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 OsH₆(PiPr₃)₂. This complex activates quinoline and 2-, 3-, 6- and 7-methyl-quinoline to afford the classical trihydride derivatives OsH₃{κ₂-C₈,N-(quinolinyl)}(PiPr₃)₂ and OsH₃{κ₂-C₈,N-(quinolinyl-n-Me)}(PiPr₃)₂ (n = 2, 3, 6, 7), containing a four-membered heterometalaring.

The C-H bond activation is among the most relevant metal-mediated σ-bond activation processes due to its connection with the functionalization of inert C-H bonds and as an intermediate step in the preparation of new materials. 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. The functionalization of the positions of the nitrogen containing ring is easier than those of the homocyclic ring, 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. In contrast to the C-H bond at 2-position, the functionalization of the C-H bond of quinoline 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 whereas, in 2011, Chang and co-workers described a protocol for the regioselective direct arylation of quinolines at the 8-position employing a Rh₂(OAc)₄(NHC) compound. Given the dimeric character of the catalyst precursor, they suggested the formation of a metalloid intermediate containing a bridge quinolinyl group, resulting from the N-coordination and C₈-H bond activation of the quinolines across the Rh-Rh bond. A similar type of addition had been previously documented by Rosenberg and co-workers to the metal cluster Os₃(CO)₁₀(CH₃CN)₂ (Scheme 1), during mechanistic study on the heterogeneous catalyzed hydrodenitrification of the heterocycles. 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. Although a few rings of this type are known, 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 OsH₆(PiPr₃)₂ (1) has shown to be active for the cleavage of C-H bonds of a wide range of organic molecules. 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 OsH₃{κ₂-C₈,N-(quinolinyl)}(PiPr₃)₂ (2), which was isolated as an orange solid in about 70% yield. 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. 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 OsH₃{κ₂-C₈,N-(quinolinyl-n-Me)}(PiPr₃)₂ (n = 2 (3), 3 (4), 6 (5), 7 (6)), as orange solids, in 60-75% yield (Scheme 2).

Scheme 1. C₈-H Bond Activation of Quinoline Promoted by the Metal Cluster Os₃(CO)₁₀(CH₃CN)₂.
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 heterometalacyle (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, and the hydride ligands separated about 1.7 Å. The 31P{1H}, 13C{1H} and the 1H NMR spectra of 2-6 in toluene-d₈ are consistent with this ligand distribution. In agreement with the presence of equivalent phosphines, the 31P{1H} NMR spectra contain a singlet between 28 and 31 ppm whereas the C 8-metalated resonance appears as a triplet (J C-P ≈ 8 Hz) between 146 and 150 ppm, in the 13C{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 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, H₂ trans to C₈ and H₂ 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(κ²-C₈,N-(quinolinyl))(η⁶-H₂)(PPr₃)₂ (TS), that with the dihydrogen ligand trans disposed to the metalated carbon atom (TSa in Figure 3; dH-H = 0.88 Å) is 7.9 kcal mol⁻¹ lower than that containing the coordinated hydrogen molecule trans to the nitrogen atom (TSb; dH-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.
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 OsH₂Cl₂(P₂Pr₃)₄ and the dichloride-hydride-iridium(III) compound IrHCl₂(P₂Pr₃)₄, which activate the C-H bond at 2-position of the heterocycles to finally afford C₂-quinolinylidene derivatives bearing an NH wingtip. The absence of 8-nor 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 π 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 the quinolines is hindered by the presence of the methyl group. In that case, the C(sp³)-H bond activation of the methyl substituent of the heterocycle is preferred over the C₂-H activation.16

In conclusion, the hexahydride complex OsH₂(P₂Pr₃)₄ promotes the direct C-H bond activation at 8-position of quinoline and methylquinolines. The absence of 8-nor 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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REFERENCES

(12) The structure of 4 has two chemically but crystallographically independent molecules in the asymmetric unit.