Osmium-Mediated Direct C-H Bond Activation at 8-Position of Quinolines

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Supporting Information Placeholder

ABSTRACT: The metal-mediated direct C-H bond activation at 8-position of quinolines, which is the essential step for the functionalization of this bond, is promoted by the hexahydride $OsH_6(P^iPr_3)_2$. This complex activates quinoline and 2-, 3-, 6- and 7-methyl-quinoline to afford the classical trihydride derivatives $OsH_3\{\kappa^2\text{-}C^8,N\text{-}(quinolinyl)\}(P^iPr_3)_2$ and $OsH_3\{\kappa^2\text{-}C^8,N\text{-}(quinolinyl\text{-}n\text{-}Me)\}(P^iPr_3)_2$ (n = 2, 3, 6, 7), containing a four-membered heterometalaring.

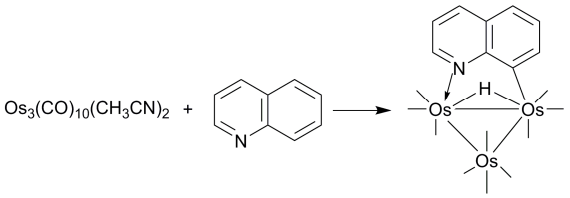
The C-H bond activation[1] is among the most relevant metal-mediated σ-bond activation processes due to its connection with the functionalization of inert C-H bonds[2] and as an intermediate step in the preparation of new materials.[3] A major goal is to control the selectivity of the process when C-H bonds of similar dissociation energies are present in the same substrate, in order to reduce the environmental impact. Particularly relevant is to achieve the regioselective C-H cleavage at unfavorable sites.

Quinoline is an important scaffold found in a wide range of natural products, with interesting biological activity, and in functional materials[4]. The functionalization of the positions of the nitrogen containing ring is easier than those of the homocyclic ring, [5] in particular the C-H bond at 2-position because of its weakness and the strengthens of the M-CN bond in the intermediates resulting from its activation.[6] In contrast to the C-H bond at 2-position, the functionalization of the C-H bond at 8-position, in the homocyclic ring, has been only achieved twice. In 2014, Steel, Marder, Sawamura and co-workers reported site selective C-H borylation of quinoline derivatives at this position by using a silica-supported phosphine-iridium system[7] whereas, in 2011, Chang and co-workers described a protocol for the regioselective direct arylation of quinolines at the 8-position employing a $Rh_2(OAc)_4(NHC)$ compound.[8] Given the dinuclear character of the catalyst precursor, they suggested the formation of bimetallic intermediates containing a bridge quinolinyl group, resulting from the N-coordination and C^8-H bond activation of the quinolines across the Rh-Rh bond of the catalyst. A similar type of addition had been previously documented by Rosenberg and co-workers to the metal cluster $Os_3(CO)_{10}(CH_3CN)_2$ (Scheme 1), during mechanistic study on the heterogeneously catalyzed hydrodenitrification of the heterocycles.[9] The observation that some mononuclear precursors also showed significant catalytic activity and regioselectivity led to Chang and co-workers to speculate that a mononuclear four-membered heterometalacycle could be also a plausible intermediate.[8] Although a few rings of this type are known,[10] the direct C-H bond activation at 8-position of quinolines promoted by a mononuclear species was unprecedented until now.

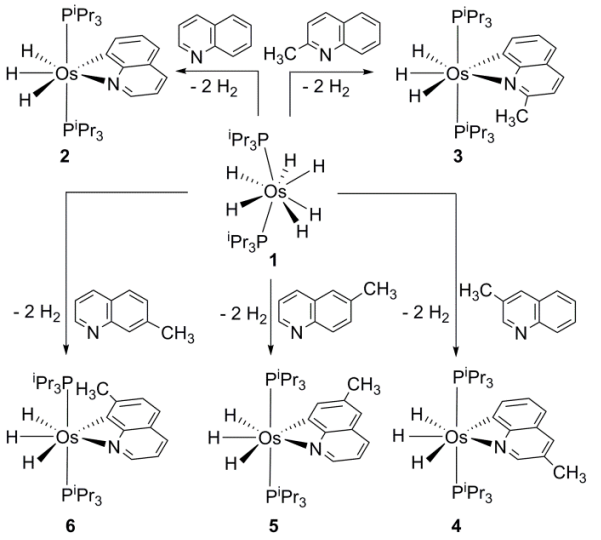
Saturated transition metal polyhydride complexes have the ability of losing molecular hydrogen to afford unsaturated species, which coordinate and subsequently activate σ-bonds. In agreement with this, the hexahydride complex $OsH_6(P^iPr_3)_2$ (**1**) has shown to be active for the cleavage of C-H bonds of a wide range of organic molecules.[11] In the search for the direct C-H bond activation at 8-position of quinolines, we have investigated the reactivity of **1** towards these heterocycles. In this communication, we report the first direct C-H bond activation at 8-position of quinolines, promoted by a mononuclear complex, which is important because gives a clue on the nature of the active species for this challenging reaction.

The reactions were carried out in toluene under reflux. Treatment of **1** with 1.0 equiv of quinoline, for 7 h, under these conditions led to classical trihydride $OsH_3\{\kappa^2\text{-}C^8,N\text{-}(quinolinyl)\}(P^iPr_3)_2$ (**2**), which was isolated as an orange solid in about 70% yied. The reaction is compatible with a methyl group at different sites of both rings of the substrate, including the adjacent position to the metalated carbon atom (C^7). Thus, the addition of 1.0 equiv of 2-, 3-, 6- and 7-methylquinoline to the toluene solutions of **1** affords the respective methyl-substituted derivatives $OsH_3\{\kappa^2\text{-}C^8,N\text{-}(quinolinyl\text{-}n\text{-}Me)\}(P^iPr_3)_2$ (n = 2 (**3**), 3 (**4**), 6 (**5**), 7 (**6**)), as orange solids, in 60-75% yield (Scheme 2).

Scheme 1. C^8-H Bond Activation of Quinoline Promoted by the Metal Cluster $Os_3(CO)_{10}(CH_3CN)_2$



Scheme 2. C^8-H Bond Activation of Quinolines Promoted by $OsH_6(P^iPr_3)_2$ (1)



The direct C-H bond activation at 8 position of the heterocycles was confirmed by means of the X-ray structures of **2** and **4**, which proved the formation of the four membered heterometalacycle (Figure 1). The coordination polyhedron around the metal center of both compounds can be rationalized as a distorted pentagonal bipyramid with the phosphines occupying axial positions. The metal coordination sphere is completed by the metalated heterocycle, with acts with C-Os-N bite angles of 65.7(5)° in **2** and 62.09(17)° and 62.52(16)° in **4**,[12] and the hydride ligands separated about 1.7 Å. The $^{31}P\{^1H\}$, $^{13}C\{^1H\}$ and the ^1H NMR spectra of **2-6** in toluene-d_8 are consistent with this ligand distribution. In agreement with the presence of equivalent phosphines, the $^{31}P\{^1H\}$ NMR spectra contain a singlet between 28 and 31 ppm whereas the C^8-metalated resonance appears as a triplet ($J_{C\text{-}P} \approx 8$ Hz) between 146 and 150 ppm, in the $^{13}C\{^1H\}$ NMR spectra. The ^1H NMR spectra at 203 K show three high field resonances at about -5.5, -13.1 and -13.9 ppm, in a 1:1:1 intensity ratio, as expected for three inequivalent hydride ligands. The signals at about -5.5 and -13.9 ppm coalesce between 233 and 243 K to afford a single resonance at temperatures higher than 243 K; Figure 2 shows the high field region of the spectrum of **2** as a function of the

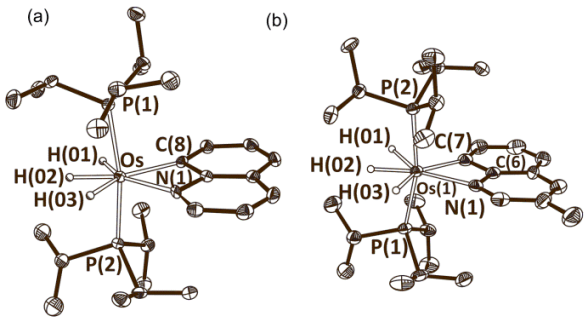


Figure 1. X-ray crystal structures of **2**(a) and **4**(b). The thermal ellipsoids are scaled at 50% probability level. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): **2**: Os-N(1), 2.238(6); Os-C(8), 2.145(8); **4**: Os(1)-C(7), 2.135(5), 2.141(5); Os(1)-N(1) 2.223(4), 2.234(4).

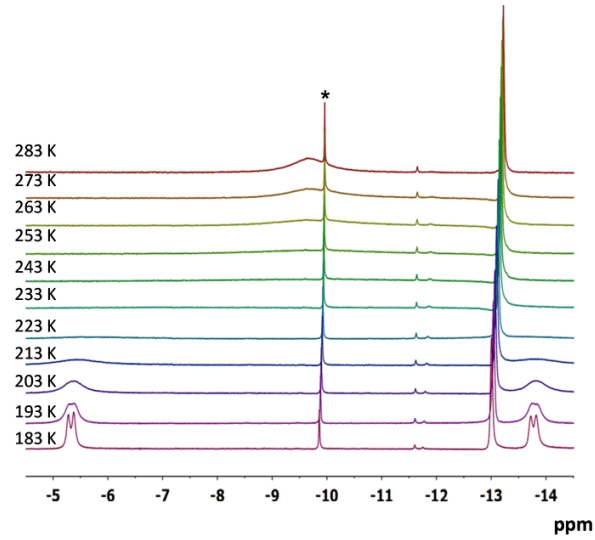


Figure 2. Variable temperature $^1H\{^{31}P\}$ NMR spectrum (400 MHz) in the high field region of complex **2** (* $OsH_6(P^iPr_3)_2$).

temperature. The behavior observed for these resonances is indicative of a thermally activated site exchange process involving the corresponding hydrides, which occurs with an activation energy of about 10 kcal·mol^{-1}. The exchange mechanism should imply Os-H stretching, H-H shortening and subsequent rotation of the resulting dihydrogen. So, the ^1H NMR spectra suggest that, from the two possible dihydrogen transition states, H_2 *trans* to C^8 and H_2 *trans* to N, one of them is more accessible than the other one. In fact, DFT calculations (B3LYP/(6-31g** + SDD)) have revealed that, from the two possible stereochemistries of $OsH\{\kappa^2\text{-}C^8,N\text{-}(quinolinyl)\}(\eta^2\text{-}H_2)(P^iPr_3)_2$ (**TS**), that with the dihydrogen ligand *trans* disposed to the metalated carbon atom (**TSa** in Figure 3; $d_{H\text{-}H}$ = 0.88 Å) is 7.9 kcal·mol^{-1} lower than that containing the coordinated hydrogen molecule *trans* to the nitrogen atom (**TSb**; $d_{H\text{-}H}$ = 0.97 Å). In addition, it should be mentioned that **TSa** only lies 11.9 kcal.mol^{-1} above **2**; a difference that is consistent with the activation energy of the exchange.

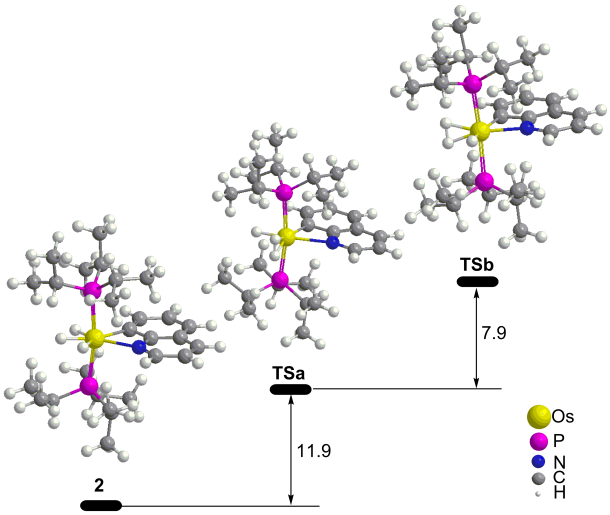


Figure 3. Calculated structures of **2**, **TSa** and **TSb** using the DFT method (complex, Gibbs energy in kcal.mol^{-1}).

The ability of **1** for activating the C-H bond at 8-position of quinolines is in contrast with the behavior previously reported for the dichloride-dihydride-osmium(IV) complex $OsH_2Cl_2(P^iPr_3)_2$[6a] and the dichloride-hydride-iridium(III) compound $IrHCl_2(P^iPr_3)_2$[6c] which activate the C-H bond at 2-position of the heterocycles[13] to finally afford C^2-quinolinylidene derivatives bearing an NH wingtip. The absence of π-donor ligands in **1**, such as chloride, which stabilize the metal quinolinylidene bond can explain this difference in behavior. Recent DFT calculations, using AIM and NBO methods, have shown that Os-NHC bonds tolerate a significant π-backdonation from the metal to the p_z atomic orbital of the carbene carbon atom. The π accepting capacity is higher than those of the aryl groups and phosphine ligands.[14] Although complex **1** promotes the activation of the NC-H bond of 2-methyl-pyridine,[15] the C-H bond activation at 2-position of quinoline and methyl-quinolines does not take place even when the 8-position is protected with a methyl group. In that case, the $C(sp^3)$-H bond activation of the methyl substituent of the heterocycle is preferred over the C^2-H activation.[16]

The reducing character of osmium also appears to be determinant for the C-H bond activation at 8-position of the quinolines. Thus, in contrast to **1**, polyhydrides of oxidizing second row metals, such as the rutenium counterpart $RuH_2(\eta^2\text{-}H_2)_2(PCy_3)_2$[17] and the molybdenum-tetraydride $MoH_4(PMe_3)_4$,[18] undergo η^6-heterocyclic coordination to subsequently hydrogenate the ring.[19]

In conclusion, the hexahydride complex $OsH_6(P^iPr_3)_2$ promotes the direct C-H bond activation at 8-position of quinoline and methylquinolines. The absence of π-donor ligands in the coordination sphere of the metal center and the reducing character of the metallic element appear to be determinant factors for the success of this metal-mediated C-H bond activation, which is essential for performing the challenging direct functionalization at 8-position of quinolines.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures, analytical data of compounds, crystallographic data (CCDC 1452609 (**2**) and 1452610 (**4**), and details of DFT calculations (PDF)
Cristallographic data for compounds **2** and **4** (CIF)
Cartesian coordinates of calculated compounds (XYZ)

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Notes

Any additional relevant notes should be placed here.

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