with no traces of the branched isomer. The substrate scope was extended to a range of terminal alkenes, and the selectivity towards the linear isomer maintained in all cases; in fact, no branched isomer was observed. The reaction for the formation of Iₖ is remarkably slower than the other examples presented in Scheme 3; therefore, a higher boiling point solvent (toluene) and higher temperatures were required. The new compounds Iₖ-g were isolated and characterized by HRMS, 1H and 13C{1H} NMR (Supporting Information).

Alkyne hydroarylation

In an attempt to identify the π-alkyne complex analogous to 5, complex 4 was reacted with 3-hexyne. Conversely, in this case, intermediate [Rh(Cl)(IPr)(κ₂C,C’-PrC–CHPr)(κ₂N,C-PyTh)] (6) was obtained as the only reaction product, which further supports the catalytic cycle previously postulated (Scheme 4).
Scheme 4. Proposed catalytic cycle for the hydroarylation of internal alkynes.

Formulation of 6 as a metallacyclopropene is based on the high frequency of the =CH-Pr signal in 1H NMR compared to literature values for alkenyl complexes,[18] and the fact that the carbon atoms at both ends of what would be the double bond show C-Rh coupling constants ca. 15 Hz. The proposed metallacyclopropene possibly originates from the parent alkenyl complex, as a consequence of the interaction between the =CH-Pr carbon atom with the rhodium center, enabled by the cis-positioned vacant coordination site. An equilibrium between the two species (metallacyclopropene and alkenyl complex) analogous to that proposed by Crabtree et al.[19] would allow for reductive elimination of the alkenyl ligand and the cyclometallated 2-(thiophen-2-yl)pyridine, thus affording the corresponding functionalized organic compound. 1H NMR shows as most representative resonances those belonging to the $\kappa^2_{C,C'}$-PrC–CHPr ligand. The signal corresponding to the CH proton appears at $\delta$ 2.47 ppm as a multiplet, while the two CH3 groups emerge at $\delta$ 1.07 and 0.71 ppm. The two protons of the cyclometallated thiophene moiety appear at $\delta$ 6.71 and 6.42 ppm with a coupling constant of 5.8 Hz. The $^{13}$C{1H} NMR spectra show two doublets at $\delta$ 66.6 and 62.1 ppm corresponding to the coordinated carbon atom (JC-Rh = 15.1 Hz) and the CH of the alkenyl ligand (JC-Rh = 16.0 Hz), respectively.

Other diagnostic signals observed in the $^{13}$C{1H} NMR spectra are the carbene carbon and the cyclometallated carbon atom of the thiophene moiety, which appear as doublets at $\delta$ 185.4 and 146.5 ppm (JC-Rh = 56.5 and 31.8 Hz respectively). 1H-1H NOE NMR experiments further support the formation of intermediate 6 (see supporting information). One of the methyl groups of the $\kappa^2_{C,C'}$-PrC–CHPr ligand (CH3CH2CH-) shows NOE with the methyl groups of the diisopropylphenyl moieties, the ortho-hydrogen of the pyridine moiety, the aromatic proton of the N-substituents, and the CH of the alkenyl ligand, which suggests that the NHC and pyridine
ligands are cis to the κ2C,C'-PrC–CHPr ligand (Supporting Information). At room temperature 6 evolves to give the functionalized organic molecule ((E)-2-(3-(oct-4-en-4-yl)thiophen-2-yl)pyridine), thus restarting the catalytic cycle.

Complex 1 proved to be an efficient pre-catalyst for the hydroarylation of a variety of internal alkynes (IIa-d); however, terminal alkynes afforded mainly polymerization and traces of cyclotrimerization products. The catalytic reactions were performed under reaction conditions analogous to those employed for alkene hydroarylation (Scheme 5). Regarding the Z / E selectivity of this reaction, exclusive formation the E isomer, the syn addition product, was confirmed by NMR data (by comparison with literature data of compound IIa[7c]). Somewhat higher temperatures were required for the rather sluggish formation of IId, which afforded the less encumbered C–C bond in excellent selectivities; in fact, C–C bond formation at the most sterically hindered carbon was not observed. The new compounds IIb-d were isolated and characterized by HRMS, 1H and 13C{1H} NMR (Supporting Information).

Scheme 5. Hydroarylation reaction of terminal alkenes with 2-(2-thienyl)pyridine. [a] Reaction conditions: 2-(thiophen2-yl)pyridine (0.23 mmol), alkyne derivative (0.23 mmol), catalyst 1 (5 mol%) in C6D6 (0.4 mL) at 80 ºC. [b] the reaction was carried out at 100 ºC.

The Rh(III) complex [Rh(µ-Cl)(H)2(IPr)]2 was the pre-catalyst of choice for the C–H bond functionalization of 2-(2-thienyl)pyrididine, while the related catalyst precursor [Rh(µ-Cl)(COE)(IPr)]2 (IPr = 1,3-bis-(2,6-diisopropylphenyl)imidazol-2-ylidene; COE = cis-cyclooctene), often used in our laboratories,[13] gave only a 33% yield after 16 h for the hydroarylation of 4-octyne under the same reaction conditions. The noticeably lower yield obtained with [Rh(µ-Cl)(COE)(IPr)]2 compared to [Rh(µ-Cl)(H)2(IPr)]2 suggests that COE coordination hampers the activity of the catalyst. In the case of the latter (1), active catalyst species 3 would be obtained from H2 elimination, which prevents catalyst poisoning by the COE ligand. In fact, reaction of [Rh(µ-Cl)(COE)(IPr)]2 with 2 equivalents of 2-(2-thienyl)pyridine afforded only a 20% conversion towards the cyclometallated complex after 2 h at room temperature.

Conclusion

In summary, we have developed a Rh-catalyzed functionalization of 2-(thiophen-2-yl)pyridine by directed C–H activation. This reaction renders moderate to excellent yields and high selectivities for the hydroarylation of a wide range of internal alkynes and terminal alkenes.
under relatively mild conditions. Theoretical calculations at the DFT level support that the reaction proceeds by loss of molecular hydrogen from 2 to give the active catalyst 3. Based on the identification of reaction intermediates 2, 4, 5 and 6, a Rh(I)/Rh(III) catalytic cycle has been proposed. The proposed reaction pathway would require the formation of active catalyst species 3, which could afford 4 after cyclometallation of the thiophene moiety. Then, migratory insertion of the unsaturated substrate into the Rh–H bond cannot take place because they are in mutual trans position. This forces reductive elimination of the activated thiophene moiety and the hydrido ligand to give intermediate 5 and its analogous alkyne complex 6. Finally, the cyclometallated intermediates, containing the coordinated olefin or alkyne cis to the hydrido ligand, undergo migratory insertion of the unsaturated molecule into the Rh–C bond, followed by reductive elimination of the functionalized organic compound.

Experimental Section

General information

All reactions and manipulations were carried out under argon atmosphere by using Schlenk-type techniques. 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 starting complexes [Rh(μ-Cl)(IPr)(coe)]2, (IPr = 1,3-bis-(2,6-diisopropylphenyl)imidazol-2-carbene, coe = cyclooctene) and [Rh(μ-Cl)(H)2(IPr)]2 (1), were prepared following procedures described in the literature.[8,9] 1H NMR and 13C NMR spectra were obtained on a Bruker ARX-300 (300 and 75 MHz respectively) spectrometer using TMS as the internal reference in toluene-d8 as solvent. All chemical shifts (δ) are reported in ppm and coupling constants (J) are reported in Hz to apparent peak multiplications. 1H-1H-COSY, 13C-APT, 1H/13C HSQC and 1H/13C HMBC sequences were used for help in the assignments of the 1H and 13C spectra.

Figure 3. Numbering of 2-(thiophen-2-yl)pyridine.

Preparation of [Rh(Cl)(H)2(IPr)(N-PyTh)] (2): The reaction was carried out in an NMR tube at –78 °C in toluene-d8 with 1 (35 mg, 0.033 mmol) and 2-(thiophen-2-yl)pyridine (11 mg, 0.066mmol). 1H NMR (300 MHz, toluene-d8, 263 K): δ 8.51 (d, J_H-H = 5.5, 1H, H6-PyTh), 7.37 (t, J_H-H = 7.6, 2H, Hlp-Ph), 7.26 (d, J_H-H = 7.6, 4H, Hm-Ph), 6.88 and 6.17 (both d, J_H-H = 5.4, 3.5, 2H, H8,10-PyTh), 6.96 (d, J_H-H = 5.3, 1H, H3-PyTh), 6.78 (dd, J_H-H = 6.6, 5.3, 1H, H4-PyTh), 6.60 (dd, J_H-H = 5.4, 3.5, 1H, H9-PyTh), 6.56 (s, 2H, =CHN), 5.97 (dd, J_H-H =6.6, 5.5, 1H, H5-PyTh), 3.40 (sept, J_H-H = 7.2, 4H, CHMeIPr), 1.49 and 1.15 (both d, J_H-H = 7.2, 4H, CHMeIPr), -18.4 (d, J_Rh-H = 39.6, 2H, HRh-H). 13C (1H)-APT NMR plus HSQC and HMBC (75 MHz, toluene-d8, 263 K): δ 185.0 (d, JC-Rh = 53.2, Rh-CIPr), 156.3 (s, C6-PyTh), 152.9 (s, C2-PyTh), 147.3 (s, Cq-lPr), 146.3 (s, C7-PyTh), 138.6 (s, CqN), 135.9 (s, C4-PyTh), 127.9 (s, Cp-Ph), 125.5 (both s, C8,10-PyTh), 127.8 (s, C9-PyTh), 124.3 (s, Cm-Ph), 123.3 (s, =CHN), 121.4 (s, C5-PyTh), 120.5 (s, C3-PyTh), 28.4 (s, CHMeIPr), 25.3 and 23.2 (both s, CHMeIPr).
Preparation of \([\text{Rh(Cl)}(\text{H})(\text{IPr})\{\kappa^2\text{N,C-PyTh}\}]\) (4): A solution of 1 (130 mg, 0.25 mmol) and 2-(thiophen-2-yl)pyridine (40 mg, 0.50 mmol) in toluene (5 mL) was stirred for 1 h at 60 °C. At the end of this time, the solvent was evaporated under vacuum. Hexane (5 mL) was added and the yellowish suspension cool down to 0 °C. The resulting cold solution was filtered to give a pale yellow solid that was dried in vacuum at room temperature. Yield: 64%. 1H NMR (300 MHz, toluene-d8, 273 K): δ 9.44 (d, JH-H = 5.4, 1H, H6-PyTh), 7.3-7.0 (all m, 6H, HPh-IPr), 7.07 (d, JH-H = 2.0, 2H, =CHN), 6.70 (d, JH-H = 7.1, 1H, H3-PyTh), 6.65 (dd, JH-H = 7.1, 6.4, 1H, H4-PyTh), 6.12 (dd, JH-H = 6.4, 5.4, 1H, H5-PyTh), 3.90, 3.59, 3.13, and 3.09 (all, sept, = JH-H = 6.8, 4H, CHMeIPr), 1.85, 1.64, 1.19, 1.12, 1.08, 1.02, 1.00, and 0.78 (all, d, JH-H = 6.8, 24H, CHMeIPr) – 26.90 (d, JRh-H = 50.0, 1H, Rh-H). 13C {1H}-APT NMR plus HSQC and HMBC (75 MHz, toluene-d8, 273 K): δ 183.9 (d, JC-Rh = 55.1, Rh-CIPr), 162.3 (d, 1JC-Rh = 35.3, C8-PyTh), 159.8 (s, C2-PyTh), 150.4 (s, C6-PyTh), 148.5, 147.9, 145.0, and 144.3 (all s, Cq-IPr), 146.0 (s, C7-PyTh), 138.5 and 135.3 (both s, CqN), 137.0 (d, 3JC-Rh = 3.8, C10-PyTh), 136.8 (s, C4-PyTh), 129.8 (d, 2JC-Rh = 15.0, C9-PyTh), 127.5, 127.4, 124.9, 124.8, 124.2, 121.4, 123.8, and 123.6 (all s, CPh-lPr), 123.9 and 123.4 (both s, =CHN), 118.3 (s, C5-PyTh), 115.8 (s, C3-PyTh), 29.3, 29.0, 28.5, and 28.2 (all s, CHMelPr), 26.9, 26.1, 25.6, 23.4, 23.3, 22.8, 22.7, and 21.9 (all s, CHMelPr).

Preparation of \([\text{Rh(Cl)}(\text{IPr})\{\eta^2-\text{PhCH=CH2})(\text{N-PyTh})\}]\) (5): An NMR tube containing a solution of complex 4 (0.022 mmol) in 0.5 mL of toluene-d8 was treated with 0.022 mmol of styrene at room temperature. 1H NMR (400 MHz, toluene-d8, 298 K): δ 8.20 (d, JH-H = 5.1, 1H, H6-PyTh), 7.61 and 7.13 (both d, JH-H = 7.6, 2H, H8,10-PyTh), 7.52 (dd, JH-H = 7.6, 1H9-PyTh), 7.4-7.0 (m, 6H, HPh-IPr), 6.77 (t, JH-H = 7.4, 1H, H5-Ph), 6.74 (d, JH-H = 6.9, 1H, H3-PyTh), 6.67 and 6.63 (both s, 2H, =CHN), 6.61 (dd, JH-H = 7.8, 7.4, 2H, Hm-Ph), 6.52 (dd, JH-H = 6.9, 6.6, 1H, H4-PyTh), 6.09 (d, JH-H = 7.8, 2H, Ho-Ph), 5.83 (dd, 6.6, 5.1, 1H, H5-PyTh), 4.94, 4.23, 2.66, and 2.22 (all, sept, JH-H = 6.4, 4H, CHMelPr), 4.60 (a t, JH-H = 8.4, 1H, CH=CH2), 2.42 (a d, JH-H = 7.7, 1H, CH=CH2), 1.84, 1.63, 1.31, 1.24, 1.14, 1.13, 1.04, and 0.96 (all d, JH-H = 6.4, 24H, CHMelPr), 1.82 (dd, JH-H = 8.4, 7.7, 1H, CH=CH2). 13C {1H}-APT NMR plus HSQC and HMBC (100 MHz, toluene-d8, 298 K): δ 182.3 (d, JC-Rh = 53.9, Rh-CIPr), 154.6 (s, C6-PyTh), 153.1 (s, C2-PyTh), 149.1, 149.0, 146.1, and 146.0 (all s, Cq-IPr), 145.9 (s, Cq-Ph), 142.7 (s, C7-PyTh), 138.0 and 137.9 (both s, CqN), 134.2 (s, C4-PyTh), 129.7, 129.5, 127.9, 127.5, 123.2, and 123.1 (all s, CPh), 127.8 and 124.9 (both s, C8,10-PyTh), 127.7 (s, Cm-Ph), 126.0 (s, Co-Ph), 125.1 (s, Cp-Ph), 125.0 (s, C9-PyTh), 121.8 (s, C3-PyTh), 120.3 (s, C5-PyTh), 54.5 (d, JC-Rh = 17.3, CH=CH2), 32.8 (d, JC-Rh = 15.9, CH=CH2), 28.8, 28.6, 28.4, and 28.2 (all s, CHMelPr), 26.8, 26.6, 26.3, 25.9, 23.5, 23.4, 22.1, and 21.9 (all s, CHMelPr).

Preparation of \([\text{Rh(Cl)}(\text{IPr})\{\kappa^2\text{C,C'-PrC–CHPr})(\kappa^2\text{N,C-PyTh})\}]\) (6): An NMR tube containing a solution of complex 4 (0.022 mmol) in 0.5 mL of toluene-d8 was treated with 0.022 mmol of 3-hexyne at 273 K. 1H NMR (300 MHz, toluene-d8, 273 K): δ 9.59 (d, JH-H = 5.2, 1H, H6-PyTh), 7.4-7.0 (m, 6H, HPh-lPr), 6.87 (d, JH-H = 7.8, 1H, H3-PyTh), 6.82 and 6.81 (br, 2H, =CHN), 6.71 and 6.42 (both d, JH-H = 5.8, 2H, H9,10-PyTh), 6.64 (dd, JH-H = 7.8, 7.1, 1H, H4-PyTh), 6.36 (dd, JH-H = 7.1, 5.2, 1H, H5-PyTh), 5.61, 5.12, 3.31, and 3.09 (all sept, JH-H = 6.9, 4H, CHMelPr), 2.47 (m, 1H, CH), 1.89, 1.27, 1.16, 1.14, 1.10, 1.08, 1.01, and 1.00 (all d, JH-H = 6.8, 24H, CHMelPr), 1.7-1.2 (m, 4H, CH2), 1.07 and 0.71 (t, JH-H = 7.4, 6H, CH3,alkenyl). 13C (1H)-APT NMR plus HSQC and HMBC (75 MHz, toluene-d8, 273 K): δ 185.4 (d, JC-Rh = 56.5, Rh-CIPr), 154.1 (s, C6-PyTh), 152.6 (s, C2-PyTh), 149.4, 149.0, 146.8, and 146.0 (all s, Cq-lPr), 147.5 (d, JC-Rh = 3.0,
C7-PyTh), 146.5 (d, JC-Rh = 31.8, C8-PyTh), 138.1 and 137.6 (both s, CqN), 135.9 (s, C4-PyTh), 127.6 and 124.3 (s, C9,10-PyTh), 125.8 and 125.5 (both s =CHN), 120.3 (s, C3-PyTh), 119.8 (s, C5-PyTh), 66.6 (d, JC-Rh = 16.0, Cq=CH), 62.1 (d, JC-Rh = 15.1, Cq=CH), 32.0 (s, CH2), 26.9 (s, CH2), 29.0, 28.4, 28.1, and 27.6 (all s, CHMeIPr), 26.6, 26.5, 26.3, 26.0, 24.7, 22.8, 22.7, and 22.1 (all s, CHMeIPr), 14.0 and 12.5 (both s, CH3).

Catalytic hydroarylation reactions. An NMR tube containing a solution of 0.011 mmol of 1 in 0.5 mL of C6D6 or toluene-d8 was treated with 0.23 mmol of alkyne or olefin and 0.23 mmol of 2-(2-thienyl)pyridine and heated at 80 ºC. The reaction course was monitored by 1H NMR and the conversion was determined by integration of the NHC-PyTh signal of free ligand with the products. Later the solution was concentrated under reduced pressure affording a crude residue, which was purified by column chromatography over silica gel (70-230 mesh), and eluted with hexane-diethylether (80/20) to isolate the organic compound.

Computational details

All DFT theoretical calculations have been carried out using the G09.D01 program package.[20] Full citation is given in supporting information. The B3LYP method[21] has been employed including the D3 dispersion correction proposed by Grimme[22] and the “ultrafine” grid. The def2-SVP basis set[23] has been selected for all atoms for geometry optimizations and calculation of free energy corrections. The nature of the stationary points has been confirmed by frequency calculations.

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Keywords: C–H functionalization • NHC • rhodium • homogeneous catalysis • C–H activation


[15] A relaxed scan for the shortening of the H-H distance from complex 2 showing the lack of transition state is provided in the Supporting Information.


[20] Gaussian 09, Revision D.01, M. J. Frisch et al

