Study Of Hydrolysis of Organophosphorus Compound in Mild Basic Condition

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***Abstract*—Organic derivative of phosphoric acid are susceptible to hydrolysis. The hydrolysis of OP pesticides and their metabolites are of great importance, because the hydrolysis results in detoxication of pesticides and their susceptibility to alkaline hydrolysis relates to their biological activity. Moreover, variety of derivatives of phosphoric and phosphonic esters were synthesized and their biological properties- such as pesticidal, fungicidal and medicinal properties were discovered. Apart from this, a few of them were found to be highly toxic and were selected for being used for defense purposes. The information about their stability in aqueous media as well as during storage, was an utmost important task for the phosphorus chemist, and in this connection, efforts were made on studies of kinetics and mechanism of these compounds under different conditions.**

I. INTRODUCTION

Paraoxon was the first member of E-600 (Lab No.) series of compounds, which were prepared by Schrader in early 1940s. Paraoxon is fairly soluble in water and able to penetrate into the plant, exerting a systemic insecticidal action [2]. The insecticidal and acaricidal properties of paraoxon are exceptional, but due to its high mammalian toxicity, it was hardly used as systemic and contact insecticide. It is however, used in ophthalmology as miotic agent under the name ®Minta Col, due to its property as a pupil dilator. Paraoxon is among the most potent cholinesterase inhibitors [13]. The oral LD_{50} for rats is 2.5 mg/kg, which is almost five times less than its thiol analog, parathion [13]. Both parathion and paraoxon possess excellent insecticidal properties, yet they are relatively toxic to mammals. Although, paraoxon is available in the market under brand names eticol, fosfacol, pestox-101, phosphacol, etc., paraoxon is on the hazardous substance list and it is banned by environmental Protection Agency (EPA) for any type of use [10]. Paraoxon quickly enters the body by breathing or by absorption through skin. Exposure to paraoxon can cause rapid and severe organophosphate poisoning with headache, sweating, nausea, vomiting, diarrhea, loss of coordination and death. Prolonged exposure can affect nervous system and it also a suspected carcinogen [10].

Paraoxon is quickly hydrolyzed in atmosphere. The rates of hydrolysis increase in alkaline solutions although, it is relatively slow in neutral and mildly acidic medium, typical of surface water and soil [3]. Though its persistency in atmosphere is less, however, sufficient for OP poisoning.

II. EXPERIMENTAL

Synthesis of paraoxon was done by the route suggested by Purnanand and Batra [11]. The method suggests one pot synthesis by the use of phase transfer catalyst, tetra butyl ammonium bromide (TBAB).

(A) *Synthesis of crude Paraoxon: PNP (2.08 gm, 0.015 M), water (25 ml), carbon tetrachloride (70 ml), NaOH (2.4 gm, 0.06 M) and TBAB (0.5 gm, 1.5×10^{-3} M) was taken in a 500 ml round bottom flask (RBF) and stirred for 15 min. To this stirred solution, diethyl phosphite (8.3 gm, 0.06 M) in CCl_4 (30 ml) was added dropwise in 10 min. A slight exothermic reaction took place, which was controlled with the help of cold-water bath. The yellow color of PNP was disappeared in first half hour. The reaction mixture was further stirred for one hour. The mixture was then filtered and organic layer separated. The organic layer was washed three times with ice cold water till free from alkaline impurity. The*

organic layer was then dried with fused $CaCl_2$; solvent first removed by distillation on a water-bath and then under reduced pressure. The crude paraoxon so obtained was distilled under vacuum (128-130°C, 0.01 mm Hg). Yield: 2.68 gm (9.7×10^{-3} M, ~65%)

(B) *Purification of Paraoxon: The crude paraoxon was subjected to thin layer chromatography (TLC) (absorbent: silica G, eluent-hexane: acetone-3:2) analysis, showed two spots, one corresponding PNP and another to that of the compound, slightly lower level. In order to remove PNP, the extraction of the crude material was done with n-hexane, till TLC showed single spot. After evaporation of n-hexane the residue was redistilled. The pure paraoxon, thus obtained, was transferred to a sample tube, properly stoppered with the help of PTFE tape (Teflon tape) and stored in a refrigerator.*

(C) *Spectral data of Paraoxon: The compound thus obtained was then subjected to UV, FT-IR and GC-MS.*

UV: λ_{max}- 274, ε = 9,300 (p.107).
IR (Neat): 3115, 2985, 1521, 1294, 1234, 1031, 860 cm^{-1} (p.108).
GC-MS M^+ (m/z): Single peak, 275, 220, 149, 139, 119, 109 (Base Peak), 99, 91, 81 (p.109).

The spectral data were in good agreement with reported values which confirmed the structure of the compound as O, O-diethyl, O- p-nitrophenyl phosphate (Paraoxon).

HYDROLYSIS OF PARAOXON

The hydrolytic study of paraoxon was performed in the presence of amine catalyst, at 80°C, and the concentration of substrates and amine catalyst in all kinetic runs unless otherwise specified [1]. All the measurement were done on the Systronics (UV-Vis double beam spectrophotometer) 2101. Results depicted in subsequent tables have shown that the concentration of parent lost and phenolate formed are equal during the hydrolysis and exclusively p-nitro phenolate is released [4]. The Kinetics was found to be of first order with respect to substrate concentration in both the free amine as well as in amine catalyzed reactions. The rate constants were determined by following the increase in the concentration of product with time. All reactions were followed for at least three half-lives. Reactions which were comparatively faster were allowed to proceed till infinity. The computerized plots of log (a/a-x) versus t, gave a straight line; passing through zero with r > 0.994, indicating that the hydrolysis in the presence and absence of metal ion catalysis are of first order with respect to the ester. The rate constant k_{obs} corresponded to the slope A of this plot. Nevertheless, here a/a-x corresponds to A_∞-A_o / A_∞-A_t, where A_o, A_t and A_∞ are absorbance of PNPA at time zero, t and infinity respectively. Each run was performed in duplicate and found to be reproducible within ±5% (max.). The kinetic rate data presented are the average values of the rate constants obtained from duplicate runs the observed free base form is the only kinetically active amine species detected. The rate law at the *p*H values examined

$$\text{Rate} = [\text{substrate}] \times \{k_2 [\text{amine}] + k_2' [OH^-] + k_2''[H_2O]\}$$

where k_2, k_2' and k_2'' are the Second-order rate constants for the reaction of amine, hydroxide ion and water, respectively. k_2 values are obtained from the slope of the observed pseudo-first order rate constants plotted as a function of amine existing in the free base form.The intercept yields the $k_2' [OH^-]$ and $k_2''[H_2O]$ quantities.Values of k_2 are independent of *p*H, which excludes specific acid and base catalyzed.

The SI unit for magnetic field strength H is A/m. However, if you wish to use units of T, either refer to magnetic flux density B or magnetic field strength symbolized as μ0H. Use the center dot to separate compound units, e.g., ―A·m^2. ‖

EFFECT OF CATALYST (AMINE) CONCENTRATION

The effect of catalyst concentrations (0.10 to 0.90 *M*) on the rate of hydrolysis of paraoxon was studied and the results are displayed in the Table 1. Apparently, the binding constant (*K*) and amine catalyzed hydrolysis rate constants (k_M) values for each amine [Table 1]

TABLE 1 – *P*H-DEPENDENCE OF PSEUDO-FIRST ORDER RATE CONSTANTS (K_{OBS}) FOR THE AMINE CATALYZED HYDROLYSIS OF PARAOXON WITH VARIOUS AMINES AT 80ºC; [SUBSTRATE] = 3×10^{-5} *M*

Amine	k_{obs} (sec^{-1})				
	[Amine] (0.1*M*)	[Amine] (0.3*M*)	[Amine] (0.5*M*)	[Amine] (0.7*M*)	[Amine] (0.9M)
Pyridine	0.68×10^{-6}	1.06×10^{-6}	1.42×10^{-6}	1.80×10^{-6}	2.16×10^{-6}
Imidazole	0.964×10^{-6}	1.828×10^{-6}	2.692×10^{-6}	3.556×10^{-6}	4.420×10^{-6}
Hydrazine	0.946×10^{-6}	1.792×10^{-6}	2.638×10^{-6}	3.484×10^{-6}	4.330×10^{-6}
Aziridine	1.126×10^{-5}	2.152×10^{-5}	3.179×10^{-5}	4.205×10^{-5}	5.232×10^{-5}
Ammonia	1.677×10^{-5}	3.24×10^{-5}	4.81×10^{-5}	6.38×10^{-5}	7.95×10^{-5}
Ethanol amine	1.742×10^{-5}	3.38×10^{-5}	4.92×10^{-5}	6.66×10^{-5}	8.30×10^{-5}
n-Butyl amine	0.446×10^{-4}	0.892×10^{-4}	1.238×10^{-4}	1.584×10^{-4}	1.930×10^{-4}
Piperidine	0.924×10^{-4}	1.748×10^{-4}	2.572×10^{-4}	3.396×10^{-4}	4.220×10^{-4}

BrØnsted correlation- BrØnsted plot pK_a v/s log k_2+7 for most of amines in table 2 follow a BrØnsted relation graph with a slope of 0.42 (r = 0.97). If the value of slope is less than 0.50 then the general base catalysis for the reaction of amines with paraoxon can be predicted**.**

TABLE -2 BRØNSTED PLOT FOR THE GENERAL BASE-CATALYZED REACTION OF AMINES WITH PARAOXON AT 80ºC

Amine	pK_a	log k_2+7
Piperidine	11.35	3.62
n-Butyle amine	10.9	3.24
Ethanol amine	10.2	2.91
Ammonia	9.42	2.62
Aziridine	8.10	2.33
Hydrazine	7.93	1.62
Imidazole	7.19	1.64
Pyridine	5.35	1.15

III. DISCUSSION

Reactions of reagents with paraoxon proceed via attack at the phosphorus center. Attack at aromatic carbon can be excluded on the grounds that it would yield smaller rate constant than those observed in this investigation [8-9]

Amine reactions of paraoxon with amines proceed exclusively by a general base pathway. The stoichiometry, rate law, BrØnsted correlation and solvent isotopes effect are completely consistent with this interpretation. The kinetically equivalent general acid-hydroxide ion reaction can be excluded. Substrate are the few examples of an acyclic organophosphorus ester showing general base behavior in its reactions with amines [5-7]. The fit and slope of the BrØnsted plot [Table-2] are of interest. General base catalyzed reactions as well as nucleophilic displacements are subject to steric effects about the nitrogen center. Steric effects are more marked for the nucleophilic cases. The apparent fit to a BrØnsted plot of amines of widely varying structure is likely fortuitous.

The magnitude of the BrØnsted slope, ca. 0.41, is consistent with a general base mechanism. It has been shown that toward the same or similar neutral substrates a nucleophilic mechanism yields a higher value of the BrØnsted slope than a general base path [12]

The reactions of hydroxide ion and water with substrate produce PNPA, which is stable under reaction conditions. The reaction of water becomes important below *p*H ca. 9. Our data below *p*H 9 are limited and subject to error in intercept estimation in plots of the form k_{obs} v/s general base or nucleophilic concentration. However, it appears that the water reaction involves general base catalysis by a second (or more) water molecule(s). General base catalysis of water attack has been reported for 2-(2, 4-dinitrophenoxy)-2-oxo-1,3,2 di oxaphosphorinane [8].

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