



# Proton, proton-decouple phosphorus and Phosphorus-decouple Proton Nuclear Magnetic Resonance (NMR) of Propyl isopropylphosphonofluoridate in water

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## ABSTRACT

Proton (<sup>1</sup>H), proton decouple phosphorus (<sup>1</sup>H{<sup>31</sup>P}), and phosphorus decouple proton (<sup>31</sup>P{<sup>1</sup>H}) NMR of propyl isopropylphosphonofluoridate in an environment of water have been produced and resonances peaks obtained have been assigned. The <sup>31</sup>P{<sup>1</sup>H} spectrum of the chemical gave two resonances peaks with chemical shifts at 28.505 and 34.129 ppm, which is an indication that propyl isopropylphosphonofluoridate has undergone degradation to produce two phosphorus containing chemicals. This does not come as surprise, since in water propyl isopropylphosphonofluoridate undergoes hydrolysis to produce to two chemicals, propyl isopropylphosphonate and isopropylphosphonic acid. The resonances at 28.505 and 34.129 ppm are assigned to isopropylphosphonic acid and propyl isopropylphosphonate respectively. The <sup>1</sup>H and the corresponding <sup>1</sup>H{<sup>31</sup>P}NMR of propyl isopropylphosphonate produced five resonances peaks in the NMR spectral. These resonances are consistent with the structure of propyl isopropylphosphonate. The <sup>1</sup>H and <sup>1</sup>H{<sup>31</sup>P} spectral of isopropylphosphonic acid also produced two resonances peaks with chemical shifts at 1.03 and 1.75 ppm respectively which is consistent with the structure.

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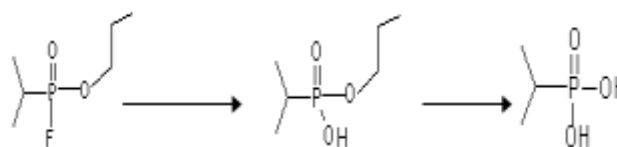
## Introduction

Propyl isopropylphosphonofluoridate is a nerve agent and therefore it does affect the transmission of neutral signal. [1]. It reacts irreversibly with acetyl cholinesterase and results in the accumulation of acetylcholine. This leads to continuous stimulation of the nervous system. For this physiological action it is used as a chemical warfare agent [2]. The chemical weapons convention (CWC) is an international convention which prohibits the development, production, stockpiling and the use of chemical weapons. The convention is administered by the organization for the prohibition of chemical weapons (OPCW) based in The Hague, of the Netherlands. An annex of the CWC lists certain toxic chemicals and their precursors in three schedules, according to the risk they pose to humans. Propyl isopropylphosphonofluoridate is one of the listed chemicals of the chemical weapon convention and its schedule number is 1.A.1 among other chemicals on the chemical weapons convention annex on chemicals [3].

An important component of the CWC is the verification regime, which may include inspection of declared or suspected chemical warfare facilities [4]. Under certain circumstances samples may be collected from these facilities and analyzed in off-site laboratories. OPCW has a network of designated laboratories for this purpose, and requires these laboratories to participate in one proficiency test within a year. Under the proficiency test these laboratories are required to identify a number of chemical warfare agents in spiked samples according to a strict set of criteria.

The primary degradation reaction of nerve agents is hydrolysis [5] hence in an environment of water propyl

isopropylphosphonofluoridate readily undergoes degradation to produce propyl isopropylphosphonate and isopropylphosphonic acid as shown in Fig 1.



propyl isopropylphosphonate isopropylphosphonic acid  
**Fig 1: Degradation pathway of propyl isopropylphosphonofluoridate**

The degradation products, propyl isopropylphosphonate and isopropylphosphonic acid are also listed chemicals of the chemical weapons convention and their schedule number is 2.B.4 [6]

The detection of these two products is very important task for verification studies since their detection can be used to indicate the presence of propyl isopropylphosphonofluoridate, which itself may have degraded completely. The Finnish Institute for Verification of Chemical Weapons Convention (VERIFIN) has successfully been able to apply a number of analytical techniques such as GC, GC/MS, LC/MS, GC/FTIR and NMR for identification of the chemical warfare agents [7] and a standard reference database of chemical warfare agents called the Verify has been developed by VERIFIN for detection and identification of chemical warfare agents. Verify gives full information on over 1,900 chemical warfare agents in terms of their mass spectrometry, infrared spectrometry, nuclear magnetic resonance spectrometry and chromatographic data [8].

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One challenge in the analysis of chemical warfare agents is the analysis of their degradation products, which are often non volatile. These non volatile products can not be analyzed directly using GC and GC/MS unless such products are derivatized. Non volatile products are often derivatized by either methylation or silylation to produce more volatile methylated or silylated products which can then be analyzed with GC and GC/MS [9]. It must however, be indicated that such non volatile chemicals can however, be analyzed without derivatization using techniques such as LC/MS, NMR and GC/FTIR [10].

This paper presents proton ( $^1\text{H}$ ), proton decouple phosphorus ( $^1\text{H}\{^{31}\text{P}\}$ ), and phosphorus decouple proton ( $^{31}\text{P}\{^1\text{H}\}$ ) NMR spectral of degradation products of propyl isopropylphosphonofluoridate, thus propyl isopropylphosphonate and isopropylphosphonic acid. The spectral were obtained by analyzing a water sample of propyl isopropylphosphonofluoridate using 400 MHz NMR spectrometer.

#### Materials and methods

This study was carried out at the Finnish Institute for verification of chemical weapon convention (VERIFIN) at Helsinki, Finland, in December 2006 as part of VERIFIN 2006 Advanced Course on analyses and verification of chemicals related to the chemical weapon convention. (CWC)

#### Sample Preparation

The chemicals and reagents used for the study were supplied by VERIFIN. The water sample of propyl isopropylphosphonofluoridate was in an aliquot form. Sample size was about 0.5 mL and was in 1.5 mL vial. Deuterated water of 0.5 mL was then added to the aliquot. The sample was then transferred into 5 mm diameter NMR tube and was used for the investigation.

#### NMR Spectrometer

The study was carried out using 400 MHz, Bruker DRX 500 NMR spectrometer and temperature was tuned to 25°C. The probe head was BBI. The sample tube diameter was 5 mm and  $^{31}\text{P}\{^1\text{H}\}$ ,  $^1\text{H}$ ,  $^1\text{H}\{^{31}\text{P}\}$  experiments were performed.

#### Results and discussion

##### $^{31}\text{P}\{^1\text{H}\}$ spectral of the sample

Fig 2 shows the results obtained when the sample was analyzed by performing phosphorus decouple proton [ $^{31}\text{P}\{^1\text{H}\}$ ] experiment.

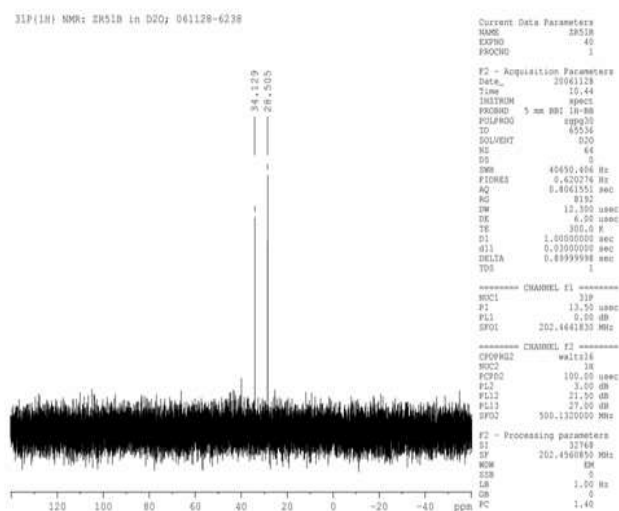


Fig 2:  $^{31}\text{P}\{^1\text{H}\}$  spectral of propyl isopropylphosphonofluoridate in water

The two peaks obtained is an indication that the sample contains two phosphorus containing compounds. This result was expecting since in water propyl isopropylphosphonofluoridate readily undergoes degradation to produce propyl isopropylphosphonate and isopropylphosphonic acid [11]. The chemical shifts of 28.505 and 34.129 ppm are characteristic peaks of alkyl phosphonates [12]. The resonance (chemical shift of 28.505 ppm) with the higher intensity is assigned to isopropylphosphonic acid since it is the final degradation product of propyl isopropylphosphonofluoridate as shown in figure 1. The other resonance is assigned to propyl isopropylphosphonate

##### $^1\text{H}$ , $^1\text{H}\{^{31}\text{P}\}$ NMR spectral of the sample

The  $^1\text{H}$  and  $^1\text{H}\{^{31}\text{P}\}$  NMR spectral of the sample is presented in Figure 3, 4 and 5.

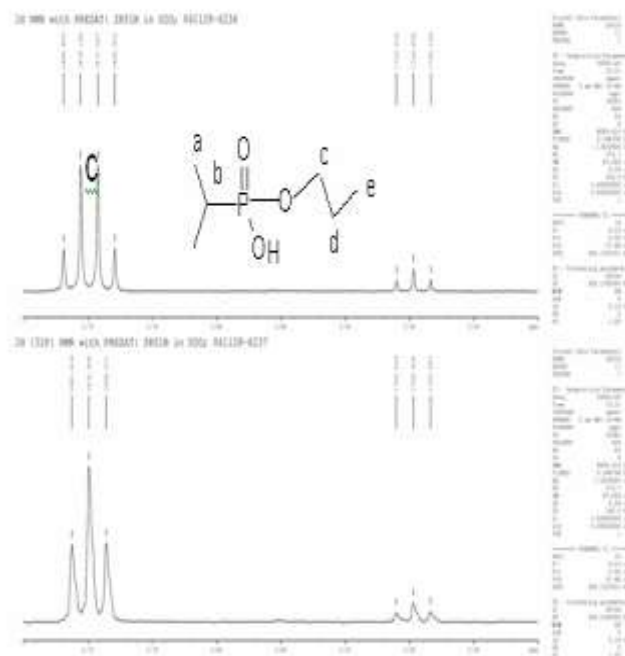


Fig 3:  $^1\text{H}$  and  $^1\text{H}\{^{31}\text{P}\}$  resonance for Hc in propyl isopropylphosphonate

The resonance with chemical shift of 3.75 ppm is assigned to the Hc protons in propyl isopropylphosphonate. The resonance is a simple quartet, with typical relative intensity of 1:3:3:1.

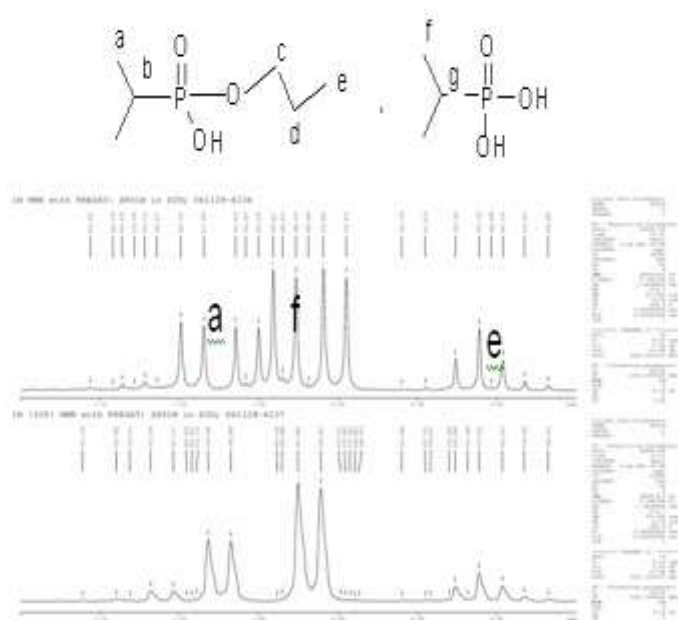
This multiplicity suggests that the Hc protons have three protons in its neighbourhood.

However, this is not the case, Hc protons have Hd protons (methylene group) and a phosphorus atom at its neighborhood.

Nevertheless it is quartet since the phosphorus is not coupled to the Hd protons (i.e.  $\text{J}_{\text{HdP}} = 0$ ). In the  $^1\text{H}\{^{31}\text{P}\}$  experiment, when the phosphorus was decoupled the quartet collapsed to triplet (the lower plot).

This should be expected, since on decoupling the phosphorus the Hc protons have only the two Hd protons in its neighborhood.

The chemical shift of 3.75 ppm is typical of chemical shift of hydrogen atoms of  $-\text{OCH}_2-$  group [13].  $3\text{J}_{\text{HcHd}}$  coupling constant of 6.7 HZ (Table 1) compares favourably with the theoretical value of 7 HZ [14].



**Fig 4:  $^1\text{H}$  and  $^1\text{H}\{^{31}\text{P}\}$  resonances of Ha, He in propyl isopropylphosphonate and Hf in isopropylphosphonic acid.**

In figure 4, the resonance with a chemical shift of 0.9 ppm is assigned to the He protons. Its multiplicity of triplet is consistent with the structure of the chemical, propyl isopropylphosphonate (it is coupled to two Hd protons).

The  $^3\text{J}_{\text{HeHd}}$  proton-proton coupling constant of 7.4 Hz is comparable to the theoretical value.

When the effect of phosphorus was removed in the  $^1\text{H}\{^{31}\text{P}\}$  experiment the resonance (in the lower plot) still remains as triplet, and this is so since the He protons is not coupled to the phosphorus.

The peak with a chemical shift of 0.98 ppm is assigned to the six chemically equivalent Hf protons.

Its multiplicity of doublet of doublet is consistent with the structure.

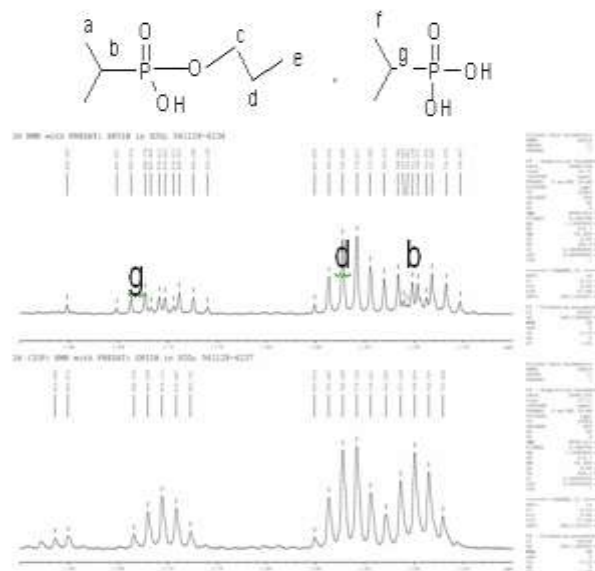
Thus the Hf protons are coupled to phosphorus and the Hg (methine) proton.

The  $^3\text{J}_{\text{HfP}}$  coupling constant of 19.9 Hz (Table 1) is consistent with the theoretical value of 19 – 21 Hz [12]. In the proton decouple phosphorus experiment [ $^1\text{H}\{^{31}\text{P}\}$ ], the doublet of doublet multiplicity collapsed to doublet since on removing the effect of phosphorus the Hf protons have only the one proton (Hg) as its neighboring proton.

The doublet of doublet peak at 1.03 ppm is assigned to the Ha protons in the propyl isopropylphosphonate and its multiplicity of doublet of doublet is so as Ha protons is coupled to both the phosphorus and one Hb proton.

Comparing the two chemicals, it is obvious that both the Ha and the Hf protons are coupled to phosphorus and a proton and this explains why the two resonances have the same multiplicity, doublet of doublet in their  $^1\text{H}$  NMR and doublet in their  $^1\text{H}\{^{31}\text{P}\}$  NMR.

However, the resonance peak with the higher intensity is assigned to the Hf protons since during degradation of propyl isopropylphosphonofluoridate, isopropylphosphonic acid is the final product of degradation (fig. 1) and is more likely to be formed in larger amount.



**Fig. 5:  $^1\text{H}$  and  $^1\text{H}\{^{31}\text{P}\}$  resonances of Hd, Hb in propyl isopropylphosphonate and Hg in isopropylphosphonic acid.**

In figure 5, the resonance of chemical shift of 1.48 ppm is assignable to Hb proton in propyl isopropylphosphonate, which from the structure of the compound ought to have been doublet of septet in its  $^1\text{H}$  NMR spectrum. However, the doublet of septet is not obvious from the spectrum, and this might have resulted from the possible overlap between the Hd and Hb resonances. The  $^2\text{J}_{\text{HbP}}$  coupling constant of 17.1 Hz compares favourably with the theoretical value of 15 – 17 Hz [12].

The  $^1\text{H}$  resonance at 1.58 ppm is produced by the Hd protons in propyl isopropylphosphonate. The Hd protons have Hc and He (five protons) protons at its neighborhood and therefore, the sextet multiplicity. Its corresponding  $^1\text{H}\{^{31}\text{P}\}$  resonance is still remains sextet since Hd protons are not coupled to the phosphorus. The  $^3\text{J}_{\text{HdHe}}$  coupling constant of 7.4 Hz is comparable to the theoretical value of 7 Hz.

The  $^1\text{H}$  peak with chemical shift of 1.75 ppm is the resonance for Hg protons in isopropylphosphonic acid, which ought to be doublet of septet. In the  $^1\text{H}\{^{31}\text{P}\}$  experiment, the doublet of septet collapsed to septet which is consistent with the structure.

### Conclusion

$^{31}\text{P}\{^1\text{H}\}$  NMR of propyl isopropylphosphonofluoridate in water produced two resonance peaks at 28.505 and 34.129 ppm in its NMR spectrum. This indicates that in an environment of water the chemical undergoes degradation by hydrolysis to produce two phosphorus containing chemicals, propyl isopropylphosphonate and isopropylphosphonic acid. Resonance at 28.505 is assigned to isopropylphosphonic acid while the one at 34.129 ppm is assigned to propyl isopropylphosphonate.  $^1\text{H}$  NMR of propyl isopropylphosphonate and isopropylphosphonic acid produced five and two resonances for propyl isopropylphosphonate and isopropylphosphonic acid respectively. These are consistent with their structures. The coupling constants obtained experimentally compared favourably with the theoretical values.

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**Table 1: Experimental and Theoretical Coupling Constants**

Coupling	Coupling Constants (Hz)	
	Experimental value	Theoretical value[14]
$^3\text{JHcHd}$	6.7	7.0
$^3\text{JHdHe}$	7.4	7.0
$^3\text{JHbHa}$	7.2	7.0
$^2\text{JHbP}$	17.1	15 - 17
$^3\text{JHgHf}$	7.1	7.0
$^2\text{JHgP}$	17.2	15 – 17
$^3\text{JHeHd}$	7.4	7.0
$^3\text{JHaP}$	19.9	19 – 21
$^3\text{JHfP}$	20.5	19 - 21