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Isolation and Crystal Structures of Both Enol and Keto Tautomer Intermediates in a Hydration of an Alkyne−Carboxylic Acid Ester Catalyzed by Iridium Complexes in Water

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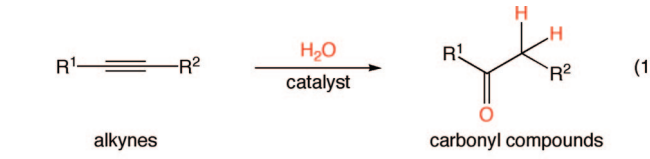
Abstract: Hydration of tetrolic acid ethyl ester as an alkyne−carboxylic acid ester catalyzed by an Ir−aqua complex $[Ir^{III}Cp^*(bpy)(OH_2)]^{2+}$ (**1**, $Cp^* = \eta^5$-C_5Me_5, bpy = 2,2′-bipyridine) in water provides ethyl acetoacetate as a β-keto acid ester. We report the successful isolation of both an Ir−enol tautomer intermediate $[Ir^{III}Cp^*(bpy)\{CH_3C(OH)=CC(O)OC_2H_5\}]^+$ (**2**) and an Ir−keto tautomer intermediate $[Ir^{III}Cp^*(bpy)\{CH_3C(O)$-$CHC(O)OC_2H_5\}]^+$ (**3**) in the catalytic hydration by optimizing the conditions of the isolation, such as pH of the solution, reaction time, and selection of counteranions. The structures of the enol and keto complexes with characteristic Ir−(sp^2carbon) bond and Ir−(sp^3 carbon) bond, respectively, were unequivocally determined by X-ray analysis, IR, electrospray ionization mass spectrometry (ESI-MS), and NMR studies including ^1H, ^{13}C, distortionless enhancement by polarization transfer (DEPT) and correlation spectroscopy (COSY) experiments. It was confirmed that the hydration of tetrolic acid ethyl ester catalyzed by **2** or **3** as initial catalysts provides ethyl acetoacetate. Mechanism of the catalytic hydration of tetrolic acid ethyl ester as an alkyne−carboxylic acid ester is discussed based on isotopic labeling experiments with the Ir−enol and Ir−keto tautomers.

Introduction

Catalytic hydration of alkynes is an atom-economically useful reaction to synthesize valuable carbonyl compounds such as ketones (eq 1).[1−4] A variety of transition metal catalysts have so far been developed for regioselective hydration of alkynes into ketones.[5−17] It has been proposed that the hydration proceeds through enol and keto tautomers of organometallic intermediates with metal−carbon (M−C) bonds (eq 2).[18] It is well-known that the enol intermediate immediately rearranged to the corresponding keto tautomers.[18]



Frontier works on observation and isolation of such enol and keto complexes have been performed so far.[19−24] There are a

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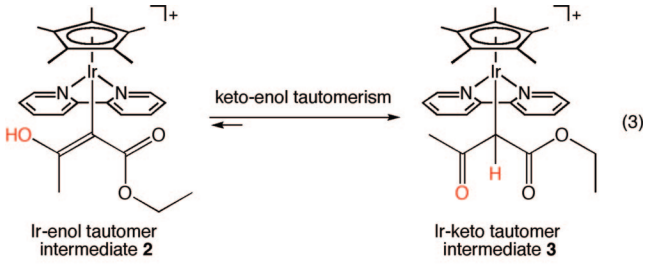
few examples of isolation of keto complexes as intermediates in catalytic hydration of alkynes.[19,21] On the other hand, however, there is no example of isolation of enol complexes as intermediates in catalytic hydration of alkynes as follows. Taube and co-workers[22] and Bergman and co-worker[23] have isolated enol complexes from a stoichiometric reaction with water and 2-butyne and a stoichiometric insertion of dimetyl acetylenedicarboxylate, respectively, but not from catalytic hydration of alkynes. Recently, Laguna and co-workers reported a direct observation of a Au−enol complex as an intermediate in catalytic hydration of phenylacetylene by NMR at low temperature.[24] Thus, the isolation and crystallization of enol intermediates in catalytic hydration of alkynes has yet to be achieved.

Here, we report the successful isolation and crystallization of $[Ir^{III}Cp^*(bpy)\{CH_3C(OH)=CC(O)OC_2H_5\}]^+$ (**2**, $Cp^* = \eta^5$-C_5Me_5, bpy = 2,2′-bipyridine) and $[Ir^{III}Cp^*(bpy)\{CH_3C(O)$-$CHC(O)OC_2H_5\}]^+$ (**3**), which are enol and keto tautomer intermediates (eq 3) in a hydration of tetrolic acid ethyl ester as an alkyne−carboxylic acid ester catalyzed by an Ir−aqua complex $[Ir^{III}Cp^*(bpy)(OH_2)]^{2+}$ (**1**). The structures of **2** and **3** with characteristic Ir−C bonds were unequivocally determined by X-ray analysis. We also report the catalytic hydration of tetrolic acid ethyl ester into a ketone (ethyl acetoacetate as a β-keto acid ester) with not only the Ir−aqua complex **1** but also the Ir−enol complex **2** or the Ir−keto complex **3** as initial catalysts (eq 4).



Experimental Section

Materials and Methods. All experiments were carried out under an air atmosphere. The aqua complex $[Ir^{III}Cp^*(bpy)(OH_2)](SO_4)$ (**1**·SO_4) was prepared by the method described in the literature.[25] Tetrolic acid ethyl ester was purchased from Tokyo Kasei Kogyo Co. Ltd. and was used as received. Ammonium hexafluorophosphate (NH_4PF_6) and sodium trifluoromethanesulfonate ($NaCF_3SO_3$) were purchased from Wako Pure Chemical Industries, Ltd. without further purification. The manipulations in the acidic media were carried out with plastic and glass apparatus (without metals). The spectra of ^1H and $^{13}C\{^1H\}$ NMR, DEPT-135, and H−H and C−H COSY (HETCOR) were recorded on JEOL-JNM-AL300 spectrometer at 25 °C. IR spectra were recorded on a Thermo Nicolet 8700 FT-IR instrument using 2 cm^{-1} standard resolution at ambient temperature. ESI-MS data were collected on an API 365 triple quadrupole mass spectrometer (PE-Sciex) in positive detection mode, equipped with an ion spray interface. The sprayer was held at a potential of +5.0 kV, and compressed N_2 was employed to assist liquid nebulization. The orifice potential was maintained at +20 V. A Nissin magnetic stirrer (Model SW-R800) was used.

pH Adjustment. In a pH range of 1−8, pH values of the solutions were determined by a pH meter (TOA, HM-18E) equipped with a pH combination electrode (TOA, GC-5015C). The pH of the solution was adjusted by using 1 M H_2SO_4/H_2O (pH 1−3), 0.1 M CH_3COOH/CH_3COONa (pH 4−5), and 0.2 M Na_2HPO_4/NaH_2PO_4 (pH 6−8) solutions. Below pH 1, the pH of the solution was estimated by the concentration of the solution; for example, pH values of 0.1 and 1.0 M H_2SO_4/H_2O were estimated to be 1.3 and 0.3, respectively. Values of pD were corrected by adding 0.4 to the observed values (pD = pH meter reading + 0.4).[26]

$[Ir^{III}Cp^*(bpy)\{CH_3C(OH)=CC(O)OC_2H_5\}]CF_3SO_3$ (2·CF_3SO_3). A reaction of $[Ir^{III}Cp^*(bpy)(OH_2)](SO_4)$ (**1**·SO_4, 100 mg, 168 μmol) with tetrolic acid ethyl ester (30 μL, 260 μmol) in H_2O (9 mL) at pH 6.5 (0.2 M Na_2HPO_4/NaH_2PO_4 buffer) at 25 °C for 1 min provided an orange solution of [**2**]$_2$·SO_4. To the solution was added CF_3SO_3Na (103 mg, 600 μmol) at pH 6.5 in H_2O (300 μL), and the mixture was stirred for 10 s to afford an orange powder of **2**·CF_3SO_3, which was collected by filtration, washed with H_2O, and dried in vacuo (yield 37.4% based on **1**·SO_4): ^1H NMR of **2**·CF_3SO_3 (300 MHz, in DMSO-d_6, reference to TMS, 25 °C) δ 0.86 (t, $^3J_{H,H}$ = 6.9 Hz, 3H), 1.65 {s, 15H}, 1.69 (s, 3H), 3.41 (q, $^3J_{H,H}$ = 6.9 Hz, 2H), 7.41 {br s, 1H}, 7.70 (t, $^3J_{H,H}$ = 6.3 Hz, 2H), 8.17 (t, $^3J_{H,H}$ = 7.8 Hz, 2H), 8.66 (d, $^3J_{H,H}$ = 7.5 Hz, 2H), 8.78 (d, $^3J_{H,H}$ = 5.7 Hz, 2H); $^{13}C\{^1H\}$ NMR of **2**·CF_3SO_3 (in DMSO-d_6, reference to TMS, 25 °C) δ 7.382 {s; η^5-$C_5(CH_3)_5$}, 14.05 {s; CH_3CH_2}, 29.64 {s; C(OH)CH_3}, 58.19 {s; CH_3CH_2}, 90.57 {s; η^5-$C_5(CH_3)_5$}, 124.18 {s; *C*H of bpy}, 128.66 {s; *C*H of bpy}, 139.44 {s; *C*H of bpy}, 151.93 {s; *C*H of bpy}, 155.22 {s; *C* of bpy}. Anal. Calcd for $C_{27}H_{32}N_2F_3IrO_6S$: C, 42.57; H, 4.23; N, 3.67. Found: C, 42.74; H, 4.43; N, 3.72.

$[Ir^{III}Cp^*(bpy)\{CH_3C(O)CHC(O)OC_2H_5\}]PF_6$ (3·PF_6). A reaction of **1**·SO_4 (100 mg, 168 μmol) with tetrolic acid ethyl ester (30 μL, 260 μmol) in H_2O (9 mL) at pH 6.5 (0.2 M Na_2HPO_4/NaH_2PO_4 buffer) at 25 °C for 15 min gave a yellow solution of [**3**]$_2$·SO_4. To the solution was added NH_4PF_6 (48.9 mg, 300 μmol) in H_2O (300 μL) at pH 6.5 to form a yellow powder of **3**·PF_6, which was collected by filtration (yield 52% based on **1**·SO_4): ^1H NMR of **3**·PF_6 (300 MHz, in $CDCl_3$, reference to TMS, 25 °C) δ 1.12 (t, $^3J_{H,H}$ = 3.9 Hz, 3H), 1.25 {s, 3H}, 1.61 {s, 15H}, 3.55 (m, 2H), 4.55 (s, 1H), 7.70 (m, 2H), 8.14 (m, 2H), 8.33 (d, $^3J_{H,H}$ = 6.3 Hz, 1H), 8.43 (d, $^3J_{H,H}$ = 6.3 Hz, 1H), 8.47 (d, $^3J_{H,H}$ = 8.1 Hz, 2H); $^{13}C\{^1H\}$ NMR of **3**·PF_6 (300 MHz, in acetone-d_6, reference to TMS, 25 °C) δ 7.925 {s; η^5-$C_5(CH_3)_5$}, 14.53 {s; CH_3CH_2}, 30.32 {s; C(O)CH_3}, 36.28 {s; *C*H}, 51.19 {s; CH_3CH_2}, 91.92 {s; η^5-$C_5(CH_3)_5$}, 124.89 {s; *C*H of bpy}, 129.25 {s; *C*H of bpy},

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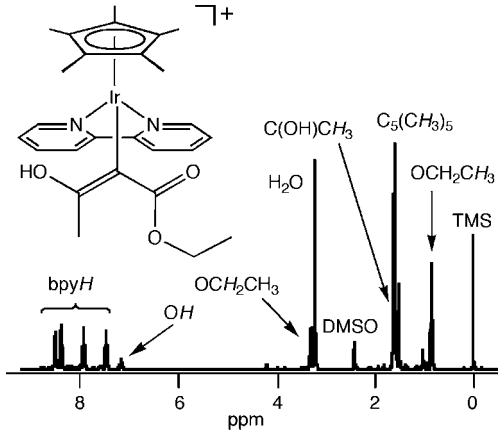


Figure 1. ^{1}H NMR spectrum of **2**·CF_3SO_3 in DMSO-d_6 at 25 °C. TMS, reference with the methyl proton resonance set at 0.00 ppm.

140.32 {s; *C*H of bpy}, 153.04 {s; *C*H of bpy}, 156.86 {s; *C* of bpy}. Anal. Calcd for $C_{26}H_{32}N_2O_3IrPF_6$: C, 41.13; H, 4.26; N, 3.75. Found: C, 41.21; H, 4.25; N, 3.69.

Typical Procedure for the pH-Dependent Hydration of Tetrolic Acid Ethyl Ester with the Ir Complexes 1, 2, or 3. The pH-dependent hydration of tetrolic acid ethyl ester catalyzed by **1**·SO_4 in water was investigated at 25 °C. The pH of the solution of **1**·SO_4 (0.12 mg, 0.2 μmol) in H_2O (2 mL) was adjusted by using 0.1 M H_2SO_4/H_2O, 0.1 M CH_3COOH/CH_3COONa and 0.2 M Na_2HPO_4/NaH_2PO_4. Five hundred equivalents of tetrolic acid ethyl ester (11.5 μL, 0.1 mmol) was added to the solution. The mixture was stirred for 1 h. It was extracted by $CDCl_3$ with 1,4-dioxane as the internal standard. The hydration of tetrolic acid ethyl ester (11.5 μL, 0.1 mmol) with **2**·CF_3SO_3 (0.15 mg, 0.2 μmol) or **3**·PF_6 (0.15 mg, 0.2 μmol) in H_2O (2 mL) was investigated at pH 1.3 at 25 °C. The turnover numbers (TONs = the number of moles of ethyl acetoacetate as the product of the hydration formed per moles of **1**, **2**, or **3**) were determined by ^{1}H NMR. It was confirmed that no reaction occurred in the absence of complexes **1**, **2**, or **3**.

X-ray Crystallographic Analysis. Crystallographic data for **2**·CF_3SO_3 and **3**·PF_6 have been deposited with the Cambridge Crystallographic Data Center as Supplementary Publication Nos. CCDC-688408 and 688409, respectively. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK {fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk}. Measurements were made on Rigaku/MSC Mercury CCD diffractometer with graphite monochromated Mo Kα radiation (λ = 0.7107 Å) and Rigaku/MSC Saturn CCD diffractometer with confocal monochromated Mo Kα radiation (λ = 0.7107 Å). Data were collected and processed using the CrystalClear program (Rigaku). All calculations were performed using the teXsan crystallographic software package of Molecular Structure Corporation.

Results and Discussion

Isolation and Structure of the Enol Complex 2. The transient Ir−enol intermediate **2** was successfully isolated as an orange powder of **2**·CF_3SO_3 by addition of CF_3SO_3Na to the solution of the hydration of tetrolic acid ethyl ester with **1**·SO_4 in H_2O at pH 6.5 in a short time (1×10^3 s; see the section of observation of keto−enol tautomerism by using ^{1}H NMR). The structure of **2**·CF_3SO_3 was determined by NMR {^{1}H and ^{13}C{^{1}H} NMR, DEPT-135, and H−H and C−H COSY (HETCOR)}, ESI-MS, and IR. Figure 1 shows the ^{1}H NMR spectrum of **2**·CF_3SO_3 in DMSO-d_6. The signal at 1.65 ppm corresponds to the Cp* protons {$C_5(CH_3)_5$} of **2**·CF_3SO_3. The ^{1}H NMR spectrum of **2**·CF_3SO_3 indicates the existence of a sp^2 carbon in **2**, which agrees with the result of the X-ray analysis of **2**. ^{1}H

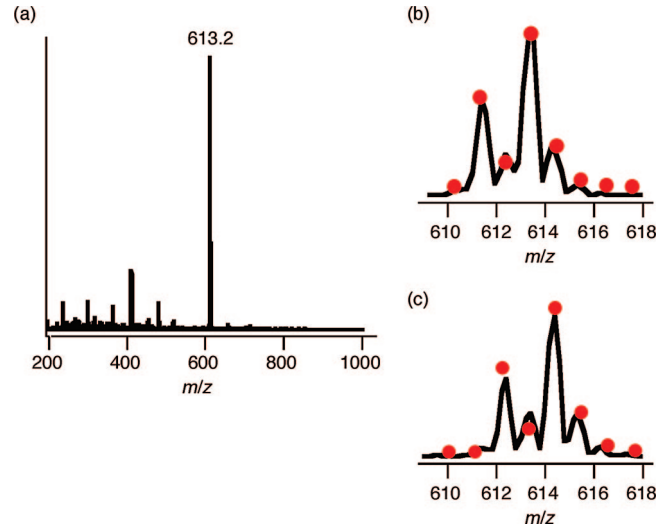


Figure 2. (a) Positive-ion ESI mass spectrum of **2**·CF_3SO_3 in MeOH. (b) Signal at *m*/*z* 613.2 for [**2**]$^+$. Red circles, calculated isotopic distribution [**2**]$^+$. (c) Signal at *m*/*z* 614.2 for D-labeled [**2**]$^+$. Red circles, calculated isotopic distribution [D-labeled **2**]$^+$.

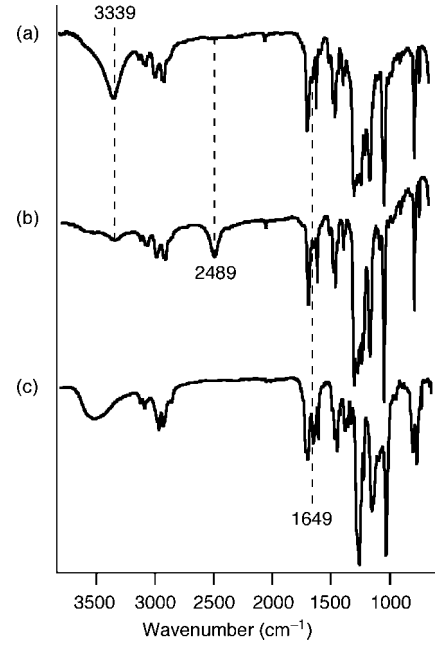


Figure 3. (a) IR spectrum of **2**·CF_3SO_3 as a KBr disk. (b) IR spectrum of D-labeled **2**·CF_3SO_3 as a KBr disk. (c) IR spectrum of **3**·CF_3SO_3 as a KBr disk. A broad peak at around 3500 cm^{-1} was derived from water.

NMR spectrum of D-labeled **2**·CF_3SO_3 (Figure S1), ^{13}C{^{1}H} NMR (Figure S2), DEPT-135 (Figure S3), H−H COSY (Figure S4), and C−H COSY (HETCOR) (Figure S5) spectra of **2**·CF_3SO_3 are shown in the Supporting Information. A positive-ion ESI mass spectrum of **2**·CF_3SO_3 in MeOH is shown in Figure 2a. The prominent signal *m*/*z* 613.2 {relative intensity (*I*) = 100% in the range of *m*/*z* 200−1000} has a characteristic distribution of isotopomers (Figure 2b) that matches well with the calculated isotopic distribution (red circles) for [**2**]$^+$. In an IR spectrum in the 650−3800 cm^{-1} region as a KBr disk of **2**·CF_3SO_3 (Figure 3a), a prominent peak at 3339 cm^{-1} was assigned to ν(O−H) that shifted to 2489 cm^{-1} by isotopic substitution of H for D in the O−H group of the enol ligand {$CH_3C(OH)$═$CC(O)OC_2H_5$, Figure 3b}. The shift value (850

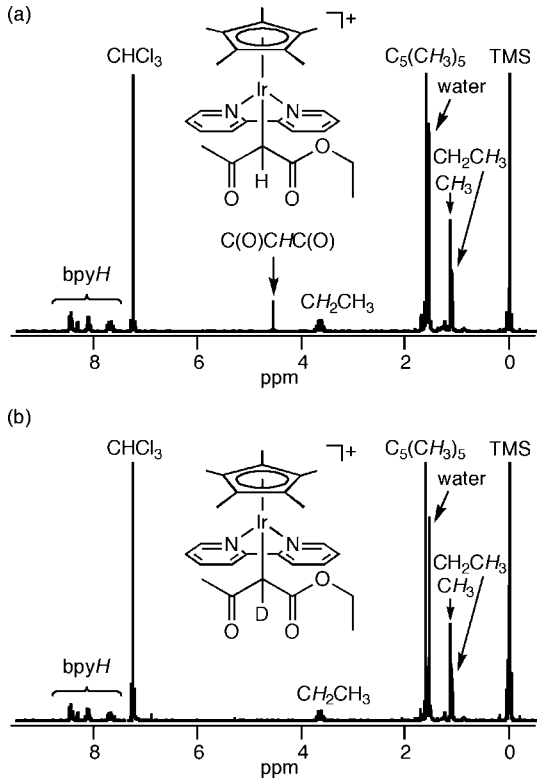


Figure 4. ^{1}H NMR spectra of **3**·PF_6 (a) and D-labeled **3**·PF_6 (b) in $CDCl_3$ at 25 °C. TMS, reference with the methyl proton resonance set at 0.00 ppm.

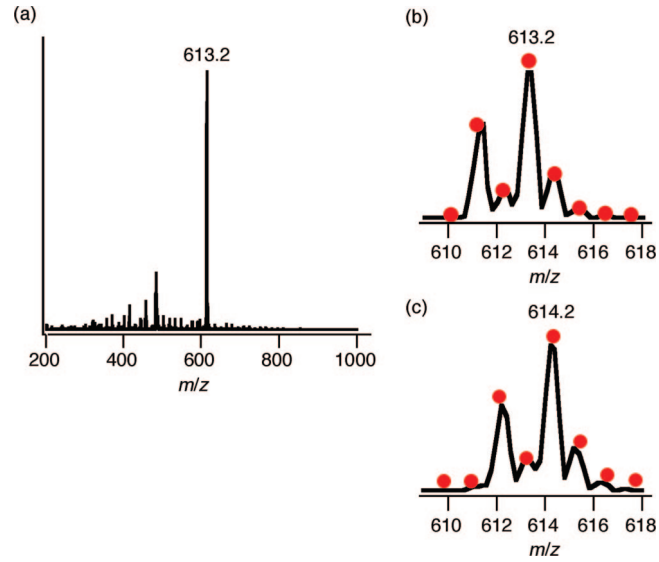


Figure 5. (a) Positive-ion ESI mass spectrum of **3**·PF_6 in MeOH. (b) Signal at *m*/*z* 613.2 for [**3**]$^+$. Red circles, calculated isotopic distribution [**3**]$^+$. (c) Signal at *m*/*z* 614.2 for D-labeled [**3**]$^+$. Red circles, calculated isotopic distribution [D-labeled **3**]$^+$.

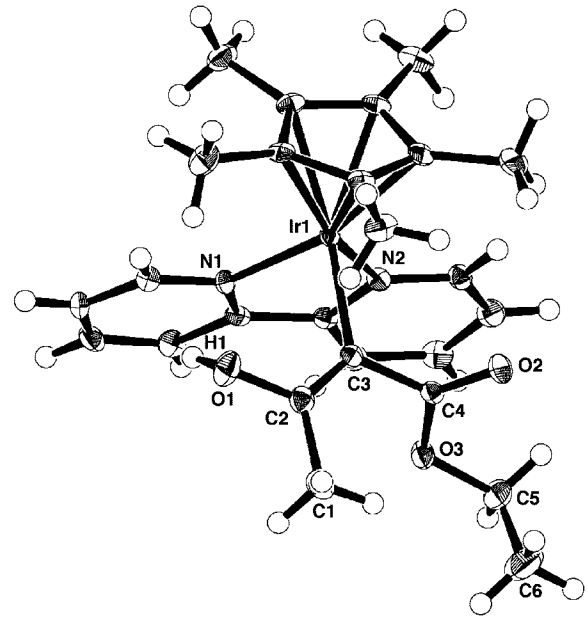


Figure 6. ORTEP drawing of **2** with ellipsoids at 50% probability. The counteranion (CF_3SO_3) is omitted for clarity.

cm^{-1}) agrees well with that expected by Hooke's law calculation for a pure OH stretching mode.[27]

Isolation and Structure of the Keto Complex 3. The water-soluble aqua complex **1**·SO_4 reacts with tetrolic acid ethyl ester in H_2O, pH 6.5, at 25 °C for 15 min to give the water-soluble keto complex [**3**]$_2$·SO_4. The stable keto complex **3** was isolated as a yellow powder of **3**·PF_6 by addition of NH_4PF_6 to the solution of [**3**]$_2$·SO_4. The structure of **3**·PF_6 was established by NMR {^{1}H and ^{13}C{^{1}H} NMR, DEPT-135, and H−H and C−H COSY (HETCOR)}, ESI-MS, and IR. Figure 4 shows ^{1}H NMR spectra of **3**·PF_6 in $CDCl_3$. The signal of the Cp* protons of **3** was observed at 1.61 ppm. The Ir−keto complex **3** shows characteristic ^{1}H NMR spectrum indicating the existence of a sp^3 carbon in **3**. ^{13}C{^{1}H} NMR (Figure S6), DEPT-135 (Figure S7), H−H COSY (Figure S8), and C−H COSY (HETCOR) (Figure S9) spectra of **3**·PF_6 are shown in the Supporting Information. A positive-ion ESI mass spectrum of **3**·PF_6 in MeOH shows a prominent signal at *m*/*z* 613.2 (I = 100% in the range of *m*/*z* 200−1000, Figure 5a), which has a characteristic distribution of isotopomers (Figure 5b) that matches well with the calculated isotopic distribution (red circles) for [**3**]$^+$. An Ir−keto complex **3**·CF_3SO_3 was prepared by dissolving isolated **2**·CF_3SO_3 in H_2O. The solution was evaporated and dried in vacuo to give **3**·CF_3SO_3 as a hydroscopic powder, which was used for IR. The IR spectrum of **3**·CF_3SO_3 (Figure 3c) showed no peak derived from ν(O−H), which was observed at 3339 cm^{-1} in the IR spectrum of **2**·CF_3SO_3 (Figure 3a). A prominent peak was observed at 1649 cm^{-1} in the IR spectrum of **3**·CF_3SO_3 (Figure 3c), which was assigned to ν(C═O). The IR spectrum of hydroscopic **3**·CF_3SO_3 showed a broad peak at around 3500 cm^{-1} derived from water.

Crystal Structure of the Enol Complex 2. To a solution of **1**·SO_4 (10 mg, 16.8 μmol) was added CF_3SO_3Na (10.3 mg, 60 μmol) at pH 6.5 in H_2O (0.9 mL). After the solution was added to tetrolic acid ethyl ester (3 μL, 26 μmol) and left at rest, complex **2**·CF_3SO_3 was quickly crystallized in a few minutes. ORTEP drawing of **2** is shown in Figure 6. Complex **2** adopts distorted octahedral coordination that is surrounded by one Cp*, one bpy, and one enol ligand. Complex **2** has the sp^2 carbon (C3 in Figure 6), as NMR studies imply the existence of sp^2 carbon. The characteristic Ir1−C3 bond length is 2.100(4) Å. The C2−C3 double bond length is 1.327(6) Å. They are close to the Ir−C bond length and C−C double bond length observed in IrCp*(PMe_3)(Ph)[C(CO_2Me)C(OH)(CO_2Me)] {2.04(2),

(27) Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, 5th ed.; Wiley: New York, 1997, and references therein.

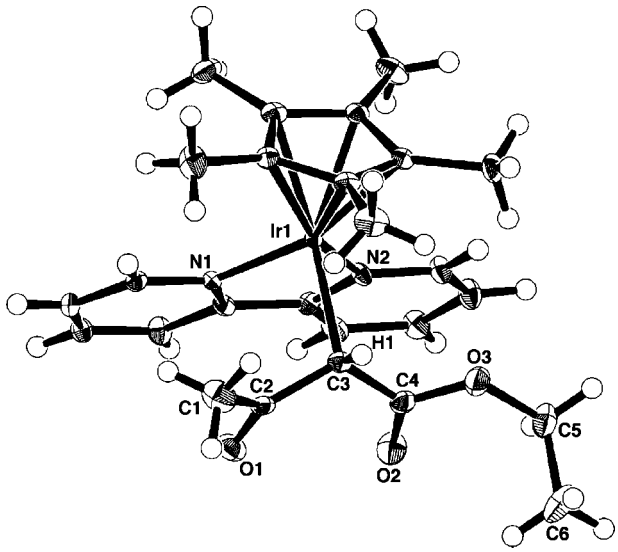


Figure 7. ORTEP drawing of **3** with ellipsoids at 50% probability. The counteranion (PF_6) and MeOH are omitted for clarity.

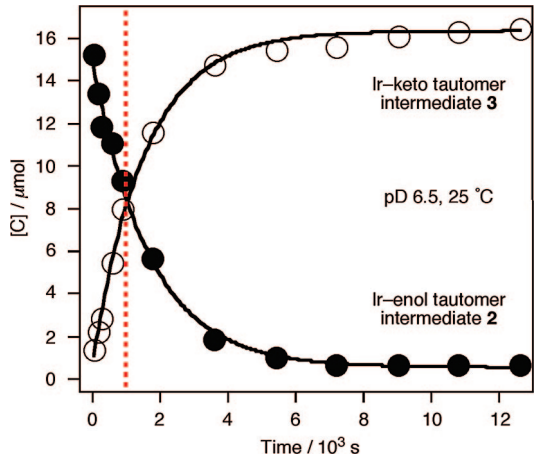


Figure 8. Time-course of conversion from **2** (●) to **3** (○) in the reaction of **1** with tetrolic acid ethyl ester in D_2O at pD 6.5 at 25 °C monitored by ^{1}H NMR. The red dotted line shows a limited period of time (1×10^3 s) for the isolation of **2**.

and 1.35(3) Å, respectively}.[23] The angles of Ir1−C3−C2, Ir1−C3−C4, and C2−C3−C4 are 114.7(3), 126.7(3), and 118.5(4)°, respectively. These results clearly indicate that C3 in **2** is sp^2 carbon. The torsion angle between the least-squares plane of bpy and that of an ester of the enol ligand is 164.1(1)°. The distances of N1−O1, N2−O2, and N2−O3 (i.e., the distance between the bpy ligand and the enol ligand of **2**) are 3.244(5), 3.147(5), and 3.455(4) Å, respectively. The coordination geometry of **2** shows that the addition of water to the carbon−carbon triple bond with **1** proceeds through a *syn* addition (see the section of Mechanism of the Hydration of Alkyne−Carboxylic Acid Esters).

Crystal Structure of the Keto Complex 3. A yellow crystal of **3**·PF_6 used for X-ray analysis was obtained from MeOH/diethyl ether. ORTEP drawing of **3** is shown in Figure 7. Complex **3** adopts a distorted octahedral coordination that is surrounded by one Cp*, one bpy, and one keto ligand. Complex **3** has the sp^3 carbon (C3 in Figure 7), as shown in NMR spectra. The characteristic Ir1−C3 (sp^3 carbon) bond length of **3** is 2.211(3) Å, which is longer than the Ir1−C3 (sp^2 carbon) bond length of **2** {2.110(4) Å}. The C2−C3 bond length of **3** is

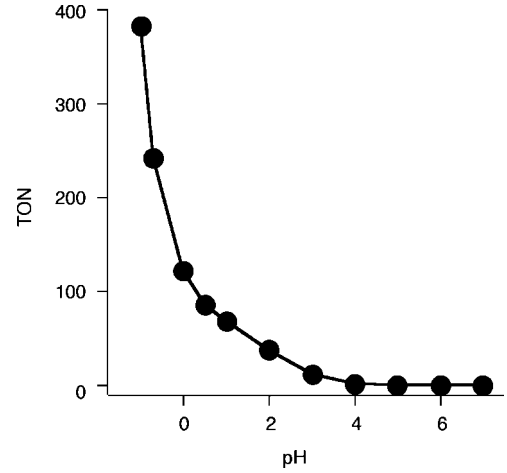
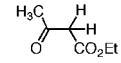
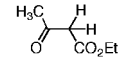
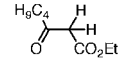
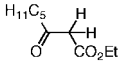
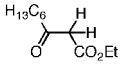
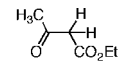
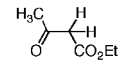


Figure 9. The pH-dependent TONs of the formation of ethyl acetoacetate in the reaction of **1**·SO_4 (0.2 μmol) with tetrolic acid ethyl ester (0.1 mmol) in H_2O (2.0 mL) at 25 °C for 1 h.

Table 1. Hydration of Alkyne−Carboxylic Acid Ethyl Esters to the Corresponding β-Keto Acid Esters Catalyzed by Water-Soluble Complexes **1**·SO_4, **2**·CF_3SO_3, or **3**·PF_6 in Water[a]

entry	substrate	product	catalyst	amt of catalyst (mol%)	time (h)	yield	TON
1	$H_3C-\equiv-CO_2Et$		**1**(SO_4)	0.2	24	99	248
2	$H_3C-\equiv-CO_2Et$		**1**(SO_4)	0.2	1	13	65
3	$H_9C_4-\equiv-CO_2Et$		**1**(SO_4)	0.2	24	31	155
4	$H_{11}C_5-\equiv-CO_2Et$		**1**(SO_4)	1.0	24	56	56
5	$H_{13}C_6-\equiv-CO_2Et$		**1**(SO_4)	2.0	24	38	19
6	$H_3C-\equiv-CO_2Et$		**2**(CF_3SO_3)	0.2	1	11	55
7	$H_3C-\equiv-CO_2Et$		**3**(PF_6)	0.2	1	11	57

[a] The reaction was carried out pH 1.3 at 25 °C with alkyne carboxylic acid esters in H_2O.

1.469(5) Å, which is longer than that of **2** {1.327(6) Å}. The Ir1−C3 length is close to the M−C bond length observed in $[Pt_2(NH_3)_4\{(CH_3)_3CCONH\}_2\{CH(CH_3)COCH_3\}](NO_3)_3$ {2.146 (13) Å}[19] and $TpRuCl\{CH_2C(O)(p\text{-}CH_3C_6H_4)\}(NO)$ {Tp = BH(prazol-1-yl)$_3$} {2.151(2) Å}.[20] The angles of Ir1−C3−C2, Ir1−C3−C4, and C2−C3−C4 are 111.4(2), 108.6(2), and 116.8(3)°, respectively. C3 in **3** is sp^3 carbon as described above. The torsion angle between the least-squares plane of the bpy ligand and that of carbonyl groups of the keto ligand is 15.4(2)°. The distances of N1−O1, N2−O2, and N2−O3 (i.e., the distance between the bpy ligand and the keto ligand of **3**) are 2.985(3), 3.045(3), and 3.416(3) Å, respectively.

Observation of Keto−Enol Tautomerism by Using ^{1}H NMR. The reaction of **1**·SO_4 (10 mg, 16.8 μmol) with tetrolic acid ethyl ester (3 μL, 26 μmol) in D_2O (0.9 mL) at pD 6.5 (0.2 M Na_2HPO_4/NaH_2PO_4 buffer) at 25 °C was monitored by ^{1}H NMR. The Ir−enol intermediate **2** was initially observed in the reaction, and the subsequent keto−enol equilibrium (eq 3) immediately afforded the Ir−keto intermediate **3** whose yields

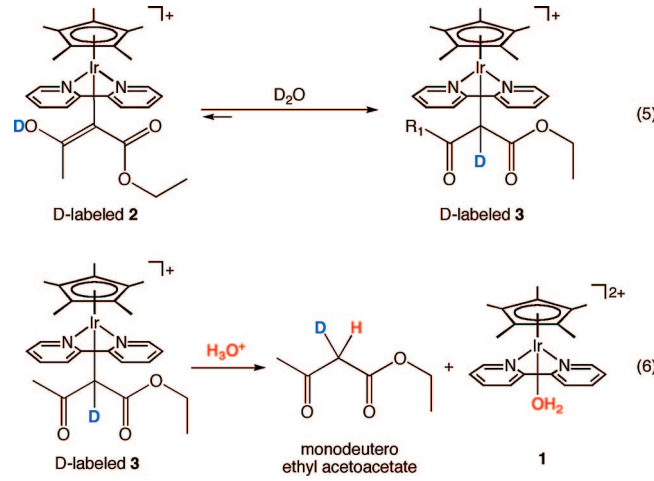
were determined by ^{1}H NMR with 3-(trimethylsilyl)propionic-2,2,3,3-d_4 acid sodium salt (TSP) as the internal standard. Figure 8 shows the time course of conversion from the Ir−enol complex **2** to the Ir−keto complex **3** in the hydration of tetrolic acid ethyl ester with **1**. The red dotted line shows a limited period time (1×10^3 s) for the isolation of **2**. The keto−enol tautmerization rate obeys first-order kinetics, and the rate constant of conversion from **2** to **3** was determined to be 6.04×10^{-4} s^{-1} at 25 °C (Figures S10 and S11 in Supporting Information).

Catalytic Hydration of Alkyne−Carboxylic Acid Esters with 1, 2, or 3. Hydration of tetrolic acid ethyl ester as an alkyne−carboxylic acid ester catalyzed by **1**·SO_4 provides ethyl acetoacetate as a β-keto acid ester regioselectively (see the section of Mechanism of the Hydration of Alkyne−Carboxylic Acid Esters). The pH-dependent turnover numbers (TONs = the number of moles of ethyl acetoacetate as the product of the hydration formed per moles of **1**) of the formation of ethyl acetoacetate from the hydration of tetrolic acid ethyl ester with **1**·SO_4 shows a maximum around pH −1 (TON = 382, Figure 9). In a pH range of −1 to 8, the lower is pH of the solution, the faster is the rate of the hydration; that is the rate of the hydration is dependent on H^+ concentration. This is the reason why the protonation of **3** gives ethyl acetoacetate to regenerate the aqua complex **1**.

Hydration of alkyne−carboxylic acid esters ($R^1C{\equiv}CCO_2C_2H_5$, $R^1 = CH_3$, C_4H_9, C_5H_{11}, and C_6H_{13}) catalyzed by the aqua complex **1**·SO_4 at pH 1.3 in H_2O at 25 °C gave the corresponding β-keto acid esters (entries 1−5 in Table 1). The larger are the alkyl groups (R^1), the lower the TONs are. The isolated enol complex **2** and keto complex **3** also catalyzed the hydration of tetrolic acid ethyl ester at TONs of 55 (entry 6) and 57 (entry 7), respectively, in Table 1. It was confirmed that the isolated enol complex **2** and keto complex **3** individually reacted with H^+ to provide the product of ethyl acetoacetate quantitatively.

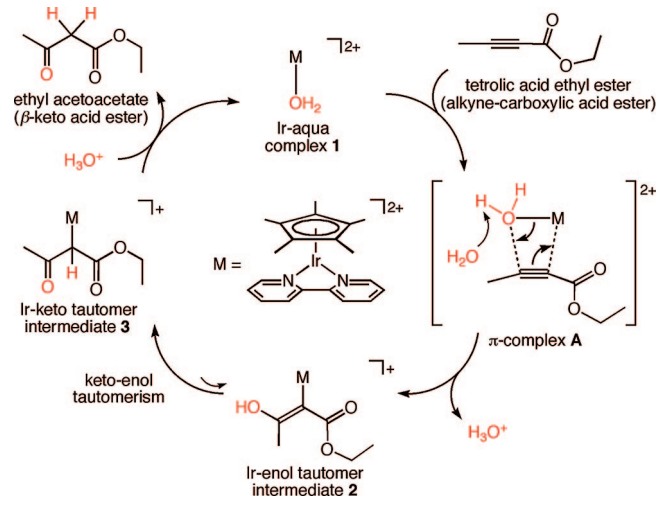
As controlled experiments, we confirmed that no reaction occurred in the absence of **1**, **2**, or **3**, and that the bpy ligands of **1**, **2**, and **3** were neither entirely nor partially dissociating under the catalytic conditions even with the excess of bpy.

Isotopic Labeling Experiments. To establish the origin of the enol ligand in **2**·CF_3SO_3, the reaction of **1**·SO_4 with tetrolic acid ethyl ester was carried out at pD 6.5 in D_2O at 25 °C. The results of ^{1}H NMR showed that the signal (observed at 7.41 ppm in Figure 1) of the OH proton of **2**·CF_3SO_3 disappeared in the ^{1}H NMR spectrum (Figure S1 in Supporting Information); that is, the D atoms derived from D_2O were incorporated into the enol ligand of **2**·CF_3SO_3. Deuterium-labeled **3** was prepared by a reaction of **1**·SO_4 with tetrolic acid ethyl ester in D_2O at pD 6.5 at 25 °C. The results of ^{1}H NMR showed that the signal (observed at 4.55 ppm in Figure 4a) of the methine proton of **3**·PF_6 disappeared in the ^{1}H NMR spectrum (Figure 4b); that is, the D atoms derived from D_2O were incorporated into the keto ligand of **3**·PF_6. Deuterium-labeled **3** was also prepared by dissolving isolated deuterium-labeled **2** in D_2O (eq 5). The reaction of isolated D-labeled keto complex **3**·PF_6 quantitatively reacted with H^+ at pH 1.3 in H_2O at 25 °C to provide monodeutero ethyl acetoacetate {$CH_3C(O)CHDC(O)OC_2H_5$} (yield 99% based on **3**·PF_6) and Ir−aqua complex **1** (eq 6), which was determined by ^{1}H NMR (Figure S12 in Supporting Information). Dideutero ethyl acetoacete {$CH_3C(O)CD_2C(O)OC_2H_5$} or ethyl acetoacetate {$CH_3C(O)CH_2C(O)OC_2H_5$} was not obtained by the hydration, which indicated that the back reaction from **3** to **2** was negligible.

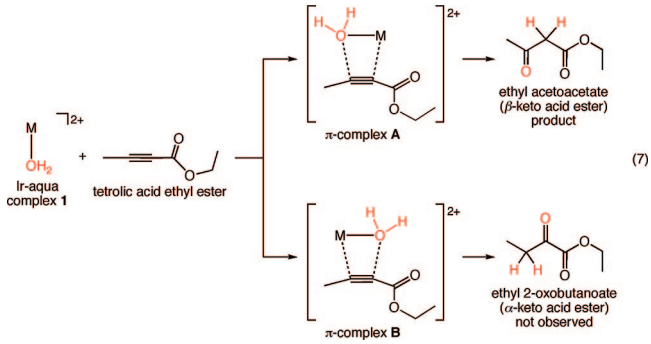


Mechanism of the Hydration of Alkyne−Carboxylic Acid Esters. The isolation and crystal structures of **2** and **3** and the isotopic labeling experiments provide excellent opportunity to elucidate the mechanism of the hydration of alkyne−carboxylic acid esters catalyzed by **1** in water. Judging from the obtained crystal structure of **2**, whose stereochemistry was determined (*Z*) by X-ray analysis (i.e., The Ir−C and O−C bonds exist in the same direction of the C−C double bonds), we propose that a *syn* addition of the H_2O ligand of **1** into the carbon−carbon triple bond of tetrolic acid ethyl ester proceeds to give π-complexes **A** or **B** (eq 7). It can be assumed that the π-complex **A** is formed selectively between the two possibilities because the product of the hydration is ethyl acetoacetate but not ethyl 2-oxobutanoate. The attack of the coordinated water molecule in **A** on coordinated tetrolic acid ethyl ester results in the formation of the Ir−enol complex **2** with the liberation of a proton. The subsequent keto−enol tautomerism affords the Ir−keto complex **3**. The protonation of **3** gives ethyl acetoacetate and regenerates **1**. Scheme 1 shows the mechanism of the hydration of tetrolic acid ethyl ester catalyzed by the Ir−aqua complex **1** via the π-complex **A**, the Ir−enol complex **2**, and the Ir−keto complex **3**.

Scheme 1



In summary, we have succeeded in the isolation of both enol tautomer intermediate **2** and keto tautomer intermediate **3** with the characteristic Ir−C bonds in the catalytic hydration of tetrolic acid ethyl ester in water by optimizing the conditions of the



(7)

isolation, such as pH of the solution, reaction time, and selection of counteranions, as well as the combination of the IrCp*(bpy) complexes and tetrolic acid ethyl ester for the first time. The structures of **2** and **3** were unequivocally determined by X-ray analysis. We have shown that the isolated complexes **2** and **3** act as the active catalysts for the hydration of tetrolic acid ethyl ester into ethyl acetoacetate.

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Supporting Information Available: Figures S1−S12 and crystallographic data (CIF) for **2**·CF_3SO_3 and **3**·PF_6. This material is available free of charge via the Internet at http://pubs.acs.org.

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