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General Synthesis, First Crystal Structure, and Reactivity of Stable *o*-Quinone Methide Complexes of Cp*Ir

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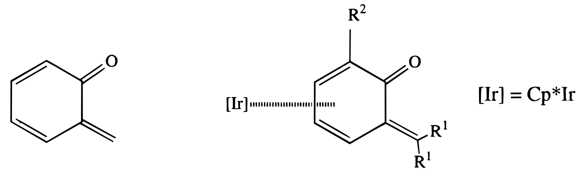
o-Quinone methides are reactive intermediates frequently used in organic synthesis.[1] They have been generated by thermal elimination of phenol Mannich bases, *o*-(α-hydroxalkyl)- or *o*-(α-methoxyalkyl)phenols, by dehydrohalogenation of *o*-(chloromethyl)phenols, by desilylation of disilylated *o*-hydroxybenzyl alcohols, by oxidation of *o*-alkylphenols, and very recently via laser flash photolysis of hydroxyl benzyl alcohols in aqueous solution.[2] *o*-Quinone methides act as heterodienes in inter- and intramolecular Diels−Alder [4 + 2] cycloadditions with electron-rich alkenes to give various substituted chromans and tetrahydrocannabinol analogues.[3] A spectacular demonstration of the potential of such cycloaddition is the total synthesis of carpanone.[4] *o*-Quinone methides are believed to act as key intermediates of several antitumor/antibiotic drugs.[5] However, despite this wide interest in *o*-quinone methides in organic and biological chemistry, examples of isolated simple *o*-quinone methides, i.e., those not bearing substituents on the exocyclic double bond, are scarce, and the parent compound (**1**) (Figure 1) has never been characterized, even in the form of a metal π-complex.[6] In fact, only two alkenyl-substituted *o*-quinone methide complexes are known [6a] and only one *p*-quinone methide complex, in which the metal is anchored by two strongly coordinating tertiary phosphine groups, is known.[6b] In contrast, here we report a general and unprecedented synthetic procedure to isolate and fully characterize a series of η^4-*o*-quinone methide complexes (**6**−**9**) (Figure 1), including the simplest *o*-quinone methide, obtained as an iridium complex [Cp*Ir(η^4-C_7H_6O)] (**6**). Further the molecular structure of one complex of this series was unambiguously identified by X-ray crystallography.



(**1**)

$R^1=R^2=H$; (**6**)
$R^1=H$, $R^2 = CH_3$; (**7**)
$R^1=CH_3$, $R^2 =H$; (**8**)
$R^1=CH_3$, $R^2=CH(CH_3)_2$ (**9**)

Figure 1.

Recently we have described a general procedure for *nucleophilic phenol functionalization*, promoted by the Cp*Ir moiety,[7] which allows efficient functionalization of tetralols and steroids.[8] Pursuing our research in this area, we discovered that oxo-η^5-dienyl iridium complexes with an alkyl group at C-2 undergo a regioselective deprotonation reaction at a benzylic position of the alkyl group with surprising ease to afford the related η^4-*o*-quinone methide complexes in quantitative yields (Scheme 1).

Thus, treatment of the oxo-η^5-dienyl iridium complexes **2**−**5** with NaOMe in methanol or more efficiently by tBuOK/CH_2Cl_2 for several hours at room temperature and subsequent reaction workup afforded the neutral η^4-*o*-quinone methide complexes **6**−**9**. Compounds **6**−**9** were obtained as yellow microcrystalline substances. All compounds were recrystallized from hexane and were obtained as analytically pure materials, in the solid state under argon. The infrared spectra of these complexes recorded in KBr displayed two bands in the area 1595−1615 cm^{-1} (s) and 1631−1643 cm^{-1} (m) similar to what was found for the one known *p*-quinone methide complex.[6b] Infrared data for *o*-quinone complexes were not reported.

The $^{13}C\{^1H\}$ NMR data obtained in toluene-d_8 for **6**−**9** at room temperature were consistent with the proposed structure for these *o*-quinone iridium complexes. For instance, the C═O group appeared around 185−195 ppm, the ═C at 130−141 ppm, and the free ═CR_2 (R = H; R = Me) group resonated around 103−110 ppm. The proposed structures for complexes **8**−**9** were also confirmed by 2D experiments; for instance, the 2D $^1H-^1H$ COSY spectrum of **6** recorded in benzene-d_6 displayed two doublet of doublets and two doublet of triplets centered at 3.61, 3.90, 4.62, and 4.77 ppm, respectively, and are attributed for the dienone C−H protons, while the methylene protons (═CH_2) appeared as pair of doublets at 4.39 ppm (J_{H-H} = 2.5 Hz) and 5.45 ppm, respectively. We also note the presence of a singlet centered at 1.62 ppm attributed to the η-Cp* methyl protons.

Despite the high solubility of **6**−**9** even in hexane, crystals of complex **9** suitable for an X-ray single-crystal analysis were obtained from hexane.[9] The structure of **9** (Figure 2) clearly shows the loss of aromaticity in the six-membered ring and coordination of Cp*Ir to four ring carbons. Loss of aromaticity is manifested by the irregularity of the C−C bond distances; the length of the uncoordinated bond C(1)−C(2) = 1.49(1) Å, while the C(2)−O(1) bond distance is 1.23(1) Å, which is characteristic of a C═O double and in the range expected for substituted quinones. Furthermore, the C(1)−C(7) bond distance is 1.34(1) Å, slightly shorter than that reported for the C═C double bond

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(9) Yellow crystal, $C_{22}H_{31}OIr$, fw = 503.7, triclinic $P\bar{1}$, a = 10.238(3) Å, b = 11.674(2) Å, c = 18.209(9) Å, α = 72.72(3)°, β = 75.24(3)°, γ = 87.50(2)°, V = 2008 (1) Å^3, Z = 4, D = 1.67 g/cm^3, T = 22 °C, R (R_w) = 0.042 (0.0487). Details of the crystallographic determinations are provided in the Supporting Information.

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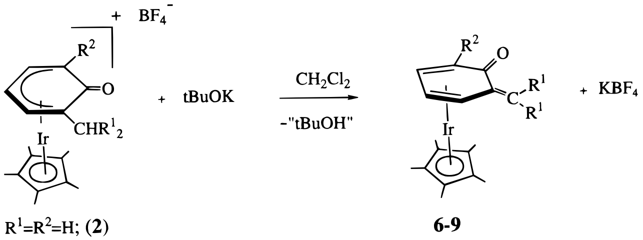
Scheme 1



$R^1=R^2=H$; (**2**)
$R^1=H$, $R^2 = CH_3$; (**3**)
$R^1=CH_3$, $R^2 =H$; (**4**)
$R1=CH_3$, $R^2=CH(CH_3)_2$ (**5**)

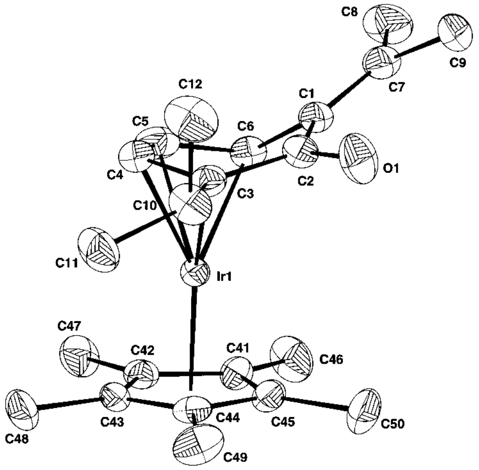
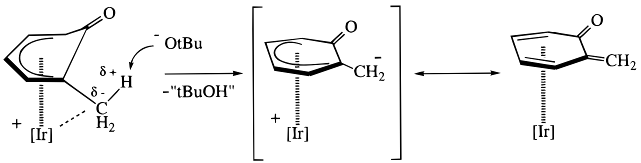


Figure 2. Ortep view of molecule **9** with thermal ellipsoids at 30% probability; one of the two independent molecules is being depicted. The hydrogen atoms are omitted for clarity. Selective bond distances (Å) and angles (deg): C(1)−C(2) = 1.49(1), C(2)−C(3) = 1.48(1), C(3)−C(4) = 1.44(1), C(4)−C(5) = 1.43(1), C(5)−C(6) = 1.42(1), C(1)−C(6) = 1.46(1), C(1)−C(7) = 1.34(1), C(2)−O(1) = 1.23(1), Ir(1)−C(3) = 2.193(8), Ir(1)−C(4) = 2.143(9), Ir(1)−C(5) = 2.122(9), Ir(1)−C(6) = 2.169(8), Ir(1)−C(41) = 2.179(8), Ir(1)−C(42) = 2.220(7), Ir(1)−C(43) = 2.246(7), Ir(1)−C(44) = 2.208(7), Ir(1)−C(45) = 2.180(8).C(2)−C(1)−C(6) = 109.7(7), C(1)−C(2)−C(3) = 114.7(7), C(2)−C(3)−C(4) = 121.4(8), C(1)−C(6)−C(5) = 120.6(8).

in duroquinone {cf. 1.352(8) Å}.[10] The distances from the metal to the centers of the π-bonded carbons are 1.76 Å for the quinonoide ligand and 1.84 Å for the η^5-C_5Me_5 ligand. The uncoordinated part of the quinonoid ligand is bent away from the metal, as the dihedral angle "hinge" across C(3)−C(6) is 33°. To our knowledge, this is the first X-ray structure of an *o*-quinone methide complex reported in the literature.

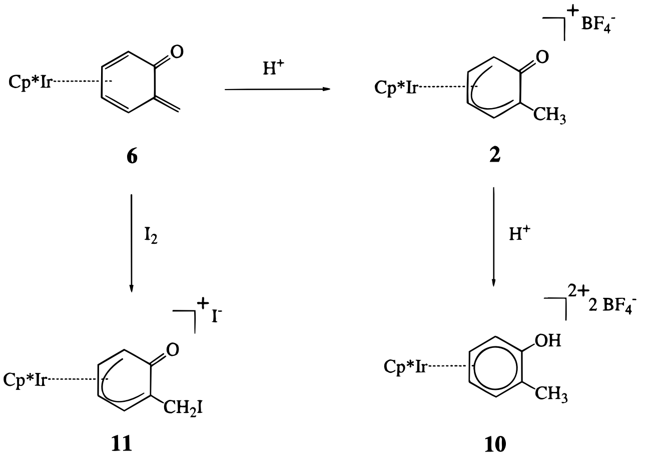
Deprotonation at the benzylic position of coordinated arenes to ruthenium and chromium have been reported in the literature.[11] However, in the coordinated oxo-η^5-dienyl unit, the scenario is completely different than the previous examples, because from our previous work[7,8] one would expect a nucleophilic attack at one terminus of the complexed η^5-dienyl ligand. We note that deprotonation succeeds even at relatively hindered isopropyl sites of **5**. This process may occur because of cationic nature of the Cp*Ir fragment which could enhance and favor the C−H abstraction. Moreover, although the X-ray structure of **6** shows no significant interaction of the Ir center with the exocyclic double bond, the transition state for the deprotonation might include some stabilization by the metal (Scheme 2).

Scheme 2



2 [Ir] = Cp*Ir **6**

Scheme 3



Protonation of complex **6** by $HBF_4 \cdot Et_2O$ afforded primarily the oxo-dienyl compound **2**; however, in the presence of an exess of $HBF_4 \cdot Et_2O$, the dicationic species **10** was obtained. It is noteworthy that reactivity of **6** toward strong electrophiles is very much different than free *o*-quinone methides, i.e., preferential protonation of the methylene group relative to the quinonoid oxygen atom. Oxidation of **6** by iodine did not lead to the free *o*-quinone methide ligand (**1**) instead the novel oxo-dienyl complex **11** was obtained (Scheme 3). Thus, starting from **2**−**5**, deprotonation followed by electrophilic addition may be a promising route to new oxo-dienyl complexes and polycyclic organic products.

In summary, an unprecedented general reaction leading to the formation of the first stable *o*-quinone methides is reported. This is only possible due to the use of the Cp*Ir moiety that stabilizes these well-known reactive intermediates by forming η^4-complexes. Complete analysis was performed on all complexes including the simplest *o*-quinone methides (**6** and **7**), which do not bear substituents at the exocyclic double bond. Preliminary reactivity of these novel η^4-*o*-quinone methide complexes shows potential for further synthetic transformation, which will be the subject of future reports. Furthermore, the X-ray molecular structure of one complex of this series is reported. Our method appears sufficiently general for the preparation of a wide variety of unprecedented stable *o*-quinone methide complexes, derivatives of important species in organic and biological chemistry.

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Supporting Information Available: Experimental details, spectral data, 2D $^1H-^1H$ and ^{13}C spectra of **6** and **7**, combustion analyses for all new compounds, X-ray crystallographic and structural data for complex **9** (11 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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