Hydrolysis of Quinalphos at High pHs and Different Temperatures

Abdelhamid A. Esbata[*], **Erwin Buncel**[**] **and Gary W. vanLoon**[**]

[*]Department of Chemistry, Faculty of Pharmacy, Misurata University,
Misurata, Libya

[**]Department of Chemistry, Queen's University, Kingston, Ontario, Canada

Abstract

Hydrolysis of quinalphos (**Q**) was studied in basic media (pH, 11.8 - 13.6) at 25°, 35° and 45°C by following spectrophotometrically the appearance of the product (2-hydroxyquinoxaline, **HQ**). The second order rate constant was determined to be 3.60 x 10^{-3} L mol^{-1} s^{-1} at 25°C. By using the second order rate constants at 25°, 35°, and 45°C, it was possible to determine the activation energy (E_a) and the activation parameters, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta G^{\ddagger}$. ^{1}H and ^{31}P NMR were used to characterize the hydrolysis products of quinalphos.

Keywords: Hydrolysis, quinalphos, basic media, rate constant.

Introduction

Hydrolysis is the principal pathway for abiotic degradation [1] and can occur via either homogeneous or heterogeneous processes. The homogeneous process applies when a nucleophile (e.g., H_2O or OH^-) interacts with the compound in solution. Temperature and pH are usually important factors affecting the rate of the hydrolytic processes [2]. One of the principle advantages for organophosphorothioate compounds (P=S) is their abilities to breakdown (hydrolyze) in a short time (hours or days). Speed of hydrolysis can be determined via determination of hydrolysis rates as well as half lives.

Hydrolysis of organophosphorus (OP) compounds have been examined extensively [1,3-15]. In a review article, it has been reported that nucleophilic attack at the phosphorus atom (P) and at a side chain carbon atom (C) through S_N2 (P) and S_N2 (C) mechanisms respectively are the two main pathways for the hydrolysis of OP compounds. In both cases, H_2O or OH^- acts as the nucleophile [1]. O,O-dimethylphosphorothioic acid is one of the products when the hydrolysis follows S_N2 (P) pathway, as in the case of diazinon [4], fenitrothion [5-7], and azinphos-methyl [8]. Recently, we have reported that ^{31}P NMR and electrospray ionization mass spectrometry (ESI-MS) are suitable techniques for organophosphorus identification. Our data revealed the

formation of Ag^{+}, Hg^{2+}, and Na^{+}-O,O-dimethylphosphorothioic anion complexes [16]. More recently, we have studied the interaction of quinalphos with different metal ions using ESI-MS/MS technique. ESI-MS/MS results show the unique opportunity to characterize complexes of quinalphos with transition metal ions (Ag^{+}, Cu^{2+}, and Hg^{2+}) [17].

This work is a continuation of a series of studies conducted in our laboratories on the hydrolysis of OP compounds under various conditions [3-7,9]. To add to our knowledge how another OP compound hydrolyzes and to investigate how some factors affect the hydrolysis rates, hydrolysis of quinalphos under various conditions is the subject of this paper.

Materials and Methods

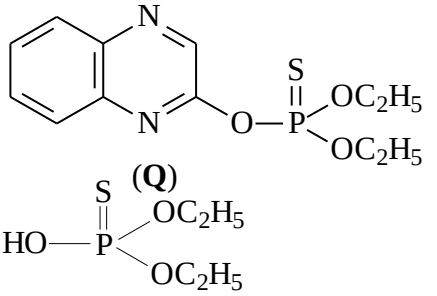
Reagents

All reagents were obtained from commercial sources and were of the highest purity available. They were used as purchased.

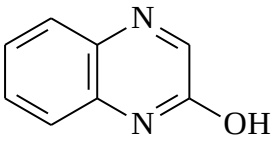
Quinalphos(**Q**,O,O-diethylO-quinoxaline-2-yl phosphorothioate, $C_{12}H_{15}N_2O_3PS$, 99.8 %) and its hydrolysis product (2-hydroxyquinoxaline, **HQ**, $C_8H_6N_2O$, 99 %) were obtained from Crescent Chemicals, U.S.A. Both were of the highest purity available and were used without further

purification. The second product (O,O-diethylphosphorothioic acid, **PA**) was prepared as described in ref. 4. The stock solutions of **Q** and **PA** were prepared individually in 1,4-dioxane, both with a concentration of 3.38 x 10^{-2} mol L^{-1}. Due to low solubility of the other product (**HQ**) in 1,4-dioxane, it was prepared in dimethyl sulfoxide, DMSO, with a concentration of 2.40 x 10^{-2} mol L^{-1}. Standard solutions from each were prepared as needed by serial dilutions of the stock solutions.

The purities of **Q** and its hydrolysis products, **HQ** and **PA** were verified by electrospray ionization mass spectrometry (ESI-MS) and nuclear magnetic resonance (NMR, 500 MHz). Structure of quinalphos (**Q**), 2-hydroxyquinoxaline (**HQ**), and O,O-diethylphosphorothioic acid (**PA**) is illustrated below.



(Q)



(HQ)

(PA)

NaOH solution (0.42 mol L^{-1}) was prepared by dissolving a weighed quantity of NaOH pellets (Aldrich Chemical Company) in deionized distilled water (DDW).

The concentration of the NaOH solution was then determined by titration against potassium hydrogen phthalate [18] ($KHC_8H_4O_4$, KHP, Aldrich), using phenolphthalein as an indicator. It was found that the concentration of the solution was 0.4197 mol L^{-1}. As required, lower concentrations were prepared by serial dilutions with DDW.

Hydrolysis of quinalphos using UV/vis spectrophotometer

In order to observe a complete spectral picture showing the disappearance of quinalphos, appearance of the product and to observe whether the reaction gave an isosbestic point, repetitive scanning was performed under basic condition using the Hewlett–Packard 8452A spectrophotometer with a circulating water bath for temperature control. Repetitive scanning was carried out at wavelengths between 200 and 600 nm in 2 min intervals over a 2 h period using a 9.46 x 10^{-5} mol L^{-1} solution of **Q** in 0.4197 mol L^{-1} NaOH (**Figure 1**). From this spectrum, it was possible to choose the optimum wavelength (λ) required to monitor either disappearance of the reactant or appearance of the product in kinetic experiments. A repetitive scanning experiment using **HQ** was also performed in the presence of the same concentration of NaOH (0.4197 mol L^{-1}) (**Figure 2**). No further degradation of **HQ** was observed under

these conditions. From **Figure 1**, it can be seen that λ_{max} for the disappearance of **Q** is 240 nm, however, this λ_{max} was inconvenient for use in the experiments because the **HQ** product absorbs light at ~240 nm as well. On the other hand, **HQ** also absorbs at 360 nm (**Figure 2**), whereas, **Q** does not, and this was selected as the optimum wavelength for monitoring the appearance of **HQ**. This wavelength was used in subsequent runs using the single wavelength spectrophotometer.

Hydrolysis of **Q** was followed experimentally using a Varian CARY3 single wavelength spectrophotometer. All kinetic experiments were carried out in duplicate under pseudo-first order conditions in which the concentration of the nucleophile (OH^-) was at least 60 times greater than the initial concentration of **Q** (9.46×10^{-5} mol L^{-1}). After the cuvettes used in the spectrophotometer had been filled with the desired concentrations of OH^-, they were placed in the cuvette holder for 15 min to temperature equilibrate before adding the substrate. A 10 μL gas tight syringe was then used to deliver a 7.0 μL aliquot of quinalphos stock solution into each cuvette at which time the run was started.

Product analysis using NMR technique

Product analysis of the hydrolysis of quinalphos in alkaline solutions were performed using 500 MHz NMR, as shown below. The experimental parameters were:

- NaOH solution (3.0 mol L^{-1}) was prepared in D_2O.
- **Q** solution (3.46 x 10^{-3} mol L^{-1}) was prepared in DMSO-d_6.
- In a 4 mL glass vial, 0.2 mL of the NaOH solution was added to 0.6 mL of the **Q** solution. The concentration of OH^- was >> the concentration of **Q**.
- ^1H and ^{31}P NMR were used to determine the hydrolysis products.

In order to confirm that the aromatic ^1H peaks belong to the hydrolysis product (**HQ**), the ^1H NMR spectrum of authentic **HQ** product was recorded under the same conditions, viz, same concentration of NaOH and concentration of **HQ** (**HQ** was also dissolved in DMSO-d_6).

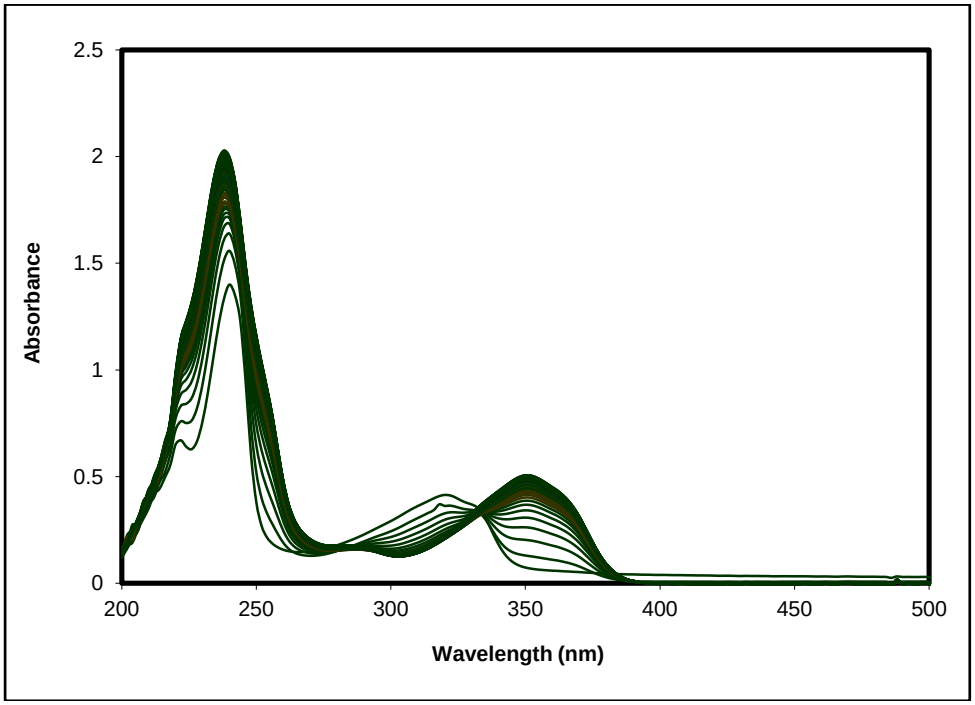


Figure 1 Repetitive scanning for two hours of quinalphos

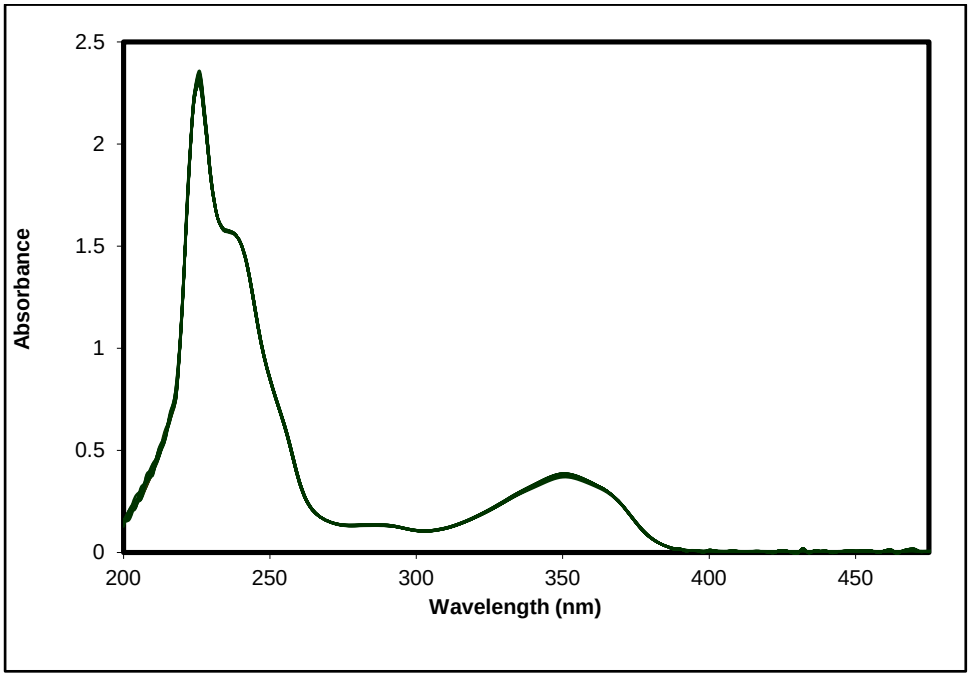


Figure 2 Repetitive scanning for two hours of 2-hyroxyquinoxaline

Results and discussion

Hydrolysis of **Q** was studied in alkaline solutions (at pHs between 11.8 and 13.6) and at three different temperatures (25, 35 and 45°C). Rate constants were determined via monitoring the formation of **HQ** product by measuring the absorbance at 360 nm as a function of time.

By plotting k_{obs} against the concentration of OH^-, the second order rate constant (k_2) at each temperature was obtained from the slope (**Figure 3**). These plots showed good linearity with the correlation coefficients (R^2) of 0.998, 0.994, and 0.996 at 25.0, 35.0, and 45.0°C, respectively (**Figure 3**). Results for the reaction of **Q** with OH^- at various temperatures are presented (**Table 1**).

The linearity of the graphs of the pseudo-first order rate constants plotted against hydroxide concentration, at the three different temperatures, demonstrates that in alkaline media the rate law based on the release of **HQ** is first order in the substrate, **Q**, and first-order in hydroxide, with an overall second order rate constant, k_2.

Table 1 Pseudo-first order rate constants for the reaction of quinalphos (9.46×10^{-5} mol L^{-1}) with various concentrations of NaOH at 360 nm and 25, 35, and 45°C.

[NaOH] (mol L^{-1})	pH[a]	$k_{obs.} \times 10^4$ (s^{-1})[b] at 25°C	$k_{obs.} \times 10^4$ (s^{-1})[b] at 35°C	$k_{obs.} \times 10^4$ (s^{-1})[b] at 45°C
0.00579	11.76	0.327±0.013	0.761±0.016	1.95 ± 0.05
0.0106	12.03	0.553±0.010	1.29 ± 0.02	2.94 ± 0.04
0.0275	12.44	1.68 ± 0.03	4.49 ± 0.03	7.15 ± 0.16
0.0688	12.84	3.15 ± 0.03	5.17 ±0.13	11.9 ± 0.1

0.165	13.22	6.26 ± 0.25	12.9 ± 0.1	24.2 ± 0.2
0.261	13.42	9.72 ± 0.29	18.6 ± 0.2	34.5 ± 0.2
0.419	13.62	15.5 ± 0.5	29.8 ± 0.2	58.5 ± 0.4

[a] Value calculated from actual NaOH concentration.

b The error in k_{obs} values were expressed as the average deviation of two

independent measurements.

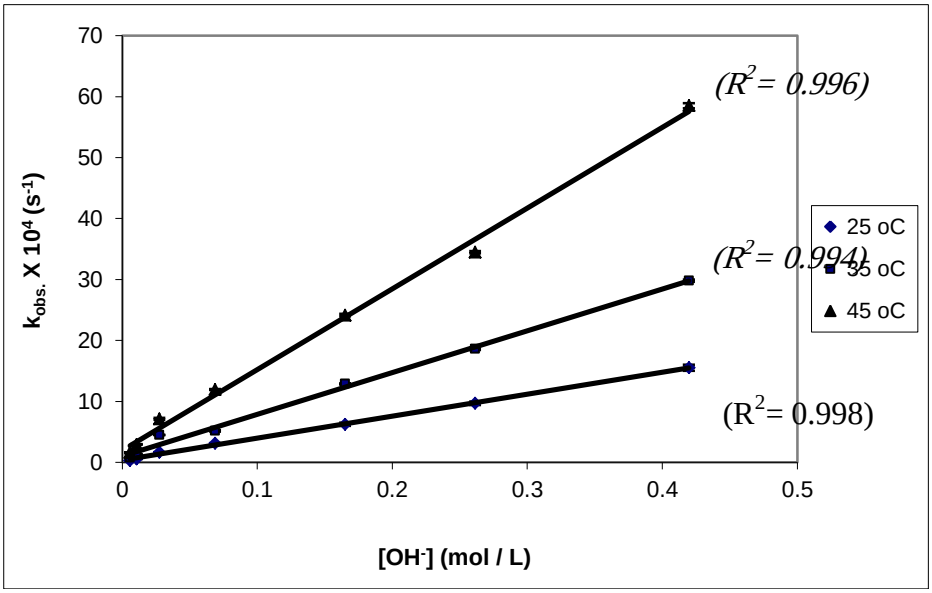


Figure 3 Effect of [OH^-] and temperature on the hydrolysis of quinalphos

Table 2 Second order rate constants at various temperatures

Rate constants, k_2	6 + ln k_2	T (^oC)*	1 / T (K^{-1})

($L.mol.s^{-1}$)			
3.60×10^{-3}	0.373	25.0	0.00335
6.85×10^{-3}	1.02	35.0	0.00324
13.2×10^{-3}	1.67	45.0	0.00314

*Temperature was maintained within ± 0.02°C

Activation parameters

The kinetic data obtained for the hydrolysis process was extended to determine the activation parameters. The activation energy (E_a) was determined from the Arrhenius plot (ln k_2 versus 1 / T) (**Figure 4**) based on:

$$k_2 = Ae^{-Ea / RT}$$

$$\therefore k_2 = \ln A - Ea / RT$$

Where R is the gas constant (8.314 J mol^{-1} K^{-1}), T is Kelvin temperature, and A is the frequency factor. The slope of this line = $-E_a / R$ and E_a was calculated to be 51.3 kJ mol^{-1} (= 12.3 kcal mol^{-1}). The data for the Arrhenius plot are listed in Table 2.

Enthalpy of activation ($\Delta H^{\ddagger}$) was calculated by using the following equation [19]:

$$\Delta H^{\ddagger} = E_a - RT$$

$$= 51.3 - 8.314 \times 10^{-3} (298.2) = 48.8 \text{ kJ mol}^{-1}$$

$$= 11.7 \text{kcal mol}^{-1}$$

Entropy of activation ($\Delta S^{\ddagger}$) was also calculated from [19]:

$$k_2 = \frac{kT}{h}\exp\left(-\frac{\Delta H^{\ddagger}}{RT}\right)\exp\left(\frac{\Delta S^{\ddagger}}{R}\right)$$

Where k_2 is the second order rate constant (3.60×10^{-3} $M^{-1}s^{-1}$), k is Boltzman's constant (1.38×10^{-23} J K^{-1}), and h is Planck's constant (6.62×10^{-34} J.s).

$$\therefore \Delta S^{\ddagger} = \frac{\Delta H^{\ddagger}}{T} + R\ln\frac{k_2 h}{kT}$$

$$= \frac{48800}{298.2} + 8.314\ln\frac{3.60x10^{-3}\left(6.626x10^{-34}\right)}{1.381x10^{-23}(298.2)}$$

$$= 163.6 + 8.314\ (-35.1) = -128.2 \text{ J mol}^{-1}\text{ K}^{-1}$$

$$= -30.6 \text{ cal mol}^{-1}\text{ K}^{-1}$$

Free energy of activation ($\Delta G^{\ddagger}$) was also calculated from:

$\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$

$$= 48800 - 298.2\ (-128.2) = 87029 \text{ J mol}^{-1} = 87.0 \text{ kJ mol}^{-1}$$

$$= 20800 \text{ cal mol}^{-1} = 20.8 \text{ kcal mol}^{-1}$$

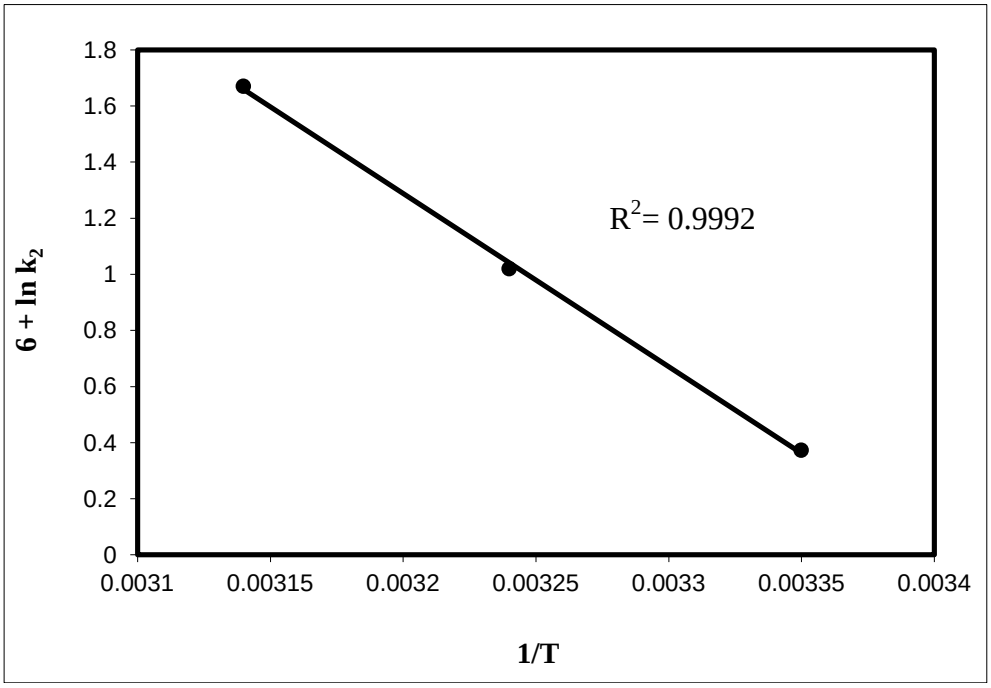
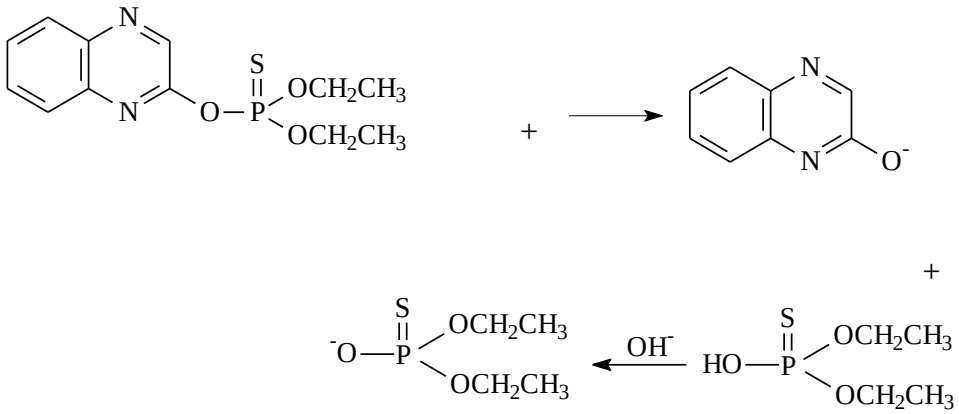


Figure 4 Arrhenius plot for the reaction of quinalphos with NaOH, using data in Table 2

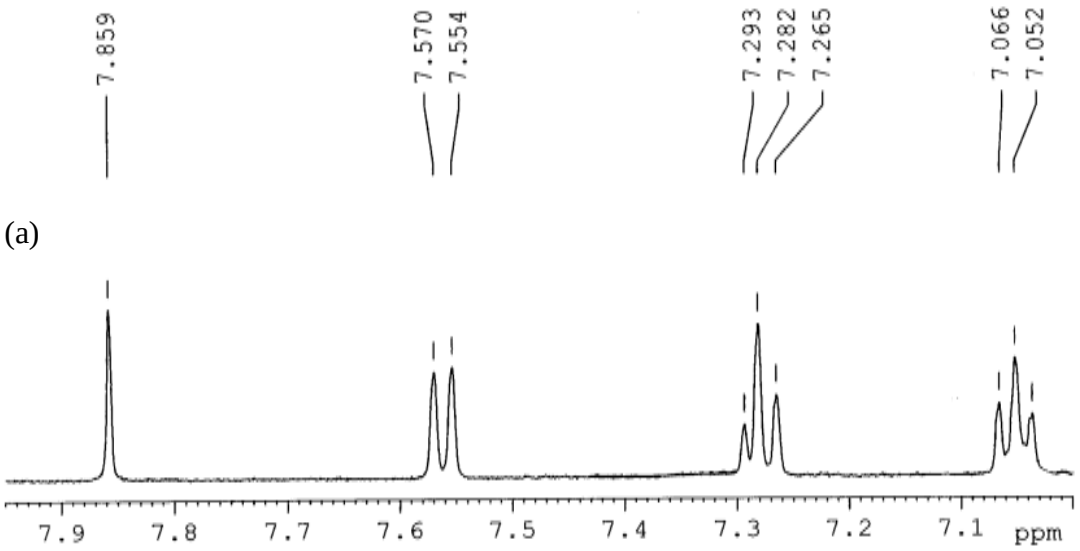
Characterization of products by NMR

In order to determine the hydrolysis products of quinalphos in the basic media, NMR experiments were carried out. ^{1}H and ^{31}P NMR spectra were recorded 20 hours after the hydrolysis had been initiated, at which time the reaction would be expected to be completed. The spectrum of authentic **HQ** and the final product of hydrolysis were found to be identical (**Figure 5**). The ^{31}P NMR spectrum (**Figure 6**) consisted solely

of a single peak for the O,O-diethylphosphorothioic acid (**PA**) as the only product containing P. Note that in **Figure 6** the ^{31}P is actually coupled with the protons of both CH_2 groups of the ethoxyls. The reaction of **Q** in alkaline media is, therefore, in agreement with the following scheme.



Scheme 1 Hydrolysis of quinalphos in alkaline media



(b)

Figure 5 (**a**) ^{1}H NMR of hydrolysis of quinalphos in the basic media (after 20 h)

(b) ^{1}H NMR of authentic 2-hydroxyquinoxaline in the basic media.

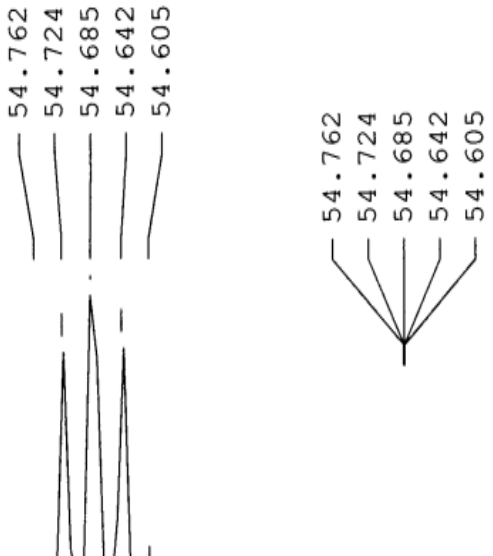


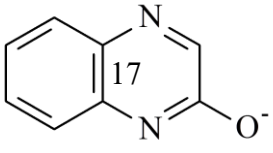
Figure 6 ^{31}P NMR of hydrolysis of quinalphos in the basic media (after 20 h)

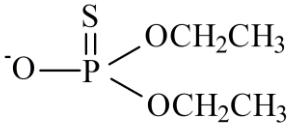
Pathways of alkaline hydrolysis of quinalphos

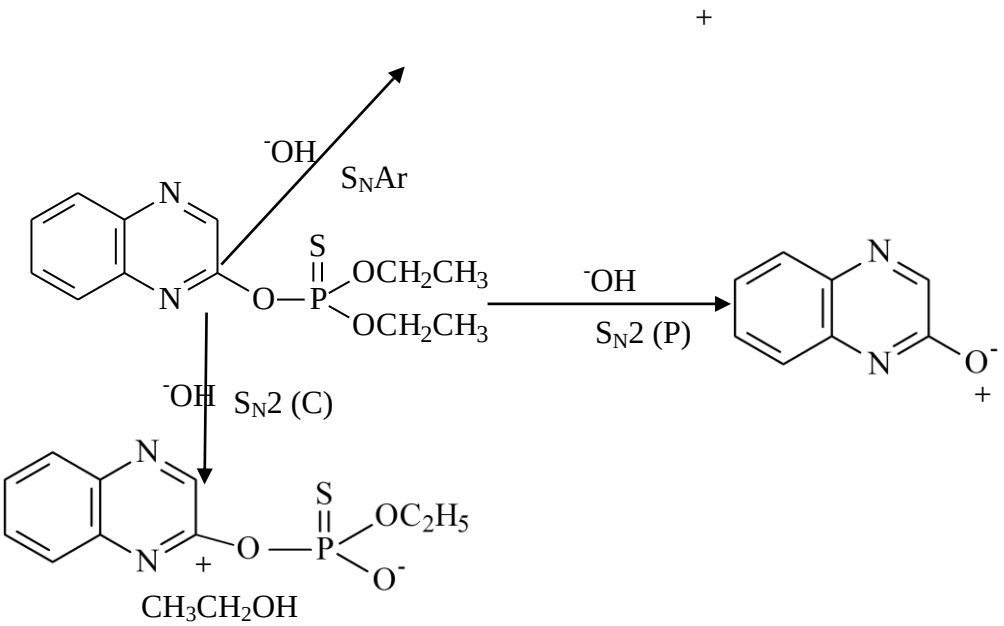
Hydrolysis of quinalphos via the nucleophilic substitution reaction could occur through one or more of the following pathways:

- Substitution at the phosphorus via S_N2 (P).
- Substitution at the aromatic carbon via S_NAr.
- Substitution at the aliphatic carbon (methylene of the ethoxy group) by S_N2 (C) process.

The three possible pathways are illustrated below.





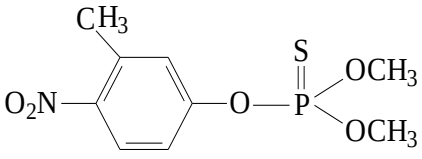


Scheme 2 Possible pathways for the hydrolysis of quinalphos.

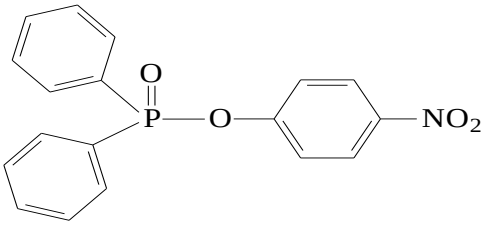
Evidence from product analysis

Pathways for the hydrolysis of quinalphos show that S_N2 (C) path occurs when the nucleophile attacks at the aliphatic carbon (Scheme 2). However, ^{31}P NMR (**Figure 6**) results excluded this path, as the ^{31}P is coupled with 4 protons of the two CH_2 groups. In addition, ^{1}H and ^{31}P NMR demonstrated that **HQ** is one of the products produced during the hydrolysis of **Q** in alkaline solutions, which can be formed via either S_N2 (P) or S_NAr paths (Scheme 2). In fact, there is a possibility of S_NAr path only when the aromatic ring is activated by electron

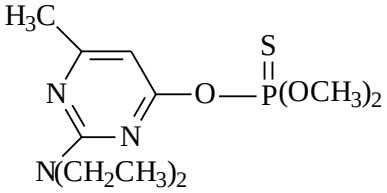
withdrawing group, EWG, (e.g. NO_2) such as in the case of fenitrothion [5,7]. As quinalphos does not contain a EWG in its structure, this path is highly unlikely to operate. Thus, S_N2 (P) is the candidate path, as reported in previous studies [3,4,13]. Greenhalgh et al. [13] have shown that under basic conditions (pH ≥ 9.0), hydrolysis of the fenitrothion occurred by attack at the phosphorus centre (P-O bond fission). Buncel and co-workers [20-22] have studied the reaction of para-nitrophenyl diphenylphosphinate with alkali metal ethoxides. They have found that reaction occurred solely at the phosphorus. In the basic environment, Eneji [3] and Pieda [4] have studied the hydrolysis of pirimiphos-methyl and diazinon, respectively. Both concluded that the most likely pathway for the hydrolysis of these compounds under alkaline conditions is S_N2 (P). In the present case, NMR data proved that hydrolysis of quinalphos followed S_N2 (P) pathway.



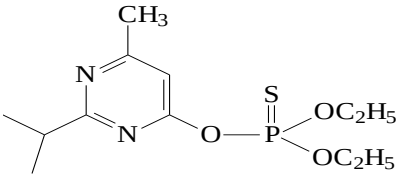
Fenitrothion



para-nitrophenyl diphenylphosphinate



Primiphos-methyl



Diazinon

Conclusions

Using UV-vis spectrophotometer, hydrolysis of the organophosphorothioate compound, quinalphos was studied in alkaline solutions at three different temperatures. The value of the second order rate constant at 25°C was determined to be 3.60×10^{-3} L mol^{-1} s^{-1}. By determining the effect of temperature on reaction rate, values of activation parameters were calculated to be $\Delta H^{\ddagger}$ = 11.7 kcal mol^{-1}, $\Delta S^{\ddagger}$ = -30.6 cal mol^{-1} K^{-1}, and $\Delta G^{\ddagger}$ = 20.8 kcal mol^{-1}. ^{1}H and ^{31}P NMR analysis revealed that hydrolysis of quinalphos in alkaline media occurred through S_N2 (P) pathway.

Acknowledgment

This work was supported by the Natural Science and Engineering Research Council of Canada (NSERC).

References

[1] Schwarzenbach R. P., Gschwend P. M., and Imboden D. M. Environmental Organic Chemistry. John Wiley and Sons, New York (2003)

[2] Mabey W. and Mill T. J. phys. Chem. Ref. Data 7, 383 (1978)

[3] Eneji, I. K. MSc thesis, Queens University (2000)

[4] Pieda D. MSc thesis, Queens University (2001)

[5] Balakrishnan V. K., Dust J. M., vanLoon G. W., and Buncel E. Can. J. Chem. 79, 157-173 (2001)

[6] Balakrishnan V. K., Han X., vanLoon G. W., Dust J. M., Toullec J., Buncel E. Langmuir 20, 6586 (2004).

[7] Balakrishnan V. K., Buncel E, and vanLoon G. W. Environ. Sci. Technol. 39, 5824 (2005)

[8] Miyata Y. and Ando H., Jpn. J. Toxicol. Environ. Health. 40, 49 (1994)

[9] Eneji I. S., Buncel E., and vanLoon G. W. J. Agric. Food Chem. 50, 5634 (2002).

[10] Dunn E. J., Moir R. Y., Buncel E., Purdon J. G., Bannard R. A. B. Can. J. Chem. 68, 1837 (1990)

[11] Cook R. D., Farah S., Ghawi L., Itani A., and Rahil J. Can. J. Chem. 64, 1630 (1986)

[12] Cook R. D. and Rahhal-A. L. Tetrahedron Lett. 26, 3147 (1985)

[13] Greenhalgh R., Dhawan K. L., and Weinberger P. J. Agric. Food Chem. 28, 102 (1980)

[14] Dyguda K. E., Roszak S., and Sokalski WA. J Phys. Chem. B 118, 7277 (2014)

[15] Sirotkina M., Lyagin I., and Efremenko E. Int. Biodeterior. Biodegrad.68, 18 (2012)

[16] Koo I. S., Dildar A., Yang K., Park Y., Esbata A. A., vanLoon G. W., and Buncel E. Can. J. Chem. 87, 433 (2009)

[17] Keller B., Esbata A. A., Buncel E., vanLoon G. W. Rapid Commun. Mass Spectrom. 27, 1319 (2013)

[18] Harris W. E. and Tochvil B. K. An introduction to chemical analysis, Saunders Golden Sunburst Series (1981).

[19] Lowry T. H. and Richardson K. S. Mechanism and Theory In Organic Chemistry. Harper and Row Publisher (1987)

[20] Pregel M. J., Dunn E. J., and Buncel E. J. Am. Chem. Soc. 113, 3545 (1991)

[21] Dunn E. J. and Buncel E. Can. J. Chem. 67, 1440 (1989)

[22] Pregel M. J., Dunn E. J., Nagelkerke R., Thatcher G. R. J., and Buncel E. Chem. Soc. Rev. 449 (1995)