Formation constants of $Ru^{II}(hedta)^-$ complexes of olefins and η^2-coordinated pyrimidines related to cytidine and uridine

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Abstract

The association constants for the formation of $Ru^{II}(hedta)L^-$, where L = an olefin or an η^2-coordinated pyrimidine nucleobase derivative of C or U, were determined for 16 ligand structures. The formation constants K_f are a sensitive function of the substituent of the α-carbon of the olefin unit. Effective K_fs range over 5 orders of magnitude (from $K_f = 7.51$, L = 3-deazauracil; $K_f = 6.33 \times 10^3$, L = 3-cyclohexen-1-methanol; to $K_f = 2.04 \times 10^6$, L = methyl vinyl ketone) depending on the electronic influence of the α substituents. π-Withdrawing groups such as a keto functionality increase K_f by 10^2 to 10^3 in magnitude. π-Donating units (R = $-NH_2$, $-OH$) reduce K_f by 10 to 10^2 in magnitude. Steric factors are of less importance for determining the overall K_f value. The sensitivity to electronic versus steric factors places Ru^{II} mid-range on a scale deduced previously by Tolman from low-oxidation state complexes of lower coordination number than $Ru^{II}(hedta)$: $Ni^0 > Pt^0 > Rh^I > Ru^{II} > Pt^{II} > Cu^I > Ag^I$. (The position of Ru^{II} is defined by the current study.) The combined influence of substituents and functionalities of uracil/uridine rings cancel each other; the net affinity ($K_f = 1.2 \times 10^3$, L = uridine) is virtually the same as a simple olefin without electronically active α substituents. This promotes η^2 coordination of uridine nucleobases to $Ru^{II}(hedta)^-$. The largest value of K_f for an olefin was found for methyl vinyl ketone, MVK. This olefin coordinates in the η^2 mode to all three stereochemical isomers of $Ru^{II}(hedta)^-$ as shown by the ^1H NMR spectrum. Two forms with the olefinic unit *trans* to the nitrogen, either the one substituted by the *N*-hydroxyethyl functionality or the nitrogen doubly substituted by glycinate units, provide unhindered coordination to MVK. The third isomer of $Ru(hedta)(MVK)^-$ is structurally more hindered and the coordinated ligand exhibits distinguishable H_a and H_b terminal MVK protons. Protons of the olefin region and the methyl group of MVK all exhibit large upfield ^1H resonance shifts upon coordination. The highest measured binding constant for $Ru(hedta)(MVK)^-$ parallels the highest stability for η^2 olefin complexes of Ru^{II} as determined by the $E_{1/2}$ values of $Ru^{III/II}(hedta)L^{0/-}$; ($E_{1/2} = 0.80$ V versus NHE for the MVK complex). It is shown, however, that K_f is not simply related to the $E_{1/2}$ values and K_f may be a function of changing solvation of olefins upon coordination.

Introduction

In spite of the importance of olefin coordination equilibria with metal centers to many catalytic industrial cycles [1], few quantitative studies of olefin complexation as a function of ligand structure have been performed. It is of particular interest to understand how substituents α to the olefin bond influence metal–olefin association constants (K_fs). Important studies of Tolman *et al.* [2] and Munakata *et al.* [3] have shown that an olefin affinity order follows the anticipated backbonding ability of the metal center. An order of several metals in lower oxidation states has shown backbonding influences with the sequence $Ni^0 > Pt^0 > Rh^I > Pt^{II} > Cu^I > Ag^I$ from their studies [2, 3]. Tolman concluded that resonance effects of α substituents (R) on the olefin bond are more important than their σ induction, and that electronic effects of the substituent greatly exceed steric effects of the R groups. The study by Tolman *et al.* emphasized trigonal Ni^0 complexes [2] while that of Munakata *et al.* examined three-coordinate Cu^I systems [3]. Other workers have also examined cases of coordination number less than six [4, 5]. Complexes of lower coordination numbers are predisposed to minimize steric effects and to emphasize electronic factors on metal–olefin K_f values.

In the present study we have found that the $Ru^{II}(hedta)(H_2O)^-$ complex undergoes association with olefinic units as in eqn. (1).

$$Ru^{II}(hedta)(H_2O)^- + L \overset{K_f}{\rightleftharpoons} Ru^{II}(hedta)L^- + H_2O \quad (1)$$

We recently reported the binding of styrenes by $Ru^{II}(hedta)^-$ [6]. The coordination in the η^2 mode at the olefinic site is readily detected by the upfield ^1H

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resonance shifts of olefinic protons or of the ^{13}C resonances [6, 7]. A characteristic $Ru^{III/II}$ half-wave potential in the range of 0.45 to 0.81 V is also observed when η^2 coordination of $Ru^{II}(hedta)^-$ occurs at an olefinic site [6–8].

A particularly important result is that $Ru^{II}(hedta)^-$ has the π-donating power sufficient to tamper with the aromaticity of pyrimidine nucleobases [8, 9]. We have shown that pyrimidine rings related to C (cytidine) and U (uridine) bind at the C-5–C-6 olefinic bond of these pyrimidines [8, 9]. The η^2 coordination of C and U derivatives occurs much in the manner of Harman and Taube's decorated arenes in which $Os(NH_3)_5^{2+}$ coordinates with dearomatization of the arene system [10–12]. We have observed that the nucleobase T (thymidine) fails to bind $Ru^{II}(hedta)^-$ in the η^2 mode [8] and that 100% of binding of T occurs by the more normal N-3 coordination [13–18]. A recent study, which is reported elsewhere [19], has shown that the halouracils and uridines (five-substituted by X=F, Cl, Br, I) all exhibit η^2 binding of these pyrimidine rings in competition with the N-3 coordination mode. The maximum yield of the η^2 isomer occurs for the Cl, Br and I derivative with *c.* 85% η^2 coordination and 15% N-3 bound $Ru^{II}(hedta)L^-$ complexes. This study shows that the absence of coordination by the T base is of electronic, and not steric origin [19].

There is a number of reasons related to both the potential uses of $Ru^{II}(hedta)(olefin)^-$ complexes and $Ru^{II}(hedta)(nucleobase)^-$ complexes in catalysis and medicine that would make a study of olefinic binding constants of these species a valuable set of data. In this report we present a study of the formation constants of sixteen ligands which bind in the η^2 mode with $Ru^{II}(hedta)^-$. The K_f values have been determined and an examination of the influence of steric and electronic factors is described.

Experimental

Reagents

$Na[Ru(hedta)(H_2O)]\cdot 4H_2O$ was synthesized and characterized as reported previously [20]. The $Ru^{II}(hedta)(H_2O)^-$ complex was obtained from the same synthesis. All ligands were obtained from Aldrich and used without further purification.

Manipulations

Solutions of $Ru^{II}(hedta)(H_2O)^-$ were prepared at the desired concentrations, such as 3 to 5×10^{-3} M for electrochemical studies, by weighing samples of the Na^+ salt which were dissolved in pipetted volumes of water. The solutions were purged with Ar gas which was prescrubbed through Cr(II) gas cleaning towers. The $Ru^{II}(hedta)(H_2O)^-$ solutions were treated with Zn/Hg for 30 min to assure remove of any trace contaminants of Ru^{II} salts via air oxidation of the stored $Na[Ru(hedta)(H_2O)]\cdot 4H_2O$ solids. These were kept in a vacuum oven except during the weighing periods. Weighed amounts of ligands were added to the Ar purged $Ru^{II}(hedta)(H_2O)^-$ solution in flasks which were sealed by rubber septa. The neck and septa were further sealed with several layers of parafilm to inhibit oxygen leakage into the Ru^{II} solutions. In order to obtain solutions at equilibrium, the $Ru(hedta)(H_2O)^-$/ligand solutions were stirred magnetically for 18 h at 22 °C. Samples were also prepared at 3×10^{-2} M by similar procedures at 1:1 ratio for study by ^1H NMR. Spectra were obtained in D_2O solutions using HOD or an internal free ligand resonance as a reference. Spectra were recorded at 300.13 MHz or 500.13 MHz on Bruker 300AF and 500AF NMRs at fields of 70.46 and 117.4 kG. Techniques were applied as reported in prior publications from these laboratories [7, 8]. The formation of η^2 olefin and pyrimidine nucleobases was confirmed by appropriate ^1H resonance splitting patterns and shifts relative to free ligand values. Electrochemical measurements as a function of time showed that a constant distribution between the free $Ru^{II}(hedta)(H_2O)^-$ and $Ru^{II}(hedta)(olefin)^-$ species is obtained within the 18 h equilibration period. All transfers were carried out under Ar using gas tight syringe techniques or by flowing solutions under Ar pressure through teflon fine-bore tubing. Solutions for equilibrium studies were prepared at $Ru^{II}(hedta)(H_2O)^-$:ligand ratios of 1:1, 1:4, 1:10 and 1:50 for evaluation by the DPP method described below.

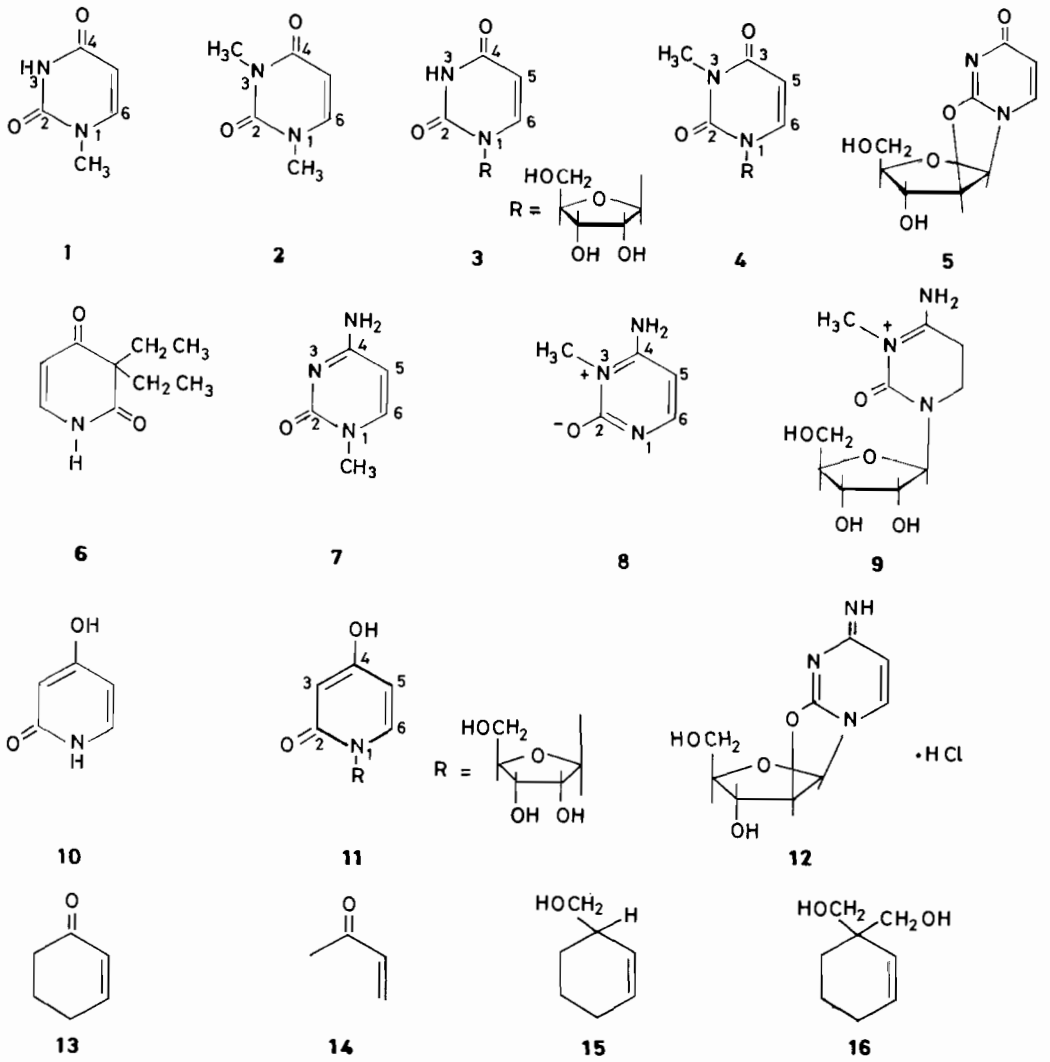
Electrochemical measurements

$Ru^{III/II}$ half waves for the $Ru^{II}(hedta)(olefin)^-$ complexes were measured under Ar with an IBM EC 225 voltammetric analyzer using the standard three-electrode assembly. Standardization with $Ru(NH_3)_6Cl_3$ was as reported previously from these laboratories [21]. Sweep rates of 50 mV/s were used for cyclic voltammetry (CV) and 40 mV/s for differential pulse polarography (DPP). A stepping voltage of 50 mV was used for DPP. Measurements were performed at a glassy carbon electrode versus a sodium chloride saturated calomel electrode reference and a shiny Pt auxiliary electrode. Measurements were made under Ar at 22 °C in 0.10 M NaCl as the electrolyte. Procedures matched those of prior studies [6–9, 21].

Results and discussion

η^2-Formation constants

The $Ru^{III/II}(hedta)(H_2O)^{0/-}$ couple exhibits its $E_{1/2}$ value at 0.00 V versus NHE at 22 °C, μ=0.10 NaCl



[7]. When samples at equilibrium according to eqn. (1) are analyzed by the CV/DPP technique, the free $Ru^{II}(hedta)(H_2O)^-$ is readily detected by this wave. The η^2-bound complexes exhibit $E_{1/2}$ values between 0.45 and 0.81 V versus NHE. Integration of the areas under the DPP waves allows the evaluation of the concentrations of $Ru(hedta)(H_2O)^-$ and the η^2-coordinated $Ru(hedta)(olefin)^-$ species from the total Ru^{II}. The amount of free ligand remaining in solution was calculated by mass balance from the total Ru^{II}:free ligand added ratio. These concentrations were used in the evaluation of an effective K_f for each complex from the concentration definition of K_f. Multiple trials showed that the reproducibility in the value of K_f was within $\pm 3\%$ from sample to sample; the cumulative error of taking ratios of three numbers sets a limit of $\pm 6\%$ on the final recorded values. The measured effective K_f values were obtained for three classes of olefinic complexes: (i) water soluble common olefins which bind in the normal metal–olefin η^2 coordination, (ii) η^2-bound complexes related to the nucleobase uridine (U), (iii) η^2-bound complexes related to the nucleobase cytidine (C). The measured K_f and the $Ru^{III/II}$ half-wave potential for the η^2 forms of the $Ru^{II}(hedta)L^-$ complexes of this report are given in Table 1. The ligand structures are shown in the associated chart together with a matching ligand number to facilitate reference.

There are three structural isomers which are possible for the pentadentate coordination of the $hedta^{3-}$ ligand with Ru^{II}. These are diagrammatically shown as **1–3**.

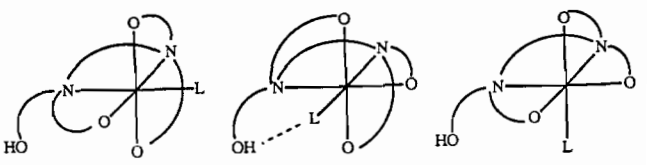
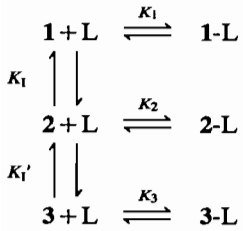


TABLE 1. Constants of the formation of $Ru^{II}(hedta)^-$ complexes with the olefinic ligands

Complex	Structure number	K_f	$E_{1/2}$
Ru^{II}(hedta)(1-methyluracil)	1	2.81×10^3	0.62
Ru^{II}(hedta)(1,3-dimethyluracil)	2	2.04×10^3	0.63
Ru^{II}(hedta)(uridine)	3	1.29×10^3	0.61
Ru^{II}(hedta)(3-methyluridine)	4	1.01×10^3	0.62
Ru^{II}(hedta)(O2,2'-cyclouridine)	5	1.76×10^3	0.72
Ru^{II}(hedta)(pyrithyldione)	6	2.05×10^3	0.65
Ru^{II}(hedta)(1-methylcytosine)	7	265	0.62
Ru^{II}(hedta)(3-methylcytosine)	8	422	0.71
Ru^{II}(hedta)(3-methylcytidine)	9	114	0.64
Ru^{II}(hedta)(3-deazauracil)	10	7.51	0.64
Ru^{II}(hedta)(3-deazauridine)	11	9.75	0.66
Ru^{II}(hedta)(cyclocytidine)	12	324	0.81
Ru^{II}(hedta)(2-cyclohexene-1-one)	13	4.68×10^5	0.70
Ru^{II}(hedta)(methyl vinyl ketone)	14	2.04×10^6	0.80
Ru^{II}(hedta)(3-cyclohexen-1-methanol)	15	6.33×10^3	0.45
Ru^{II}(hedta)(3-cyclohexen-1,1-dimethanol)	16	2.00×10^3	0.45

Ru^{II}(polyaminocarboxylate) aqua complexes are known to interconvert on a time-scale which promotes broadening of the glycinato rings in the ^1H NMR spectra [23, 24]. Rapid exchange of the more labile ions (Zn^{II}, Cd^{II}, Hg^{II}, Tl^{I}, Al^{III}) which promotes scrambling and isomerization of the polyaminocarboxylate complexes is also well-known [25]. Dissociation of carboxylate donors from $(NH_3)_5Ru^{2+}$ is rapid [26] and $Ru^{II}(edta)^{2-}$ and $Ru^{II}(hedta)^-$ species are even more labile [27]. The ^1H NMR broadening exhibited by the glycinato resonances for the pentadentate $Ru^{II}(edta)(H_2O)^{2-}$ systems shows that processes which equilibrate isomers **1–3** are rapid compared to the 18 h period required to achieve olefin ligand substitution and equilibrium [6–8]. The effective equilibrium represented by eqn. (1) is therefore somewhat more complex and can be written as in Scheme 1 where the symbols **1**, **2**, **3** refer to the isomers of the aqua species and **1**-L, **2**-L, **3**-L refer to the olefin ligated products.

It is anticipated on the basis of atom size for Ru^{II} and the lesser ring strain of axially coordinated glycinato groups compared to in-plane glycinato units that isomers **1** and **2** will have nearly equal population whereas **3** should be less favored [28–31]. The effective K_f value will be equal to $K_1\alpha_1+K_2\alpha_2+K_3\alpha_3$ where α is the fractional abundance of each isomer in the total $Ru(hedta)(H_2O)^-$ pool.



Scheme 1.

All three isomers have been detected by ^1H NMR for only the methyl vinyl ketone complex (MVK). Isomer **3** is sterically hindered for most ligands as described later in the text. Isomers **1** and **2** are sterically similar in terms of spacial availability at the coordination site, number of axial and equitorial rings and having an NO_3 donor face with a *trans* N donor with respect to the ligand L. These two isomers are assumed to have nearly identical affinities for L ($K_1\cong K_2$) on both steric and electronic grounds. In related studies of the $Ru^{II}(Me_2edda)$ complex which favors a structure similar to **3**, we have observed no η^2 coordination of pyrimidine or olefins as large as 2-cyclohexane-1-one without the switch of an in-plane glycinato group into an axial position [22]. This opens a site similar to the aqua position of **1** and **2**. Thus for most larger olefins $K_3\cong0$. In the case of methyl vinyl ketone ^1H NMR data show that $K_1\alpha_1{:}K_2\alpha_1{:}K_3\alpha_3$ are in the ratio of 2.59:2.29:1.00. In only two previous cases (3Me-C and 3Me-U) has more than one species been observed upon coordination with $Ru(hedta)(H_2O)^-$ [8]. In these cases two isomers of nearly equal abundance are observed. This is consistent with binding to either **1** or **2** with nearly equal binding constants, but with $K_3\cong0$. This further implies $\alpha_1\cong\alpha_2$ as would be predicted on the basis of structural factors [31]. Therefore $\alpha_1K_1\cong\alpha_2K_2$.

The ability of $Ru(hedta)^-$ to bind olefins which are small enough to ligate all three isomers is probably dominated by the overall N_2O_3 electronic environment of the Ru^{II} center and not by steric effects as supported by general conclusions from this work. In order to obtain an estimate of the relative aqua isomer distribution, we will assume $K_1=K_2=K_3$ for the MVK com-

plex. The observed distribution of products for the three MVK isomers implies, $\alpha_1 \cong 0.44$ $\alpha_2 \cong 0.39$ and $\alpha_3 \cong 0.17$. This leads to reasonable conclusions. The value of $K_1 \cong 0.9$ (e.g. α_2/α_1) is in good agreement with what is anticipated on similar structural energetics for isomers **1** and **2**. The estimate of $K_1' = 0.4$ (e.g. α_3/α_2) is smaller than K_1. It is also properly smaller than the value of $K_1' = 2.0$ found for $Co(edta)Br^{2-}$ [28] as predicted for the larger Ru^{II} center [31]. For all the other ligands reported in Table 1, their true binding constants will become $(K_f/0.83) = 1.20\ K_f$. Since this means that all the other constants of Table 1 are multiplied by a factor of 1.20, we have adopted the policy of comparing raw effective binding constants as deduced from electrochemical data. The influences which we have observed that are of chemical importance change the effective K_f by factors of 10 to 10^3, not by small changes in the magnitude of $\alpha_1 + \alpha_2$.

The results are in agreement with Tolman's observations on metal–olefin complexes of lower coordination member. Electronic influences of R dominate steric factors for either regular olefins or pyrimidine nucleobase-related rings with $Ru^{II}(hedta)^-$. Minor changes of less than a factor of 4.5 in K_f are involved in constraining the olefinic binding site in a cyclic versus straight chain structure (compare K_fs for methyl vinyl ketone versus 2-cyclohexene-1-one; ratio of K_fs = 4.36). The influence of an unhindered olefinic region is not substantially perturbed by the presence of a branched moiety at the α carbon (compare 3-cyclohexen-1-methanol versus 3-cyclohexene-1,1'-dimethanol, K_f ratio = 3.17) A major influence is detected when an α-keto group or an α-amino group is present adjacent to the olefin bond. An α withdrawing keto oxygen raises K_f *c.* 75 to 325-fold; a π-donating α-amino group or α-hydroxyl group decreases K_f *c.* 100 to 200-fold. These influences are seen in the comparison of K_fs for complexes of methyl vinyl ketone and 2-cyclohexene-1-one with 3-cyclohexen-1-methanol and 3-cyclohexene-1,1'-dimethanol. The presence of a π-donating nitrogen within the pyrimidine ring effectively cancels the withdrawing influence of an α-keto group (compare 1-methylcytosine and dimethyl uracil with 3-cyclohexen-1,1'-dimethanol). The presence of a ribose moiety at N-1 of either the uracil/uridine series or the cytosine/cytidine series shows little steric influence. Only slightly larger K_fs (between K_f ratios of 2.81 to 1.71) are observed for uracil/uridines and 2.32 for cytosine/cytidines. Therefore the large bulky ribose functionality does not inhibit coordination of the η^2 forms for derivatives of C and U.

The sensitivity of $Ru^{II}(hedta)(olefin)^-$ complexes to steric versus electronic factors places Ru^{II} mid-range on Tolman's metal π-donor order, between Rh^I and Pt^{II} [2, 3]. The combined influence of the internal ring nitrogen at N-1 and the presence of the α-keto group at C-4 in uracils/uridines is such that the uracil binding K_fs (*c.* 2.0×10^3) are within a factor of 3 of olefins lacking electronically active substituents. The doubly donating influence of an internal N-1 donor and an exo C-4 donating amino group for the cytosine/cytidine series results in a lower binding constant than for simple olefins. It is also notable than the binding constant does not directly parallel the $E_{1/2}$ value. The highest $E_{1/2}$ values are for complexes of cyclocytidine (0.81 V) and methyl vinyl ketone (0.80 V). These complexes exhibit K_f values of 3.24×10^2 and 2.04×10^6 which are near the lower and upper limits of the K_f range. This suggests that there can be major influences on the difference in solvation of the free ligand and complexed ligand which contribute to K_f, but which have much less influence on the $E_{1/2}$ value, a parameter measuring only the stabilizing influence of the olefinic unit on Ru^{II} versus Ru^{III}. Solvation of the two oxidation states of the $Ru^{III/II}(hedta)L^{0/-}$ complexes may not be all that different, given the requirements of each ligand to perturb the water structure as it projects away from the Ru(hedta) center. But solvation changes as the complex is assembled from $Ru^{II}(hedta)(H_2O)^-$ and each free L can strongly influence K_f, particularly if making a charged complex from a hydrophobic olefin. Releasing solvent molecules from the frozen out structure around the hydrophobic group upon coordination with $Ru^{II}(hedta)^-$ could reduce the total number of bound waters, increasing ΔS of formation and aiding the complexation process. The more solvated derivatives of C and U would not benefit as greatly as the regular olefinic units.

Methyl vinyl ketone complex

A complete discussion of the ^1H NMR spectra of all sixteen complexes is outside the scope of the present report. We have provided detailed treatment of the ^1H NMR and ^{13}C NMR spectra of key complexes of the uracil/uridine series and the cytosine/cytidine series in our prior reports on η^2 coordination [8, 9, 19]. Since the methyl vinyl ketone (MVK) ligand yielded the highest effective binding constant ($K_f = 2.04 \times 10^6$), its coordination behavior is deemed of special interest for the series of simple olefinic complexes described in Table 1. The 500 MHz ^1H NMR spectrum for the CH_3 region and the shift region above HOD is shown in Fig. 1 at 1:1 stoichiometry. It is clear from the three distinct methyl singlets at 2.26, 2.12 and 1.96 ppm, that there are three different isomers **1–3** of $Ru(hedta)(MVK)^-$ in solution at 22 °C which differ in the modes of glycinato coordination of the $hedta^{3-}$ ligand.

By using 5-fluorouridine (5-FU) we have shown elsewhere that only isomers **1** and **2** contribute to the

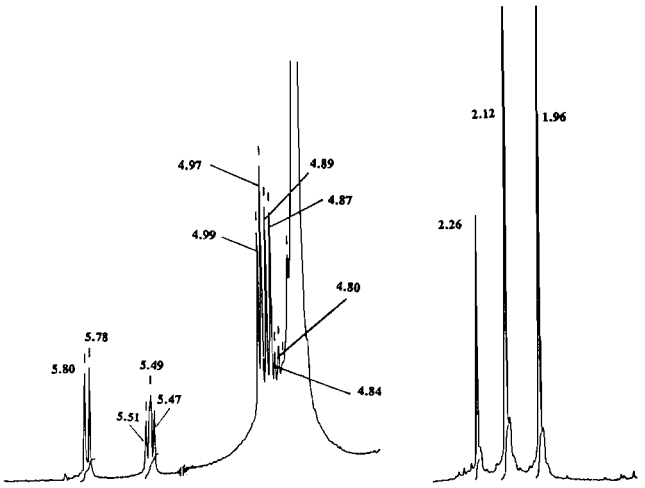
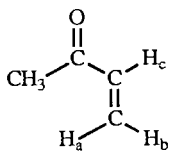


Fig. 1. 500 mHz ^{1}H NMR spectrum of Ru^{II}(hedta)(MVK) in the methyl region and region downfield of HOD.

coordination of 5-FU with Ru^{II}(hedta)$^-$ [19]. We have synthesized the dimethyl derivative of *N,N'*-ethylenediamminediacetate and prepared its Ru^{II}-(Me_2edda)$(H_2O)_2$ complex. The full disclosure of the chemistry of Ru^{II}(Me_2edda) will be presented elsewhere [22]. However, for the purposes of this report it is of interest that Ru_2(Me_2edda) is similar to structure **3**, but it lacks the axial carboxylate donor of Ru^{II}(hedta)$^-$ in isomer **3**. Ru^{II}(Me_2edda) does not bind 1,3-dimethyluracil [22]. It does, however, bind smaller olefins including MVK [22]. Thus, the evidence from prior work and the Ru(Me_2edda) system provides evidence that all three structures of Ru^{II}(hedta)L$^-$ may exist for Ru^{II}(hedta)(MVK)$^-$. This is consistent with the presence of three isomers of Ru^{II}(hedta)(MVK)$^-$ in abundance of 17.4%, 44.1% and 38.6% corresponding to the ones with CH_3 singlets at 2.26, 2.12 and 1.96 ppm, respectively. The areas of the methyl protons match up with sets of doublets in the region downfield of HOD. These are the olefinic protons of MVK:



The set for CH_3 $\delta = 1.96$ matches with doublets at 5.80; 5.78 ppm (area 1) and 4.93; 4.91 ppm (area 2) which are shown by decoupling to be interconnected. The CH_3 with $\delta = 2.12$ is connected with a doublet at 5.51, 5.49 (which is overlapped with another unrelated doublet at 5.49; 5.47 ppm) and the larger doublet at 4.99; 4.97 ppm. The CH_3 resonance of least intensity is connected to the doublet at 5.49; 5.47 (overlapped with the prior set) and another doublet 4.89; 4.87 ppm which rides the HOD resonance on the low-field side. The equivalent of the third proton needed to match the ones at 5.49; 5.47 (area 1) and 4.89; 4.87 (area 2) appear nearly buried by the HOD resonance, but are detected as a pair at 4.84; 4.80 ppm. Thus three distinct isomers of the Ru(hedta)(MVK)$^-$ complex are detectable. All of these complexes exhibit strong upfield shifts for the H_a, H_b pair and the H_c proton. The free ligand MVK resonances are at 6.35; 6.30 δ for H_a, H_b and 6.10; 6.08 δ for H_c. These peaks are split into doublets due to H_{ab} coupling and H_{ac} coupling. Coordination of MVK to Ru(hedta) causes an upfield shift of the H_a and H_b protons by 1.35 and 1.41 ppm ($\Delta\delta$) for the more abundant isomers with methyl singlets at 2.12 δ and 1.96 δ, respectively, and about a 1.48 ppm upfield shift in H_a, H_b for the lesser abundant isomer. H_a and H_b are distinguished in the lesser isomer.

The absence of differentiation of the H_a and H_b protons for two of the Ru(hedta)(MVK)$^-$ isomers, but the discrimination of them by the third requires comment. Models show that Ru(hedta)$^-$ isomers **1** and **2** are relatively open at the olefin binding site, whereas isomer **3** has a crowded binding pocket. In isomers **1** and **2** the MVK ligand may approach the Ru^{II} center more closely resulting in lesser or coincident coupling to H_c as observed previously for linear olefins [7]. In isomer **3** the crowded binding pocket may force a slightly longer Ru^{II}–olefin and lesser equivalence of H_a and H_b. This is discerned by distinctly separate doublets at 5.49, 5.47; 4.89, 4.87; and 4.84, 4.80 ppm. It is also interesting to observe that the most crowded Ru(hedta)(MVK)$^-$ isomer, **3**, is also the one of least abundance, representing only 17.4% in comparison with higher, nearly equal, contributions from **1** and **2** (44.1% and 38.6%). Our data does not allow us to assign which isomer, **1** or **2**, is the 44.1% isomer. It is interesting to observe, however, that the models show that **1** and **2** are nearly equally unhindered for the approach of olefins or the η^2 bonding site of pyrimidine nucleobases. In concert with the observations of the smaller MVK ligand, only **1** and **2** are available for η^2-pyrimidine type coordination [8, 9, 19], whereas small olefins bond to all three geometrical arrangements of Ru^{II}(hedta)$^-$.

Appraisal of η^2 coordination

The above results with Ru^{II}(hedta)$^-$ in complexation with regular olefins and the η^2-site of pyrimidine nucleobases reveal a number of important results.

(i) The olefin coordination of Ru^{II}(hedta)$^-$ follows the behavior of organometallic complexes of lower coordination number of studies by Tolman *et al.* [2] and Munakata *et al.* [3]; metal–olefin association in Ru^{II}(hedta)$^-$ is dominated by electronic factors and not steric effects. The same conclusion was recently drawn from the differences in the coordination of five-substituted halouracils and halouridines in comparison

with the absence in η^2 coordination by thymidine [19, 8].

(ii) There are three stereochemical isomers of Ru^{II}(hedta), and these are capable of discriminating on the basis of ligand size as to which olefinic units may be coordinated to each isomer.

(iii) The crowded isomer **3** will bind only with the smallest olefinic structures such as ethylene, propylene, MVK and linear butenes [22].

(iv) The measured η^2 binding constants in Table 1 represent an effective binding constant which averages the binding abilities of isomers **1**, **2** and **3** toward the substrate. Thus comparisons between series of differing structure such as a straight chain olefin versus an olefin in a cyclic system places the linear complex at an advantage if it can bind all three isomers. Thus it is difficult to get a 'pure' estimate of the difference a steric effect might contribute in even a seemingly simple comparison, as between MVK and 3-cyclohexen-1-one.

(v) The stabilization of the $E_{1/2}$ value of the $Ru^{III/II}$(hedta)$L^{0/-}$ couple cannot be taken as a measure of the affinity of the olefinic unit in L for Ru^{II}(hedta)$^-$; solvation factors on the substitution equilibrium are very important and contributory to the magnitude of K_f for olefin coordination in aqueous solution.

(vi) Small linear chain olefins which lack significant branching about the olefinic unit can exhibit fluxional coordination which equilibrates the coordination above and below the plane of the olefin; this behavior is not observed with cyclic systems whose planes are defined within the cyclic ring. The ring structure further prevents tumbling between the top and bottom surfaces. This feature leads to the detection of two stereochemical isomers when large bulky groups define the steric aspects of the olefin region. This has been most delicately observed for the cases of 3-methyluridine [8] and 5-fluorouridine [19] where the ribose unit at N-3 promotes differentiation of the η^2 complexes with ribose above or below the olefin plane with Ru(hedta) isomers **1** and **2**.

(vii) The sensitivity of K_f to ligand geometry and substituents, and the type of metal-centered stereochemical isomers active in controlling η^2 coordination to pyrimidine nucleobases points to the ability for synthetic control of tailor-made Ru^{II} reagents which would favor η^2 binding to C and T of DNA chains. Efforts toward this exciting prospect and its potential implications for molecular recognition, medicine and molecular biology are currently being pursued in our laboratories.

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