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Review

Organometallic chemistry in aqueous solution: Reactions catalyzed by water-soluble molybdocenes

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Contents

Abstract

The aqueous chemistry of molecules containing the Cp_2Mo^{2+} unit (referred to as "molybdocenes" in this paper) is reviewed. Aqueous molybdocenes are generated by hydrolysis of the Mo–X bonds in Cp_2MoX_2 complexes (X = halide or pseudo-halide) or by dissolving isolable dimers of the form $[Cp_2Mo(\mu\text{-}OH)_2MoCp_2{}^{2+}][OTs^-]_2$ in water. The nature of the molybdocene species in solution is pH dependent: $Cp_2Mo(H_2O)_2{}^{2+}$ has $pK_{a1} = 5.5$ and $pK_{a2} = 8.5$; thus, at neutral and physiological pH, $Cp_2Mo(OH)(OH_2)^+$ is the dominant monomer in aqueous solution. This monomer is in equilibrium with $[Cp_2Mo(\mu\text{-}OH)]_2{}^{2+}$ ($K_{eq} = 3.5 \times 10^{-2}$ M $\pm 1.3 \times 10^{-3}$ M at pD 3.5). $Cp_2Mo(OH)(OH_2)^+$ and $Cp_2Mo(H)(OH_2)^+$ (and the Cp′ analogs) are catalysts for a variety of reactions in aqueous solution, including H/D exchange reactions that proceed through C–H bond activation pathways, transfer hydrogenation reactions of ketones and aldehydes, nitrile hydration, and the hydrolysis of ethers, carboxylic esters, phosphate esters, and thiophosphinates. In these reactions, the molybdenum center acts as a Lewis acid, activating substrates toward intra- or intermolecular nucleophilic attack by a bound hydroxo ligand or a free water molecule. Mechanistic evidence suggests that the intramolecular hydration and hydrolysis reactions proceed via strained, four-membered ring intermediates.

Keywords: Catalytic hydration; Catalytic hydrolysis; Water-soluble metallocenes; *ansa*-Molybdocenes

1. Introduction

Water has traditionally not been used as a solvent in organometallic chemistry because the M–C bonds in organometallic complexes are frequently susceptible to hydrolysis. Depending on the organometallic complex, a variety of aqua, hydrido, hydroxo, and oxo products may be formed as a result of the reactions with water. However, not all organometallic complexes degrade when exposed to water, and over the past 15 years, aqueous organometallic chemistry has received increased attention. This chemistry has been well documented in a number of books and review articles [1,2]. Three main reasons may be given for the interest in water as a solvent for organometallic reactions. First, water is abundant, cheap, environmentally

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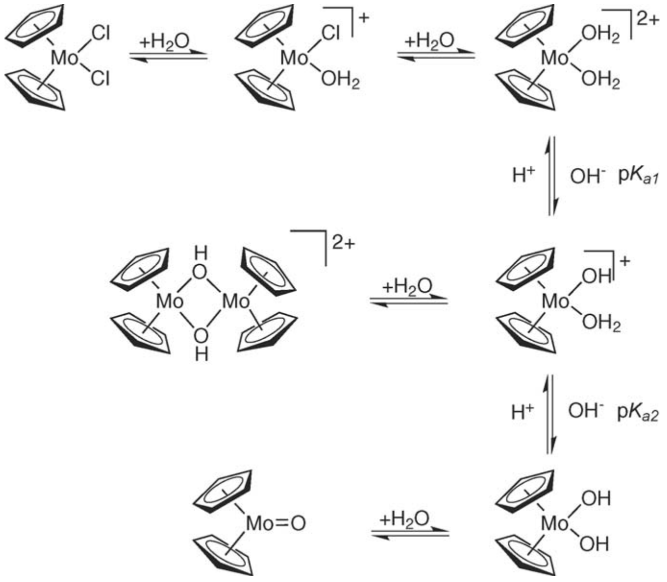
benign, and it has a high heat capacity. This is appreciated both in the laboratory as well as in industry [3], where organometallics are used as catalysts in a number of important reactions and processes [4–7]. Second, the use of organometallic catalysts in an aqueous phase may lead to easy workup procedures. For example, in aqueous biphasic reaction systems, catalysts and products can be easily separated [8]. The third promising aspect of aqueous organometallic chemistry is the possibility of finding reactions that outperform their analogs, or are even unprecedented, in organic solvents [9] (a classic example being the Ruhrchemie/Rhône-Poulence process for the production of butyraldehyde under biphasic conditions [10]).

The insolubility of organometallic complexes in water is often an important hurdle in doing aqueous organometallic chemistry. To deal with this problem, a variety of new water-soluble ligands have been synthesized [2,7,11,12]. When incorporated into metal complexes, these ligands impart water-solubility to the complexes. However, it is often overlooked that many organometallic complexes are intrinsically water-soluble. Among these compounds [13,14] are those containing aqua and hydroxo ligands in their coordination sphere such as $Cp'_2Mo(OH)(H_2O)^+$. These types of complexes are soluble by virtue of their ionic charge and their hydrogen-bonding ability through the aqua or hydroxo ligands.

Because of the emerging importance of water as a solvent in organometallic chemistry and because an extensive aqueous chemistry has developed for the $Cp'_2Mo(OH)(H_2O)^+$ complex, this paper reviews the aqueous chemistry of this molecule and that of its related molybdocene derivatives. Particular emphasis is placed on the homogeneous catalytic reactivity of molybdocene species and the pathways of these catalytic reactions. Initial investigations of the *ansa*-effect on the catalytic reactivity are also discussed. (Note that, as used in this review, molybdocene refers to the Cp_2Mo^{2+} unit and not just to Cp_2Mo^0.) The bioorganometallic chemistry of molybdocenes was recently reviewed and will not be covered here [15].

2. Molybdocenes in aqueous solution

Metallocenes of the group VI metals have received considerable attention since the first report of the Cp_2MCl_2 complexes ($Cp = \eta^5\text{-}C_5H_5$, M = Mo, W) by Cotton and Wilkinson in 1954 [16]. A vast number of theoretical, physicochemical, and chemical studies on molybdocenes have been carried out since then [17,18]. However, only a few of the early reports commented on the chemistry of the group VI metallocenes in water [19,20]. It was not until the discovery of the anti-tumor activity of metallocenes of the type Cp_2MX_2 (M = Ti, V, Mo; X = halide or pseudo-halide) that researchers began to focus on the aqueous chemistry of these species [21,22], and over the past 15 years, the aqueous chemistry of metallocenes containing Ti, Zr, Hf, V, Nb, Cr, and Mo has been explored in considerable detail. The hydrolysis chemistry of these compounds is complex, typically involving the formation of a number of dimeric and oligomeric species. The structure of the hydrolysis products is highly dependent on the pH and is often inferred only from titration studies. In most cases, hydrolysis of the coordinated halide or pseudo-halide ligands occurs first and affords aquated metallocene complexes, with OH or OH_2 ligands replacing X (Scheme 1). In a few cases, aqua and hydroxo complexes can be isolated by controlled hydrolysis of the metallocene precursors [23,24]. In the specific case of Cp_2MoCl_2, the first chloride dissociation is rapid, and by the time of complete dissolution [25], the $[Cl^-]/[Mo]$ ratio is already 1.2.



Scheme 1. Equilibria of the various molybdocene species in aqueous solution.

The dissociation rate of the second X^- from the metallocene is dependent on the metal but the reaction typically occurs in 5–45 min. For the metallocene dichlorides of Ti ($k_2 = 0.84\ h^{-1}$), Zr ($k_2 = 1.31\ h^{-1}$), and V ($k_2 = 1.73\ h^{-1}$), the dissociation rate constant (k_2) of the second chloride is much smaller than for Mo [26], for which the half-life for loss of the second chloride ligand was estimated to be 6.7 min [25]. This hydrolysis behavior is independent of X in Cp_2MoX_2, as X = NCS, F, Br, I, Cl, N_3, or OC(O)R all shows similar activity [27,28]. In the case of Cp_2MoCl_2, the pH of the aqueous solution drops to ∼3.5 during the hydrolysis due to the acidity of the coordinated H_2O ligand (Scheme 1) [25].

The other important hydrolytic process in aqueous metallocene chemistry is the loss of the cyclopentadienyl ligands. Table 1 gives an overview of metallocene M–Cp hydrolysis for different metals under a variety of conditions. Note that the rate of M–Cp hydrolysis is again pH dependent and varies significantly with the metal. Also note that molybdocene stands out from the other metallocenes in Table 1 in that it is surprisingly stable with respect to Cp hydrolysis. (In fact, if oxygen is excluded, no Mo–Cp hydrolysis can be detected in aqueous solutions of molybdocenes over a period of several weeks.) Thus, while hydrolysis and subsequent degradation of the Cp_2M core are observed with most metallocenes in aqueous solution, the molybdocene core (Cp_2Mo^{2+}) remains intact in water.

The behavior of bis(aqua)molybdocene is noteworthy in at least one other regard: it is the least acidic of the bis(aqua)metallocenes, with $pK_{a1} = 5.5$ and $pK_{a2} = 8.5$. In contrast, titanocene is the most acidic of the aqueous-stable metal-