Intermolecular C-H activation with an Ir-METAMORPhos piano-stool complex: multiple reaction steps at a reactive ligand

Oldenhof, S.; Lutz, M.; van der Vlugt, J.I.; Reek, J.N.H.

DOI
10.1039/c5cc05916j

Publication date
2015

Document Version
Final published version

Published in
Chemical Communications

License
Article 25fa Dutch Copyright Act (https://www.openaccess.nl/en/in-the-netherlands/you-share-we-take-care)

Citation for published version (APA):

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: https://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 426, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (https://dare.uva.nl)
Intermolecular C–H activation with an Ir-METAMORPhos piano-stool complex – multiple reaction steps at a reactive ligand†

S. Oldenhof, M. Lutz, J. I. van der Vlugt* and J. N. H. Reek*

Substrate activation by means of a reactive ligand is a topic of much interest. Herein we describe a stoichiometric anti-Markovnikov C–N bond formation involving ligand reactivity in multiple steps along the reaction coordinate, including ligand assisted substrate (de)protonation and C–N bond formation, as illustrated by a combined experimental, spectroscopic and computational study. This affords a highly unusual four-membered iridacycle bearing an exo-cyclic C=C double bond.

Fig. 1 Sequential C–H and N–H bond activation with subsequent C–N bond formation on a reactive ligand scaffold.

Metal–ligand bifunctional substrate activation has recently evolved as a valuable strategy in homogeneous catalysis. Hydrogen-bond interactions and acid–base reactivity are often-encountered strategies in this context.1,2 Prime examples of reactive ligands with internal Brønsted-active sites that can undergo reversible deprotonation are those containing primary or secondary amines. The nitrogen atom may be in the coordination sphere of the transition metal or located in the ligand backbone, having no direct interaction with the metal.3 C–H activation remains to be a topic of intense research, with a major focus on site-specific and regioselective functionalization. Intramolecular ligand-assisted metal-mediated C–H activation, via a directing group, is frequently utilized4 but intramolecular C–H activation facilitated by a reactive ligand (Fig. 1) that functions as internal base is much less explored.5

However, elegant work by Grotjahn using imidazolylphosphines as reactive ligands to enhance alkyne C–H activation has demonstrated the feasibility of this approach for the hydration of alkynes.6 The related hydroaddition of amines to unsaturated hydrocarbons is an attractive and atom-efficient protocol to form C–N bonds. Hydroamination with late transition metal complexes typically proceeds via initial coordination and activation of the hydrocarbon, with follow-up (external) nucleophilic attack of the (activated) amine and proton transfer.7 Examples where C–H activation of an unsaturated hydrocarbon precedes the overall syn-addition of an amine are rare8 and no structurally characterized complex has been reported, to the best of our knowledge. We hypothesized that metal–ligand bifunctional activation of a hydrocarbon would allow for direct observation of this unusual pathway, which could potentially open up new avenues for hydroaddition chemistry and catalysis. Ligands that combine more than one type of reactivity in the scaffold are uncommon9 but these designs could provide entry into site-selective activation and functionalization of substrates.

Sulfonamidophosphine ligands (coined METAMORPhos), which are accessible from commercially available sulfonamides and chlorophosphine precursors, have been demonstrated to combine proton responsive character at nitrogen with hydrogen bonding properties upon coordination to transition metals.10 Intermolecular C–H activation mediated by this ligand scaffold has not been observed to date. METAMORPhos contains two potentially reactive ligand sites, namely the sulfonyl oxygen and the nitrogen, of which the former can coordinate to metal ions (both as neutral or anionic donor), while the latter is part of the second coordination sphere. Iridium piano-stool complexes have been used regularly for a number of bond activation processes, including the use of noninnocent ligands in the coordination sphere of Ir.11 Herein, we demonstrate the key steps of METAMORPhos-assisted C–H activation of alkenes in the coordination sphere of Ir and subsequent overall syn-addition of the H–N(R) ligand fragment over the C=C bond. The end-product contains a unique four-membered metallacycle with an exo-cyclic double bond, as

† Electronic supplementary information (ESI) available: Characterization details of new compounds, computational details, crystallographic details, NMR spectra. CCDC 1410768, 1410769 and 1412995. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5cc05916j
confirmed by X-ray crystal structure determination and NMR spectroscopy. DFT calculations provide insight in the pathway for this unusual transformation.

Mixing two molar equivalents of ligand 1H with Ir-precursor [IrCl(Cp*)(μ-Cl)]2 in C2D2Cl2 instantly led to complete consumption of starting materials and formation of a single species, which was characterized by multinuclear NMR spectroscopy and HR-MS spectrometry as neutral P-coordinated complex 2 (see Scheme 1). An X-ray crystal structure determination supports this conformation in the solid state (Fig. 2, left). Hydrogen bond interactions between the N–H of the METAMORPhos ligand and the chloride ligands Cl1 and Cl2 were observed [N1⋯Cl1 3.1451(13), N1⋯Cl2 3.2529(14)] (see Table S1 in the ESI†). Addition of 2 to a suspension of sodium acetate (NaOAc) in CH2Cl2 at room temperature led to complete conversion of this complex to a new species 3 (as could easily be observed by 31P NMR spectroscopy), formulated as IrCl(Cp*)(k3-P,O-1) (see Scheme 1), based on multinuclear NMR spectroscopy and HR-MS spectrometry and supported by single crystal X-ray structure determination (Fig. 2, right). Compared to the bond lengths found in the precursor species 2, the N1–S1 bond is shortened (1.5464(13) Å) while the S–O 1 bond (1.5098(11) Å) is indeed undergone deprotonation.

Scheme 1 Preparation of neutral monodentate P-coordinated complex 2 from 1H with [IrCl(Cp*)(μ-Cl)]2 and subsequent deprotonation to give P,O-coordinated complex 3.

Selected bond lengths (Å) and angles (°): for 2, Ir1–P1 2.2838(4), Ir1–Cl1 2.3956(4), Ir1–Cl2 2.4061(4), Ir1–N1 2.077(3), Ir1–C1 2.077(3), Ir1–Cl1 2.3981(4), N1–Cl1 3.1451(13), N1–Cl2 3.2529(14), N1⋯Cl1 3.1451(13), N1⋯Cl2 3.2529(14), N1⋯HCl1 119.8(19), N1⋯HCl2 115.9(19). For 3, Ir1–N1 2.2968(4), Ir1–P1 2.1630(10), Ir1–Cl1 2.3981(4), Ir1–Cl2 2.430(3), P1–Ir1–N1 101.91(19), P1–Ir1–C1 100.26(19), N1–Ir1–C1 101.91(19), N1–P1–N1 100.26(19), N1–P1–Cl1 88.48(9), N1⋯Ir1 101.91(19).

Addition of phenylacetylene to 3 led to the formation of a new species (13C{1H} NMR: δ 31.0 ppm) after two hours at 50 °C. The 1H NMR spectrum showed a singlet at 6.88 ppm. The identity of the starting materials and formation of a single species, which was characterized by multinuclear NMR spectroscopy and HR-MS spectrometry as neutral P-coordinated complex 2 (see Scheme 1), based on multinuclear NMR spectroscopy and HR-MS spectrometry and supported by single crystal X-ray structure determination, obtained via slow diffusion of pentane into a THF solution of complex 4. The resulting X-ray structure establishes the formation of an Ir-vinyl complex containing an unusual four-membered Ir-P-N-C ring, see Fig. 3.

Scheme 2 Complex 3 reacts with phenylacetylene to generate Ir-acetylide complex 5, which rearranges to Ir-vinyl complex 4 within 3 hours at 50 °C.

With pre-activated species 3 in hand, we decided to investigate the ligand assisted intermolecular activation of allynes, generating an Ir-phenylacetylide species via proton transfer from the terminal alkyne to the proton responsive ligand, which might allow for alternative reaction pathways in the context of selective hydrofunctionalization. Addition of phenylacetylene to 3 led to the formation of a new species (13C{1H} NMR: δ 31.0 ppm) after two hours at 50 °C. The 1H NMR spectrum showed a singlet at 6.88 ppm. The identity of the complex obtained could be determined via single crystal X-ray structure determination, obtained via slow diffusion of pentane into a THF solution of complex 4. The resulting X-ray structure establishes the formation of an Ir-vinyl complex containing an unusual four-membered Ir-P-N-C ring, see Fig. 3.

The Ir–P–N–C ring is essentially flat, with a torsion angle ∠Ir1–P1–N1–C1 of –3.13°. The geometry of the metallacycle is very asymmetric, with bond angles of ∠P1–Ir1–C1: 69.21(9), ∠Ir1–P1–N1: 88.48(9), ∠P1–N1–C1: 100.26(19)° and ∠N1–C1–Ir1: 101.91(19)°. Compared to complex 3, the P–N bond lengths are slightly elongated (P1–N1 1.6535(13), P1–N1 1.717(3) Å for 3 and 4 respectively). The N1–S1 bond length of 1.653(3) Å clearly points toward an N–S single bond, while the C1–C2 bond length of 1.338(5) Å indicates a C–C double bond. To the best of our
knowledge only three complexes containing a four-membered M–P–N–C ring with an sp2 hybridized carbon atom have been reported in literature. This is the first example reported with iridium as well as the first structure that is generated from an alkynyl, making the vinyl fragment a unique exo-cyclic entity. Four-membered M–P–N–C rings wherein C is a divalent carbene are more common in literature, particularly with ruthenium. Alkyne activation likely proceeds by concerted metatllation–deprotonation after initial coordination of the π-system to IrIII, facilitated by Cl– dissociation in THF. Proton-transfer to the more basic sulfonamide nitrogen is favored over protonation of the S–O, but temporary formation of –OH as a kinetic intermediate can not be excluded.

Monitoring the unique conversion from 3 to this novel complex 4 by 31P{1H} NMR spectroscopy directly after addition of phenylacetylene at room temperature revealed the intermediary of another species (31P NMR: δ 33.1 ppm). In an attempt to characterize this complex, the reaction of phenylacetylene and complex 3 was monitored by 1H, 31P and 13C NMR spectroscopy at 0 °C. Signals at 102.70 (d, J = 6.4 Hz, Cquat) and 94.86 (s, Cquat), in the 13C{1H} NMR spectrum support the involvement of the initially anticipated IrIII(C≡CPh) species 5 in this reaction (Scheme 2).

Complex 4 is proposed to form via initial proton transfer from the phenylacetylene to the METAMORPhos backbone (generating 5), followed by a formal intramolecular anti-Markovnikov hydroamination onto the resulting acetylide species. This selective C–N bond formation, which occurs in an overall syn addition, would involve nucleophilic attack of the nitrogen onto the electrophilic β-carbon of the Ir(C≡CPh) species 5. To support this proposed mechanism, DFT calculations were performed (BP86, def2-TZVP); the energetically most favored obtained energy profile is displayed in Fig. 4 (see ESI† for comparison with experimental metric parameters). The combination of (3 + HCCPh) was used as reference point (0.0 kcal mol−1). Formation of Ir-acetylide complex 5 is slightly downhill by 1.5 kcal mol−1. From this observable intermediate, the most energetically favored pathway to 4 proceeds via initial proton transfer from the N–H of the ligand to the β-carbon of the acetylide through TS1, which is endergonic by 17.6 kcal mol−1. This generates intermediate Int (13.7 kcal mol−1), wherein the anionic ligand is only monodentate P-coordinated. The calculated HOMO and LUMO of this intermediate species support formulation as an electrophilic iridium(III)-vinylidene (Fig. 5). Subsequent nucleophilic attack of the nitrogen of the ligand onto the β-carbon of the vinylidene via TS2 (endergic by 18.3 kcal mol−1) generates complex 4, bearing a unique exo-cyclic vinyl unit. This product is exergonic by 6.7 kcal mol−1 relative to the starting materials. We were unable to find a transition state for the alternative concerted mechanism involving direct N–H syn-addition over the C≡C bond. The pathway involving protonation via a sulfone O–H was found to be slightly higher in energy (initial proton transfer step was endergonic by 18.6 kcal mol−1; see ESI† Fig. S1) relative to the described pathway. A solvation model (COSMO) did not affect the turnover-limiting step.

In conclusion, we have demonstrated the reactivity of IrIII piano-stool complexes with sulfonamidophosphine ligand 1H (METAMORPhos) for the heterolytic activation of alkynyl C–H bonds. The initially generated species 2, featuring monodentate P-coordination, reacts with exogenous base to generate complex 3, bearing a reactive P,O-coordinated METAMORPhos ligand. In the presence of terminal alkynes, the ligand is reprotonated via PhC≡C–H activation to generate acetylide compound 5. This intermolecular C–H activated species undergoes facile anti-Markovnikov hydroamination reaction in the coordination sphere of IrIII. This represents a novel reaction mode for this ligand class, making this a versatile design in the context of chemically non-innocent ligand reactivity. The resulting unique four-membered Ir-PNC metallacycle 4, featuring an exocyclic vinyl group, is structurally characterized and DFT calculations support the transient formation of an IrIII, vinylidene intermediate. The insights presented potentially provide an entry into selective intra- and intermolecular C–H activation protocols with, e.g., alkynes.

This research was funded by a TOP-grant from NWO-CW to J.N.H.R. The ApexII X-ray diffractometer at Utrecht University was funded by NWO-CW. We thank Ed Zuidinga for mass spectrometry measurements, Daniël L. J. Broere for providing MO figures and computational assistance, Prof. Dr Bas de Bruin for helpful suggestions regarding the DFT calculations and Dr Maxime Siegler for advice on X-ray crystallography.

Notes and references

‡ Crystallographic details, for 2; C29H34ClIrNO2PS, Fw = 795.77, orange needle, 0.63 × 0.33 × 0.16 mm3, triclinic, P1 (no. 2), α = 10.16597(16) Å,
b = 10.5116(3) Å, c = 15.5310(3) Å, α = 76.18(3), β = 78.361(3), γ = 80.796, \ V = 1569.58(6) Å³, Z = 2, D_M = 1.684 g cm⁻³, μ = 4.57 mm⁻¹. 22217 reflections were measured up to a resolution of (sin(θ/λ)_{max} = 0.65 Å). 7214 reflections were unique (R_int = 0.012), of which 7109 were observed \[[I > 2σ(I)\]]. 371 parameters were refined with no restraints. R_I = 0.0117/0.0297. R_F = 0.0120/0.0298. S = 1.005. 9.14 and 1.12 e Å⁻³. For 3: C_{40}H_{44}ClIrNO_{2}PS, F_w = 78.29, P. H. Dixneuf, S. de Boer, M. Kuil, K. M. Kubo, T. Baba, T. Mizuta and K. Miyoshi, Organometallics, 2013, 32, 3893–3898; K. A. Bunten, D. H. Farrar, A. J. Poe and A. J. Lough, Organometallics, 2000, 19, 3674–3682.


