

TETRAVALENT METAL CATALYZED HYDROLYSIS OF CYANOFENPHOS: A DELAYED NEUROTOXIC ORGANOPHOSPHORUS COMPOUND

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Received: April 15, 2011; Accepted: May 06, 2011

Abstract-Hydrolysis of O-ethyl O-p-cyanophenyl, phenyl phosphonothionate (Cyanofenphos) has been studied in the acidic medium with catalyst such as Zr⁴⁺, Ce⁴⁺, Hf⁴⁺ and Th⁴⁺ cations, and the rate maxima observed were at around pH 2.0. Since the metal aquo complex are known to exist in equilibrium with deprotonated species, and therefore metal bound OH-nucleophile might be available abundantly even in acidic aqueous solutions. Thus an interaction of sulphur of P=S group with metal cation followed by an intramolecular nucleophilic attack of hydroxy anion at the ester phosphorus atom would result in the cleavage of P-O bond.

Keywords- cyanofenphos, tetravalent, divalent, octameric, dimeric

INTRODUCTION

The development of new methods for accelerating hydrolysis of organophosphorus esters under the mild acidic conditions is an important area of industrial and academic research [1]. Phosphorus triesters (e.g., Paraoxon etc.) are accepted as suitable mimics of G-type nerve agents (e.g., Sarin, Soman etc) [2,3]. These compounds are not only highly toxic but also highly persistent in the environment. A significant body of information on the effect of divalent[4-6] and trivalent[7-10] ions on the hydrolysis of diesters like DNA and RNA has already been reported. Recent work has demonstrated extraordinary catalytic effect of tetravalent[11-14] cations on the hydrolysis of phosphate diester as well as nucleotides. Here, we report the acidic hydrolysis of a model compound -Cyanofenphos (CFP) of phosphonothionate series, in the presence of tetravalent metal cations. CFP, being an important insecticide could control rice stem borer, cotton ball worm, cabbage worm and aphids[15]. Moreover CFP is highly toxic to mammals; the oral LD₅₀ for rats is about 43 mg/kg (ref.16) and besides toxicities, one another problem associated to exposure of cyanofenphos is its potential for the development of delayed neuropathy[16]. Although, it is detoxified quickly in alkaline solutions, but persist under neutral and slightly acidic conditions, typical in surface water, soil etc. In order to avoid accidental exposure to birds, animals and humans from the spillage and used containers etc. all these sources of contamination must be decontaminated by economically viable method. This study includes hydrolysis of cyanofenphos, catalyzed by Zr (IV), Ce(IV), Hf (IV) and Th(IV) in mild acidic aqueous solutions.

EXPERIMENTAL

4-Cyanophenol(99%), Zirconium(IV) Chloride(98%), Hafnium(IV) Chloride(97%),Ceric Ammonium Nitrate(98%), and Thorium Nitrate(98%) were purchased from Aldrich (Sigma Aldrich Chemie, Germany) and used as supplied. AR grade KCl obtained from Central Drug House (P) Ltd. Mumbai was used in all our kinetic runs. Double distilled water was used throughout our experimental work.

Cyanofenphos was synthesized according to the standard procedure[17]. All our measurements were done on the Systronics (UV-Vis double beam spectrophotometer)-2101. Since the reaction medium was acidic, the λ_{max} values of the substrate (232 nm, $\epsilon = 15,800$) and p-cyanophenol (246 nm, $\epsilon = 38,400$) overlapped. Therefore, p-cyanophenol was converted into p-cyanophenolate anion ($\lambda_{max} = 275$ nm, $\epsilon = 48,000$), by adding 0.1 ml of triethyl amine (1M) in dioxan to each of the 5ml aliquot.

A typical kinetic run was made by adding KCl (0.037g, 10mM), ZrCl₄ (0.004g, 3×10^{-4} M) in water in 50ml flask to which approximately 40-45 ml water was added. The pH of the medium was adjusted by using 0.1 N HCl or 0.1 N KOH. HEPES buffer (0.122, 10mM) was used to maintain pH ≥ 6.0 . The solution was chilled and 0.15 ml of solution of cyanofenphos in dioxan (5×10^{-3} M) was added to it. It was made upto mark with chilled water, mixed well and equal volume of this was then quickly transferred to separate test tubes for the convenience of our measurements. The properly stoppered test tubes were placed in a digital water bath maintained at 83°C ($\pm 0.5^\circ\text{C}$), such that the temperature inside the test tubes were at 80°C. The test tubes were withdrawn one by one

at definite time intervals and the measurement of liberated p-cyanophenol was made as p-cyanophenolate anion as described earlier. All other runs (i.e., pH 1.0-5.0) were carried out in unbuffered aqueous solutions, as metal salt solutions acts as self buffers[18]. Similar kinetic runs were performed for varied [Substrate/Metal] ratio e.g., 1:30, 1:15, 1:10, 1:5 and 1:1 at pH value 2.0.

RESULTS AND DISCUSSION

All reactions were observed for more than three half lives and plots of $\log A_{\infty}-A_0 / A_{\infty}-A_t$ (where, A_0 , A_t and A_{∞} are absorbance of p-cyanophenolate anion at time zero, t and infinity respectively) versus time were linear indicating that the hydrolysis occurs via first order kinetics with respect to the parent compound. All runs were performed in duplicate and found reproducible within $\pm 5\%$ (max.) and the mean value of pseudo-first order rate constant obtained has been given in Table-1. Our experiments showed that all the metals require at least 20 fold excess over [substrate] for showing maximum catalysis. All the metal cations showed rate maxima at pH 2.0 which indicates the presence of catalytically more active species around this pH. The Rate constants for Zr(IV), Ce(IV), Hf(IV) and Th(IV) at pH 2.0 were $10.4 \times 10^{-5} \text{ sec}^{-1}$, $7.6 \times 10^{-5} \text{ sec}^{-1}$, $5.5 \times 10^{-5} \text{ sec}^{-1}$ and $4.9 \times 10^{-5} \text{ sec}^{-1}$ respectively showed the enhancement of 43, 31, 22 and 20 fold compared to those of uncatalyzed reactions. The decreases in k_{obs} values with increasing pH, suggested a reduction in the concentration of catalytically active species, and which might happens due to the precipitation of the metal ion as their hydroxide above pH 5.0(ref.19). The literature reports indicated that at around pH 2.0, Zr(IV) exists as coordination complex of water {e.g. $\text{Zr}_8(\text{OH})_{20}(\text{H}_2\text{O})_{24}\text{Cl}_{12}$ }, whose geometry has been determined to be octameric[20], and under similar conditions Hf(IV) has been reported to exhibit a similar chemistry[19]. These octameric species may be formed by bridging of two tetramers via four single OH- bridges and each metal cations of the octamer would bind to three H_2O molecules. Ce(IV) at pH 2.0 exists as dimeric Ce(IV) - hydroxo species $\{\text{Ce}_2(\text{OH})_4(\text{H}_2\text{O})_2\}^{4+}$, which has found to be a more reactive entity[21]. However, the geometry of aquo complex of Th(IV) has been proposed to be more or less similar to that of Ce(IV)[21].

The rate equation for ester hydrolysis including metal catalysis may be given by the Eq. 1

$$d[\text{p-cp}]/dt = (k_a [\text{H}^+] + k_n [\text{H}_2\text{O}] + k_b [\text{OH}^-] + k_m [\text{Metal hydroxo species}]) [\text{Parent}] \quad (1)$$

Where k_a , k_n , k_b and k_m are the rate constants for the hydrolysis of cyanofenphos by acid, water, base and the metal ion present as hydroxo complex, respectively. Moreover the hydroxide ion $[\text{OH}^-]$ is stronger nucleophile, but its concentration in neutral and acidic solutions being low, have negligible contribution to the reaction rates and at the same time the reaction rate at around pH 6.5-7.0 are very small (table-1), therefore k_n & k_b terms can be dropped out from the equation 1 .

Again we found that metal catalyzed reaction rates are much greater than the acid catalyzed rates, thus, contribution of $k_a[\text{H}^+]$ term appears to be negligible and hence the final form of the rate equation may be written as equation 2.

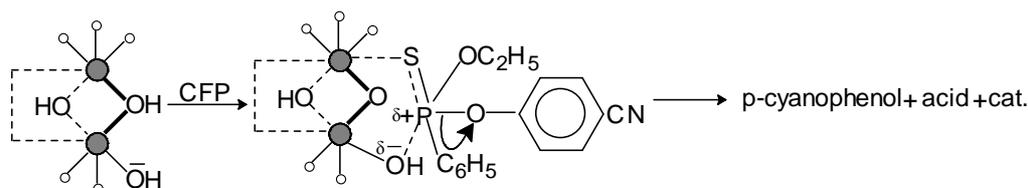
$$\text{Rate} = k_m [\text{Metal hydroxo complex}] [\text{Parent}] \quad (2)$$

In all our reactions metal hydroxo species being present in large excess; hence the rate is governed by first order kinetics. It has been reported that, because of increasing Lewis acid strength and deprotonation ability of metal bound water molecule, due to increasing positive charge on metal cation, the tetravalent metal cations like Zr^{4+} , Ce^{4+} , Hf^{4+} and Th^{4+} are found to be highly reactive towards activated phosphodiester like bis(p-nitrophenyl phosphate)[11,19], dimethyl phosphate[14], hydroxyethyl p-nitrophenyl phosphate[19] etc. and neutral triesters like methyl parathion [22]. The metal ester binding constant K_M obtained, dividing intercept by the slope of the linear plots between $1/k_{\text{obs}}$ vs. $1/[\text{M}^{4+}]$, are 4.1×10^{-3} , 3.8×10^{-3} , 3.5×10^{-3} and 2.6×10^{-3} for Zr^{4+} , Ce^{4+} , Hf^{4+} , and Th^{4+} respectively. Since, the pK_a values of the metal bound water molecule for Zr^{4+} , Ce^{4+} , Hf^{4+} and Th^{4+} are found to be around -0.6 (ref.23), -0.7 (ref.23), -1.1 (ref.23) and -2.3 (ref.11) respectively which explains that deprotonation of H_2O molecule attached to Zr^{4+} and Ce^{4+} occurs faster than H_2O molecules linked to Hf^{4+} and Th^{4+} in acidic solutions. From the magnitude of K_M and pK_a values, it became evident that hydroxo species formed from Zr^{4+} would bind more efficiently to esters molecules than those with other metal ions and additionally might facilitate intramolecular nucleophilic attack by metal bound hydroxide ion at phosphorus atom initiating the formation of a six membered ring intermediate. Thus the reaction appears to follow a push-pull mechanism as described in the case of bivalent metal catalyzed hydrolysis of phosphorus compounds[22,24-28]. Therefore considering the above facts it has been proposed that, electrons of sulfur atom of the P=S bond binds with complexed metal ions making phosphorus an electron deficient centre, which subsequently being attacked by OH^- ion of the adjacent metal ion to liberate the cyanophenol as shown by the Scheme -1.

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Deprotonated Species Six membered Intermedtate

Where the dotted line (---) represents the rest portion of the octamer or tetramer, the symbols

○ and ● stands for H₂O and Metal cations involved in the complex formation respectively

Scheme-1

Effect of pH on the metal catalyzed hydrolysis of cyanofenphos kept at concentration 1.5 × 10⁻⁵ M at 80° C

Metal (3 × 10 ⁻⁴ M)	k _{obs} × 10 ⁻⁵ sec ⁻¹												
	pH												
	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	6.0	6.5	7.0
Zr	6.5	9.8	10.4	8.7	6.5	6.4	6.3	5.8	5.3	4.3	3.3	1.2	0.3
Ce	4.2	6.2	7.6	5.9	5.1	4.8	4.1	3.8	3.1	2.7	2.1	1.1	0.2
Hf	3.7	4.9	5.3	4.6	3.8	3.6	3.4	3.1	2.9	2.3	1.5	0.8	0.2
Th	3.1	4.2	4.9	3.8	3.3	2.9	2.6	2.2	2.1	1.8	1.2	0.6	0.1
Blank	0.18	0.21	0.24	0.22	0.21	0.19	0.18	0.15	0.14	0.11	0.07	0.04	0.01