with $I > 2.0\sigma I$) (28848 independent reflections, $R_{int} = 0.0922$), for 2θ in the range 1.56 to 50.0° ($GOF = 0.900$). Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-140825. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[9] L. Zhao, C. J. Matthews, L. K. Thompson, S. L. Heath, *Chem. Commun.* **2000**, 265–266.

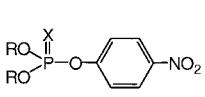
[10] Variable temperature magnetic measurements were carried out in the range 2–300 K using a SQUID magnetometer (Quantum Design MPMS5S) in fields of 0.1–5.0 T. Background corrections for the sample holder and diamagnetic portions of the complex were applied.

[11] A. M. Garcia, F. J. Romero-Salguero, D. M. Bassani, J.-M. Lehn, G. Baum, D. Fenske, *Chem. Eur. J.* **1999**, *5*, 1803–1808.

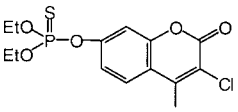
Highly Efficient Degradation of Thiophosphate Pesticides Catalyzed by Platinum and Palladium Aryl Oxime Metallacycles**

Gregory M. Kazankov, Victoria S. Sergeeva, Elena N. Efremenko, Larissa Alexandrova, Sergey D. Varfolomeev, and Alexander D. Ryabov*

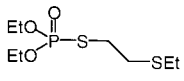
Thiophosphoric acid esters such as **1** and **4**, pesticides with an annual world production of hundred thousands of tons, are strong pollutants and their accumulation in the environment is a recognized ecological threat.[1] Some neurotoxins and V-type chemical warfare agents are chemically similar, and a potential danger is emerging from their aging stockpiles.[2]



1 (R = Et, Z = S; parathion)
2 (R = Me, Z = S; methyl parathion)
3 (R = Et, Z = O; paraoxon)



4 (coumaphos)



5 (demeton-S)

[*] Prof. Dr. A. D. Ryabov, Dr. G. M. Kazankov, V. S. Sergeeva, Dr. E. N. Efremenko, Dr. L. Alexandrova,[+] Prof. Dr. S. D. Varfolomeev
Department of Chemistry
Moscow State University
119899 Moscow (Russia)
Fax: (+7) 95-939-5417
E-mail: ryabov@enz.chem.msu.ru

[+] Permanent address:
Instituto de Investigaciones en Materiales
UNAM, Circuito Exterior s/n, Ciudad Universitaria (Mexico)

[**] Financial support from the Russian Foundation for Basic Research (grant no. 98-03-33023a) and INTAS (project 97-0166) is gratefully acknowledged.

Needless to say, creation of "green" catalytic processes for degradation of thiophosphoric acid esters is an urgent task of contemporary chemical technology and biotechnology. Significant progress has recently been made by the use of organophosphate hydrolases (OPH), a class of metal-dependent enzymes whose vital virtue is in the detoxification of organophosphoric species by reaction (1).[3] These enzymes

$$RR'P(=X)Z + H_2O \xrightarrow{OPH} RR'P(=X)OH + HZ \quad (1)$$

are superior to their low molecular weight analogues in terms of catalyst specificity and activity, but the latter are often also efficient, more stable, and less subject to inactivation. Chemical catalysts with the features of enzyme active sites are believed to be particularly promising.[4]

Recently, we introduced orthometalated complexes of Pd^{II} and Pt^{II} as mimetics of metal-dependent esterases. The catalysts display regio- and stereoselectivity as well as reasonable rate accelerations at neutral pH values.[5] However, the rates of hydrolysis of amino acid esters were not very striking, although the catalysts had features typical of metallohydrolases.[5b] It could be argued that a square-planar metal configuration, which is not reported in enzymes, is less favorable for catalysis, and that Pd^{II} and Pt^{II} are "soft" acids which require "softer" bases for efficient catalysis. The thiophosphoric acid esters **1**–**5** are examples of such bases, and therefore metallacycles **6** and **7** (dmso = dimethyl sulfoxide, py = pyridine) have been tested as catalysts for the hydrolysis of pesticides **1**–**5**. Here we show that **6** and **7**[6] as well as the Pt^{IV} complex **8**[6] are excellent catalysts for the degradation of thiophosphate pesticides and neurotoxins.

Parathion (**1**) is spontaneously hydrolyzed at pH 8.5 at an immeasurably slow rate. Addition of a catalytic amount of the Pt^{II} complex **6a** enhances the rate of hydrolysis of **1** (by reaction (1)), which proceeds to completion and follows first-order kinetics.[7] Methyl parathion (**2**) and coumaphos (**4**) behave similarly (Figure 1). No intercept is observed in the

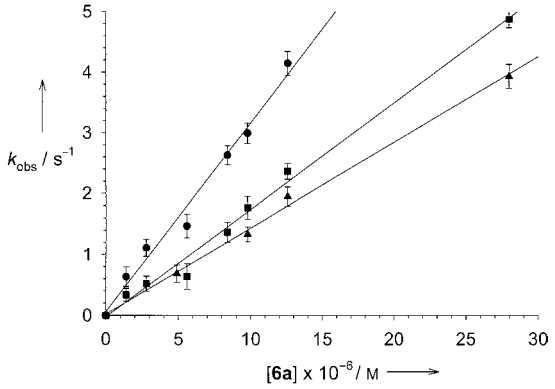
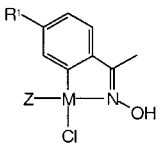


Figure 1. Dependencies of k_{obs} for the hydrolysis of parathion (**1**, ●), methyl parathion (**2**, ■), and coumaphos (**4**, ▲) catalyzed by Pt^{II} complex **6a** at different concentrations. Conditions: [ester] = 1×10^{-4} M, 0.005 M $Na_2B_4O_7$/NaOH buffer, pH 8.5, 0.01 M $NaClO_4$, 25 °C.

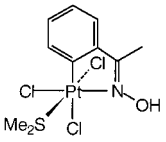
plot of the observed rate constant versus the concentration of **6a**, indicating good catalysis according to the rate law (2).

$$k_{obs} = k_2[\text{catalyst}] \quad (2)$$

Kinetic data were obtained for all the esters **1**–**5** in combination with complex **6a**, and for parathion (**1**) with complexes **6**–**8**. The rate law (2) holds throughout. The values



	M	R^1	Z
6a	Pt	H	dmso
6b	Pt	MeO	dmso
6c	Pt	Me	dmso
6d	Pt	F	dmso
6e	Pt	Cl	dmso
6f	Pt	H	py
7	Pd	H	py



8

of k_2 are summarized in Table 1; the rates of the hydroxide-catalyzed hydrolysis of several esters were also measured at 0.001–1.0 M NaOH, and the k_2 values are included for comparison. The catalytic activity of **6** in the hydrolysis of **1**

Table 1. Observed second-order rate constants k_2 [$M^{-1}s^{-1}$] for the catalyzed hydrolysis of phosphoric acid triesters **1**–**5**.[a]

Catalyst	Ester				
	1	**2**	**3**	**4**	**5**
6a	310 ± 17	175 ± 7	10.2 ± 0.1	141 ± 5	27.8 ± 0.3
6b	914 ± 21				
6c	773 ± 29				
6d	429 ± 8				
6e	452 ± 17				
6f	230 ± 8				
7	54 ± 3				
8	10.9 ± 0.4				
OH^-	$(9.5 \pm 0.6) \times 10^{-5}$	$(2.6 \pm 0.4) \times 10^{-4}$	7.5×10^{-2}[b]		

[a] Conditions: pH 8.5, 25 °C, 0.01 M $NaClO_4$. [b] Reference [3].

is 10^6–10^7 times higher than that of hydroxide. Assuming that only the OH^--catalyzed pathway is operative in the absence of a metal catalyst at pH 8.0, the metal-catalyzed hydrolysis is 10^9 times more efficient than the spontaneous reaction for a **6b** concentration as low as 10^{-4} M! This is in fact a significant number. In other systems where the hydrolysis of nitrophenyl phosphates catalyzed by biomimetically relevant transition metal catalysts was investigated,[8] the catalytic effects were usually in the range of 10^4–10^6. However, these estimates should be treated with care, since they often refer to the promoted hydrolysis rather than the catalyzed reaction, and the kinetic data are sometimes not used carefully enough. For example, the estimate of 10^{11} reported by Williams et al. corresponds to the *promoted* cleavage of 4-nitrophenyl methyl phosphate coordinated to a dinuclear Co^{III} complex.[9]

A comparison of the catalytic activity of complexes **6** and OPH in the hydrolysis of **1** shows that the low molecular weight catalyst is fairly competitive, although OPH is a very reactive enzyme ($k_{cat} = 600\ s^{-1}$ and $K_M = 2.8 \times 10^{-4}$ M).[3] Recalculation for a gram of catalyst provides $k_2 \approx 1$ and $k_{cat}/K_M \approx 60\ g^{-1}s^{-1}$, which nicely advertises for the Pt^{II} catalysts taking into account that the rate of the enzymatic reaction levels off at high concentrations of **1**.

The data in Table 1 are indicative of several remarkable features. First, the catalysis of paraoxon (**3**) hydrolysis by **6a** is 30 times less efficient than that of parathion (**1**) hydrolysis. Thus, a soft sulfur donor center is more favorable than the harder oxygen. Interestingly, the base hydrolysis of paraoxon is about 1000 times faster than that of parathion. Second, the square-planar Pt^{II} complexes **6** are 30-fold more catalytically active than the structurally similar octahedral Pt^{IV} species **8**, presumably due to steric effects imposed by a more crowded coordination sphere. Third, the catalytic activity of **6** can be increased threefold by introducing substituents at the benzene ring of the cyclometalated ligand. Remarkably, both electron-donating and electron-withdrawing groups favor the catalysis. Fourth, comparison of the "twin" Pt^{II} and Pd^{II} complexes **6f** and **7** shows that the former is about five times more catalytically active. The hard–soft principle seems to hold here as well.

The hydrolysis of **1** catalyzed by **6a** is pH-dependent in the range 6–10 (Figure 2). The profile suggests two catalytically

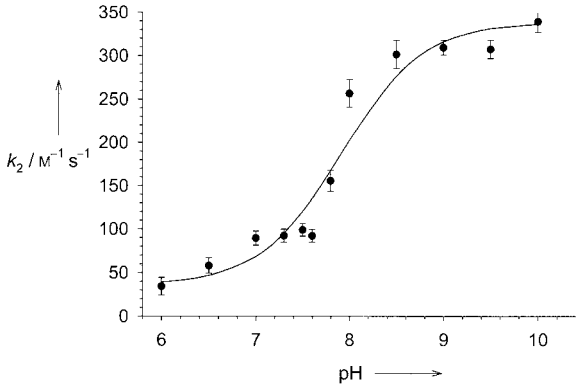


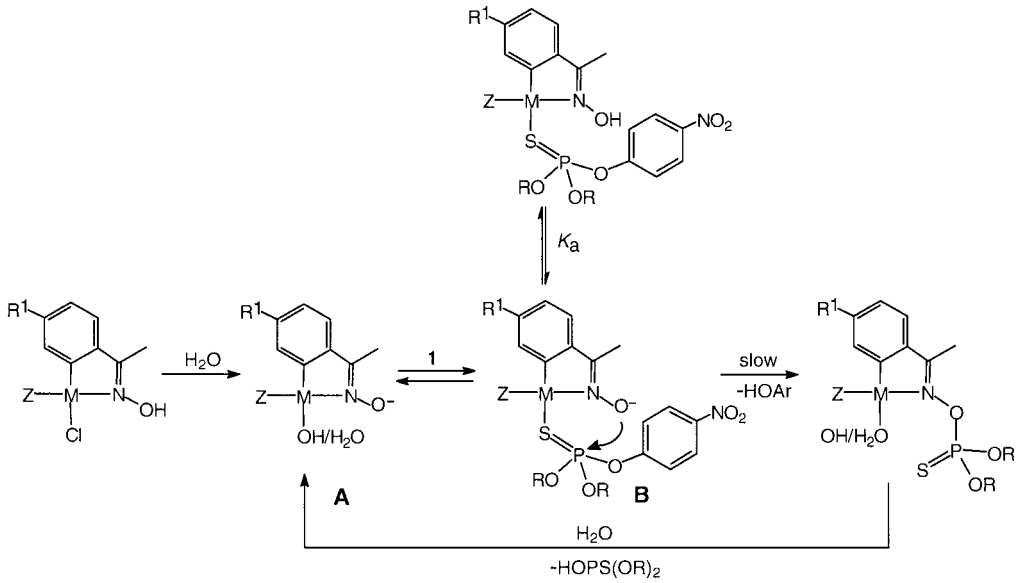
Figure 2. The pH profile for **6a**-catalyzed hydrolysis of parathion (**1**). Conditions: [**1**] = 1×10^{-4} M, 0.01 M $NaClO_4$, 25 °C. The buffer components were 0.005 M $Na_2B_4O_7$ (pH 8–10) and 5,5′-diethylbarbituric acid (pH 6–7.8).

active species. Fitting the data to Equation (3) leads to the rate constants $k_{AH} = 40 \pm 20\ M^{-1}s^{-1}$ and $k_A = 340 \pm 20\ M^{-1}s^{-1}$, and a K_a value of $(1.2 \pm 0.5) \times 10^{-8}$ M ($pK_a = 7.9$). As in our previous work,[10] the acid–base equilibrium is ascribed to the deprotonation of the NOH group of the orthometalated oxime, a key nucleophilic center in the reaction.

$$k_2 = \frac{k_{AH}[H^+] + k_A K_a}{[H^+] + K_a} \quad (3)$$

It is well documented by us[10] and others[11] that the coordinated halides *trans* to the σ-bound phenyl carbon in **6** or **7** are rapidly and completely hydrolyzed in water. Therefore, the reaction mechanism shown in Scheme 1 can be envisioned. The esters form sulfur-bonded intermediates **B** with aqua/hydroxo species **A**. Subsequently intramolecular nucleophilc attack of the oximate oxygen at P^V takes place.[12] Thus, Pd^{II} or Pt^{II} play a dual role in the catalysis. The metal centers are binding sites for the substrate in close proximity to the coordinated oxime, the pK_a of which is substantially lowered

  0044-8249/00/11217-3248 $ 17.50+.50/0



Scheme 1. Plausible reaction mechanism for the hyrolyisis of **1**–**5** catalyzed by complexes **6** and **7**.

due to coordination with the metal. As a result, a strong nucleophile is generated at neutral pH values.

Coordination of the esters and the metals should also cause an increase in the effective positive charge at P^V, and thus facilitate the intramolecular nucleophilic attack by the oximate. The replacement of DMSO or pyridine ligands at Pt^{II} in **6** and **7** is unlikely since no characteristic bands for free pyridine were observed in the UV/Vis spectrum of a mixture of **5** and **7**. The mechanism in Scheme 1 is supported by the UV/Vis and ^{31}P NMR study of the **6a**-promoted hydrolysis of neurotoxin demeton-S (**5**). The ^{31}P NMR resonance for intact **5** is at $\delta = 30.005$ in aqueous 1×10^{-4} M $NaClO_4$. Addition of **6a** generates a new signal at $\delta = 0.655$ for the reaction product $(EtO)_2P(=O)OH$.[13] Although the rate of hydrolysis of **5** increases tremendously in the presence of **6a**, there is no true catalysis and a stoichiometric amount of **6a** is necessary. Cleavage of **5** liberates the potentially good ligand $HSCH_2CH_2SEt$, which on interaction with the Pt^{II} C,N-metallacycle blocks the substrate binding site, making intramolecular nucleophilic attack impossible.

In conclusion, cyclometalated Pt^{II} complexes efficiently catalyze the degradation of thiophosphoric acid pesticides (**1**–**3**). Comparison with related Pd^{II} and Pt^{IV} complexes indicates that the Pt^{II} catalysts are more active and exhibit an increased selectivity towards sulfur-containing triesters. It has been previously noticed that Pd^{II} complexes could be promising catalysts in reaction (1).[14] Cycloplatinated compounds with coordinated oxime could be used to create even more specific and reactive catalysts.

Received: March 20, 2000 [Z14871]

[1] M. A. Gallo, N. J. Lawryk, *Organic Phosphorous Pesticides. The Handbook of Pesticide Toxicology*, Academic Press, San Diego, CA, **1991**.

[2] J. K. Grimsley, V. K. Rastogi, J. R. Wild, *Biological Detoxification of Organophosphorus Neurotoxins, Vol. 2*, Technomic Publishing Company, Inc, Lancaster, PA, **1998**.

[3] D. P. Dumas, S. R. Caldwell, J. R. Wild, F. M. Raushel, *J. Biol. Chem.* **1989**, *33*, 19659–19665.

[4] a) J. Chin, *Acc. Chem. Res.* **1991**, *24*, 145–152; b) J. Suh, *Acc. Chem. Res.* **1992**, *25*, 273–279.

[5] a) A. K. Yatsimirsky, G. M. Kazankov, A. D. Ryabov, *J. Chem. Soc. Perkin Trans. 2* **1992**, 1295–1300; b) E. V. Krooglyak, G. M. Kazankov, S. A. Kurzeev, V. A. Polyakov, A. N. Semenov, A. D. Ryabov, *Inorg. Chem.* **1996**, *35*, 4804–4806; c) A. D. Ryabov, G. M. Kazankov, S. A. Kurzeev, P. V. Samuleev, V. A. Polyakov, *Inorg. Chim. Acta* **1998**, *280*, 57–61; d) G. M. Kazankov, O. G. Dyachenko, A. V. Nemukhin, A. D. Ryabov, *Mendeleev Commun.* **1997**, 159–162; e) S. A. Kurzeev, G. M. Kazankov, A. D. Ryabov, *Zh. Org. Khim.* **2000**, in press; f) S. A. Kurzeev, G. M. Kazankov, A. D. Ryabov, *Inorg. Chim. Acta* **2000**, *305*, 1–6.

[6] Complexes **6b**–**f** were prepared as described for **6a**: A. D. Ryabov, G. M. Kazankov, I. M. Panyashkina, O. V. Grozovsky, O. G. Dyachenko, V. A. Polyakov, L. G. Kuz'mina, *J. Chem. Soc. Dalton Trans.* **1997**, 4385–4391. Their full characterization has been reported: L. Alexandrova, O. G. D'yachenko, G. M. Kazankov, V. A. Polyakov, P. V. Samuleev, E. Sansores, A. D. Ryabov, *J. Am. Chem. Soc.* **2000**, *122*, 5189–5200. The Pd^{II} complex **7** was obtained as described in ref. [10].

[7] Stock solutions of **1** (Sigma) or **2**–**4** (Fluka) in MeCN were added to a UV/Vis cuvette ($d = 1$ cm) with a solution of **6** or **7** in a buffer, and the progress of reaction (1) was monitored at $\lambda = 405$ ($\varepsilon = 17000\,M^{-1}cm^{-1}$) for **1**–**3** and at $\lambda = 384$ nm ($\varepsilon = 9000\,M^{-1}cm^{-1}$) for **4**. Pseudo-first-order rate constants were calculated from the graphs of absorbance (A) versus time (t) obtained by plotting $\ln[A_\infty/(A_\infty - A_t)]$ against t. Linearity was observed for three to five half-lives. Every reported rate constant is a mean value of three determinations.

[8] a) P. Hendry, A. M. Sargeson, *J. Am. Chem. Soc.* **1989**, *111*, 2521–2527; b) Y. Chung, E. U. Akkaya, T. K. Venkatachalam, A. W. Gzarnik, *Tetrahedron Lett.* **1990**, *31*, 5413–5416; c) L. Y. Kuo, S. Kuhn, D. Ly, *Inorg. Chem.* **1995**, *34*, 5341–5345; d) W. H. Chapman, R. Breslow, *J. Am. Chem. Soc.* **1995**, *117*, 5462–5469; e) I. O. Kady, B. Tan, Z. Ho, T. Scarborough, *J. Chem. Soc. Chem. Commun.* **1995**, 1137–1138; f) M. Wall, B. Linkletter, D. Williams, A.-M. Lebuis, R. C. Hynes, J. Chin, *J. Am. Chem. Soc.* **1999**, *121*, 4710–4711.

[9] N. H. Williams, W. Cheung, J. Chin, *J. Am. Chem. Soc.* **1998**, *120*, 8079–8087.

[10] A. D. Ryabov, G. M. Kazankov, A. K. Yatsimirsky, L. G. Kuz'mina, O. Y. Burtseva, N. V. Dvortsova, V. A. Polyakov, *Inorg. Chem.* **1992**, *31*, 3083–3090.

[11] M. Schmülling, D. M. Grove, G. van Koten, R. van Eldik, N. Veldman, A. L. Spek, *Organometallics* **1996**, *15*, 1384–1391.

[12] The solvent isotope effect of 1.2 ± 0.1 was determined in the reaction of **1** and **6c** at pD = 10.05 (borate buffer) and is consistent with the nucleophilic mechanism; see M. L. Bender, R. J. Bergeron, M. Komiyama, *The Bioorganic Chemistry of Enzymatic Catalysis*, Wiley, New York, **1984**.

[13] K. Lai, N. J. Stolowich, J. R. Wild, *Arch. Biochem. Biophys.* **1995**, *318*, 59–64.

[14] J. H. Mendez, R. C. Martinez, J. S. Martin, *Anal. Chem.* **1986**, *58*, 1969–1972.