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Article

Remarkably Efficient Hydrolysis of Methylparathion Catalyzed by [2-(2-Pyridyl)phenyl-*C*,*N*]palladium(II) Complexes

Mieock Kim, Alexandre Picot, and François P. Gabbaï*

Chemistry Department, Texas A&M University, 3255 TAMU, College Station, Texas 77843-3255

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The reaction of the palladium(II) acetate derivative $[Pd(N\wedge C)(OAc)]_2$ ($N\wedge C = (NC_5H_4\text{-}2\text{-}C_6H_4(C^2,N)$ or (2-(2-pyridyl)-phenyl-*C,N*)) with methylparathion and water in THF leads to the formation of $[Pd(N\wedge C)(\mu\text{-}SP(=O)(OCH_3)_2)]_2$ (**1**), which reacts with PPh_3 in THF to afford mononuclear complex $[Pd(N\wedge C)(SP(=O)(OCH_3)_2)(PPh_3)]$ (**2**). Compounds **1** and **2** have been characterized by ^1H, ^{13}C, and ^{31}P NMR spectroscopy; elemental analysis; and single-crystal X-ray diffraction. When dissolved in water, **1** serves as a precatalyst for the hydrolysis of methylparathion. Kinetic and spectroscopic studies suggest that compound **1** dissociates in aqueous solution to afford cationic diaqua complex $[Pd(N\wedge C)(OH_2)_2]^+$ (**A**). At basic pH, **A** is converted into its deprotonated form $[Pd(N\wedge C)(OH_2)(OH)]$ (**B**), which dimerizes to afford a dinuclear complex, presumably $[Pd(N\wedge C)(\mu\text{-}OH)]_2$ (**C**). At pH 7, the reaction is first order in substrate and first order in palladium catalyst **A**, with $k_2 = 146 \pm 9\ M^{-1}\ s^{-1}$ at 303 K. At more-basic pH, the reaction rate increases and shows an apparent half-order dependence in palladium catalyst. These observations suggest that the active form of the catalyst at basic pH is **B**, whose concentration is controlled by an equilibrium with inactive **C**. Analysis of the data obtained at pH 9 yields a dimer formation constant $K_f = [\mathbf{C}]/[\mathbf{B}]^2 = (6.6 \pm 5.6) \times 10^6\ M^{-1}$ and a second-order rate constant k_2 of $(8.6 \pm 3.6) \times 10^3\ M^{-1}\ s^{-1}$ at 298 K. The pH dependence of the reaction rate as well as a spectroscopic titration indicates that the pK_a of **A** is in the 9.5–9.7 range. Determination of the activation parameters at both pH 7 and 9 suggests that catalysis occurs via an associative mechanism whose rate-determining step involves the substitution of a water ligand of **A** by a molecule of methylparathion at neutral pH and nucleophilic attack of the phosphorus center of methylparathion by a hydroxide ligand of **B** at basic pH.

Introduction

The study of catalytic systems that promote the hydrolytic decomposition of organophosphorus neurotoxins continues to generate interest.[1] Thus far, the greatest hydrolytic activities have been observed with enzymatic systems such as the organophosphorus hydrolase (OPH) of *pseudoma diminuta*. This metalloenzyme, which possesses a dinuclear zinc active site, promotes the hydrolysis of a broad range of organophosphorus compounds, including the thiophosphate triester methylparathion.[2] Despite many attempts, however, efforts to discover metal-based catalysts that parallel the activity of this enzyme for the hydrolysis of thiophosphate triesters have remained largely unsuccessful.[3,4] A noteworthy exception concerns cyclometalated palladium and platinum complexes.[5−9] For example, palladium and platinum aryl oxime complexes have been shown to greatly accelerate the hydrolysis of substrates such as ethylparathion.[5] According to Ryabov, the activity of such catalysts can be explained by invoking the coordination of ethylparathion at the metal

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* To whom correspondence should be addressed. E-mail: gabbai@mail.chem.tamu.edu.

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center followed by an intramolecular nucleophilic attack by the neighboring supernucleophilic oximate functionality.[5] In an effort to determine which factors control the activity of such catalysts, we have studied phenyloxazoline palladium (II) complexes and discovered that their activity in the hydrolysis of methylparathion parallels those reported for cyclometalated palladium and platinum aryl oxime complexes.[7,8] These results suggest that the presence of a supernucleophilic functionality in the catalysts may in fact not be needed to achieve high activity. To further explore this hypothesis, we have decided to investigate the catalytic activity of a simple *ortho*-metalated palladacycle that does not possess any available nucleophilic groups. In this contribution, we report on the remarkable catalytic activity of palladium complexes bearing the 2-(2-pyridyl)-phenyl-*C*,*N* ligand.

Experimental Section

General Considerations. ***Caution****: Methylparathion is highly toxic and should be handled in a well-ventilated fume hood. All glassware exposed to methylparathion should be decontaminated with bleach.* Solvents were dried by standard methods. All NMR studies were carried out on Inova NMR spectrometers (300 or 500 MHz for ^{1}H, 75.4 or 125.7 MHz for ^{13}C, 121.4 MHz for ^{31}P NMR). H_3PO_4 (85%) was used as an external standard for the solution ^{31}P NMR spectra. The proton and carbon signals of the deuterated solvents were used as internal standards for the ^{1}H and ^{13}C NMR spectra, respectively. Elemental analyses were performed by Atlantic Microlab Inc., at Norcross, GA. Melting points were measured on a Laboratory Devices Mel-Temp apparatus and were not corrected. All UV−vis absorption spectra and spectrophotometric measurements were recorded on a JASCO V530 UV−vis spectrometer equipped with an automatic cell changer. For pH titrations, a Radiometer PHM290 pH meter with VWR SympHony electrode was used. The methylparathion solution was provided by A/S CHEMINOVA, Lemvig, Denmark, as a gift. $[Pd(OAc)(N\wedge C)]_2$ ($N\wedge C = (NC_5H_4\text{-}2\text{-}C_6H_4(C^2,N)$ or (2-(2-pyridyl)-phenyl-*C*,*N*)) was prepared in accordance with a literature procedure.[10]

Synthesis of $[Pd(N\wedge C)(\mu\text{-}SP(=O)(OCH_3)_2)]_2$ (1). A solution of $[Pd(OAc)(N\wedge C)]_2$ (320 mg, 0.5 mmol) in THF (10 mL) was added to a solution of methylparathion (145 mg, 0.55 mmol) in THF (20 mL). Following the addition of water (0.5 mL), the resulting yellow solution was stirred overnight at 65 °C. Evaporation of the solvents yielded a residue that was washed with ether and dichloromethane and extracted with THF. The compound was further purified by crystallization from DMF upon slow evaporation of the solvent. Yield: 297 mg, 74%. Mp: 281 °C. ^{1}H NMR (500 MHz, DMSO): δ 3.65 (d, $^3J_{HP} = 9.3$ Hz, 12H, OC*H*$_3$), 6.99 (m, 2H), 7.41 (m, 2H), 7.52 (m, 2H), 7.65 (m, 2H), 8.07 (m, 6H), 8.46 (m, 2H). ^{13}C NMR (125.7 MHz, CDCl$_3$): δ 53.0, 119.2, 123.1, 124.3, 124.5, 129.0, 137.7, 140.1, 145.7, 147.7, 149.7, 163.3. ^{31}P{^{1}H} NMR (121.4 MHz, DMSO/D$_2$O): δ 50.5. Solid-state ^{31}P{^{1}H} NMR: δ 35.9, 32.9, 29.3. Elemental Anal. Calcd for $C_{26}H_{28}N_2O_6P_2Pd_2S_2$: C, 38.87; H, 3.51; N, 3.49. Found: C, 39.25; H, 3.60; N, 3.51.

Synthesis of $[Pd(N\wedge C)(SP(=O)(OCH_3)_2)(PPh_3)]$ (2). To a solution of complex **1** (40 mg, 50 μmol) in THF (10 mL) was added a solution of triphenylphosphine (13 mg, 50 μmol) in THF (10 mL). After 20 h at room temperature, the colorless solution was evaporated under vacuum. Slow recrystallization of the white residue in acetone led to the formation of colorless needles that were suitable for further X-ray analysis. Yield:45 mg, 85%. Mp: 281 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ 3.32 (d, $^3J_{HP} = 7.2$ Hz, 6H, OC*H*$_3$), 6.47 (m, 1H), 6.57 (m, 1H), 6.94 (m, 1H), 7.28 (m, 2H), 7.37 (m, 6H), 7.43 (m, 3H), 7.55 (m, 1H), 7.78 (m, 1H), 7.83 (m, 7H). ^{13}C NMR (75.4 MHz, CDCl$_3$): δ 53.0, 119.2, 123.1, 124.3, 124.5, 129.0, 137.6, 140.1, 145.7, 147.7, 149.6, 163.2. ^{31}P NMR (121.4 MHz, THF): δ 43.1, 44.5. Elemental Anal. Calcd for $C_{31}H_{29}NO_3P_2SPd$: C, 56.07; H, 4.40; N, 2.11. Found: C, 55.89; H, 4.33; N, 2.25.

Catalytic Hydrolysis of Methylparathion. In a typical experiment, the cell was filled with 3.0 mL of a 1 × 10^{-2} M buffer solution (HEPES, 6 < pH < 7; EPPS, 7.5 < pH < 8.5; CHES, 9 < pH < 10.5) and 0.139 mL of a stock solution of catalyst in dioxane ($[Pd_{tot}] = 2 \times [\mathbf{1}] = 8.8 \times 10^{-5}$ M). Following the addition of 0.278 mL of a stock solution of methylparathion ([methylparathion] = 4.4×10^{-4} M in dioxane), the total volume of the solution was adjusted to 3.5 mL by addition of water; the reaction was followed by monitoring the release of *p*-nitrophenol, which features an absorption band at 400 nm. The dependence of the reaction rate on methylparathion was established by varying the methylparathion concentration at constant catalyst concentration ($[Pd_{tot}] = 3.5 \times 10^{-6}$ M). The dependence of the reaction rate on the catalyst was established by varying the catalyst concentration at constant methylparathion concentration (3.5×10^{-5} M).

Spectrometric Titration. Titrations were performed by addition of a solution of NaOH (1.0 M) or a solution of HNO_3 (1.0 M) to an aqueous solution of compound **1** (4.4×10^{-5} M) containing 16% dioxane. The absorbance and pH of the solution were measured after each addition of titrant.

Single-Crystal X-ray Analysis. X-ray data for **1** and **2** were collected on a Bruker Smart-CCD diffractometer using graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). Specimens of suitable size and quality were selected and mounted onto a glass fiber with Apezion grease and run at 110 K. The structures were solved by direct methods, which successfully located most of the non-hydrogen atoms. Subsequent refinement on F^2 using the SHELXTL/PC package (version 6.1) allowed for location of the remaining non-hydrogen atoms. Additional crystallographic details are compiled in Table 1.

Results and Discussions

Synthesis. The reaction of the palladium(II) acetate derivative $[Pd(N\wedge C)(OAc)]_2$[10] with methylparathion and water in THF leads to the formation of $[Pd(N\wedge C)(\mu\text{-}SP(=O)(OCH_3)_2)]_2$ (**1**), which can be obtained as a crystalline solid (Scheme 1). This compound has been characterized by elemental analysis, MAS ^{31}P{^{1}H} NMR spectroscopy, and X-ray crystallography. The solid-state MAS ^{31}P{^{1}H} NMR spectrum of **1** shows two different sets of signals, which most likely correspond to the cis (29.3 and 35.9 ppm) and trans isomers (32.9 ppm), as shown in Scheme 1.[11] These ^{31}P NMR

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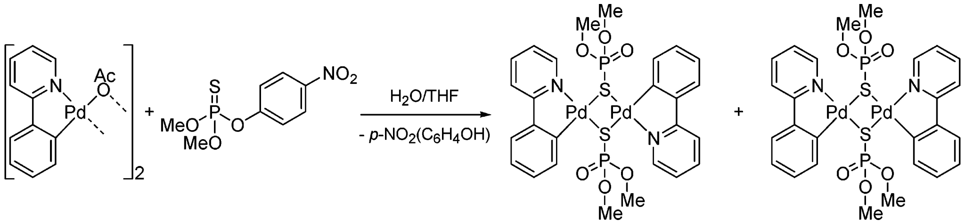
Scheme 1



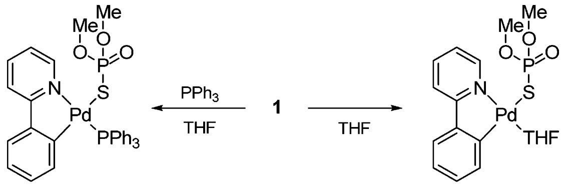
1

Table 1. Crystal Data, Data Collection, and Structure Refinement for **1** and **2**

	1	**2**
formula	$C_{26}H_{28}N_2O_6P_2Pd_2S_2$	$C_{31}H_{29}NO_3P_2PdS$
M_r	803.36	663.95
cryst size (mm^3)	0.32 × 0.35 × 0.42	0.15 × 0.32 × 0.20
cryst system	orthorhombic	triclinic
space group	*Pbca*	$P\bar{1}$
a (Å)	7.8374(16)	9.0616(18)
b (Å)	19.451(4)	17.793(4)
c (Å)	19.600(4)	19.315(4)
α (deg)		112.91(3)
β (deg)		96.39(3)
γ (deg)		94.58(3)
V (Å^3)	2987.9(10)	2824.9(10)
Z	4	4
ρ_{calcd} (g cm^{-3})	1.786	1.561
μ (Mo K) (mm^{-1})	1.493	0.878
F(000) (e)	1600	1352
T (K)	163(2)	163(2)
scan mode	ω	ω
hkl ranges	$-8 \le h \le 8$, $-22 \le k \le 14$, $-20 \le l \le 22$	$-11 \le h \le 5$, $-22 \le k \le 23$, $-23 \le l \le 25$
no. of measured reflns	12 111	17 862
no. of unique reflns [R_{int}]	2281 [0.0780]	12 514 [0.0368]
no. of reflns used for refinement	2281	12 514
abs corr	SADABS	SADABS
$T_{\min}/T_{\max}$	0.790290	0.330042
no. of refined params	181	707
R1[a], wR2[b] [$I > 2\sigma(I)$]	0.0767, 0.1510	0.0548, 0.1028
ρ_{fin} (max/min) (e Å^{-3})	2.129, −0.690	0.942, −0.887

[a] $R1 = \sum(F_o - F_c)/\sum F_o$. [b] $wR2 = \{[\sum w(F_o^2 - F_c^2)^2]/[\sum w(F_o^2)^2]\}^{1/2}$; $w = 1/[\sigma^2(F_o^2) + (ap)^2 + bp]$; $p = (F_o^2 + 2F_c^2)/3$; $a = 0.02$ (**1**), 0.0394 (**2**); $b = 50$ (**1**), 3.4354 (**2**).

Scheme 2



2 **3**

chemical shifts are comparable to that of 29 ppm measured for [Pd{*C*,*N*-($C_6H_4C(CH_3)$═NOH)-2}(μ-*S*P(═O)($OCH_3)_2$)]$_2$, which retains its dimeric structure in solution.[7] Compound **1** crystallizes in $P\bar{1}$ triclinic space group in the form of a centrosymmetrical dimer (Figure 1, Table 1). The two square planar palladium moieties (∑(angle at Pd) = 360.2(2)°) are linked by the sulfur atoms of the bridging dimethylthiophosphate ligands. The Pd−S and Pd−S(0A) distances of 2.418(3) and 2.467(3) Å are comparable to those observed in related complexes such as (*R*,*S*)-di-μ-(dimethylthiophosphate-*S*,*S*)-bis{2-[2-(4-carbomethoxy)-oxazolinyl]-phenyl-*C*,*N*}-dipalladium(II) (average Pd−S = 2.40 Å) which also features bridging thiophosphate groups.[8] The remaining coordination sites of the palladium center are occupied by the phenylpyridine carbon and nitrogen donor atoms. The quality of the X-ray measurement did not allow us to directly determine the identity of the phenylpyridine atoms bound to palladium nor did it allow us to unambiguously rule out a possible disorder. Instead, the atom located trans from the sulfur atom with the longest Pd−S bond was assigned to carbon because phenyl exerts a greater trans effect than pyridine. Accordingly, the atom trans from the sulfur atom with the shortest Pd−S bond was assigned to nitrogen. The resulting Pd−C(1) (2.049(11) Å) and Pd−N (2.060(11) Å) bonds are comparable to those observed for [Pd(N∧C)(μ-Cl)]$_2$.[12]

To assess the lability of the palladium sulfur bridges in **1**, its reaction with triphenylphosphine has been studied. In THF, this reaction afforded mononuclear complex [Pd(N∧C)(*S*P(═O)($OCH_3)_2$)(PPh_3)] (**2**) (Scheme 2). The formation of **2** is confirmed by the appearance of two new ^{31}P NMR signals at 43.1 and 44.5 ppm that correspond to the phosphorus atom of the dimethylthiophosphate and triphenylphosphine ligand, respectively. Compound **2** crystallizes in the triclinic space group $P\bar{1}$, with two independent molecules in the asymmetric unit (Figure 2, Table 1). In both of these molecules, the palladium center adopts a square planar environment, with the triphenylphosphine and the carbon of the phenylpyridine ligand in a cis arrangement. This observation agrees with the documented tendency of phosphines to avoid coordinating trans to carbon donor

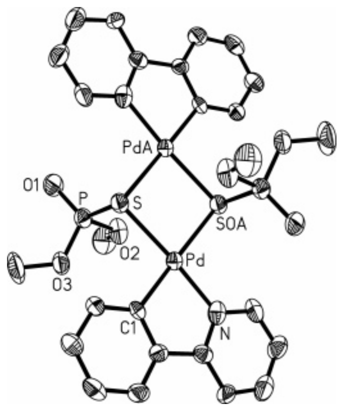


Figure 1. ORTEP view of one of the two independent molecules in the structure of **1** (50% probability level ellipsoid). Selected bond lengths (Å) and angles (deg): Pd−C(1) 2.049(11), Pd−N 2.060(11), Pd−S 2.418(3), Pd−S#1 2.467(3), S−Pd#1 2.467(3); C(1)−Pd−N 80.9(5), C(1)−Pd−S 96.7(3), N−Pd−S 175.5(3), C(1)−Pd−S#1 177.3(3), N−Pd−S#1 98.6(3), S−Pd−S#1 83.98(11), P−S−Pd 101.75(17), P−S−Pd#1 97.72(16), Pd−S−Pd#1 96.02(11).

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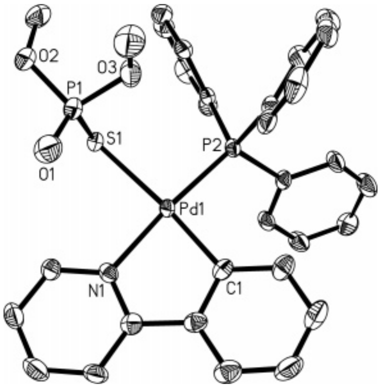


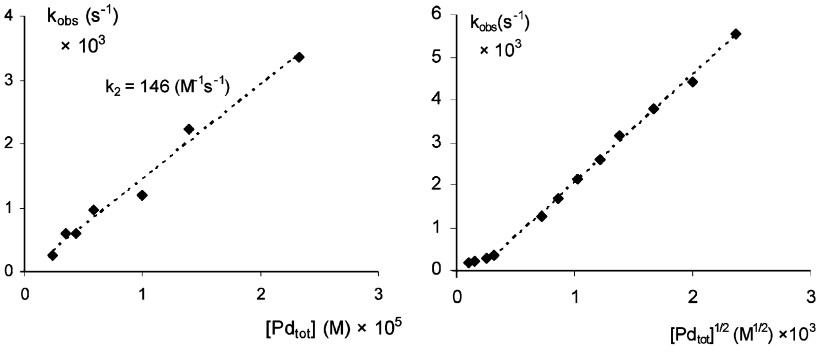
Figure 2. ORTEP view of one of the two independent molecules in the structure of **2** (50% probability level ellipsoid). Selected bond lengths (Å) and angles (deg), with the corresponding metrical parameters of the second independent molecule given in brackets. Pd(1)−C(1) 2.024(5) [Pd(2)−C(18) 2.026(5)], Pd(1)−N(1) 2.089(4) [Pd(2)−N(2) 2.080(4)], Pd(1)−P(2) 2.2612(15) [Pd(2)−P(2) 2.2548(15)], Pd(1)−S(1) 2.4139(14) [Pd(2)−S(2) 2.4427(14)]; N(1)−Pd(1)−P(2) 173.68(11) [N(2)−Pd(2)−P(2) 173.97(11)], C(1)−Pd(1)−S(1) 172.67(13) [C(18)−Pd(2)−S(2) 172.95(14)], N(1)−Pd(1)−S(1) 93.51(12) [N(2)−Pd(2)−S(2) 91.81(11)], P(2)−Pd(1)−S(1) 90.50(6) [P(4)−Pd(2)−S(2) 94.21(5)].

ligands.[13] The resulting Pd−P (2.261(15) and 2.255(15) Å)[11a,13,14] and Pd−S (2.414(14) and 2.443(14) Å)[5,6,15] distances fall within the expected ranges for these types of linkages. When dissolved in neat THF, ^{31}P NMR measurements also suggest dissociation of **1** and formation of the mononuclear derivative [Pd(N∧C)(*S*P(=O)(OCH$_3$)$_2$)(THF)] (**3**) (Scheme 2). The ^{31}P NMR resonance of the dimethylthiophosphate ligand in **3** appears at 50.5 ppm. This chemical shift is comparable to that measured for the dimethylthiophosphate ligand in **2**. It is also comparable to that measured at 53.6 ppm for the monomeric complex [Pd{*C*,*N*-(C$_6$H$_4$C(CH$_3$)=NOH)-2}(*S*P(=O)(OCH$_3$)$_2$)(py)] that we previously reported.[7]

Catalytic Studies

Complex **1** serves as a precatalyst for the hydrolysis of methylparathion, which can be conveniently followed by monitoring the release of *p*-nitrophenol using UV−vis spectroscopy. In the 6−7.5 pH range, the activity of the catalyst remains essentially constant with HEPES, EPPS, or CHES as a buffer. Although the catalyst may be active below pH 6, studying the reaction at acidic pH is complicated by the fact that the extinction coefficient of *p*-nitrophenol decreases with the pH. Kinetic studies carried out at pH 7 indicate that the reaction rate follows second-order kinetics with a first-order dependence in both substrate and palladium catalyst (Figure 3). Similar rate laws have been observed for other palladium catalysts such as phenyloxazoline palladium (II) complexes and cyclometalated palladium aryl oxime complexes.[5,7,8] Unlike in previous palladium catalysts, however, we note that the catalyst generated by dissolution of **1** in water is active at neutral or even slightly acidic pH. The k_2 value of 146 ± 9 M^{-1} s^{-1} measured at pH 7 and 303 K (Table 2) is the highest ever recorded for a synthetic catalyst at neutral pH, which is a significant achievement. In fact, the k_2 value obtained for this catalysts at neutral pH is comparable to those previously reported for palladium complexes in the 8.5−9.5 pH range.[5] Under basic conditions, the observed rate of the reaction increases substantially. This increase, which occurs over a narrow range,[16] is accompanied by a change in the order of the reaction rate. Indeed, at pH 9, the rate follows an apparent half-order dependence in palladium catalyst (Figure 3). The half-order dependence can be rationalized by invoking a catalytically active mononuclear palladium complex whose concentration is controlled by an equilibrium with a catalytically inactive dimer.[17] As the catalyst concentration decreases and passes below 1.0 × 10^{-7} M, the initial rate of the reaction ceases to follow an apparent half-order dependence in palladium catalyst. Such behavior has been previously observed and rationalized.[18] At low catalyst concentrations, the concentration in the inactive dimer becomes negligible, which is the reason the apparent half-order dependence does not hold any longer. We note in passing that the palladium catalyst in 3.5 × 10^{-6} M concentration accelerates the reaction by a factor of about 5000−6000 at pH 7 and 20 °C and about 1200 at pH 9 and 25 °C when compared to the uncatalyzed hydrolysis of parathion at $k_1 = (6.2 \pm 0.2) \times 10^{-8}$ s^{-1} at pH 7.4 and 20 °C and $k_1 = (3.5 \pm 0.2) \times 10^{-6}$ s^{-1} at pH 9 and 25 °C.[19]

The low solubility of compound **1** in water prevented a straightforward characterization of the resulting aqueous palladium species by NMR spectroscopy. Nonetheless, the system could be satisfactorily modeled (vide infra) by considering a palladium diaqua catalyst, presumably [Pd(N∧C)(OH$_2$)$_2$]$^+$ (**A**), in equilibrium with its deprotonated



(a)

(b)

Figure 3. k_{obs} for the hydrolysis of methylparathion catalyzed by **1** (a) at pH 7 as a function of [Pd$_{tot}$] and (b) at pH 9 as a function of [Pd$_{tot}$]$^{1/2}$. (k_{obs} = initial rate/[S$_o$], [Pd$_{tot}$] = total concentration in palladium, and [S$_o$]= initial methylparathion concentration = 3.5 × 10^{-5} M).

Table 2. Temperature Dependence of the Rate Constant for the Hydrolysis of Methylparathion by **1** and the Dimer Formation Constant of **1**

pH 9				pH 7	
T (°C)	$k_{1.5}$ ($M^{-1/2}\ s^{-1}$)[a]	K_f (M^{-1})	k_2 ($M^{-1}\ s^{-1}$)	T (°C)	k_2 ($M^{-1}\ s^{-1}$)
25	2.35 ± 0.07	$(6.6 \pm 5.6) \times 10^6$	$(8.57 \pm 3.65) \times 10^3$	20	$(1.00 \pm 0.07) \times 10^2$
30	2.43 ± 0.13	$(0.5 \pm 10.8) \times 10^6$	$(1.00 \pm 0.64) \times 10^4$	30	$(1.46 \pm 0.10) \times 10^2$
38	2.63 ± 0.11	$(1.0 \pm 1.4) \times 10^6$	$(1.18 \pm 0.85) \times 10^4$	35	$(1.71 \pm 0.12) \times 10^2$
45	2.86 ± 0.08	$(1.2 \pm 1.4) \times 10^6$	$(1.42 \pm 0.79) \times 10^4$	44	$(2.29 \pm 0.15) \times 10^2$
55	3.09 ± 0.26	$(1.5 \pm 4.9) \times 10^6$	$(1.67 \pm 2.81) \times 10^4$	52	$(2.79 \pm 0.19) \times 10^2$

[a] $k_{1.5}$ was obtained experimentally by dividing the initial rate by [S] and $[Pd_{tot}]^{1/2}$.

form [Pd(N∧C)(OH$_2$)(OH)] (**B**) (eq 1), which dimerizes to afford an inactive dinuclear complex, presumably [Pd(N∧C)(μ-OH)]$_2$[20] (**C**) (eq 2). To confirm the dissociation of **1** in water, we recorded the ^{31}P NMR spectrum of **1** (1.43×10^{-5} M) in water at pH 7 using CHES (10 mM) as a buffer. These experiments allowed for the detection of the dimethylthiophosphate anion at δ 57.1[21] thus confirming that the dimethylthiophosphate anion is liberated by **1** in water at neutral pH. A simple derivation (eq 3−7) shows that the concentrations of three palladium species involved in this model can be expressed as a function of the total concentration in palladium [Pd$_{tot}$], the proton concentration [H$^+$], the acidity constant of the diaqua complex **A** (K_a), and the formation constant of dinuclear complex **C** (K_f) (eq 7−9).

$$\underset{\mathbf{A}}{[Pd(N\wedge C)(OH_2)_2]^+} \overset{K_a}{\rightleftharpoons} H^+ + \underset{\mathbf{B}}{[Pd(N\wedge C)(OH_2)(OH)]} \quad (1)$$

$$2\underset{\mathbf{B}}{[Pd(N\wedge C)(OH_2)(OH)]} \overset{K_f}{\rightleftharpoons} 2H_2O + \underset{\mathbf{C}}{[Pd(N\wedge C)(\mu\text{-}OH)]_2} \quad (2)$$

$$[Pd_{tot}] = [\mathbf{A}] + [\mathbf{B}] + 2[\mathbf{C}] \quad (3)$$

$$K_a = [H^+][\mathbf{B}]/[\mathbf{A}] \quad (4)$$

$$K_f = [\mathbf{C}]/[\mathbf{B}]^2 \quad (5)$$

$$[Pd_{tot}] = [\mathbf{A}] + K_a[\mathbf{A}]/[H^+] + 2K_fK_a^{\,2}[\mathbf{A}]^2/[H^+]^2 \quad (6)$$

$$[\mathbf{A}] = \frac{[H^+]^2\{-1-K_a[H^+]+\sqrt{(1+K_a/[H^+])^2+8[Pd_{tot}]K_fK_a^{\,2}/[H^+]^2}\}}{4K_fK_a^{\,2}} \quad (7)$$

$$[\mathbf{B}] = \frac{K_a[\mathbf{A}]}{[H^+]} \quad (8)$$

$$[\mathbf{C}] = \frac{K_fK_a^{\,2}[\mathbf{A}]^2}{[H^+]^2} \quad (9)$$

Assuming that, at pH 9, the concentration in **A** is negligible, the data obtained at this pH can be fitted to eq 10, where k_{obs} is equal to the initial rate divided by the initial methylparathion concentration [S$_o$] and is dependent on the total concentration in palladium [Pd$_{tot}$] and K_f, the formation constant of **C**, as defined in eq 5.[17,20,22] A plot of the k_{obs} as a function of $[Pd_{tot}]^{1/2}$ followed by a least-squares linear fit and graphical analysis affords a second-order rate constant of $(8.6 \pm 3.6) \times 10^3$ M^{-1} s^{-1} and a K_f value of $(6.6 \pm 5.6) \times 10^6$ M^{-1} at 298 K (Table 1). The kinetic data obtained by this method indicate that the second-order rate constant observed at pH 9 is 2 orders of magnitude larger than that at pH 7. Although the errors affecting the parameters determined by this method are often neglected, a rigorous error propagation calculation indicates that, at least in the present case, the uncertainties on both k_2 and K_f are considerable.

$$k_{obs} = \text{initial rate}/[S_O] = k_2[\mathbf{B}] = k_2(-{}^1/_2 + ({}^1/_4 + 2K_f[Pd_{tot}])^{1/2})/2K_f \quad (10)$$

To further evaluate the model, we have studied the pH dependence of k_{obs} at 298 K between pH 6 and 10.5. Because both **A** and **B** are brought to coexist in this pH range, the data obtained in these experiments was manually fitted to eq 11, which accounts for the contribution of catalysts **A** and **B** to the overall rate of the reaction. In eq 11, [**A**] and [**B**] are expressed as a function of K_a and K_f as per eq 7 and 8, respectively. The fit presented in Figure 4 was obtained manually with $K_a = 1 \times 10^{-9.7}$ M, $K_f = 6.6 \times 10^6$ M^{-1}, a second-order rate constant at neutral pH ($k_{2(neutral)}$) of 140

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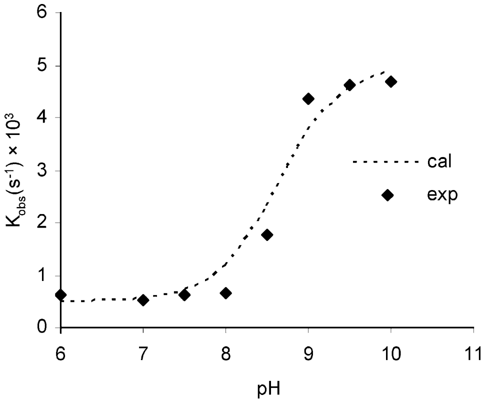

Figure 4. pH dependence of the hydrolysis of methylparathion catalyzed by **1** ([Pd_{tot}] = 1.75×10^{-6} M, [methylparathion] = 3.5×10^{-5} M). The fit (dotted line) was obtained using eq 11 with pK_a = 9.7, $K_f = 6.6 \times 10^6$ M^{-1}, $k_{2(neutral)} = 140$ M^{-1} s^{-1}, and $k_{2(basic)} = 10.5 \times 10^3$ M^{-1} s^{-1}.

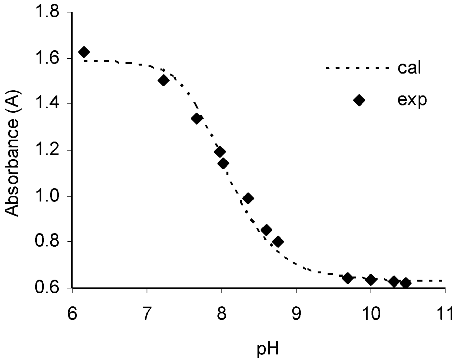

Figure 5. Spectrophotometric titration curve of **1** in aqueous solution with 16% dioxane at 240 nm and 25 °C ([**1**] = 4.4×10^{-5} M). The fit (dotted line) was obtained using eq 12 with pK_a = 9.5, $K_f = 6.6 \times 10^6$ M^{-1}, ϵ_A = 18 000 M^{-1} cm^{-1}, ϵ_B = 12 000 M^{-1} cm^{-1}, and ϵ_c = 14 000 M^{-1} cm^{-1}.

M^{-1} s^{-1}, and a second-order rate constant at basic pH ($k_{2(basic)}$) of 10.5×10^3 M^{-1} s^{-1}. We note that the values of $k_{2(neutral)}$ and $k_{2(basic)}$ are similar, within error, to those determined by analyzing the initial rates at pH 7 and pH 9, respectively, whereas the value of K_f is identical to that determined by studying the dependence of the initial rate as a function of $[Pd_{tot}]^{1/2}$ (Table 1). This fit also suggests that the pK_a of the cationic diaqua complex **A** is close to 9.7. This pK_a value is intermediate between that usually observed for cationic cyclometalated palladium monoaqua complexes[23,24] and that recently reported for the cationic cyclopalladated diaqua arylphosphinate complex [Pd{*C*,*P*-(4-MeC$_6$H$_3$-2-(OP*i*Pr$_2$))}-(OH$_2$)]$^+$ (pK_a = 10.9).[25]

$$k_{obs} = \text{initial rate}/[S] = [\mathbf{A}]k_{2(\text{neutral})} + [\mathbf{B}]k_{2(\text{basic})} \quad (11)$$

The pK_a of cationic diaqua complex **A** was also measured by a spectrophotometric titration. To this end, the absorbance of a solution of **1** as a function of pH in water/dioxane was measured at 240 nm between pH 6 and 10.5 (Figure 5). The change observed in the absorbance of the sample as a function of pH is consistent with the formation of **B** and **C** by deprotonation of **A**. The theoretical absorbance (Abs) can be approximated using eq 12, where [**A**], [**B**], and [**C**] are expressed as a function of K_a and K_f (eq 7−9) and where ϵ_A, ϵ_B, and ϵ_C are the extinction coefficients of **A**, **B**, and **C**, respectively. ϵ_A was derived from the absorbance at pH 6−7, where **A** is the predominant species. Because **B** and **C** coexist above pH 9.5, a direct determination of their respective extinction coefficients is complicated. We monitored the absorbance of a solution of **1** at pH 10 in the $2.01 \times 10^{-5} < [Pd_{tot}] < 1.13 \times 10^{-4}$ range and observed an essentially linear variation of the absorbance. One might expect that the equilibrium between **B** and **C** would result in a nonlinear dependence of the absorbance as a function of [Pd_{tot}]. However, the large equilibrium constant K_f of 6.6×10^6 M^{-1} as derived from the aforementioned kinetic studies (Figure 4) indicates that **C** is the major species ([**C**]/[**B**] = 7.8 for [Pd_{tot}] = 2.01×10^{-5}; [**C**]/[**B**] = 19 for [Pd_{tot}] = 1.13×10^{-4}) and therefore the major contributor to the observed absorbance. Increasing the level of dilution to better study the equilibrium between **B** and **C** was not possible because of the limited magnitude of the extinction coefficients. For these reasons, the extinction coefficient of **B** and **C** cannot be independently determined and were instead derived by the following method.

$$\text{Abs} = [\mathbf{A}]\epsilon_A + [\mathbf{B}]\epsilon_B + [\mathbf{C}]\epsilon_C \quad (12)$$

Using $K_f = 6.6 \times 10^6$ M^{-1}, ϵ_A = 18 000 ± 200 M^{-1} cm^{-1}, fitting of the spectrophotometric data to eq 12 affords pK_a = 9.5 ± 0.1 and ϵ_B = 12 000 ± 6000 M^{-1} cm^{-1}, ϵ_c = 14 000 ± 500 M^{-1} cm^{-1}. The pK_a value determined by this method is almost identical to that determined by analyzing the pH dependence of the initial reaction rate. The value of ϵ_B is affected by a large error, because **B** remains a minor species at all pH levels.

To get additional mechanistic information, the rate of the reaction was studied at different temperatures (Table 1). The k_2 values obtained at pH 7 and pH 9 (Table 1) were analyzed using the Eyring equation, which afforded the following activation parameters: $\Delta H^{\ddagger} = 22.9 \pm 0.15$ kJ mol^{-1}, $\Delta S^{\ddagger} = -129 \pm 0.5$ J K^{-1} mol^{-1} at pH 7; $\Delta H^{\ddagger} = 15.8 \pm 4.2$ kJ mol^{-1} and $\Delta S^{\ddagger} = -117 \pm 13$ J K^{-1} mol^{-1} at pH 9. The data collected at pH 9 were also used to calculate K_f at each temperature. A van't Hoff analysis of the K_f values indicates that the formation of **C** is endothermic ($\Delta H_f^0 = 21.3 \pm 4.2$ kJ mol^{-1}). Comparable thermodynamic parameters have been calculated for the dimerization of platinum complexes[26] or copper hydroxide complexes.[22b]

The very negative value of the entropy of activation measured at neutral and basic pH indicates that the association of the catalyst with the substrate is involved in the rate-determining step of the reaction (Scheme 3). It is well-known that ligand-substitution reactions in square planar palladium-

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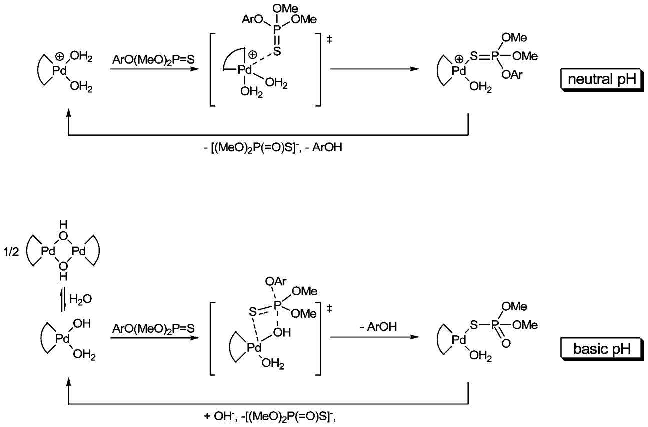
Scheme 3



(II) complexes often proceed by associative mechanisms,[27] which are also characterized by very negative activation entropies.[28] By analogy, we propose that the rate-determining step of the reaction at neutral pH may in fact involve the substitution of a water ligand by a molecule of methylparathion, which would proceed via a five-coordinate intermediate.[29] This ligand-substitution reaction would be followed by rapid hydrolysis of the methylparathion and release of *p*-nitrophenol and dimethylthiophosphate. At basic pH, the experimental observations can be reconciled on the basis of a mechanism in which the catalyst−substrate interaction involves nucleophilic attack of the phosphorus center by a hydroxide ligand. Taking into account the thiophilic character of palladium, this event may in fact be concomitant with coordination of the sulfur atom to the palladium center. Such a mechanism, which has been proposed for zinc-containing hydrolysis catalysts,[30] may in fact be applicable to other palladium-catalyzed hydrolysis reactions that we have previously reported but not studied in detail.[8]

In summary, simple cyclopalladated complexes based on the 2-(2-pyridyl)-phenyl-*C,N* ligand yield remarkably active catalysts for the hydrolysis of methylparathion. The data that we have gathered indicate the formation of a palladium(II) diaqua complex (**A**) that is moderately active at acidic and neutral pH. At pH 7, the reaction follows a second-order rate law with a first-order dependence in palladium catalyst and methylparathion. Deprotonation of this complex affords a palladium(II) aqua hydroxo complex (**B**) whose activity at pH 9 is much greater than that observed for **A** at neutral pH. This increase is somewhat tempered by the fact that catalyst **B** is in equilibrium with a nonactive dinuclear species (**C**). This unproductive equilibrium becomes negligible at low concentrations, where the catalyst exists mostly in the dissociated active form. Finally, these results indicate that the presence of a supernucleophilic functionality is not necessary for achieving high catalytic activity.[5] In fact, the second-order rate constant observed at pH 9 with **1** as a precatalyst is 1 to 2 orders of magnitude larger than those reported for palladium and platinum aryl oxime complexes.[5]

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Supporting Information Available: Calculation details and X-ray crystallographic data for complexes **1** and **2** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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