C−O Coupling of $LPt^{IV}Me(OH)X$ Complexes in Water (X = ^{18}OH, OH, OMe; L = di(2-pyridyl)methane sulfonate)

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The C−O reductive elimination from $LPt^{IV}Me(OH)_2$ (**1**, Me = CH_3; **1-*d*$_3$**, Me = CD_3; L = di(2-pyridyl)methanesulfonate) leading to methanol, dimethyl ether, and $LPt^{II}(OH_2)_2BF_4$ (**3**) was studied in acidic solutions (60 and 120 mM HBF_4) in H_2O and $H_2{}^{18}O$ at 80 °C. In ^{18}O-labeled water a mixture of two isotopologous methanols, $Me^{18}OH$ and $Me^{16}OH$, formed in 1:1 to 5:1 ratios. At a given acidity and a ∼10% conversion of **1-*d*$_3$** the $Me^{18}OH/Me^{16}OH$ ratio was inversely proportional to the concentration of the complex **1-*d*$_3$** (29−120 mM). ESI-MS study showed that a slow $^{18}O/^{16}O$ exchange in hydroxo ligands of complexes **1** and **1-*d*$_3$** occurred that led to higher $Me^{18}OH/Me^{16}OH$ ratios by the end of the reaction. Similarly, a mono-^{18}O-labeled complex, **1-^{18}O**, reacted in $H_2{}^{16}O$ in the presence of HBF_4 to form a mixture of $Me^{16}OH$ and $Me^{18}OH$. A number of intermediates of C−O elimination from **1** in acidic aqueous solution were identified, prepared independently, and characterized by NMR, X-ray diffraction, and elemental analysis: $LPt^{IV}Me(OH)(OMe)$ (**4**), *sym*-$LPt^{IV}Me(OMe)_2$ (**5**), and isomeric dinuclear heterovalent cationic complexes $[LPt^{IV}Me(\mu\text{-}OH)_2Pt^{II}L]BF_4$ (*cis*- and *trans*-**6**). It was shown that an isomer of **4**, methoxo platinum(IV) complex **13**, hydrolyzed in acidic $H_2{}^{18}O$ solution to produce $Me^{16}OH$ isotopologue exclusively. Kinetic studies established that C−O elimination from **1** was first order in **1**; it was catalyzed by acids and by one of the reaction products, complex **3**. In the latter case reversible formation of intermediates **6** occurred. A suggested reaction mechanism for the formation of $Me^{16}OH$ from **1** in $H_2{}^{18}O$ solutions involves a bimolecular nucleophilic attack of a hydroxo ligand of **1** or **4** at the electrophilic carbon atom of the methyl group in the cationic species **1·H**$^+$ (complex **2**) or **6**, leading to non-^{18}O-labeled intermediates **4** or **5**, respectively. Subsequent hydrolysis of these intermediates in $H_2{}^{18}O$ solution leads to $Pt^{IV}{-}^{16}OMe$ bond cleavage and formation of $Me^{16}OH$. Similarly, a bimolecular nucleophilic attack of a methoxo ligand of **4** or **5** at the electrophilic carbon atom of complex **2** or **6** leads to intermediate dimethyl ether Pt^{IV} complexes **7** and/or **8**. These intermediates are responsible for the formation of dimethyl ether. The C−O coupling of **4** leading to dimethyl ether, methanol, and transient complex **5** was studied in neutral and acidic aqueous solutions. The $Me_2O/MeOH$ ratio was found to increase with decreasing $[H^+]$ and increasing concentration of **4**.

Introduction

C−O reductive coupling reactions mediated by late transition metal complexes play an important role in homogeneous catalysis.[1] In particular, $C(sp^3)$−O reductive coupling at a d^6 Pt^{IV} center is involved in Shilov-type chemistry relevant to catalytic methane functionalization.[2−7] C−O coupling of alkoxo iridium(I) carbonyls with methyl and acyl halides to produce esters was proposed to proceed via d^6 Ir^{III} intermediates.[8]Highly regioselective Pd^{II}-catalyzed oxidative aminoacetoxylation of olefins was shown to include a C−O coupling step at a Pd^{IV} center.[9] The $C(sp^2)$−O reductive coupling, one of the key steps in Pd-catalyzed nucleophilic substitution in aromatic substrates, was studied extensively at a Pd^{II} center[10,11] and was suggested recently to be operative for d^6 Pd^{IV} derivatives as well.[12] Despite these significant efforts and a growing number of synthetic applications,[10,11] not much yet is known about the mechanisms of C−O coupling of transition metal complexes. Elimination of products with a new $C(sp^3)$−O bond relevant to Pt-mediated methane functionalization was considered to proceed by nucleophilic attack at the $C(sp^3)$ atom attached to the Pt^{IV} center, with water,[3,4] AcO^-, or ArO^- acting as a nucleophile.[7] Our recent studies on the elimination of methanol from a monomethyl dihydroxoplatinum(IV) complex $LPt^{IV}Me(OH)_2$ (**1**, Scheme

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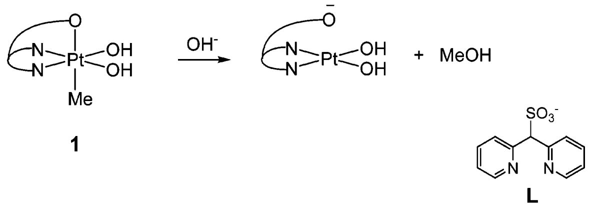
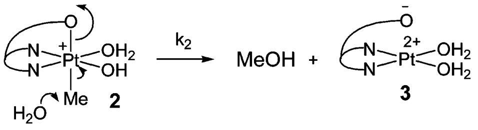
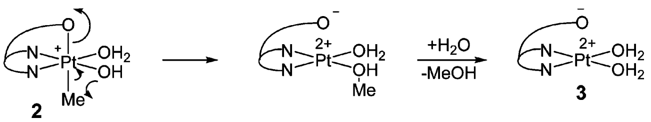
Scheme 1



Scheme 2



Scheme 3



1) in alkaline aqueous solutions (eq 1)[13] agreed well with the S_N2 mechanism involving strongly nucleophilic OH^-:

$$\underset{\mathbf{1}}{\mathrm{LPt^{IV}Me(OH)_2}} + \mathrm{OH^-} \rightarrow \mathrm{MeOH} + \mathrm{LPt^{II}(OH)_2^-} \qquad (1)$$

At the same time, it may be important to explore mechanisms of C−O coupling in *acidic* media that are widely used in the Shilov-type chemistry.[2−7] In the simplest scenario, water or another suitable solvent might be the major nucleophile involved in an acid-catalyzed S_N2-type reaction with the electrophilic substrate **2** produced upon protonation of **1** (eq 2).

$$\underset{\mathbf{1}}{\mathrm{LPt^{IV}Me(OH)_2}} + \mathrm{H^+} \overset{K_1}{\rightleftharpoons} \underset{\mathbf{2}}{\mathrm{LPt^{IV}Me(OH)_2{\cdot}H^+}} \qquad (2)$$

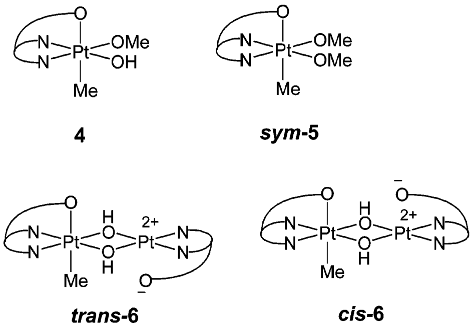
In the case of aqueous solutions such a nucleophilic attack (Scheme 2) would lead to the formation of methanol (Scheme 2, eq 3):[13]

$$\underset{\mathbf{1}}{\mathrm{LPt^{IV}Me(OH)_2}} + \mathrm{H^+} + \mathrm{H_2O} \rightarrow \mathrm{MeOH} + \underset{\mathbf{3}}{\mathrm{LPt^{II}(OH_2)_2^+}} \qquad (3)$$

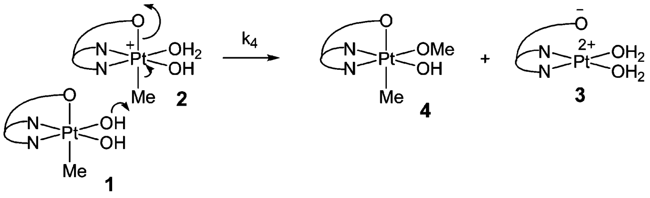
However, nucleophilic substitution at the methyl carbon of **2** may not be the only possible pathway for C−O elimination. Recently a C(sp^3)−I reductive elimination from another d^6 metal center, Rh^{III}, was reported as unlikely to proceed via an S_N2 attack of iodide anion formed upon dissociation of the starting Rh^{III} iodo complex.[14] An *intramolecular*[15] mechanism was also suggested for the C(sp^2)−O coupling of diaryl carboxylato palladium(IV) derivatives[12] and for the C(sp^2)−I coupling of diaryl Pt^{IV}X$_2$ diphosphine complexes (X = I, Br).[16] On the basis of these reports, we also considered *intramolecular* C−O coupling as an alternative path of methanol elimination from complex **2** (Scheme 3).

A possible way to distinguish between the two mechanisms presented in Schemes 2 and 3 is by using an isotopically labeled solvent such as $H_2{}^{18}O$. The reaction in Scheme 2, which involves the solvent as a nucleophile, would produce an ^{18}O-labeled methanol, $Me^{18}OH$, whereas the reaction in Scheme 3, which does not involve the solvent as a nucleophile, would give the unlabeled product $Me^{16}OH$.

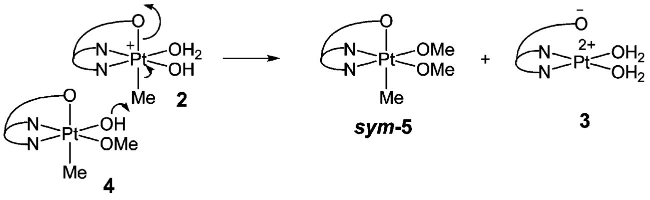
Scheme 4



Scheme 5



Scheme 6



In this work we report the results of our mechanistic studies of C−O reductive elimination from complex **1** in acidic solutions of $H_2{}^{18}O$ or $H_2{}^{16}O$. Remarkably, we found that when reaction 3 was set up in 98% enriched $H_2{}^{18}O$, two isotopologous methanols, $Me^{18}OH$ and $Me^{16}OH$, formed in comparable amounts. This observation suggested that at least two different mechanisms of methanol elimination were operative. In addition to methanol, noticeable amounts of dimethyl ether were found (eq 4):

$$\underset{\mathbf{2}}{\mathrm{2LPt^{IV}Me(OH)_2{\cdot}H^+}} + \mathrm{H_2O} \rightarrow \mathrm{Me_2O} + \underset{\mathbf{3}}{\mathrm{2LPt^{II}(OH_2)_2^+}} \qquad (4)$$

A number of intermediates from reactions 3 and 4, such as complexes **4** and **5** and isomeric dinuclear heterovalent complexes *cis*- and *trans*-**6** (Scheme 4), were detected by ^{1}H NMR and electrospray ionization mass spectrometry (ESI-MS). These complexes were prepared independently in analytically pure form and characterized by NMR spectroscopy and, in most cases, by X-ray diffraction.

Our analysis of the reactivity of **1** and **4**−**6** and a kinetic analysis of reaction 3 showed that formation of $Me^{16}OH$ in weakly acidic (pH ≥ 1) $H_2{}^{18}O$ solutions and formation of dimethyl ether as well as mono- (**4**) and dimethoxo (**5**) MePt^{IV} intermediates resulted from a nucleophilic *intermolecular* C−O coupling of **2** and **1**, **4**, or **5** (Schemes 5−7). The coupling was possible because of a relatively low basicity and relatively high nucleophilicity of these complexes that allowed for a significant fraction of **1** to be present in its acidic solutions along with its

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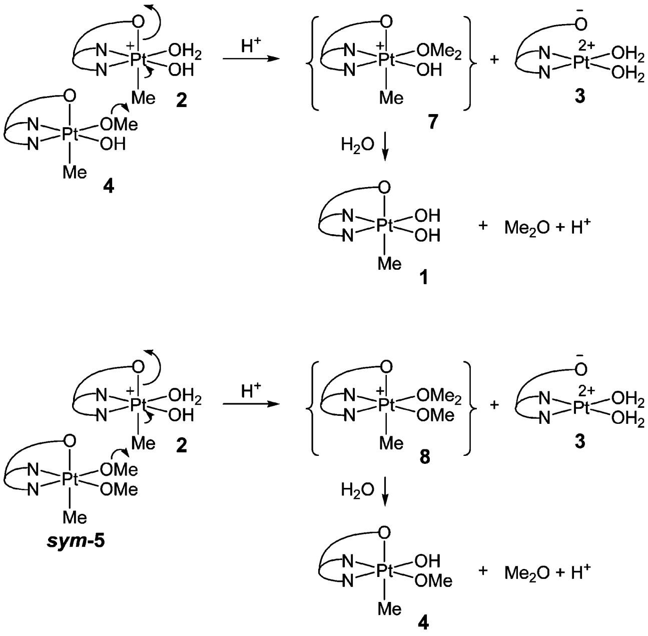
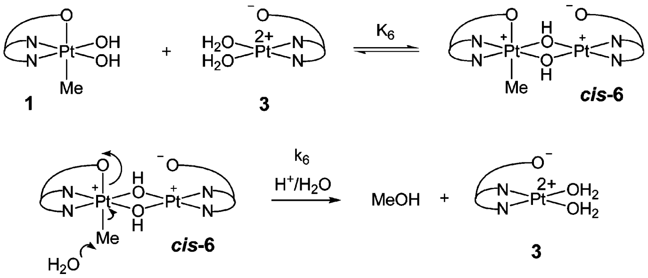
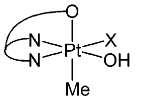
Scheme 7



Scheme 8

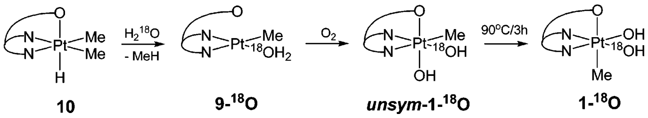


Scheme 9



1 (Me = CH$_3$; X = OH)
1-^{18}O (Me = CH$_3$; X = ^{18}OH)
1-d_3 (Me = CD$_3$; X = OH)

Scheme 10

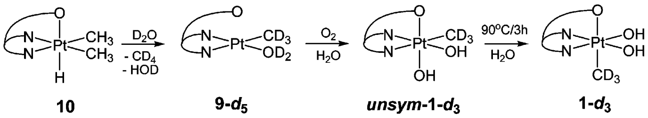


protonated form **2** at [H$^+$] = 60−120 mM (eq 2). The C−O coupling reactions shown in Schemes 5−7 occurred concurrently with the expected S$_N$2 reaction between water and complex **2** (Scheme 2). Notably, an electrophilic activation of **1** toward nucleophilic attacks could be achieved not only by protonation but also by formation of cationic isomeric dinuclear heterovalent complexes **6** (Scheme 4) as a result of a reversible aqua ligand exchange at the Pt^{II} center of **3** (Scheme 8). A report on this aqueous organoplatinum chemistry relevant to aerobic Pt^{II}−Me bond cleavage leading to methanol[13] is presented below.

Results

Preparation of LPt^{IV}CH$_3$(^{18}OH)(OH), 1-^{18}O. Complex **1-^{18}O** containing an ^{18}O-label in one of the equatorial hydroxo ligands (Scheme 9) was synthesized via a multistep reaction sequence given in Scheme 10, which is similar to that used for the parent complex **1**.[13] First, a water-soluble ^{18}O-labeled aqua methyl platinum(II) complex, **9-^{18}O**, LPt^{II}Me(^{18}OH$_2$), was prepared in virtually quantitative yield by dissolving dimethyl hydride **10**, LPt^{IV}Me$_2$H, in H$_2$^{18}O at 40−45 °C (eq 5):

Scheme 11



$$\underset{\mathbf{10}}{\mathrm{LPt^{IV}Me_2H}} + \mathrm{H_2{}^{18}O} \rightarrow \mathrm{MeH} + \underset{\mathbf{9\text{-}^{18}O}}{\mathrm{LPt^{II}Me(^{18}OH_2)}} \tag{5}$$

Complex **9-^{18}O** was used without isolation for subsequent oxidation under an oxygen atmosphere. The reaction produced cleanly, according to ^{1}H NMR, *unsymmetrical* **1-^{18}O** (eq 6, Scheme 10):

$$\underset{\mathbf{9\text{-}^{18}O}}{\mathrm{2LPt^{II}Me(^{18}OH_2)}} + \mathrm{O_2} \rightarrow 2\ \underset{unsym\text{-}\mathbf{1\text{-}^{18}O}}{unsym\text{-}\mathrm{LPt^{IV}Me(^{18}OH)(OH)}} \tag{6}$$

According to ESI-MS analysis, after 5 h all of the LPt^{II}CH$_3$(^{18}OH$_2$) complex had reacted to form a singly labeled *unsym*-LPt^{IV}Me(^{18}OH)(OH) complex. The unsymmetrical **1-^{18}O** was isomerized to the target symmetrical **1-^{18}O** containing an axial methyl group and two equatorial hydroxo ligands at 90 °C in a dilute aqueous solution. The mixture was filtered to remove a small amount of a precipitate characterized as complex **11**, L$_2$Pt^{II}$_2$(μ-OH)$_2$,[13] which formed according to eq 7 (^{18}O labels are omitted for clarity):

$$\underset{\mathbf{1}}{\mathrm{4LPt^{IV}Me(OH)_2}} \rightarrow \underset{\mathbf{4}}{\mathrm{2LPt^{IV}Me(OMe)(OH)}} + \underset{\mathbf{11}}{\mathrm{L_2Pt^{II}{}_2(\mu\text{-}OH)_2}} + \mathrm{2H_2O} \tag{7}$$

Trace amounts of complex **4** (2−5%) could be seen in ^{1}H NMR spectra of the resulting solution when isomerization was carried out at concentrations of **1** higher than 5 mM. Upon removal of the solvent under vacuum at room temperature, **1-^{18}O** was isolated in 96% yield, pure according to ^{1}H NMR. To obtain complex **1-^{18}O** in a pure form, it is critical to carry out the thermal isomerization of LPt^{IV}Me(OH)$_2$ in dilute solutions.

Preparation of LPt^{IV}CD$_3$(OH)$_2$, 1-d_3. The symmetrical complex **1-d_3** containing a completely deuterated methyl ligand was synthesized according to Scheme 11 in a manner similar to that described above for **1-^{18}O**.

The d_5-labeled aqua methyl platinum(II) complex **9-d_5**, LPt^{II}CD$_3$(OD$_2$), was prepared in virtually quantitative yield by dissolving dimethyl hydride **10** in D$_2$O at 40−45 °C (eq 8):

$$\underset{\mathbf{10}}{\mathrm{LPt^{IV}(CH_3)_2H}} + \mathrm{8D_2O} \rightarrow \mathrm{CD_4} + \underset{\mathbf{9\text{-}}d_5}{\mathrm{LPt^{II}CD_3(OD_2)}} + \mathrm{7HOD} \tag{8}$$

Complete H/D exchange in the Pt-bound methyl groups preceded the C−D reductive elimination of methane as established in an earlier report.[17] Aerobic oxidation of the resulting **9-d_5** was performed in regular water. The reaction produced cleanly, according to ^{1}H NMR, the *unsymmetrical* **1-d_3** (eq 9, Scheme 11):

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$$\underset{\mathbf{9\text{-}}\boldsymbol{d_3}}{2\mathrm{LPt^{II}CD_3(OH_2)}} + \mathrm{O_2} \rightarrow 2\ \underset{unsym\text{-}\mathbf{1\text{-}}\boldsymbol{d_3}}{unsym\text{-}\mathrm{LPt^{IV}CD_3(OH)_2}} \tag{9}$$

An ESI-MS analysis of the reaction mixture diluted with H_2O showed that after 5 h all $\mathrm{LPt^{II}CD_3(OH_2)}$ complex had reacted and the deuterium-labeled complex $\mathrm{LPt^{IV}CD_3(OH)_2}$ formed. Upon removal of the solvent under vacuum at room temperature, the residue was dissolved in a large volume of distilled water and isomerized at 90 °C. After 3 h, according to ^{1}H NMR, the unsymmetrical dihydroxo $\mathrm{Pt^{IV}}$ complex had transformed to the symmetrical isomer $\mathrm{LPt^{IV}CD_3(OH)_2}$. Upon filtration of the mixture, the solvent was removed under vacuum at room temperature to produce symmetrical **1-*d*₃** in 87% yield, pure according to ^{1}H NMR.

Preparation and Characterization of Isomeric $\mathbf{LPt^{IV}Me(OMe)(OH)}$, 4 and 13. Complex **4** was prepared using a multistep reaction sequence shown in Scheme 12 in a manner similar to that for complexes **1-*d*₃** and **1-^{18}O**. The difference was that methanol was used as a solvent to prepare $\mathrm{LPt^{II}Me(MeOH)}$, **12**, a methanol analogue of the aqua complex **9** (eq 10):

$$\underset{\mathbf{10}}{\mathrm{LPt^{IV}Me_2H}} + \mathrm{MeOH} \rightarrow \mathrm{MeH} + \underset{\mathbf{12}}{\mathrm{LPt^{II}Me(MeOH)}} \tag{10}$$

Complex **12** formed quantitatively and was pure according to ^{1}H NMR.

Complex 13. (a) Synthesis and Characterization. Oxidation of **12** to produce the $\mathrm{Pt^{IV}}$ methoxo hydroxo methyl complex **13** with equatorial methoxo and methyl ligands was performed in methanol without isolation of **12** (eq 11):

$$\underset{\mathbf{12}}{2\mathrm{LPt^{II}Me(MeOH)}} + \mathrm{O_2} \rightarrow \underset{\mathbf{13}}{2\mathrm{LPt^{IV}Me(OMe)(OH)}} \tag{11}$$

The reaction was complete after 5 h at room temperature, according to ^{1}H NMR, and yielded the single reaction product $\mathrm{LPt^{IV}Me(OMe)(OH)}$, **13**, as a pale yellow precipitate. The compound was isolated by filtration in 75% yield in an analytically pure form. Its ^{1}H NMR spectra in D_2O exhibited a singlet of the methyl ligand at 2.44 ppm with two platinum-195 satellites and $^2J_{\mathrm{195PtH}} = 67$ Hz. Two platinum-195 satellites were seen near the signal of the methoxo ligand at 2.96 ($^3J_{\mathrm{195PtH}} = 23$ Hz). The dpms ligand in **13** produced eight multiplets integrating as 1H each and one singlet of the CH bridge at 6.67 ppm.

(b) Structure. X-ray quality crystals of **13** were obtained by slow vapor diffusion of diethyl ether into a saturated solution of **13** in a MeOH−H_2O mixture containing 0.5 equiv of HBF_4 added to increase solubility of **13**. The structure (Figure 1a; Table 1) was shown to have two enantiomeric hydrogen-bonded moieties of **13** and a methanol molecule in a unit cell. Both enantiomers of **13** had practically identical geometrical parameters. The configuration at the platinum(IV) atom was slightly distorted octahedral with methoxo and methyl ligands in the equatorial plane defined as the plane of the platinum and two nitrogen atoms of the dpms ligand. The Pt1−N1 bond length, 2.156 Å, *trans* to the methyl ligand, was significantly longer than the Pt1−N2 bond, 2.052 Å, which was *trans* to the methoxo ligand.

Complex 4. (a) Synthesis and Characterization. Complexes **4** and **13** turned out to be hydrolytically unstable in aqueous solutions and slowly produced complex **1** or *unsym*-**1**, respectively, and methanol already at room temperature (see, for instance, eq 12):

$$\underset{\mathbf{4}}{\mathrm{LPt^{IV}Me(OH)(OMe)}} + \mathrm{H_2O} \rightarrow \underset{\mathbf{1}}{\mathrm{LPt^{IV}Me(OH)_2}} + \mathrm{MeOH} \tag{12}$$

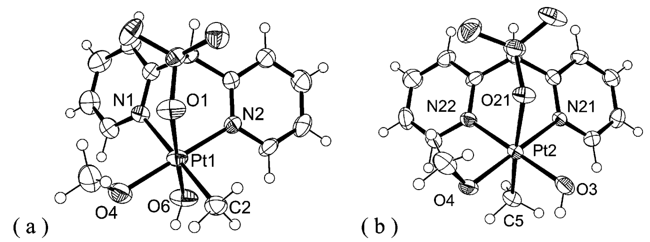
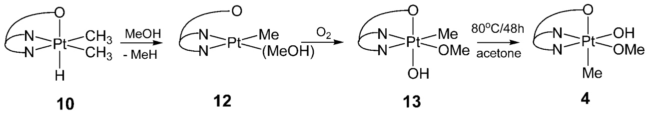


Figure 1. ORTEP drawings of complex **13** (a) and one of the isomeric moieties **4** (b) present in $\mathbf{4_2}\cdot\mathrm{HBF_4}$, 50% probability ellipsoids. Selected bond distances, Å, and angles, deg, for complex **13**: Pt1−O1, 2.101; Pt1−O4, 1.977; Pt1−O6, 1.952; Pt1−N1, 2.156; Pt1−N2, 2.052; Pt1−C2, 2.099; O1−Pt1−N1, 89.57; O1−Pt1−N2, 89.28; O1−Pt1−O4, 95.15; O1−Pt1−C2, 89.92; N1−Pt1−N2, 86.99; N2−Pt1−C2, 93.65; N1−Pt1−O4, 90.31; O1−Pt1−O6, 178.39. For moiety **4**: Pt2−O3, 1.982; Pt2−O4, 1.990; Pt2−O21, 2.220; Pt2−N21, 2.040; Pt2−N22, 2.020; Pt2−C5, 2.025; O21−Pt2−N22, 91.76; O21−Pt2−N21, 84.54; O21−Pt2−O4, 96.18; O21−Pt2−O3, 87.62; N21−Pt2−N22, 89.99; N21−Pt1−O3, 90.31; N22−Pt2−O4, 90.08; O21−Pt2−C5, 176.51.

Scheme 12



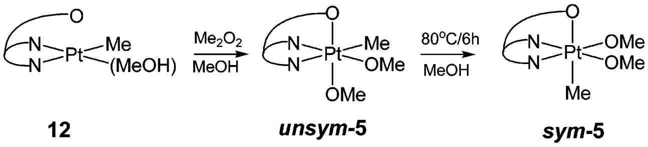
Because of the hydrolytic instability, subsequent isomerization of **13**, having the equatorial PtMe group, to complex **4**, featuring the axial PtMe, was performed in refluxing acetone. The poorly soluble reaction product **4** was filtered off after 48 h and washed with hot acetone. An analytically pure yellowish complex was obtained in 66% yield after drying under high vacuum. Similar to its isomeric complex **13**, **4** exhibited in its ^{1}H NMR spectra in aqueous solutions a singlet at 2.58 ppm with two platinum-195 satellites ($^2J_{\mathrm{195PtH}} = 77$ Hz), corresponding to the methyl ligand. Two platinum-195 satellites belonging to the methoxo ligand were seen near the signal at 3.08 ppm ($^3J_{\mathrm{195PtH}} = 28$ Hz). The dpms ligand in **4** produced eight multiplets, integrating as 1H each, and one singlet assigned to the CH bridge at 6.53 ppm. A carbon-13 NMR spectrum of **4** in D_2O showed the presence of a signal of the PtMe group at 12.5 ppm ($^1J_{\mathrm{PtC}} = 641$ Hz), a signal of the PtOMe group at 56.0 ppm ($^2J_{\mathrm{PtC}} = 14$ Hz), and 10 signals originating from the CH bridge and two pyridine rings, one of the signals integrating as 2C, consistent with the assigned C_1 symmetric structure. ESI-MS of **4** in methanol acidified with one drop of HBF_4 showed a signal expected for a protonated **4**.

(b) Structure. Comparison with 13. X-ray quality crystals of the salt $\mathbf{4_2}\cdot\mathrm{HBF_4}$ were produced by layering saturated methanolic solution of **4** containing 0.5 equiv of HBF_4 with an equal volume of benzene. The structure (Figure 1b; Table 1) was shown to have two noninteracting enantiomeric fragments of **4**. On average, one of the two fragments was protonated on the oxygen of the hydroxo ligand. Bond lengths in the protonated and nonprotonated fragments differed by up to 0.02 Å. The platinum atom had a slightly distorted octahedral geometry with

Table 1. Crystal Structure Data and Structure Refinement for Complexes 4_2·HBF$_4$, 13, and *cis*-6

	4_2·HBF$_4$	**13**	***cis*-6**
formula	$C_{27.625}H_{39.50}BF_4N_4O_{11.625}Pt_2S_2$	$C_{14}H_{20}N_2O_6PtS$	$[C_{23}H_{23}N_4O_8Pt_2S_2](BF_4)\ 6H_2O$
fw	1154.74	539.47	1132.66
cryst syst	triclinic	monoclinic	triclinic
space group	$P\bar{1}$	$P2_1/c$	$P1$
a (Å)	11.1100(16)	8.457(3)	11.3558(10)
b (Å)	11.5756(17) Å	24.941(9)	11.5175(10)
c (Å)	15.568(2) Å	8.718(3)	15.3258(14)
α (deg)	99.996(3)	90°	111.3060(10)
β (deg)	100.958(3)	107.501(6)°	106.321(2)
γ (deg)	109.545(2)	90°	96.637(2)
Z	2	4	2
density, calc (g/cm^3)	2.142	2.043	2.164
abs coeff (mm^{-1})	8.006	8.152	8.249
F(000)	1111 ē	1040 ē	1084 ē
cryst size (mm^3)	0.12 × 0.07 × 0.06	0.095 × 0.085 × 0.045	0.275 × 0.175 × 0.032
cryst habit	colorless prism	colorless prism	colorless prism
θ range (deg)	2.57 to 25.00	2.53 to 25.00	2.68 to 25.00
index ranges	$-13 \le h \le 13$	$-10 \le h \le 9$	$-13 \le h \le 12$
	$-13 \le k \le 13$	$-29 \le k \le 29$	$-13 \le k \le 12$
	$-18 \le l \le 18$	$-10 \le l \le 10$	$0 \le l \le 18$
no. of reflns collected	18 131	8399	6752
no. of indep reflns	6046	3072	6759
no. of obs reflns	4490	2455	5494
final R indices	R_1, $I > 2\sigma(I)$ 0.0321	0.0359	0.0514
	wR_2, all data 0.0712	0.0787	0.1282
	R_{int} 0.0312	0.0344	0.0000
	R_{sig} 0.0499	0.0428	0.0265

Scheme 13



the hydroxo and the methoxo ligands in the equatorial and the methyl group in the axial position. Remarkably, in spite of the positive charge delocalization between two moieties of **4** in 4_2·H$^+$, the length of the Pt−O bond including the sulfonate group oxygen atom was much longer in the moiety **4**, 2.220 versus 2.101 Å in **13**. The difference was due to a much stronger *trans* influence of the methyl ligand as compared to the *trans* influence of the hydroxo ligand, both *trans* to the sulfonate in **4** and **13**, respectively.

Preparation and Characterization of Isomeric LPt^{IV}Me(OMe)$_2$, *sym*-5 and *unsym*-5. Dimethoxo hydroxo methyl platinum(IV) complex *sym*-**5** was synthesized using a two-step procedure as shown in Scheme 13. First, methanol methyl platinum(II) complex **12** was oxidized by dimethylperoxide to produce the unsymmetrical isomer, *unsym*-**5** (eq 13):

$$\underset{\mathbf{12}}{\mathrm{LPt^{II}Me(MeOH)}} + \mathrm{Me_2O_2} \rightarrow \underset{unsym\text{-}\mathbf{5}}{\mathrm{LPt^{IV}Me(OMe)_2}} + \mathrm{MeOH} \qquad (13)$$

The resulting *unsym*-**5** was characterized by ^{1}H and ^{13}C NMR and used for thermal isomerization to *sym*-**5** in methanol solution without isolation. A ^{1}H NMR spectrum of *unsym*-**5** in methanol showed the presence of three signals of equal intensity integrating as 3H and originating from the PtMe group (2.40 ppm, $^2J_{195PtH} = 70$ Hz), two methoxo ligands at 2.65 ($^3J_{195PtH} = 55$ Hz) and 2.89 ppm ($^3J_{195PtH} = 25$ Hz), along with a singlet of the dpms ligand CH bridge at 6.51 ppm and a set of eight partially overlapping multiplets, all integrating as 1H, typical for C_1 symmetric dpms complexes. A carbon-13 NMR spectrum of *unsym*-**5** was consistent with the assigned configuration of a low symmetry.

Isomerization of *unsym*-**5** to *sym*-**5** was achieved by heating a solution of *unsym*-**5** in methanol at 80 °C for 6 h. The isolated yield of the analytically pure complex **5** was 46%. The ^{1}H NMR spectrum of *sym*-**5** in D$_2$O exhibited the presence of a signal of the PtMe group at 2.50 ppm with two platinum-195 satellites ($^2J_{195PtH} = 77$ Hz) integrating as 3H, a signal of the methoxo ligands at 3.08 ppm with the platinum-195 satellites ($^3J_{195PtH} = 27$ Hz) integrating as 6H, a singlet of the dpms CH bridge at 6.50 ppm (1H), and four multiplets of the dpms pyridine rings integrating as 2H each, consistent with the expected C_s symmetric structure. According to ESI-MS, aqueous solutions of *sym*-**5** showed a signal expected for protonated *sym*-**5**.

Preparation of Isomeric [LPt^{IV}Me(μ-OH)$_2$Pt^{II}L]BF$_4$, *cis*- and *trans*-6. (a) Synthesis and Characterization. Isomeric cationic complexes *cis*- and *trans*-**6**, [LPt^{IV}Me(μ-OH)$_2$Pt^{II}L]BF$_4$ (Scheme 4), were prepared by mixing an aqueous solution of LPt^{IV}Me(OH)$_2$ and a HBF$_4$-acidified solution of [LPt^{II}(OH$_2$)$_2$]BF$_4$[13] (eq 14, Scheme 8):

$$\underset{\mathbf{1}}{\mathrm{LPt^{IV}Me(OH)_2}} + \underset{\mathbf{3}}{\mathrm{LPt^{II}(OH_2)_2}^+} \overset{K_6}{\rightleftharpoons} \underset{cis\text{- and }trans\text{-}\mathbf{6}}{\mathrm{LPt^{IV}Me(\mu\text{-}OH)_2Pt^{II}L^+}} + 2\mathrm{H_2O} \qquad (14)$$

The mixture was heated at 95 °C for a short time, cooled to room temperature, and left for 1 week. Isomeric complexes [LPt^{IV}Me(μ-OH)$_2$Pt^{II}L]BF$_4$ crystallized from the reaction mixture as colorless crystals that were collected, washed with water, and dried. The isolated yield of an analytically pure product containing *cis*- and *trans*-**6** in a 3:1 ratio was 41%. Depending on the crystallization conditions, solid *cis*-**6** could be produced in a more isomerically pure form. According to ^{1}H NMR, both isomeric complexes **6** produced similar sets of signals in aqueous solutions. In particular, the signal originating from the PtMe group appeared at 3.56 ppm ($^2J_{195PtH} = 64$ Hz) for the *cis* and at 3.38 ppm for the *trans* isomer. Two singlets of two dpms CH bridges integrating as 1H each and eight partially overlapping multiplets of the dpms pyridyl groups integrating as 2H each were also observed. According to ESI-MS, aqueous

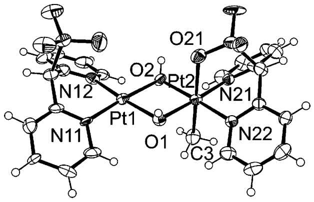


Figure 2. ORTEP drawings of cationic complex ***cis*-6**, 50% probability ellipsoids. Selected bond distances, Å: Pt1−O1, 2.085; Pt1−O2, 2.041; Pt2−O1, 2.019; Pt2−O2, 2.029; Pt1−Pt2, 3.076; Pt2−C3, 2.033; Pt2−O21, 2.221.

solutions of **6** produced peaks expected for [LPt^{IV}Me(μ-OH)$_2$Pt^{II}L]$^+$.

When dissolved in water, **6** formed complexes **1** and **3** and a poorly water-soluble dinuclear species L$_2$Pt$_2$(μ-OH)$_2$.[13] The half-life for disappearance of **6** was 11 h at 22 °C.

In the presence of 60 mM HBF$_4$, **6** produced complexes **1** and **3** with a half-life of 9 h at 22 °C. Methanol and intermediate **4** (traces) formed upon heating of acidic solutions.

(b) Structure. X-ray quality crystals of *cis*-**6** were prepared by a slow crystallization from a reaction mixture. The structure (Figure 2, Table 1) was shown to have two platinum atoms at a distance of 3.076 Å, one platinum atom in a square-planar and another platinum atom in an octahedral environment. Both platinum atoms, two bridging oxygens, and four nitrogen atoms of two dpms ligands are located in one plane. Two sulfonate groups are above the plane; hence the term "*cis*" was used to designate this isomer. The lengths of Pt−O, Pt−N, and Pt−C bonds around the Pt^{IV} center are almost the same as in complex **4**; for instance, the Pt−sulfonate oxygen bond was 2.221 Å long.

Kinetic Studies of Reaction between 1 and H$_2$O in Acidic Solutions. (**a) Reaction 3 Balance.** Complex **1** reacted in clear, acidic, aqueous solutions at 25−80 °C to ultimately produce methanol, complex **3**[13] (eq 3), and dimethyl ether (eq 4). The fraction of dimethyl ether depended on the concentration of **1** and the acidity of the reaction mixture, and it never exceed 5−7%. By the end of the reaction, methanol (93−95% yield) and dimethyl ether (5−7%) were the only organic products formed in virtually quantitative combined yield. Formation of methanol and Me$_2$O was confirmed by ESI-MS and by ^{1}H NMR spectroscopy. The methanol peak appeared at 3.3−3.5 ppm depending on the acidity of solution, and the ESI mass spectra showed the peak of the CH$_3$^{16}OH$_2$$^+$ ion with $m/z = 33.03176$. When methanol was present at concentrations well below 1 mM, this peak was weak and could interfere with a signal of adventitious ^{16}O$_2$H$^+$ (calc $m/z = 32.99765$). When this was the case, the peak could not be integrated accurately. Dimethyl ether produced a ^{1}H NMR signal at 3.2−3.4 ppm, always slightly upfield shifted compared to the methanol peak. ESI mass spectra of Me$_2$O showed a signal at $(m+\mathrm{H}^+)/z = 47.042$.

Besides the products of reactions 3 and 4, formation of intermediates **4** and **5** and isomeric complexes **6** was observed in the beginning of the reaction. These intermediates persisted at the middle stages and eventually disappeared when the reaction was complete. Figure 3 shows the concentration dependence of complexes **1**, **3**, **4**, **5**, **6**, methanol, and Me$_2$O on reaction time for a 41 mM solution of **1** in 60 mM HBF$_4$ at 80 °C. Assuming that equilibrium 2 is very fast on the NMR time scale, the concentration of complex **1** determined by NMR integration represented the total concentration of free **1** and its protonated form, complex **2**.

Considering methanol, dimethyl ether, **1**, **3**, **4**, **5**, and **6** as the major species involved in the reaction of complex **1** in acidic aqueous solutions (Figure 3), the balance of all methyl groups originating from the MePt^{IV} fragment of **1** and all dpms ligands also having their origin in complex **1** was calculated. The combined concentrations of methanol, complex **1**, isomeric complexes **6**, doubled concentrations of dimethyl ether and complex **4**, each bearing two methyl groups, and a tripled concentration of **5** incorporating three methyls remained constant at 41 ± 2 mM up to a 95% conversion of complex **1**. Similarly, the combined concentration of complexes **1**, **3**, **4**, and **5** and a doubled concentration of isomeric dinuclear complexes **6** remained constant, 41 ± 2 mM, for the same period of time.

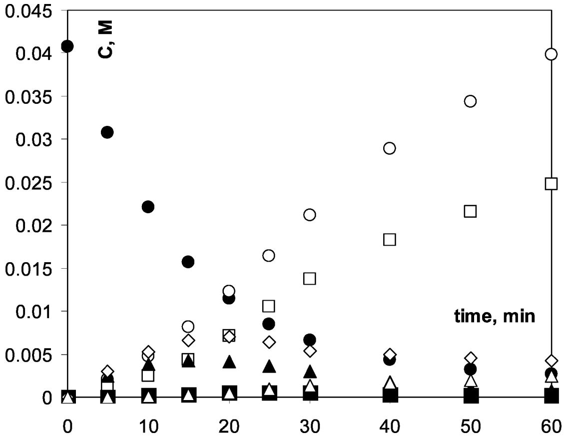


Figure 3. Concentration of components of a reaction mixture composed by 41 mM complex **1** and D$_2$O in the presence of 60 mM of HBF$_4$, 80 °C, as a function of reaction time: **1** (filled circles), MeOH (empty circles), Me$_2$O (empty triangles), **3** (empty squares), **4** (filled triangles), two isomeric complexes **6** (diamonds), and **5** (filled squares).

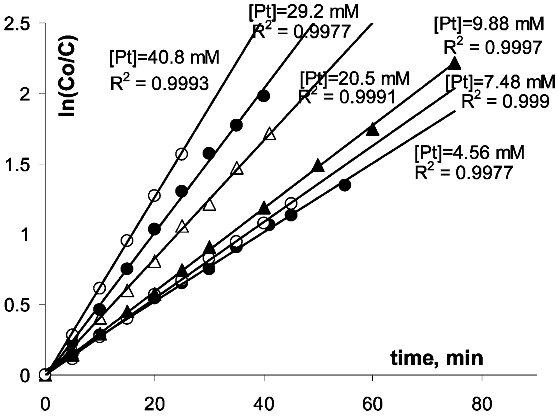


Figure 4. First-order kinetic plots of reaction between complex **1** and D$_2$O at [HBF$_4$] = 60 mM and 80 °C; C_0 and C are initial and current concentrations of **1**.

(b) Effect of Reactants' Concentration, [H$^+$] and [Pt^{IV}], on the Rate of Disappearance of Complex 1. A kinetic study of reaction 3 was carried out in 60 and 120 mM HBF$_4$ solutions in D$_2$O at 80 °C with the initial concentration of complex **1**, C_0, ranging from 4.6 to 40.8 mM.

Good linear plots of ln(C_0/C) versus time were obtained for [HBF$_4$] = 60 and 120 mM (Figure 4), suggesting that reaction 3 was first-order in complex **1**. Corresponding pseudo-first-order rate constants, k_{obs}, were found to be dependent on the *initial* concentration of complex **1**, [Pt]$_0$ (Table 2).

The pseudo-first-order rate constants for the formation of methanol, $k_{obs,MeOH}$, were independent of [Pt]$_0$ $(6.0 \pm 0.2) \times 10^{-4}$ s^{-1} for [H$^+$] = 120 mM and $(3.7 \pm 0.1) \times 10^{-4}$ s^{-1} for [H$^+$] = 60 mM.

(c) Effect of Additives of Complex 3 and MeOH on the Rate of Disappearance of Complex 1. Kinetic experiments

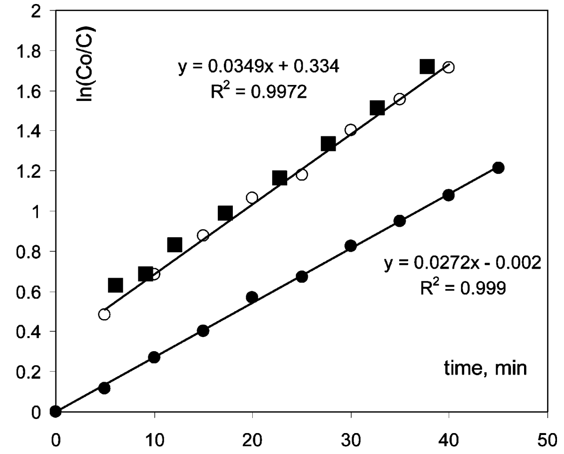


Figure 5. First-order kinetic plot for (i) reaction of 7.48 mM **1** in D_2O (filled circles), (ii) reaction of 7.63 mM **1** in D_2O in the presence of 7.48 mM **3** (empty circles); (iii) reaction of 7.44 mM **6** in D_2O (filled squares). In all experiments $[HBF_4] = 60$ mM and temperature is 80 °C. C_0 is the initial concentration of **1** measured before addition of **3** (experiment i or ii) or initial concentration of **1** expected as a result of complete dissociation of **6** used instead of **1** and **3** in experiment iii. C is the current concentration of **1** as determined by ^{1}H NMR integration of the PtMe signal of **1**.

Table 2. Observed Pseudo-First-Order Rate Constants of Disappearance of Complex 1, k_{obs}, Measured at Various Initial Concentrations, $[Pt]_0$, and HBF_4 Additive; 80 °C

$[H^+] = 60$ mM		$[H^+] = 120$ mM	
$[Pt]_0$, mM	$k_{obs} \times 10^4$, s^{-1}	$[Pt]_0$, mM	$k_{obs} \times 10^4$, s^{-1}
4.56	4.10 ± 0.15	5.01	7.69 ± 0.31
7.48	4.53 ± 0.15	9.88	8.18 ± 0.36
9.88	4.92 ± 0.07	20.8	9.67 ± 0.49
20.5	6.99 ± 0.19	28.4	10.57 ± 0.38
29.2	8.52 ± 0.37	40.0	12.31 ± 0.79
40.8	10.63 ± 0.23		

performed with acidic aqueous solutions of complex **1** showed that both the rate of disappearance of **1** and the rate of formation of methanol could be accelerated by reaction 3 product, complex **3**, and remained unaltered by methanol additives.

A 7.48 mM solution of **1** was reacted with 60 mM HBF_4 in D_2O at 80 °C (eq 3). The reaction followed first-order kinetics with the observed rate constant $k_{obs} = (4.53 \pm 0.05) \times 10^{-4}$ s^{-1} (Figure 5, lower line). When the reaction was complete, a small sample of the resulting solution of **3** was diluted 100-fold with regular water. An ESI mass spectrum of the dilute solution showed one mass envelope of a platinum-containing complex that corresponded to $L^{195}Pt(OH_2)_2{}^+$.

A sample of solid **1** was combined with a 7.48 mM solution of **3** above in 60 mM HBF_4 in D_2O at room temperature so that the resulting mixture contained 7.48 mM **3** and 7.63 mM **1**. Heating the mixture at 80 °C led to very fast consumption of some part of **1** in the first few minutes (time <5 min, Figure 5). An ESI-MS analysis evidenced formation of complexes **6** (eq 14, Scheme 4). The plot of $\ln(C_0/C)$ versus time was practically linear after 5 min (Figure 5, upper line), with the observed pseudo-first-order rate constant $k_{obs} = (5.82 \pm 0.30) \times 10^{-4}$ s^{-1}.

When instead of a mixture of 7.63 mM **1** and 7.48 mM **3** (Figure 5, upper line, empty circles) a 7.44 mM solution of isomeric complexes **6** was used, an undistinguishable kinetic plot was observed (Figure 5, upper line, filled squares).

In contrast to the effect of complex **3** additives on the *initial* rate of disappearance of **1** (Figure 5), formation of methanol was first-order in **1** for the *whole* period of reaction. At the same time, methanol formed faster in a 1:1 mixture of **1** and **3**, with the observed pseudo-first-order rate constant $k_{obs,MeOH} = (3.70 \pm 0.27) \times 10^{-4}$ s^{-1} (upper line, Figure 6). Pure complex **1** produced methanol at 80 °C with the observed pseudo-first-order rate constant $k_{obs,MeOH} = (2.74 \pm 0.09) \times 10^{-4}$ s^{-1} (lower line, Figure 6):

$$\frac{d[MeOH]}{dt} = k_{obs,MeOH}[Pt^{IV}]$$

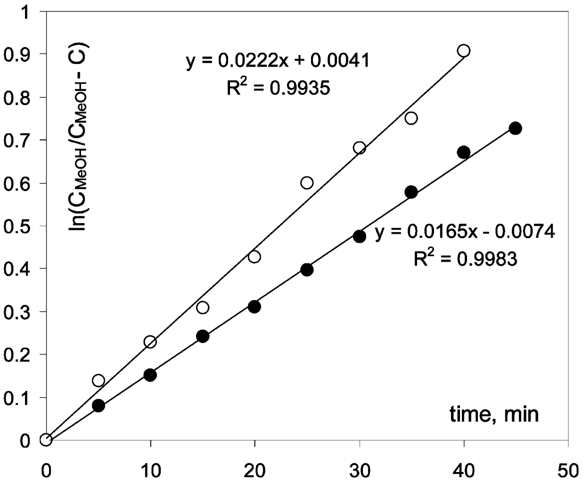


Figure 6. Kinetic plot of formation of methanol in a reaction between a 7.48 mM solution of **1** and D_2O (filled circles) and a reaction between a 7.63 mM solution of **1** and D_2O in the presence of 7.48 mM **3** (empty circles); $[HBF_4] = 60$ mM and 80 °C; C_{MeOH} and C are the final and current concentrations of MeOH.

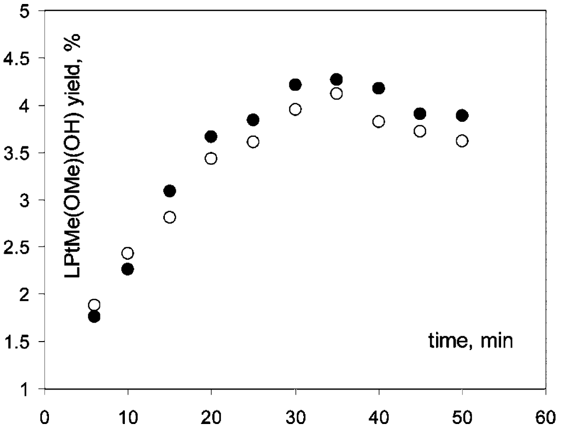


Figure 7. Formation of intermediate **4** in a 8.8 mM solution of complex **1** in D_2O in the absence (filled circles) and in the presence of 50 mM MeOH (empty circles) at 80 °C; $[HBF_4] = 60$ mM.

In order to establish the effect of another reaction 3 product, methanol, on the rate of disappearance of **1**, an experiment was set up where an 8.8 mM solution of complex **1** reacted with D_2O at 80 °C in the presence of 50 mM methanol. Thus, the initial concentration of MeOH exceeded more than 5-fold the concentration of methanol expected in this system upon completion of reaction 3. The experiment showed the rate of disappearance of **1** of $(4.55 \pm 0.23) \times 10^{-4}$ s^{-1}. Virtually the same reaction rate was observed in the absence of methanol additives $(4.60 \pm 0.15) \times 10^{-4}$ s^{-1}. No change in the rate of formation of methoxo complex **4** was seen in the presence of the methanol additive (Figure 7).

(d) Isotopic Labeling Experiments. (i) Reaction of Complexes 1 and 1-*d*$_3$ with $H_2{}^{18}O$. A reaction between 38 mM **1**

Table 3. Ratio of Isotopologous Alcohols, $CH_3{}^{18}OH/CH_3{}^{16}OH$, Established by ESI-MS as a Function of Reaction Time; 63 mM HBF_4 and 38 mM 1 in 98% Enriched $H_2{}^{18}O$ at 80 °C

	time, min			
	12	25	40	70
$CH_3{}^{18}OH/CH_3{}^{16}OH$	1.7	2.1	2.4	2.4

Table 4. $CD_3{}^{18}OH/CD_3{}^{16}OH$ Ratio at the Early Stages of Reaction between 1-d_3 and 120 mM [HBF_4] in $H_2{}^{18}O$ Solution at 80 °C, as Established by ESI-MS at Various Concentration of Complex 1-d_3

	[Pt], mM			
	29	39	60	120
$CD_3{}^{18}OH/CD_3{}^{16}OH$	4.8	2.7	2.2	1.2
[Pt]•($CD_3{}^{18}OH/CD_3{}^{16}OH$)	140	110	130	140

and 63 mM HBF_4 in 98% enriched $H_2{}^{18}O$ at 80 °C resulted in the formation of *two* isotopologous alcohols, $Me^{18}OH$ (eq 15) and $Me^{16}OH$ (eq 16):

$$\underset{\mathbf{1}}{LPt^{IV}Me(^{16}OH)_2} + H^+ + 3H_2{}^{18}O \rightarrow \underset{\mathbf{3\text{-}^{18}O_2}}{LPt^{II}(^{18}OH_2)_2{}^+} + Me^{18}OH + 2H_2{}^{16}O \quad (15)$$

$$\underset{\mathbf{1}}{LPt^{IV}Me(^{16}OH)_2} + H^+ + 2H_2{}^{18}O \rightarrow \underset{\mathbf{3\text{-}^{18}O_2}}{LPt^{II}(^{18}OH_2)_2{}^+} + Me^{16}OH + H_2{}^{16}O \quad (16)$$

The ratio of the major products, $Me^{18}OH/Me^{16}OH$, as established by ESI mass spectrometry, was 1.7/1 in the beginning of the reaction (12 min, 13% conversion of **1**; see Table 3) and steadily increased over time, reaching 2.4/1 when the reaction was almost complete (70 min, 95% conversion).

According to ESI-MS, signals belonging to $LPt^{IV}Me(OMe)OH_2{}^+$, $LPt^{IV}Me(OMe)_2H^+$, and $LPt^{IV}Me(\mu\text{-}OH)_2Pt^{II}L^+$ grew over time, passed a maximum, and then diminished and disappeared. No peaks of comparable intensity were seen for ^{18}O-isotopologous compounds, such as $LPt^{IV}Me(OMe)^{18}OH_2{}^+$, $LPt^{IV}Me(OMe)(^{18}OMe)H^+$, and $LPt^{IV}Me(\mu\text{-}^{18}OH)(\mu\text{-}OH)Pt^{II}L^+$, up to at least 80% conversion of **1**.

Similar ESI-MS experiments were performed with the deuterium-labeled complex $LPt^{IV}CD_3(OH)_2$, **1-*d*₃**, and 120 mM HBF_4 in $H_2{}^{18}O$. Concentration of complex **1-*d*₃** was varied from 29 to 120 mM. Peaks derived from isotopologous methanols, $CD_3OH_2{}^+$ with $m/z = 36.05256$ $CD_3{}^{16}OH_2{}^+$ and $CD_3{}^{18}OH_2{}^+$ with $m/z = 38.05686$, did not interfere with a peak of adventitious O_2H^+ (calc $m/z = 32.99765$), so that the ratio of the alcohols could be determined more reliably compared to analogous nondeuterated isotopologous species CH_3X ($X = {}^{16}OH$ and ^{18}OH). The results given in Table 4 show that the $CD_3{}^{18}OH/CD_3{}^{16}OH$ ratio measured at low conversions of **1-*d*₃** (~10%) decreased approximately linearly with 1/[**1-*d*₃**].

(ii) Reaction of Complex 1-^{18}O with $H_2{}^{16}O$. In a similar experiment a 26 mM solution of ^{18}O-labeled complex **1-^{18}O**, $LPt^{IV}Me(^{18}OH)(OH)$, was reacted with 63 mM HBF_4 in $H_2{}^{16}O$ at 80 °C. Formation of the 17/83 mixture of the ^{18}O-labeled and a nonlabeled methanol was observed at ~83% conversion of **1-^{18}O**.

(iii) Attempted $^{16}O/^{18}O$ Exchange between CH_3OH and $H_2{}^{18}O$ and a $^{16}O/^{18}O$ Exchange between 1 and $H_2{}^{18}O$. According to ESI mass spectrometry, a solution of 44 mM $CH_3{}^{16}OH$ and 60 mM HBF_4 in $H_2{}^{18}O$ exposed to 80 °C for 3 h had no detectable amounts of $CH_3{}^{18}OH$.

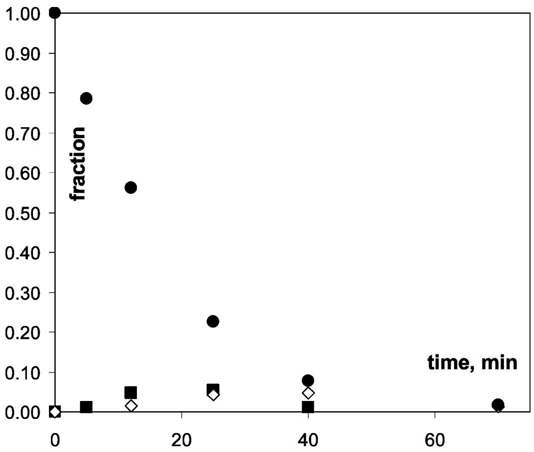
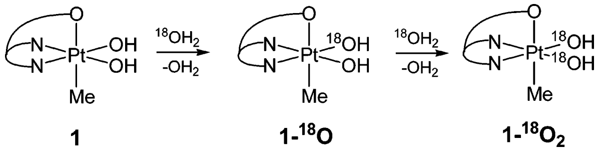


Figure 8. Relative concentrations of isotopologous complexes $LPt^{IV}Me(^{18}OH)_n(^{16}OH)_{2-n}$, $n = 0$ (filled circles), 1 (filled squares), 2 (empty diamonds), given as a fraction of the initial concentration of complex **1** (38 mM), determined by ESI-MS as a function of the reaction time at 80 °C and [H^+] = 63 mM.

Scheme 14



In contrast, ESI-MS monitoring of a 38 mM solution of **1** and 63 mM HBF_4 in $H_2{}^{18}O$ showed that a slow $^{16}O/^{18}O$ exchange took place at 80 °C and both **1-^{18}O** (eq 17) and **1-^{18}O₂** (eq 18) formed (Scheme 14, Figure 8).

$$\underset{\mathbf{1}}{LPt^{IV}Me(^{16}OH)_2} + H_2{}^{18}O \rightarrow \underset{\mathbf{1\text{-}^{18}O}}{LPt^{IV}Me(^{18}OH)(^{16}OH)} + H_2{}^{16}O \quad (17)$$

$$\underset{\mathbf{1\text{-}^{18}O}}{LPt^{IV}Me(^{18}OH)(^{16}OH)} + H_2{}^{18}O \rightarrow \underset{\mathbf{1\text{-}^{18}O_2}}{LPt^{IV}Me(^{18}OH)_2} + H_2{}^{16}O \quad (18)$$

At 75% conversion of $LPt^{IV}Me(OH)_2$, which was observed after 25 min of the reaction, ca. 40% of complex **1** contained either one or two ^{18}O-labels. During this period of time the fraction of the monolabeled isotopologue **1-^{18}O** exceeded that of the doubly labeled **1-^{18}O₂**. Isotopologues with more than two ^{18}O labels were not detected.

(iv) Hydrolysis of Complex 13 in 129 mM HBF_4 Solution in $H_2{}^{18}O$. In order to establish whether the Pt^{IV}−OMe or the Pt^{IV}O−Me bond is cleaved by water (eq 12), an experiment was set up with methoxo hydroxo methylplatinum(IV) complex **13** and acidified $H_2{}^{18}O$. In the case of the Pt^{IV}−OMe bond cleavage formation of $Me^{16}OH$ was expected. If the Pt^{IV}O−Me bond was cleaved by water, isotopologous $Me^{18}OH$ would form. The experiment might be inconclusive if complex **1** resulting from the hydrolysis produced $Me^{18}OH$ at a comparable rate. Since *unsym*-**1** is virtually unreactive in methanol elimination in acidic solutions at room temperature,[13] we studied hydrolysis of methoxo complex **13**, which produced *unsym*-**1**.

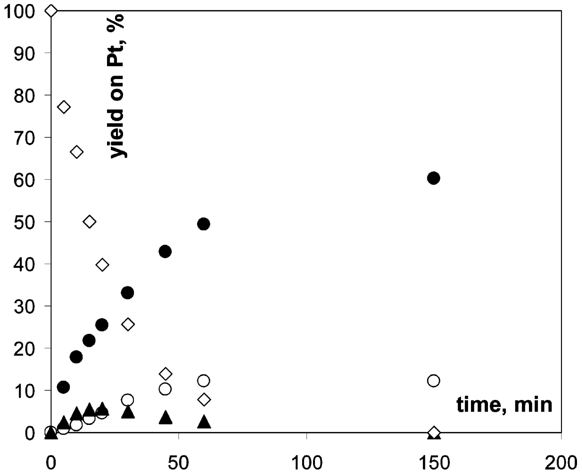


Figure 9. Yield of water-soluble products of reaction of 39 mM **4** (diamonds) with 60 mM HBF_4 in D_2O at 80 °C: MeOH (filled circles), Me_2O (empty circles), *sym*-$LPt^{IV}Me(OMe)_2$, **5** (triangles).

According to GC-MS, a room-temperature hydrolysis of methoxo complex **13** in 129 mM HBF_4 in $H_2{}^{18}O$ solution showed clean formation of $Me^{16}OH$ exclusively (23% conversion of **13** after 3.5 days, eq 19):

$$\underset{\mathbf{13}}{LPt^{IV}Me(OH)(OMe)} + H_2{}^{18}O \xrightarrow{H^+} \underset{unsym\text{-}\mathbf{1}\text{-}^{18}\mathbf{O}}{LPt^{IV}Me(OH)(^{18}OH)} + MeOH \quad (19)$$

No $Me^{18}OH$ isotopologue was found in the reaction mixture.

(v) Effect of Complex 3 Additives on the Reaction between 1 and $H_2{}^{18}O$. An isotope labeling experiment was performed in which complex **3-^{18}O$_2$** was allowed to react with **1-*d*$_3$**. For this purpose 39 mM **3-^{18}O$_2$** was prepared from **1** and 120 mM HBF_4 in 98% $H_2{}^{18}O$. The product was combined with complex **1-*d*$_3$** (39 mM) at 80 °C. After 5 min the $CD_3{}^{18}OH/CD_3{}^{16}OH$ ratio was 2.7:1, which matched the ratio of the methanol isotopologues found in experiments performed under the same conditions but without the additive of **3** (Table 3). Formation of isomeric complexes **6** containing no ^{18}O labels in them, $[LPt^{IV}CD_3(\mu\text{-}^{16}OH)_2Pt^{II}L]^+$, was observed by ESI-MS.

Kinetics and Product Distribution in Reaction between 4 and H_2O at Various [H^+]. A 39 mM solution of complex **4** reacted with 60 mM HBF_4 in D_2O to produce, according to ^1H NMR spectroscopy and ESI mass spectrometry, up to 12% of Me_2O (Scheme 7, eq 20) and up to 5% of dimethoxo complex $LPt^{IV}Me(OMe)_2$, **5** (Scheme 6, eq 21), along with complexes **3** and **14** and methanol (Figure 9):

$$\underset{\mathbf{4}}{LPt^{IV}Me(OH)(OMe)} + H^+ + H_2O \rightarrow \underset{\mathbf{3}}{LPt^{II}(OH_2)_2{}^+} + Me_2O \quad (20)$$

$$\underset{\mathbf{4}}{4LPt^{IV}Me(OH)(OMe)} \rightarrow \underset{\mathbf{14}}{L_2Pt^{II}{}_2(\mu\text{-}OMe)_2} + \underset{\mathbf{5}}{2LPt^{IV}Me(OMe)_2} + 2H_2O \quad (21)$$

The observed pseudo-first-order rate constant of disappearance of **4** in the experiment described above with 39 mM **4** and 60 mM HBF_4 in D_2O solution was found to be (7.1 ± 0.1) × 10^{-4} s^{-1} at 80 °C.

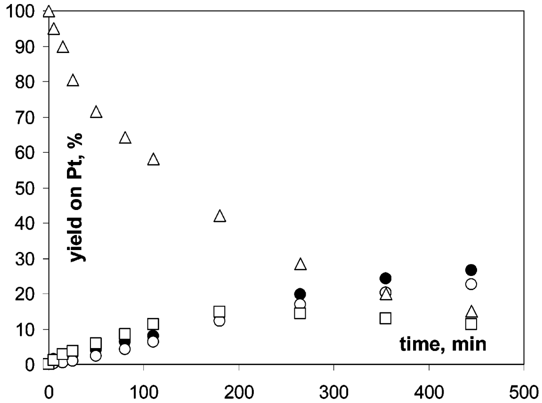


Figure 10. Yield of water-soluble products of reaction of 42 mM **4** (triangles) in neutral D_2O solution at 80 °C: MeOH (filled circles), Me_2O (empty circles), and *sym*-$LPt^{IV}Me(OMe)_2$, **5** (squares).

Intermediate formation of complex **1** resulting from a partial hydrolysis of **4** in the reaction mixtures was evidenced by ^1H NMR (eq 12). After 3 h, by the end of the reaction, intermediate **5** disappeared to form MeOH and Me_2O in a 5:1 ratio, 60% and 12% yield, respectively, complex **3**, and a small amount of water-insoluble white product **14** (~20% by mass), which was characterized by mass spectrometry, elemental analysis, and acidic hydrolysis as $L_2Pt^{II}{}_2(\mu\text{-}OMe)_2$, a methoxo analogue of $L_2Pt^{II}{}_2(\mu\text{-}OH)_2$ described earlier.[13] The mass spectrum of an acidic aqueous solution of **14** exhibited a signal corresponding to a protonated species $L_2{}^{195}Pt_2(\mu\text{-}OMe)_2H^+$.

A reaction performed with a more dilute, 10.0 mM solution of complex **4** and 60 mM HBF_4 in water showed a much higher, 21:1, $MeOH/Me_2O$ ratio by the end of the reaction.

No methylplatinum(IV) intermediates that could be identified as dimethyl ether complexes such as **7** or **8** (Scheme 7) were detected in reaction mixtures by ^1H NMR at the level of ≥1%. ESI-MS could not be used for detecting $LPt^{IV}Me(OH)(OMe_2)^+$, **7**, since this complex is an isomer of the protonated complex *sym*-**5** present in solution. Still, the use of ESI-MS was efficient for detecting **8** in acidified reaction mixtures containing *sym*-**5**. A solution of complex *sym*-**5** and 60 mM HBF_4 in D_2O produced cation **8** after 30 min of heating at 80 °C.

Finally, in the absence of HBF_4 a slow transformation of 42 mM **4** to a mixture of methanol, dimethyl ether, **5**, and **14** was observed at 80 °C (Figure 10). After 6 h, when the conversion of **4** was 80%, methanol (24% yield), Me_2O (20% yield), and **4** (13% yield) formed, along with ~30% by mass of water-insoluble complex **14**, which was isolated as a solid.

Discussion

Synthesis of Isotopically Labeled Complexes 1-^{18}O and 1-*d*$_3$. The method of preparation of the parent methyl dihydroxo platinum(IV) complex was reported earlier.[13] In this work it was successfully applied to the synthesis of isotopically substituted complexes (Schemes 10 and 11). The configuration of the Pt^{IV} atom in *unsym*-**1-^{18}O** with the ^{18}O-labeled hydroxo ligand in the equatorial position (Scheme 10) was assigned arbitrarily, based on the assumption that equatorial groups in a starting platinum(II) complex do not change their position in the course of aerobic oxidation. The assumption was proven correct for the case of the oxidation of methanol analogue **12** (eq 11, Scheme 12, Figure 1a) and is consistent with the proposed mechanism of oxidation of $LPt^{II}(Alk)(OH)^-$.[18]

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[18] Khusnutdinova, J. R.; Zavalij, P. Y.; Vedernikov, A. N. *Organometallics* **2007**, *26*, 2402.

Synthesis of Isomeric Methoxo Hydroxo Methyl Platinum(IV) Complexes LPt^{IV}Me(OMe)(OH), 4 and 13. Compared to isotopologous aqua methyl platinum(II) complexes **9**, **9-^{18}O**, and **9-*d*$_5$**, their methanol analogue **12** did not show any diminished activity in the oxidation by O_2 (eq 11), suggesting that solvento ligands ROH, which are similar to H_2O, may provide the same level of reactivity.

Importantly, results of structure determination of complex **13** obtained by X-ray diffraction showed that upon oxidation of **12** the platinum atom retained the methyl and methoxo ligands in the equatorial positions. In the simplest mechanistic scenario this means that dioxygen attacked the platinum(II) atom from one of the axial sites.[18,19]

The results of the thermal isomerization of **13** to **4**, similar to the isomerization of *unsym*-**1** to **1**,[13] suggest that complex **4**, the isomer with the methyl ligand *trans* to the sulfonate, as compared to **13**, where the methyl group is *trans* to one of the dpms nitrogen atoms, has greater thermodynamic stability. Significant elongation of the bonds *trans* to the methyl in complexes **4** and **13** suggests a significant weakening of the corresponding bonds. In particular, in complex **4** the *trans* influence of the methyl facilitates dissociation of the best leaving group available there, the sulfonate, which is necessary for the C−O elimination[7] (Scheme 2). Thus, the isomerization of *unsym*-**1** to **1**[13] and **13** to **4** enhances the reactivity of the methyl group toward nucleophilic attacks.

Synthesis of Isomeric Dimethoxo Methyl Platinum(IV) Complexes LPt^{IV}Me(OMe)$_2$, *sym*-5 and *unsym*-5. According to ^{1}H NMR, oxidative addition of Me_2O_2 to LPt^{II}Me(MeOH) leads to an unsymmetrical dimethoxo methyl Pt^{IV} complex, *unsym*-**5** (eq 13). These results suggest that the methyl ligand in the "equatorial" position of the Pt^{II} atom does not relocate in the course of addition. The results do not exclude an option where the oxidant attacks an electron-rich Pt^{II} center at one of the axial sites, as in the case of O_2.[18,19]

Synthesis of Dinuclear Heterovalent Isomeric Complexes LPt^{IV}Me(μ-OH)$_2$Pt^{II}L, *cis*- and *trans*-6. Acidity of Complexes 2 and 3. Formation of isomeric dinuclear complexes **6** (eq 14) is an example of an aqua ligand substitution in the coordination sphere of a platinum(II) atom in the relatively labile complex **3**. The attacking nucleophilic groups originate exclusively from dihydroxo platinum(IV) complex **1**, as is confirmed by the results of ESI-MS analysis of the reaction between **1-*d*$_3$** and **3-^{18}O$_2$**, which produced complex **6** (eq 14) containing no ^{18}O labels in it. Aqua ligand substitution in **3** is expected to be most efficient in acidic solutions where the fraction of cationic **3** is high compared to its less electrophilic conjugated base LPt^{II}(OH)(OH$_2$), **15** (eq 22):

$$\underset{\textbf{15}}{\mathrm{LPt^{II}(OH)(OH_2)}} + \mathrm{H^+} \overset{K_{15}}{\rightleftharpoons} \underset{\textbf{3}}{\mathrm{LPt^{II}(OH_2)_2^{\;+}}} \qquad (22)$$

Complex **15** is unstable in solution and eliminates an aqua ligand readily to form $L_2Pt^{II}_2(\mu\text{-}OH)_2$ **11**.[13] To estimate K_{15}, solutions of LPt^{II}(OH$_2$)$_2$(NO$_3$) were prepared by protonolysis of a KLPt^{II}Me$_2$ complex[17] with an excess of 0.09704 M HNO_3 (see Supporting Information for details). Potentiometric titration of these solutions with 0.1000 M NaOH allowed us to calculate the value of log K_{15} as 4.81 ± 0.01, suggesting that at $[H^+] \approx 0.1$ M most Pt^{II} should be in the form of complex **3**.

To favor formation of **6** (eq 14), the fraction of neutral complex **1** should be high enough compared to the fraction of a less nucleophilic conjugated acid, cationic Pt^{IV} complex **2**, which imposes an upper limit on the acidity of a reaction mixture. The available estimate of the protonation constant of dimethyl hydroxo complex *sym*-LPt^{IV}Me$_2$(OH),[13] a *di*methyl analogue of **1**, was found to be $K \approx 46 \pm 5$ at 97 °C in water. Assuming that *sym*-LPt^{IV}Me$_2$(OH) is more basic than *sym*-LPt^{IV}Me(OH)$_2$, we can get $K_2 < 46$. Therefore, at $[H^+] \approx 0.1$ M equilibrium concentrations of **2** and **1** are expected to be of the same order of magnitude.

Isotopic Labeling Experiments. (**i**) **Reaction of Complex 1 with H$_2$^{18}O.** While the heavier isotopologue Me^{18}OH could result from a bimolecular nucleophilic attack of H$_2$^{18}O at the methyl group carbon of electrophilic complex **2** (Scheme 2, eq 15), the unlabeled, ^{16}O-methanol must form predominantly from starting **1** or **1-*d*$_3$** in a coupling reaction that does *not involve solvent as a nucleophile* (eq 16).

(ii) Reaction of Complex 1-^{18}O with H$_2$^{16}O. The fact that a C−O coupling reaction that does not involve solvent as a nucleophile can occur in solutions of complex **1** was additionally confirmed in an experiment with the ^{18}O-labeled compound **1-^{18}O**, which was allowed to react with H$_2$^{16}O. As in the case of the **1**−H$_2$^{18}O system, a mixture of an ^{18}O-labeled and a nonlabeled methanol formed here. This time the ^{18}O-labeled methanol, Me^{18}OH, could not be a product of a nucleophilic attack of the solvent, H$_2$^{16}O, at **1-^{18}O** (Scheme 2, eq 23):

$$\underset{\textbf{1-}^{\mathbf{18}}\textbf{O}}{\mathrm{LPt^{IV}Me(^{16}OH)(^{18}OH)}} + \mathrm{H^+} + \mathrm{H_2{}^{16}O} \rightarrow \underset{\textbf{3}}{\mathrm{LPt^{II}(^{16}OH_2)_2^{\;+}}} + \mathrm{Me^{18}OH} \qquad (23)$$

Therefore, in both reactions (eqs 16 and 23), a noticeable fraction of an appropriate isotopologous methanol formed, which did not incorporate oxygen from the solvent.

(iii) Attempted ^{16}O/^{18}O Exchange between CH$_3$OH and H$_2$^{18}O, ^{16}O/^{18}O Exchange between 1 and H$_2$^{18}O, and Attempted Pt^{IV}-to-Pt^{II} Methyl Group Transfer. Before any analysis of possible mechanisms of C−O elimination from complex **1** based on the isotopic labeling experiments described above could be performed, the factors that might be responsible for the Me^{18}OH/Me^{16}OH ratio change over time should be considered. Accordingly, the following factors were analyzed: (i) the ^{16}O/^{18}O exchange between the reaction product, Me^{16}OH, and bulk H$_2$^{18}O (eq 24); (ii) the ^{16}O/^{18}O exchange between reactants, complex **1** and H$_2$^{18}O, leading to **1-^{18}O** and **1-^{18}O$_2$** (eqs 17, 18), and (iii) a methyl group transfer between an electrophilic MePt^{IV} complex **2** and a potentially nucleophilic Pt^{II} complex **3-^{18}O$_2$** leading to **3** and **2-^{18}O$_2$** (eq 25):[20]

$$\mathrm{Me^{16}OH} + \mathrm{H_2{}^{18}O} \rightarrow \mathrm{Me^{18}OH} + \mathrm{H_2{}^{16}O} \qquad (24)$$

$$\underset{\textbf{2}}{\mathrm{LPt^{IV}Me(^{16}OH)_2{\cdot}H^+}} + \underset{\textbf{3-}^{\mathbf{18}}\textbf{O}_\mathbf{2}}{\mathrm{LPt^{II}(^{18}OH_2)_2^{\;+}}} \rightarrow \underset{\textbf{3}}{\mathrm{LPt^{II}(^{16}OH_2)_2^{\;+}}} + \underset{\textbf{2-}^{\mathbf{18}}\textbf{O}_\mathbf{2}}{\mathrm{LPt^{IV}Me(^{18}OH)_2{\cdot}H^+}} \qquad (25)$$

According to ESI mass spectrometry, no ^{16}O/^{18}O exchange between 44 mM CH$_3$^{16}OH and 60 mM HBF$_4$ in H$_2$^{18}O (eq 24)

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(19) Rostovtsev, V. V.; Henling, L. M.; Labinger, J. A.; Bercaw, J. E. *Inorg. Chem.* **2002**, *41*, 3608.

(20) (a) Ling, S. S. M.; Puddephatt, R. J.; Manojlovic-Muir, L.; Muir, K. W. *J. Organomet. Chem.* **1983**, *255*, C11. (b) Hill, G. S.; Puddephatt, R. J. *Organometallics* **1997**, *16*, 4522. (c) Than, A. K.; Canty, A. J.; Crespo, M.; Puddephatt, R. J.; Scott, J. D.; Watson, A. A. *Organometallics* **1989**, *8*, 1518.

occurred after 3 h at 80 °C. In turn, the results of an ESI-MS monitoring of a solution of complex **1** in acidic $H_2{}^{18}O$ showed that a slow $^{16}O/^{18}O$ exchange took place at 80 °C and both **1-^{18}O** and **1-$^{18}O_2$** formed (eqs 17, 18, Figure 8). Therefore, reactions 17 and 18 might be responsible for the $Me^{18}OH/Me^{16}OH$ ratio increase over time (Table 3).

Because of a relatively fast aqua ligand exchange at the platinum(II) atom in **3**, complex **3-$^{18}O_2$** was the only platinum(II) aqua complex present in reaction mixtures with $H_2{}^{18}O$ as a solvent, as established by ESI-MS. Therefore, if reaction 25 rate was fast compared to reactions 17 and 18, the fraction of **1-$^{18}O_2$** in reaction mixtures would be greater than that of **1-^{18}O**. Since this was not observed up to high conversions of **1** (Figure 8), the doubly labeled **1-$^{18}O_2$** resulted predominantly from a consecutive $^{16}O/^{18}O$ exchange in **1** driven forward by the high $[H_2{}^{18}O]/[H_2{}^{16}O]$ ratio (eqs 17, 18) and not from a methyl group transfer between complexes **1** and **3-$^{18}O_2$** (eq 25). Additional arguments against the Pt^{IV}-to-Pt^{II} methyl group transfer arise from an analysis of the isotopologous methanols' distribution in experiments between **1-*d*$_3$** and **3-$^{18}O_2$** (see discussion below).

Importantly, to eliminate the effect of reactions 17 and 18 on the observed $Me^{18}OH/Me^{16}OH$ ratio to the maximum extent, the ratio should be measured at the early stages of reaction 3, when conversion of complex **1** is low.

(iv) Reaction of Complex 1-*d*$_3$ with $H_2{}^{18}O$. Experiments on the C−O reductive elimination from **1-*d*$_3$** (Table 4) showed that the $CD_3{}^{18}OH/CD_3{}^{16}OH$ ratio measured at low conversions of the complex (∼10%) decreased approximately linearly with 1/[Pt], so that the product of $[Pt]\cdot(CD_3{}^{18}OH/CD_3{}^{16}OH)$ remained approximately constant at 130 ± 10. Assuming that the reaction producing $CD_3{}^{18}OH$ followed an expected S_N2 mechanism (eq 15, Scheme 2) and therefore was first-order in complex **1-*d*$_3$**, these results suggested that the reaction leading to $CD_3{}^{16}OH$ was second-order in complex **1-*d*$_3$**. A deuterium-labeled complex $LPt^{IV}CD_3(OH)_2$, **1-*d*$_3$**, was used in these experiments since corresponding $CD_3OH_2{}^+$ peaks could be integrated more reliably than those of isotopologous $CH_3OH_2{}^+$.

Plausible Mechanisms of Reaction between 1 and H_2O in Acidic Solutions. Two paths of the C−O reductive elimination not involving solvent as a nucleophile were considered: (i) a *monomolecular* (intramolecular) C−O coupling of **2** (Scheme 3);[15] (ii) an *intermolecular* nucleophilic reaction leading to an intermediate **4** (Scheme 5, eq 26) with a subsequent hydrolysis of **4** (eq 12).

$$\underset{\mathbf{2}}{LPt^{IV}Me(OH)_2\cdot H^+} + \underset{\mathbf{1}}{LPt^{IV}Me(OH)_2} \rightarrow \underset{\mathbf{4}}{LPt^{IV}Me(OH)(OMe)} + \underset{\mathbf{3}}{LPt^{II}(OH_2)_2{}^+} \quad (26)$$

The mechanism (i) may be similar to the mechanisms suggested for diaryl carboxylato palladium(IV) derivatives,[12] elimination of aryl halides from diphosphine diaryl $Pt^{IV}X_2$ complexes (X = I, Br),[16] or elimination of methyl iodide from $(PCP)Rh^{III}$ iodo methyl complexes.[14] The expected reaction order in complex **1** is one, which is not consistent with the results of experiments with various concentrations of complex **1-*d*$_3$** in acidic $H_2{}^{18}O$ solutions: the $CD_3{}^{18}OH/CD_3{}^{16}OH$ ratio was found to be proportional to 1/[Pt] (Table 4), which corresponded to the reaction leading to $Me^{16}OH$ being second-order in **1**.

In the case of the mechanism (ii) **2** could serve as an electrophilic component, whereas one of the hydroxo ligands of a nonprotonated **1** could play the role of a nucleophile. Because **2** and **1** were in a fast equilibrium (eq 2), reaction 26 was expected to be second-order in complex **1**. Complex **4**, which might form in reaction 26, was shown to be able to react with water (eq 12) to produce methanol. Importantly, complex **4** generated in $H_2{}^{18}O$ solutions did not contain noticeable amounts of ^{18}O-labels up to a conversion of **1** of at least 80%. According to our experimental data and reactivity studies for methoxo platinum(IV) complex *fac*-$Me_2(MeO)Pt^{IV}(OH_2)_3{}^+$,[21] a $Pt^{IV}-OMe$ and not a $Pt^{IV}O-Me$ bond cleavage occurs during their hydrolysis. Therefore, a sequence of reactions 26 and 12 allows us to account for the formation of $Me^{16}OH$ in $H_2{}^{18}O$ solutions of **1**. The presence of intermediate **4** in reaction mixtures further confirms the viability of mechanism (ii).

Using a sample of **4** prepared independently, we established by means of ^1H NMR spectroscopy and ESI mass spectrometry that complex **4** formed in acidic (eq 26) and concentrated neutral aqueous solutions of **1** (eq 7). Typically, the fraction of complex **4** increased slowly and reached a maximum of about 4−5% after a few minutes in acidic reaction mixtures containing **1** (Figure 3). Eventually the intermediate disappeared, consistent with its ability to undergo an acid-catalyzed hydrolysis (eq 12).

Besides reaction 26, a fast acid-catalyzed OH/MeO ligand exchange between complex **1** and methanol formed in reaction 3 could be responsible for the formation of intermediate **4** (eq 27):

$$\underset{\mathbf{1}}{LPt^{IV}Me(OH)_2} + MeOH \rightarrow \underset{\mathbf{4}}{LPt^{IV}Me(OH)(OMe)} + H_2O \quad (27)$$

If path 27 was viable, high concentrations of methanol present in solution before reaction 3 had started would lead to a faster accumulation of **4** and higher concentrations of the intermediate. In fact, in the presence of 50 mM methanol in a solution of 10 mM **1** and 60 mM HBF_4 neither significant change of the fraction of the methoxo complex **4**, nor the rate of its formation, nor any statistically significant change of the reaction 3 rate was observed as compared to the control reaction with no methanol additive (Figure 7). Thus, complex **4** was a reaction 3 intermediate and not a secondary product of the OH/MeO ligand exchange in complex **1**.

Interestingly, at [Pt] = 120 mM the fractions of two isotopologous alcohols were almost equal (Table 4), suggesting that nucleophilic attacks of the solvent (eq 15) and hydroxo complex **1** at the methyl group of electrophilic cation **2** (eq 16) occurred at comparable rates.

Although the results obtained strongly support the viability of the *intermolecular* path for the C−O coupling of complex **1** (Scheme 5), the precision of data in Table 4 does not allow us to completely rule out a minor (few percent) contribution of an intramolecular mechanism to the C−O elimination from **1** (Scheme 3).

Reaction Balance. On the basis of the available observations, a typical reaction 3 mixture contained methanol, dimethyl ether, and complexes **1**, **3**, **4**, **5**, and **6** as main components at the middle stages of reaction. Whereas complex **3** and methanol formed as a result of reactions summarized by eq 3 and, in particular, following a path shown in Scheme 2, complex **6** formed most likely as the result of a secondary reaction between **1** and **3** (eq 14).

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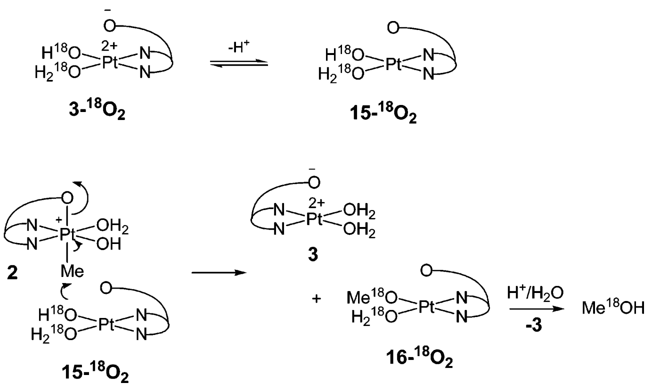
[21] Hadi, S.; Appleton, T. G.; Ayolo, G. A. *Inorg. Chim. Acta* **2003**, *352*, 201.

Scheme 15



Accepting the mechanism of formation of **4** given by Scheme 5 and eq 26 as viable, we can account for the formation of complex **5** by postulating a similar mechanism of alkylation of the hydroxo ligand of **4** by complex **2** (Scheme 6, eq 28):

$$\underset{\mathbf{2}}{LPt^{IV}Me(OH)_2\cdot H^+} + \underset{\mathbf{4}}{LPt^{IV}Me(OMe)(OH)} \rightarrow \underset{\mathbf{5}}{LPt^{IV}Me(OMe)_2} + \underset{\mathbf{3}}{LPt^{II}(OH_2)_2^+} \tag{28}$$

We can also account for the formation of dimethyl ether via alkylation of the methoxo ligand in complexes **4** and/or **5** by electrophilic **2** leading to cationic dimethyl ether Pt^{IV} intermediates such as **8**, which was detected by ESI-MS (eq 29, Scheme 7):

$$\underset{\mathbf{2}}{LPt^{IV}Me(OH)_2\cdot H^+} + \underset{\mathbf{5}}{LPt^{IV}Me(OMe)_2} + H^+ \rightarrow \underset{\mathbf{8}}{LPt^{IV}Me(OMe_2)(OMe)^+} + \underset{\mathbf{3}}{LPt^{II}(OH_2)_2^+} \tag{29}$$

Subsequent hydrolysis of dimethyl ether complexes such as **8** is responsible for the formation of dimethyl ether (eq 30):

$$\underset{\mathbf{8}}{LPt^{IV}Me(OMe_2)(OMe)^+} + H_2O \rightarrow \underset{\mathbf{4}}{LPt^{IV}Me(OH)(OMe)} + Me_2O + H^+ \tag{30}$$

Because of a relatively low concentration and presumably high reactivity, complex **8** could not be reliably detected in reaction mixtures by ^{1}H NMR spectroscopy.

Test of the Viability of Pt^{IV}-to-O Methyl Group Transfer between Complexes 2 and 15. Since Pt^{IV}-to-O methyl group transfer between **2** and **1** was proven to be viable (Scheme 5, eq 26), we investigated the viability of a similar Pt^{IV}-to-O methyl group transfer between an electrophilic complex **2** and complex **15** that possessed a nucleophilic hydroxo ligand. Complex **15** could form in acidic reaction mixtures in low equilibrium concentrations (eqs 2, 31, Scheme 15):

$$\underset{\mathbf{2}}{LPt^{IV}Me(^{16}OH)_2\cdot H^+} + \underset{\mathbf{15\text{-}^{18}O_2}}{LPt^{II}(^{18}OH_2)(^{18}OH)} \rightarrow \underset{\mathbf{3}}{LPt^{II}(^{16}OH_2)_2^+} + \underset{\mathbf{16\text{-}^{18}O_2}}{LPt^{II}(^{18}OH_2)(^{18}OMe)} \tag{31}$$

The reaction would lead to the presumably readily hydrolyzable methoxo Pt^{II} complex **16**. The viability of the Pt^{IV}-to-O methyl transfer reaction (eq 31) could not be proven directly since **15** is much more basic than **1**; log $K_{15} = 4.81 \pm 0.01$, see eq 22. To obtain evidence in favor or against viability of the path 31, an isotope labeling experiment was performed in which complex **3-^{18}O$_2$** was allowed to react with **1-*d*$_3$** and 120 mM HBF$_4$ in H$_2{}^{18}$O at 80 °C. After 5 min the CD$_3{}^{18}$OH/CD$_3{}^{16}$OH ratio was 2.7:1, which matched the ratio of isotopologues found in experiments performed under the same conditions but with no additive of **3** (Table 4). Since no dramatic changes in the CD$_3{}^{18}$OH/CD$_3{}^{16}$OH ratio were observed, we can conclude that reaction 32 did not contribute noticeably to the C−O elimination from complex **1**. These results also provide evidence against the Pt^{IV}-to-Pt^{II} methyl group transfer between **1** and **3** discussed above. If such transfer occurred, one could expect the CD$_3{}^{18}$OH/CD$_3{}^{16}$OH ratio to be higher than the observed 2.7:1.

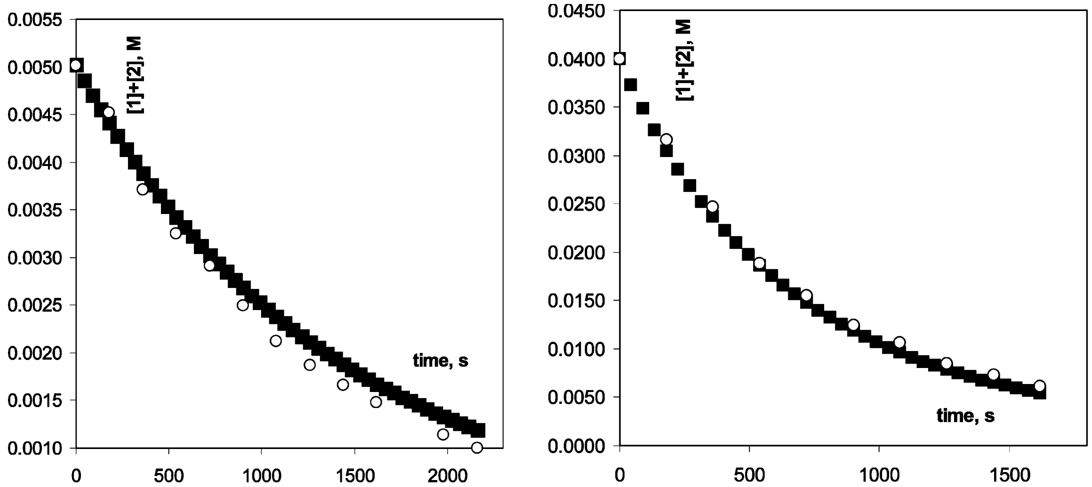
Kinetic Studies of Reaction of 1 and H$_2$O in Acidic Solutions. Possible Role of Heterovalent Dinuclear Complexes 6 in the C−O Elimination from 1. As follows from experiments illustrated in Figures 5 and 6, additives of complex **3** accelerated methanol elimination from **1** substantially. We postulate that the acceleration was due to the formation of cationic electrophilic complexes **6** that are prone to nucleophilic attack of water (Scheme 8, eq 32), hydroxo, and methoxo ligands of complexes **1** (eq 33), **4**, and **5**:

$$\underset{\textit{\textbf{cis}}\text{- and }\textit{\textbf{trans}}\text{-}\mathbf{6}}{LPt^{IV}Me(\mu\text{-}OH)_2Pt^{II}L^+} + 3H_2O + H^+ \rightarrow \underset{\mathbf{3}}{2LPt^{II}(OH_2)_2^+} + MeOH \tag{32}$$

$$\underset{\textit{\textbf{cis}}\text{- and }\textit{\textbf{trans}}\text{-}\mathbf{6}}{LPt^{IV}Me(\mu\text{-}OH)_2Pt^{II}L^+} + 2H_2O + \underset{\mathbf{1}}{LPt^{IV}Me(OH)_2} + H^+ \rightarrow \underset{\mathbf{3}}{2LPt^{II}(OH_2)_2^+} + \underset{\mathbf{4}}{LPt^{IV}Me(OMe)(OH)} \tag{33}$$

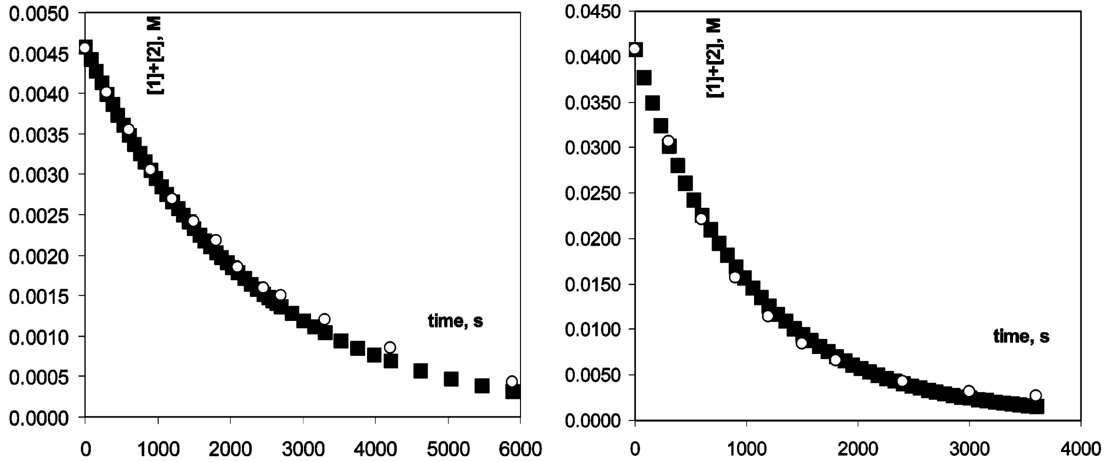
Since undistinguishable kinetic results were obtained for reactions involving an equimolar mixture of **1** and **3** in one case and complex **6** in another case (Figure 5), the rate of establishing an equilibrium between **1**, **3**, and **6** (eq 14) was much faster than the rate of subsequent nucleophilic reactions of complex **6**.

Modeling the Rate of Disappearance of Complex 1. An additional evidence in favor of the mechanisms of C−O coupling discussed here might be an appropriate modeling of available kinetic data on the combined rate of disappearance of complexes **1** and **2** (Table 2). Therefore, an analysis of reaction 3 kinetics was performed. Our analysis was based on the following assumptions: (i) the value of the protonation constant for **1**, K_1(eq 2), is low enough to allow for coexistence of **1** and **2** in comparable amounts at [H$^+$] = 60−120 mM and 80 °C. This hypothesis is consistent with the available upper estimate of K_1, which is the protonation constant for a presumably more basic dimethyl hydroxo analogue of **1**, *sym*-LPt^{IV}Me$_2$(OH),[13] $K \approx 46 \pm 5$ at 97 °C in D$_2$O. (ii) Weakly acidic complex **3** did not produce its conjugate base **15** in noticeable amounts (eq 22). Indeed, the protonation constant for **15** is large, log K_{15} = 4.81 ± 0.01 at 22 °C. (iii) Concentration of complex **4** was low enough to neglect its bimolecular reactions with **2** and with itself (Schemes 6 and 7), and the formation of complex **5** can be neglected. The plot in Figure 3 shows that the fraction of **4** never exceeded a few percent of the initial concentration of **1** and the fraction of **5** was close to zero at all times. (iv) The rate constants for C−O elimination from **1** (Scheme 2) and **4** in acidic solutions leading to MeOH and **3** are essentially the



a) $[Pt]_0$ = 5.01 mM, $[HBF_4]$ = 120 mM; standard deviation = $1.03 \cdot 10^{-4}$

b) $[Pt]_0$ = 40.0 mM, $[HBF_4]$ = 120 mM; standard deviation = $3.83 \cdot 10^{-4}$



c) $[Pt]_0$ = 4.56 mM, $[HBF_4]$ = 60 mM; standard deviation = $5.9 \cdot 10^{-5}$

d) $[Pt]_0$ = 40.8 mM, $[HBF_4]$ = 60 mM; standard deviation = $1.23 \cdot 10^{-3}$

Figure 11. Least-squares fitting for combined concentration of complexes **1**+**2** versus time. Calculated values are represented by filled squares; experimentally determined concentrations are shown with empty circles.

same. This assumption is based on the measured observed pseudo-first-order rate constants for reactions of **1** and **4** with water at 80 °C and $[HBF_4] = 60$ mM, $(10.6 \pm 0.2) \times 10^{-4}$ s^{-1} for **1** at $[Pt^{IV}] = 40.8$ mM (Table 2) and $(7.1 \pm 0.1) \times 10^{-4}$ s^{-1} for **4** at $[Pt^{IV}] = 39$ mM. (v) Complexes **6** formed from **1** and **3** reversibly (eq 14) at a much faster rate than they reacted with water (eq 32) or with other nucleophiles. In particular, the reaction plot in Figure 5 provides evidence for that. While subsequent reaction of **6** with water (eq 32) should be taken into consideration here, we could neglect second-order reactions between **6** and **1** (eq 33) since the concentration of **6** is low (see Figure 3).

First of all, we derived an expression describing the rate of disappearance of complex **1** measured in our NMR experiments. If *C* is a combined concentration of complexes **1** and **2** in a solution as determined by ^{1}H NMR, then using the expression for the equilibrium constant K_1(eq 2) we can get eq 34:

$$[\mathbf{2}] = \frac{K_1[H^+]}{1 + K_1[H^+]}C \text{ and } [\mathbf{1}] = \frac{C}{1 + K_1[H^+]} \tag{34}$$

Using steady-state approximation for complex **6** and considering three major reaction paths given in Schemes 2, 5, and 8 and contributing to the rate of disappearance of **1** + **2**, we can get eq 35 for the total rate of disappearance of **1** + **2**:

$$-\frac{dC}{dt} = k_2[\mathbf{2}] + k_4[\mathbf{1}][\mathbf{2}] + k_6[\mathbf{6}] \tag{35}$$

Here the first term corresponds to the pseudo-first-order reaction of **2** with water (Scheme 2), the second term accounts for the bimolecular reaction of **2** with **1** (Scheme 5), and the third term corresponds to the reaction between water and complexes **6** that exist in fast equilibrium with **1** and **3** and are present at a steady concentration, [**6**] ≈ const (eq 14). At the early stages of reaction, the steady-state approximation for **6**, [**6**] ≈ const, may not be correct, and the fourth term corresponding to the change of the concentration of **6** over time (eq 14), d[**6**]/d*t*, should be added. Therefore, eq 35 is to be modified to give a four-term equation, eq 36:

$$-\frac{dC}{dt} = k_2[\mathbf{2}] + k_4[\mathbf{1}][\mathbf{2}] + k_6[\mathbf{6}] + \frac{d[\mathbf{6}]}{dt} \tag{36}$$

Using numerical integration to calculate *C* after consecutive short periods of time and calculating concentrations of **1**, **2**, **3**,

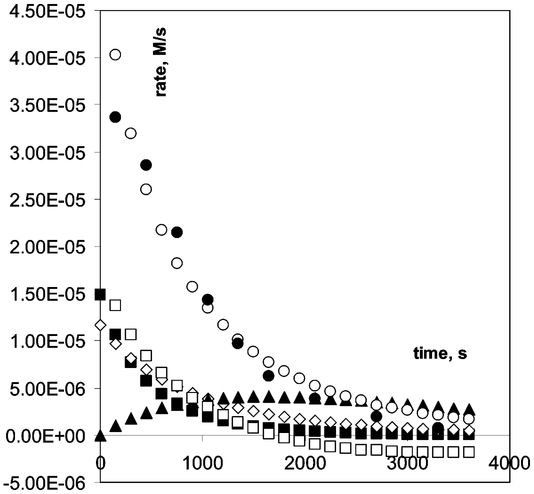


Figure 12. Experimentally determined (filled circles) and calculated using eq 36 (empty circles) rate of reaction of 40.8 mM **1** and 60 mM HBF_4 in D_2O at 80 °C. Relative contributions of four terms of eq 36 to the total reaction rate: (a) the first term accounting for the reaction between **2** and water and leading to $Me^{18}OH$ in $H_2{}^{18}O$ solutions (empty diamonds), (b) the second term accounting for the bimolecular reaction of **2** with **1** leading to **4** and subsequently to $Me^{16}OH$ (filled squares), (c) the third term accounting for the complex **6**-mediated transformation of **1** to methanol and **3** (filled triangles), (d) the fourth term accounting for the change of concentration of **6** with time (empty squares).

4, [H$^+$], and **6** after each step using eq 34 and eqs 37−39 given below (see Supporting Information for details), one can describe the dependence of C on time if all necessary constants, k_2, k_4, k_6, K_1, and K_6, are known.

$$[\mathbf{6}] = K_6[\mathbf{1}][\mathbf{3}] \tag{37}$$

$$\frac{d([\mathbf{3}] + [\mathbf{6}])}{dt} = k_2[\mathbf{2}] + \frac{1}{2}k_4[\mathbf{1}][\mathbf{2}] + k_6[\mathbf{6}] + k_2\frac{K_1[H^+]}{1 + K_1[H^+]}[\mathbf{4}] \tag{38}$$

$$\frac{d[\mathbf{4}]}{dt} = \frac{1}{2}k_4[\mathbf{1}][\mathbf{2}] - k_2\frac{K_1[H^+]}{1 + K_1[H^+]}[\mathbf{4}] \tag{39}$$

Vice versa, by performing least-squares fitting of the 12 experimentally found dependences between C and reaction time given in Figures 4 and 5 and in the Supporting Information one can find the necessary set of constants: $K_1 = 4.5 \pm 0.1$, $K_6 = 90 \pm 1$, $k_2 = (1.50 \pm 0.01) \times 10^{-3}$ s^{-1}, $k_4 = (5.8 \pm 0.1) \times 10^{-2}$ M^{-1} s^{-1}, $k_6 = (7.9 \pm 0.1) \times 10^{-4}$ s^{-1} (Figure 11; see also Supporting Information). The model also allows for a satisfactory description of the dependence of concentrations of complexes **3** and **6** and methanol on reaction time (see Supporting Information). Since the quality of the fit between experimental and calculated data is acceptable, we can conclude that the kinetic model proposed is correct.

Using the model developed we estimated relative contributions of all terms of eq 36 to the total rate of disappearance of complex **1**. These contributions for a representative case of $[Pt]_0 = 40.8$ mM and $[HBF_4] = 60$ mM are given in Figure 12 as a function of reaction time. In the beginning of the reaction the contribution of the first term accounting for the reaction between **2** and water, which leads ultimately to $Me^{18}OH$ in $H_2{}^{18}O$ solutions (Scheme 2), and the contribution of the second term accounting for the bimolecular reaction of **2** with **1** leading to **4** and subsequently to $Me^{16}OH$ in $H_2{}^{18}O$ solutions (Scheme 5) are almost equal. Of note is that the rate of formation of intermediate **4**, which is responsible for the formation of Me^{16}-OH, is 2 times lower than the magnitude of the second term (eq 26). As a result, the $Me^{18}OH/Me^{16}OH$ ratio is expected to be close to 2:1, which was indeed the ratio that was actually observed in the beginning of reaction 3 for $[Pt]_0 = 38$ mM and $[HBF_4] = 63$ mM (Table 3).

The contribution of the third term accounting for complex **6**-mediated transformation of **1** to methanol and **3** (Scheme 8) is small in the beginning, increases in the middle stage of reaction, and diminishes subsequently. At the middle and later stages of reaction 3, when this term from eq 36 is relatively large, the contribution of reaction of dinuclear complexes **6** with water (eq 32) should be comparable with that of reactions given in Schemes 2 and 5. If so, a noticeable acceleration of reaction between complex **1** and water in the presence of **3** should be expected and was actually observed (Figures 5, 6).

Finally, the contribution of the fourth term of eq 36 is very large in the beginning but diminishes at a later time, so that the steady-state approximation is not correct at the early stages of reaction 3.

C−O Coupling of Methoxo Platinum(IV) Complex 4 at Various [H$^+$]. One might anticipate that methoxo $MePt^{IV}$ complex **4**, which contains a more nucleophilic methoxo ligand as compared to hydroxo ligands in complex **1**, may be even more prone to compete with water for electrophilic $MePt^{IV}$ species. Indeed, in contrast to complex **1**, for which a C−O coupling in neutral solutions was not typical (see eq 7 and a comment nearby), a slow reaction of ~40 mM **4** was observed in the absence of HBF_4 at 80 °C (Figure 10). After 6 h, the conversion of **4** was 80%. Main reaction products were methanol (24% yield), Me_2O (20% yield), and **5** (13% yield), along with ~30% of water-insoluble complex **14** (eqs 21, 40, 41). Thus, MeOH and M_2O formed in a 1.2:1 ratio.

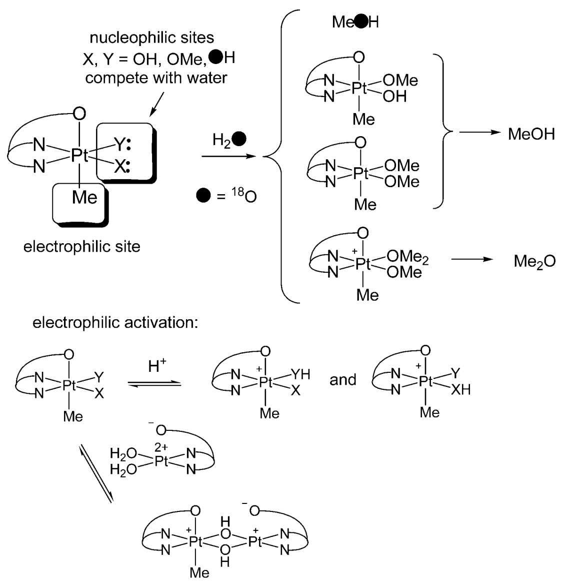
$$\underset{\mathbf{4}}{4LPt^{IV}Me(OMe)(OH)} \rightarrow \underset{\mathbf{14}}{2L_2Pt^{II}{}_2(\mu\text{-}OMe)_2} + 2Me_2O + 2H_2O \tag{40}$$

$$\underset{\mathbf{4}}{2LPt^{IV}Me(OMe)(OH)} \rightarrow \underset{\mathbf{14}}{L_2Pt^{II}{}_2(\mu\text{-}OMe)_2} + 2MeOH \tag{41}$$

In the presence of 60 mM HBF_4 a ~40 mM solution of **4** produced Me_2O and complex **5** in much lower yields. A 12% yield of Me_2O was found by the end of the reaction, and up to 5% of an *intermediate* dimethoxo complex $LPt^{IV}Me(OMe)_2$, **5**, formed after about 20 min (Figure 9). Both products were the result of methylation reactions shown in Schemes 6 and 7, along with complex **3** and methanol (60% yield). Thus, MeOH and Me_2O formed in a much higher, 5:1, ratio as opposed to the result obtained in the absence of the acid.

A reaction with a more dilute, 10.0 mM, solution of complex **4** and 60 mM HBF_4 in water showed an even higher, 21:1, MeOH/Me_2O ratio by the end of the reaction. This result was consistent with the expected second-order in complex **4** for the reaction leading to Me_2O (Scheme 7) and a first-order in **4** for the reaction leading to methanol (eq 12 and Scheme 2). Hence, higher concentration of acid and lower concentration of complex **4** allowed us to decrease the fraction of C−O coupling products

Scheme 16



not involving solvent as a nucleophile, such as Me_2O and **5**. Similar behavior was observed for complex **1**.

Summary

In summary, we have shown that in poorly nucleophilic neutral and acidic *aqueous* media hydroxo and methoxo methyl Pt^{IV} complexes can be involved in nucleophilic reactions with two different nucleophiles: water and themselves (Scheme 16). The latter reaction is second-order in Pt^{IV} and results in the formation of C−O coupling products where both the “C” and the “O” part originate from the starting complex. Both reactions can be very competitive. The outcome of the competition between the nucleophiles is reflected in the ratio of the products formed, $Me^{18}OH/Me^{16}OH$, in the case of the reaction between **1** and $H_2{}^{18}O$ solvent, or $MeOH/Me_2O$ in the case of reaction of **4** with water. These ratios depend on concentration of $MePt^{IV}$ species, acidity, and the nature (nucleophilicity and basicity) of hydroxo and methoxo Pt^{IV} complexes present. Higher acidity and lower Pt^{IV} concentrations allowed us to suppress C−O coupling that involved Pt complexes behaving as a nucleophile. Interestingly, cationic diaqua platinum(II) complex **3**, one of the products of C−O elimination, was responsible for accelerating the rate of the C−O coupling. This effect might result from an electrophilic activation of $LPt^{IV}Me(OH)_2$ via formation of cationic dinuclear μ-hydroxo-bridged heterovalent $Pt^{II}-Pt^{IV}$ complexes. Ultimately, this information may be valuable for designing aqueous Pt-based systems for selective methane functionalization.

Experimental Section

General Procedures. All manipulations were carried out under purified argon using standard Schlenk and glovebox techniques. All reagents for which synthesis is not given were commercially available from Aldrich, Acros, or Pressure Chemical and were used as received without further purification. Symmetrical methyldihydroxo di(2-pyridyl)methanesulfonato platinum(IV) complex **1** was synthesized according to a published procedure.[17] Water-^{18}O with the isotopic composition of 97.9% ^{18}O, 0.5% ^{17}O, and 1.6% ^{16}O from the Cambridge Isotope Laboratories was used as received.

^1H (400.132 MHz) and ^{13}C NMR (100.625 MHz) spectra were recorded on a Bruker Avance 400 spectrometer. Chemical shifts are reported in ppm and referenced to residual solvent resonance peaks. Elemental analyses were carried out by Chemisar Laboratories Inc., Guelph, Canada. ESI-MS experiments were performed using a JEOL AccuTOF-CS instrument. GC-MS (EI) experiments were performed using a JEOL JMS-SX 102A instrument.

Preparation of $LPt^{IV}CH_3(^{18}OH)(OH)$, 1-^{18}O. In an argon-filled glovebox a 5 mL Schlenk flask was charged with 40 mg of dimethyl hydride $LPtMe_2H$[13] (84 μmol), 1.0 g of air-free water $H_2{}^{18}O$, and a stirring bar. The flask was placed in a 45 °C water bath, and the mixture was vigorously stirred under argon for 1 h to produce a clear, colorless solution of $LPtCH_3(^{18}OH_2)$. Air was then admitted into the flask and vigorous stirring continued for a further 5 h. After that time, according to the ESI-MS analysis of a slightly acidified sample of the reaction mixture, all $LPtCH_3(^{18}OH_2)$ complex had reacted and the singly labeled complex $LPtMe(^{18}OH)(OH)$ had formed. The reaction mixture was diluted with distilled water (5 mL) and heated at 93 °C for 3 h. After that time, all the starting complex isomerized to the “symmetrical” isomer of $LPtMe(^{18}OH)(OH)$, according to ^1H NMR.

The mixture was filtered through Celite, and the solvent was removed under vacuum at room temperature to produce **1-^{18}O**, 40 mg (96%). The product was pure according to ^1H NMR. It was redissolved in regular water (960 mg) and stored at 5 °C in a sealed vial.

ESI-MS of a solution of **1-^{18}O** in H_2O acidified with HBF_4, m/z = 496.074. Calculated for (**2-^{18}O**), $C_{12}H_{15}{}^{16}O_4{}^{18}ON_2{}^{195}Pt^{32}S$, 496.03924. Calculated isotopic pattern matched the experimentally observed one.

Preparation of $LPt^{IV}CD_3(OH)_2$, 1-*d*$_3$. In an argon-filled glovebox a 25 mL Schlenk flask was charged with 100 mg of dimethyl hydride $LPt^{IV}Me_2H$[16] (210 μmol), 3.0 mL of air-free D_2O, and a stirring bar. The flask was placed in a 45 °C water bath, and the mixture was vigorously stirred under argon for 1 h to produce a clear, colorless solution of $LPt^{II}CD_3(OD_2)$. Air was then admitted to the flask and vigorous stirring continued for 5 h. After that time, according to the ESI-MS analysis, all $LPt^{II}CD_3(OD_2)$ complex has reacted and the labeled complex $LPt^{IV}CD_3(OH)_2$ formed. The solvent was removed under vacuum at room temperature. The residue was dissolved in distilled water (10.0 mL) and heated at 93 °C for 3 h. After that time, according to ^1H NMR, all the dihydroxo Pt^{IV} complex isomerized to the “symmetrical” isomer $LPt^{IV}CD_3(OH)_2$.

The mixture was filtered through Celite, and the solvent was removed under vacuum at room temperature to produce **1-*d*$_3$**, 91 mg (87%), pure according to ^1H NMR. The product was redissolved in regular water (5.91 g) and kept in a refrigerator in a sealed vial at 5 °C.

The ^1H NMR spectrum of **1-*d*$_3$** is identical to that of **1**[13] with the exception that there are only weak residual resonances for the PtMe group.

In the ^{13}C NMR spectrum of **1-*d*$_3$** the signal of the PtMe group was not observed due to the high multiplicity of the signal leading to a set of short lines masked by noise.

ESI-MS of a solution of **1-*d*$_3$** in H_2O acidified with one drop of HBF_4, m/z = 497.081. Calculated for (**1-*d*$_3$·H$^+$**), $C_{12}H_{12}D_3O_5N_2{}^{195}Pt^{32}S$, 497.05348. Calculated isotopic pattern matched the experimentally observed one.

Preparation of $LPt^{II}Me(MeOH)$, 12, and Isomeric $LPt^{IV}Me(OMe)(OH)$, 4 and 13. $LPt^{II}Me(HOMe)$, 12. In an argon-filled glovebox a 25 mL Schlenk flask was charged with 95 mg of dimethyl hydride $LPt^{IV}Me_2H$[17] (200 μmol), 10.0 mL of air-free methanol, and a stirring bar. The flask was placed in a 45 °C water bath, and the mixture was stirred under argon for 1 h to produce a clear, colorless solution of $LPt^{II}Me(HOMe)$, pure according to ^1H NMR.

^1H NMR (CD_3OD, 22 °C), δ: 0.94 ($^2J_{195PtH}$ = 75 Hz, 3H), 5.89 (s, 1H), 7.27 (ddd, J = 2.0, 6.1, 7.6 Hz, 1H), 7.55 (ddd, J = 1.4, 5.4, 7.1 Hz, 1H), 7.74 (vd, J = 7.9 Hz, 1H), 7.86 (vd, J = 8.0 Hz, 1H), 8.01 (dt, J = 1.6, 8.0 Hz, 1H), 8.05 (dt, J = 2.0, 8.0 Hz, 1H), 8.70 (m, 2H).

Complex 13. Air was admitted into a flask containing **4** prepared as described above, and vigorous stirring was continued for 5 h. After that time according to ^{1}H NMR all LPt^{II}Me(HOMe) complex had reacted and a pale yellow precipitate of the *poorly soluble* product LPt^{IV}Me(OMe)(OH), **5**, with an equatorial Me ligand, formed. The mixture was filtered; the precipitate was washed with 1 mL of methanol and dried. Yield: 76 mg (75%).

^{1}H NMR (D_2O, 22 °C), δ: 2.44 ($^2J_{195PtH}$ = 67 Hz, 3H), 2.96 ($^3J_{195PtH}$ = 23 Hz, 3H), 6.67 (s, 1H), 7.80 (ddd, J = 1.4, 6.0, 7.5 Hz, 1H), 7.80 (ddd, J = 1.0, 5.0, 7.7 Hz, 1H), 8.06 (vd, J = 7.8 Hz, 1H), 8.08 (vd, J = 8.0 Hz, 1H), 8.29 (vt, J = 7.8 Hz, 2H), 8.52 (vd, J = 6.0 Hz, $^3J_{PtH}$ = 25 Hz, 1H), 8.90 (vd, J = 5.3 Hz, 1H).

The relatively small $^2J_{195PtH}$ = 67 Hz for the PtMe group is an indication of the presence of a ligand *trans* to the methyl with a relatively strong *trans* effect (py rather than SO_3 group).

^{13}C NMR (D_2O, 22 °C), δ: 5.7, 55.0, 71.8, 127.4, 127.8, 128.0, 129.2, 142.6, 143.5, 147.8, 148.1, 150.6, 150.7. Due to the limited solubility of **13** in water and weak NMR signals, platinum satellites for the PtMe and PtOMe groups were not observed.

X-ray quality crystals of **13** were obtained by slow diffusion of vapors of diethyl ether into a saturated solution of **13** in a MeOH−H_2O mixture containing 0.5 equiv of HBF_4.

Anal. Found: H, 3.31; C, 31.0; N, 5.68; S, 6.15. Calcd for $C_{13}H_{16}O_5N_2PtS$: H, 3.18; C, 30.8; N, 5.52; S, 6.32.

Complex 4. Subsequent isomerization of complex **13** with an equatorial PtMe group to **3** featuring an axial PtMe was performed in refluxing acetone. Complex **13** (120 mg) was placed in a Teflon-sealed Schlenk flask with 5 mL of dry acetone and heated in an oil bath at 80 °C for 48 h. After cooling, the mixture was filtered and the precipitate washed with hot acetone. It was dried to yield pure target complex: yellowish powder, 80 mg (66%).

X-ray quality crystals were produced by layering a saturated methanolic solution of **4** and 0.5 equiv of HBF_4 with an equal volume of benzene.

^{1}H NMR (D_2O, 22 °C), δ: 2.58 ($^2J_{195PtH}$ = 77 Hz, 3H), 3.08 ($^3J_{195PtH}$ = 28 Hz, 3H), 6.53 (s, 1H), 7.83 (m, 2H), 8.09 (m, 2H), 8.33 (m, 2H), 8.56 (vd, J = 6.0 Hz, $^3J_{PtH}$ = 28 Hz, 1H), 8.65 (vd, J = 6.0 Hz, $^3J_{PtH}$ = 29 Hz, 1H). ^{13}C NMR (D_2O, 22 °C), δ: 12.5 ($^1J_{PtC}$ = 641 Hz), 56.0 ($^2J_{PtC}$ = 14 Hz), 72.7 ($^3J_{PtC}$ = 34 Hz), 127.6 (J_{PtC} = 28 Hz), 127.7 (J_{PtC} = 29 Hz), 128.9 (J_{PtC}=15 Hz), 129.1 (J_{PtC} = 14 Hz), 143.3 (2C), 148.9, 149.2, 149.3, 149.5.

ESI-MS of a solution of **4** in methanol acidified with one drop of HBF_4, m/z = 508.034. Calculated for (**4**·H^+), $C_{13}H_{17}O_5N_2{}^{195}Pt^{32}S$, 508.0506. Calculated isotopic pattern matched the experimentally observed one.

Preparation of Isomeric LPt^{IV}Me(OMe)$_2$, *sym-* and *unsym-*5. A solution of 55.2 mg (112 μmol) of LPt^{II}Me(HOMe) in 5 mL of air-free methanol was placed in a 50 mL Schlenk flask. Then 3.7 mL of 0.6 M solution of Me_2O_2 in benzene (2.2 mmol) prepared according to ref 22 was added. The mixture was stirred overnight under argon and then heated at 45 °C for 3 h to produce unsymmetrical LPt^{IV}Me(OMe)$_2$ along with ca. 14% of the isomeric *sym*-LPt^{IV}Me(OMe)$_2$.

Caution: Me_2O_2 can explode during preparation. The explosion can be caused even by friction between glass joints if a drop of the reaction mixture is present on their surface. We therefore recommend using a reaction flask without attached devices such as a dropping funnel, a condenser, or stoppers. In addition, we scaled the synthesis of Me_2O_2[22] down to 2.5 mL of Me_2SO_4 and used extraction of the reaction mixture with benzene instead of distillation. Concentration of Me_2O_2 in the extract was determined by ^{1}H NMR spectroscopy.

unsym-LPt^{IV}Me(OMe)$_2$, ^{1}H NMR (CD_3OD, 22 °C), δ: 2.40 ($^2J_{195PtH}$ = 70 Hz, 3H), 2.65 ($^3J_{195PtH}$ = 55 Hz, 3H), 2.89 ($^3J_{195PtH}$ = 25 Hz, 3H), 6.51 (s, 1H), 7.76−7.81 (m, 1H), 7.89 (ddd, J = 1.2, 5.2, 7.9 Hz, 1H), 8.00−8.07 (m, 2H), 8.22−8.30 (m, 2H), 8.59−8.71 (m, 1H), 8.95−9.00 (m, $^3J_{PtH}$ = 26 Hz, 1H). ^{13}C NMR (CD_3OD, 22 °C), δ: 8.4, 57.6, 73.2, 127.8, 128.3, 128.7, 129.8, 143.1, 144.0, 149.6, 151.1, 151.6, 153.7.

Due to the limited solubility of *unsym*-LPt^{IV}Me(OMe)$_2$ in methanol and weak NMR signals, platinum satellites for the PtMe and PtOMe groups were not observed.

unsym-LPt^{IV}Me(OMe)$_2$ was used without isolation for isomerization to the symmetrical isomer. Solvent was removed by evaporation under vacuum. The solid residue was redissolved in 50 mL of methanol and heated in a sealed Schlenk tube at 80 °C for 6 h. The mixture was cooled, its volume was reduced to 2 mL, and the resulting white precipitate was filtered and washed with 1 mL of methanol, then with 1 mL of CH_2Cl_2, and dried under vacuum for 5 h. Yield: 26.8 mg, 46%. **5** reacted slowly in water to produce methanol and **4**.

^{1}H NMR (D_2O, 22 °C), δ: 2.50 ($^2J_{195PtH}$ = 77 Hz, 3H), 3.08 ($^3J_{195PtH}$ = 27 Hz, 6H), 6.50 (s, 1H), 7.84 (ddd, J = 1.4, 6.1, 7.6 Hz, 2H), 8.08 (vd, J = 8.0 Hz, 2H), 8.31 (dt, J = 1.3, 7.8 Hz; 2H), 8.63 (vd, J = 5.8 Hz, $^3J_{PtH}$ = 28 Hz, 2H).

Limited solubility of **5** in water prevented obtaining a good-quality ^{13}C NMR spectrum.

ESI-MS of solution of **5** in water, m/z = 522.076. Calculated for (**5**·H^+), $C_{14}H_{19}O_5N_2{}^{195}Pt^{32}S$, 522.06625. Calculated isotopic pattern matched the experimentally observed one.

Anal. Found: H, 3.22; C, 31.81; N, 5.59; S, 5.88. Calcd for $C_{14}H_{18}O_5N_2PtS$: H, 3.48; C, 32.25; N, 5.37; S, 6.15.

Preparation of Isomeric [LPt^{IV}Me(μ-OH)$_2$Pt^{II}L]BF$_4$, *cis-* and *trans-*6. Complex *sym*-LPt^{IV}Me(OH)$_2$ (102.5 mg, 208 μmol) was dissolved in 4 mL of 120 mM HBF_4 solution in D_2O containing [LPt^{II}(OH$_2$)$_2$]BF$_4$ (36.6 mg, 64.5 μmol). The mixture was kept at 95 °C for 5 min, cooled slowly to room temperature, and left for 1 week. Isomeric complexes [LPt^{IV}Me(μ-OH)$_2$Pt^{II}L]BF$_4$ crystallized slowly from the mixture as colorless crystals, which were collected and washed with water until the filtrate was neutral to give 27.3 mg of a colorless, crystalline solid (3:1 *cis*:*trans*, yield 41%). The product is poorly soluble in water and HBF_4.

^{1}H NMR (D_2O, 22 °C), δ: *cis*-isomer: 3.56 ($^2J_{195PtH}$ = 64 Hz, 3H), 6.16 (s, 1H), 6.71 (s, 1H), 7.58 (m, 2H), 7.83−7.93 (m, 4H), 8.08−8.18 (m, 4H), 8.38 (vt, J = 7.7 Hz, 2H), 8.64 (vd, J = 6.1 Hz, 2H), 8.74 (vd, J = 6.0 Hz, 2H). *trans*-isomer: 3.38 (3H), 6.21 (s, 1H), 6.83 (s, 1H), 7.52 (m, 2H), 8.47 (vd, J = 6.1 Hz, 2H), 8.54 (vd, J = 6.1 Hz, 2H); other signals of the pyridyls overlap with signals of the *cis*-isomer. ESI-MS: m/z 937.02124 (calc for [LPt^{IV}Me(μ-OH)$_2$Pt^{II}L]$^+$ 937.024292). Calculated isotopic pattern matched the experimentally observed one. ^{19}F NMR (D_2O, 22 °C), δ: −150.8. Anal. Found: H, 2.75; C, 24.73; N, 5.00; S, 6.08. Calcd for $C_{23}H_{35}O_{14}N_4Pt_2S_2BF_4$ ($L_2Pt_2Me(\mu\text{-}OH)_2\cdot 6H_2O$): H, 3.11; C, 24.39; N, 4.95; S, 5.66.

Formation of Intermediates LPt^{IV}Me(OMe)OH, 4, LPt^{IV}Me(OMe)$_2$, 5, Isomeric LPt^{IV}Me(μ-OH)$_2$Pt^{II}LBF$_4$, 6, Complex 3, Methanol, and Dimethyl Ether in the C−O Reductive Elimination from Complex 1. Heating a 41 mM solution of **1** in 60 mM HBF_4 in D_2O solvent resulted in the appearance of complex **4** already after 5 min (2%, 13% conversion of **1**) and reached the maximum (4%) after approximately 15 min (30% conversion of **1**). By the end of the reaction (3 h) no complex **4** was detected. The behavior of intermediates **5** and **6** was similar (Figure 3). Formation of methanol (93% yield) and small amounts of dimethyl ether (7% yield) was observed. Concentrations of complex **3** and methanol as a function of time are given in Figure 3.

Me_2O, ^{1}H NMR (D_2O, 22 °C), δ: 3.18 (s). Mass spectrum after 100-fold dilution with H_2O, $(m+H^+)/z$ = 47.042. Calculated for C_2H_7O, 47.04969.

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[22] Hanst, P. L.; Calvert, J. G. *J. Phys. Chem*. **1959**, *63*, 104.

In the absence of acids a 41 mM solution of **1** in D_2O produced complex **4** in 5% yield along with water-insoluble $L_2Pt^{II}_2(\mu\text{-}OH)_2$[13] after heating the solution at 90 °C for 3 h. Only traces of free methanol (<1%) could be found in the mixture.

Kinetics of the C−O Elimination from Complex 1 in Acidic Aqueous Solutions. HBF_4 solutions (60 and 120 mM) were prepared by dissolving 141.9 and 225.2 mg of HBF_4 (50% by mass) in 13.5 (14.9751 g) and 10.6 mL (11.6868 g) of D_2O, respectively. The following procedure was used for all kinetic experiments with a varied Pt concentration.

A sample of $LPt^{IV}Me(OH)_2$ (3.6−16.1 mg, 7.3−32.6 μmol) was dissolved in 0.8−1.6 mL of a 60 or 120 mM solution of HBF_4 in D_2O. The solutions were placed in NMR Young tubes and Teflon-sealed. ^1H NMR spectra were recorded before heating to determine the ratio of signals of the complex to HOD used as an internal standard. The tubes were placed in an 80 °C heating bath. Periodically the tubes were removed and cooled with ice water, and ^1H NMR spectra were recorded. The observed rate constants of the disappearance of complexes **1** + **2**, k_{obs} (Figure 4, Table 2), were determined from the rates of disappearance of a central line of the PtMe signal of **1** at 2.7−2.8 ppm.

Effect of MeOH on the Kinetics of Formation of $LPt^{IV}Me(OMe)OH$, 4, and Disappearance of $LPt^{IV}Me(OH)_2$, 1. A sample of $LPt^{IV}Me(OH)_2$ (12.5 mg, 25.3 μmol) was dissolved in 2.89 mL of a 60 mM HBF_4 solution in D_2O ([**1**] = 8.77 mM). The solution (0.8 mL) was placed in a vial, and 1.1 μL of MeOH was added, which corresponded to a 5.7:1 MeOH/Pt molar ratio, as confirmed by an NMR integration, [MeOH] = 50 mM. Another 0.8 mL portion of the solution was used in a control experiment without MeOH additive. The reaction mixtures were transferred into NMR Young tubes, Teflon-sealed, and heated at 80 °C. No statistically meaningful difference in the observed rate constants of disappearance of complex **1** was seen: $(4.60 \pm 0.15) \times 10^{-4}\ s^{-1}$ in the absence and $(4.55 \pm 0.23) \times 10^{-4}\ s^{-1}$ in the presence of the methanol additive.

Effect of 1 equiv of $LPt^{II}(OH_2)_2BF_4$ Additive on the Kinetics of the C−O Elimination from $LPt^{IV}Me(OH)_2$ in Acidic D_2O Solutions. A solution of complex **3** was prepared as follows. A sample of 4.8 mg of $LPt^{IV}Me(OH)_2$ (9.7 μmol) was dissolved in 1.3 mL of 60 mM HBF_4 solution in D_2O ([Pt] = 7.48 mM). Then 0.817 g of the resulting solution was placed into an NMR Young tube and heated at 80 °C in a heating bath. The disappearance of $LPt^{IV}Me(OH)_2$ was monitored by ^1H NMR. After heating for ca. 190 min a complete conversion of $LPt^{IV}Me(OH)_2$ to $LPt^{II}(OH_2)_2BF_4$ and MeOH was reached.

Another sample of $LPt^{IV}Me(OH)_2$ (2.9 mg, 5.9 μmol) was placed in a vial and dissolved in the acidic solution of $LPt^{II}(OH_2)_2BF_4$ above. The resulting mixture was transferred into an NMR Young tube. According to NMR, the $LPt^{IV}Me(OH)_2/LPt^{II}(OH_2)_2BF_4$ ratio was 1.02:1, $LPt^{II}(OH_2)_2BF_4$ = 7.48 mM and $LPt^{IV}Me(OH)_2$ = 7.63 mM. The solution was heated at 80 °C in a temperature-controlled bath. Periodically the Young tube was removed from the bath and cooled quickly to room temperature, and NMR spectra were recorded. After heating for 5 min at 80 °C a new PtMe peak was observed at 3.56 ppm ($^2J_{195PtH}$ = 64 Hz), corresponding to *cis*-$LPt^{IV}Me(\mu\text{-}OH)_2Pt^{II}LBF_4$, as confirmed by independent synthesis and ESI-MS analysis. After rapid consumption of $LPt^{II}Me(OH)_2$ due to the formation of isomeric $[LPt^{IV}Me(\mu\text{-}OH)_2Pt^{II}L]BF_4$, **6**, which were observed during the first 5 min, the reaction followed first-order kinetics. The calculated pseudo-first-order rate constant $k_{obs} = (5.82 \pm 0.30) \times 10^{-4}\ s^{-1}$.

Dissociation of $[LPt^{IV}Me(\mu\text{-}OH)_2Pt^{II}L]BF_4$, 6, to Produce 1 and 3 and Its Reaction with Water. A sample of isomeric complexes **6** (6.1 mg, 5.95 μmol) was placed into a Young tube, and 0.8 mL of 60 mM HBF_4 solution in D_2O was added. The mixture was heated at 80 °C. After 5 min of heating crystals of $LPt^{IV}Me(\mu\text{-}OH)_2Pt^{II}LBF_4$ dissolved to produce $LPt^{IV}Me(OH)_2$ and $LPt^{II}(OH_2)_2^+$. The kinetic curves for $LPt^{IV}Me(OH)_2$, $LPt^{II}(OH_2)_2^+$, and $LPt^{IV}Me(\mu\text{-}OH)_2Pt^{II}L^+$ obtained after 5 min of heating were identical to those observed upon heating of the solution containing 7.48 mM $LPt^{II}(OH_2)_2BF_4$ and 7.63 mM $LPt^{IV}Me(OH)_2$ with 60 mM HBF_4.

C−O Elimination from Complexes 1 and 1-*d*$_3$ in Acidic $H_2{}^{18}O$. A solution of complex **1** (17.0 mg, 34.5 μmol) and 10.0 mg of 50% HBF_4 in 987 mg of $H_2{}^{18}O$ ($[H^+]$ = 63 mM; [Pt] = 38 mM) was placed in an NMR tube, securely capped and heated in an oil bath at 80 °C. A 0.10 mL sample was picked up with a syringe before the heating began. The mixture was periodically sampled during the reaction. The composition of the mixture was analyzed using ESI-MS to determine the $Me^{18}OH/Me^{16}OH$ ratio and by ^1H NMR to determine conversion of the starting complex (Table 3). No methanol was detected in the solution before the reaction. Similar experiments were performed with $[HBF_4]$ = 120 mM and complex **1-*d*$_3$**, with concentration of the latter of 29 and 39 mM and 60 and 120 mM (Table 4).

Over time signals belonging to $LPt^{IV}Me(OMe)OH_2^+$, m/z = 508.0487, calc 508.0506, and $LPt^{IV}Me(OMe)_2H^+$, m/z = 522.0646, calc 522.06625, grew in intensity. No peaks of comparable intensity were seen for ^{18}O-isotopologous compounds, $LPt^{IV}Me(OMe)^{18}OH_2^+$ and $LPt^{IV}Me(OMe)(^{18}OMe)H^+$, up to 80% conversion of **1**.

ESI-MS, $CH_3{}^{16}OH_2^+$, m/z = 33.03176, calc 33.03404; $CH_3{}^{18}OH_2^+$, m/z = 35.03557, calc 35.03834. $CD_3{}^{16}OH_2^+$, m/z = 36.05450, calc 36.05256; $CD_3{}^{18}OH_2^+$, m/z = 38.06127, calc 38.05686.

C−O Elimination from Complex 1-^{18}O, $LPt^{IV}CH_3(^{18}OH)(OH)$, in Acidic H_2O. A solution of complex **1-^{18}O** (14.0 mg, 28.3 μmol) and 5.6 mg of 50% HBF_4 in 1074 mg of H_2O ($[H^+]$ = 59 mM; [Pt] = 26 mM) placed in an NMR tube was heated in an oil bath at 80 °C. A 0.10 mL sample of the mixture was picked up with a syringe before the heating had begun and periodically after the reaction had started. The composition of the mixture was analyzed using ESI-MS to determine the $Me^{18}OH/Me^{16}OH$ ratio and ^1H NMR to determine conversion of the starting complex. No methanol was detected in the solution before the reaction. After 70 min when the conversion of the starting complex was 83% the $Me^{18}OH/Me^{16}OH$ ratio was 16/83.

$^{16}O/^{18}O$ Exchange between Complexes 1, 1-*d*$_3$, and $H_2{}^{18}O$. A solution of complex **1** or **1-*d*$_3$** (17.0 mg, 34.5 μmol) and 10.1 mg of 50% HBF_4 in 992 mg of $H_2{}^{18}O$ ($[H^+]$ = 63 mM; [Pt] = 38 mM) placed in an NMR tube was heated in an oil bath at 80 °C. A 0.10 mL sample of the mixture was picked up with a syringe before the heating began and periodically after the reaction had started. The composition of the mixture was analyzed using ESI-MS to determine both the $Me^{18}OH/Me^{16}OH$ ratio and relative concentration of isotopomeric complexes $L^{195}PtMe(^{18}OH)_n(OH)_{2-n}$:

1, $n = 0$; $(m+H^+)/z$ = 494.070. Calc for ($\mathbf{1}\cdot H^+$), $C_{12}H_{15}{}^{16}O_5N_2{}^{195}Pt^{32}S$, 494.0349.

1-^{18}O, $n = 1$; $(m+H^+)/z$ = 496.084. Calc for (**1-^{18}O**$\cdot H^+$), $C_{12}H_{15}{}^{16}O_4{}^{18}O_1N_2{}^{195}Pt^{32}S$, 496.0392.

1-^{18}O$_2$, $n = 2$. $(m+H^+)/z$ = 498.094. Calc for (**1-^{18}O$_2$**$\cdot H^+$), $C_{12}H_{15}{}^{16}O_3{}^{18}O_2N_2{}^{195}Pt^{32}S$, 498.0435.

The signal at $(m+H^+)/z$ = 492.068, which belonged to the adventitious $LPt^{IV}Me_2(OH)$ complex, inert under the reaction conditions,[13] was used as an internal standard.

The contribution to the peak of ^{195}Pt-**1** coming from $L^{197}PtMe_2(OH)$ (16.1%) was taken into account when the relative concentrations of **1**, **1-^{18}O**, and **1-^{18}O$_2$** were calculated. Similarly taken into account were the contributions to the peak of ^{195}Pt-**1-^{18}O** coming from ^{197}Pt-**1** (16.1%) and the contribution to the signal of ^{195}Pt-**1-^{18}O$_2$** coming from ^{197}Pt-**1-^{18}O** (16.1%) (Figure 8).

Very weak peaks ($\ll$1%) with $(m+H^+)/z$ = 500, 502, and 504, which could correspond to **1-^{18}O$_3$**, **1-^{18}O$_4$**, and **1-^{18}O$_5$**, did not change their intensity in the course of the reaction. Therefore, $^{18}O/^{16}O$ exchange in the sulfonate group did not take place. Doubly

^{18}O-labeled complex **3-^{18}O$_2$**, LPt^{II}(^{18}OH$_2$)$_2^+$, was observed only in the mass spectrum of the reaction solutions.

ESI-MS of the reaction mixture composed by **3**, HBF$_4$, and H$_2$^{18}O, *m*/*z* = 484.044. Calculated for (**3**-^{18}O$_2$), $C_{11}H_{13}O_3{}^{18}O_2N_2{}^{195}Pt^{32}S$, 484.0279. Calculated isotopic pattern matched the experimentally observed one.

Similarly, for **1-*d*$_3$** peaks of **1-*d*$_3$-^{18}O** and **1-*d*$_3$-^{18}O$_2$** appeared and grew in relative intensity in the course of the reaction.

1-*d*$_3$, *n* = 0; ($m+H^+$)/*z* = 497.081. Calc for (**1-*d*$_3$**·H$^+$), $C_{12}H_{12}{}^2H_3{}^{16}O_5N_2{}^{195}Pt^{32}S$, 497.0534.

1-*d*$_3$-^{18}O, *n* = 1; ($m+H^+$)/*z* = 499.112. Calc for (**1-*d*$_3$-^{18}O**·H$^+$), $C_{12}H_{12}{}^2H_3{}^{16}O_4{}^{18}O_1N_2{}^{195}Pt^{32}S$, 499.0577.

1-*d*$_3$-^{18}O$_2$, *n* = 2; ($m+H^+$)/*z* = 501.094. Calc for (**1-*d*$_3$-^{18}O$_2$**·H$^+$), $C_{12}H_{12}{}^2H_3{}^{16}O_3{}^{18}O_2N_2{}^{195}Pt^{32}S$, 501.0620.

Inertness of Me^{16}OH in Acidic H$_2$^{18}O at 90 °C. To confirm the inertness of MeOH in acidic H$_2$^{18}O solutions, 1 μL of CH$_3$OH (22 μmol) was dissolved in 0.5 mL of H$_2$^{18}O containing 60 mM HBF$_4$. A 0.1 mL sample of the mixture was picked up with a syringe, and the mixture in a Teflon-sealed Young tube was placed in a heating bath for 3 h (80 °C). According to mass spectrometry, both before and after heating no CH$_3$^{18}OH was detected.

Reaction of LPt^{IV}CD$_3$(OH)$_2$, 1-*d*$_3$, in the Presence of 1 equiv of LPt^{II}(^{18}OH$_2$)$_2$BF$_4$ in Acidic H$_2$^{18}O Solutions. A 38.9 mM solution of LPt^{II}(^{18}OH$_2$)$_2$BF$_4$ was prepared by heating LPt^{IV}Me(OH)$_2$ (8.99 mg) in 119 mM HBF$_4$ in H$_2$^{18}O (0.5149 g) for 3 h at 80 °C. LPt^{IV}CD$_3$(OH)$_2$ (9.02 mg) was dissolved in the resulting mixture ([LPt^{IV}CD$_3$(OH)$_2$] = 38.8 mM). The reaction mixture was heated at 80 °C in a sealed NMR Young tube for 5 min. The composition of the mixture was analyzed using ESI-MS to determine the CD$_3$^{18}OH/CD$_3$^{16}OH ratio, which was found to be 2.7:1. Formation of [LPt^{IV}CD$_3$(μ-^{16}OH)$_2$Pt^{II}L]$^+$ was observed after 5 min of heating, *m*/*z* = 940.04649 (calculated for $C_{23}H_{20}D_3O_8N_4{}^{195}Pt_2{}^{32}S_2$, 940.04312).

Hydrolysis of LPt^{IV}Me(OMe)(OH), 13, in 129 mM HBF$_4$ Solution in H$_2$^{18}O. A sample of complex **13** (8.3 mg, 16 μmol) was combined with 10.2 mg (58 μmol) of 50% (mass) HBF$_4$ in water and 0.4947 g of H$_2$^{18}O to produce a solution with [**13**] = 36.4 mM and [HBF$_4$] = 129 mM. The solution was left at 20 °C for 3.5 days and then analyzed by GC-MS (EI) and ^{1}H NMR (after dilution with D$_2$O). According to GC-MS, only one methanol isotopologue was present in the mixture, CH$_3$^{16}OH, with *m*/*z* 32.0264 (calc for CH$_4$^{16}O 32.0262). No peaks that could be assigned to CH$_3$^{18}OH were detected at the level $\geq$ 1% of the intensity of the CH$_3$^{16}OH signal. Immediately after GC-MS analysis, the reaction mixture was diluted with D$_2$O and analyzed by ^{1}H NMR. According to NMR, conversion of complex **13** was 23%, and the product of hydrolysis was identified as *unsym*-LPt^{IV}Me(OH)$_2$ (*unsym*-**1**).[13]

Transformations of LPt^{IV}Me(OMe)(OH), 4, in Neutral and Acidic Aqueous Solutions. Formation of *sym*-LPt^{IV}Me(OMe)$_2$, 5, and L$_2$Pt$^{II}_2$(μ-OMe)$_2$, 14. The experiments were set up in Teflon-sealed NMR Young tubes to avoid possible loss of volatile reaction products. In neutral aqueous solution methanol formed very slowly at room temperature, <1% conversion was seen after 24 h. At 80 °C in neutral 42 mM solutions of **4** a slow ($t_{1/2} \approx$ 90 min) reaction proceeded, leading to complex **1**, MeOH, and water-insoluble white precipitate **14**, L$_2$Pt$^{II}_2$(μ-OMe)$_2$. Other reaction products were a perfectly water-soluble Me$_2$O and a symmetrical LPt^{IV}Me(OMe)$_2$, **5** (Figure 10). According to ^{1}H NMR, after 6 h the conversion of **4** was 80%; the MeOH/Me$_2$O/**5** ratio and yields of complex **4** were as follows: 7.2 (24%):3 (20%):1 (13%).

L$_2$Pt$^{II}_2$(μ-OMe)$_2$, **14**: white, amorphous powder, insoluble in water; dissolved slowly in acids to produce complex **3** and methanol. ESI-MS of a solution of **14** in diluted HBF$_4$, *m*/*z* = 951.086. Calculated for (**14**·H$^+$), $C_{24}H_{25}O_8N_4{}^{195}Pt_2{}^{32}S_2$, 951.04095. Calculated isotopic pattern matched the experimentally observed one. Anal. Found: H, 2.27; C, 29.9; N, 5.76. Calcd for $C_{12}H_{12}O_4N_2PtS$, H, 2.54; C, 30.32; N, 5.89.

The rate of the acid-catalyzed reaction of **4** in water at 80 °C, [Pt] = 39 mM and [H$^+$] = 60 mM, defined as the rate of disappearance of **4** was almost twice as fast as that involving complex **1** under the same conditions. As a result, complex **1** was seen in the reaction mixtures. Up to 5% yield of the intermediate complex **5** could be observed after 20 min, but eventually it reacted completely. Methanol and dimethyl ether were the major reaction products; the yield of methanol reached 60% and the yield of Me$_2$O was 12% by the end of reaction (3 h, Figure 9). A small amount of complex **14** (~20% by mass) was observed in the reaction mixture by the end of the reaction, while the major part of Pt was converted to complex **3**.

An acidic dilute solution of **4** (10.0 mM) in 60 mM [HBF$_4$] produced methanol as a main reaction product. After 92 min at 80° the MeOH/Me$_2$O molar ratio was 21 (70%):1 (3.3%).

C−O Coupling of *sym*-LPt^{IV}Me(OMe)$_2$, 5. A solution of *sym*-LPt^{IV}Me(OMe)$_2$ (15.0 mg) in 1 mL of 60 mM HBF$_4$ in D$_2$O was placed in an NMR Young tube and heated at 80 °C for 30 min. According to ESI-MS, the resulting solution contained LPt^{IV}Me(OMe)(OMe$_2$)$^+$, *m*/*z* = 536.08052. Calculated for $C_{15}H_{21}O_5N_2{}^{195}Pt^{32}S$, 536.082022.

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Supporting Information Available: Potentiometric titration data for **3**, all details of kinetic data fitting, crystallographic details, and CIF files for **4**$_2$·HBF$_4$, **13**, and ***cis*-6** are available free of charge at http://pubs.acs.org.

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