International Journal of Mass Spectrometry 369 (2014) 59–70

Contents lists available at ScienceDirect

International Journal of Mass Spectrometry

journal homepage: www.elsevier.com/locate/ijms

Fragmentation mechanisms in mass spectrometry of Chemical Weapons Convention related spiro alkylphosphonates and alkyldioxaphosphinane oxides

Hamid Saeidian [a,*], Mehran Babri [b,*], Zohreh Mirjafary [c], Mohammad Taghi Naseri [b], Mansour Sarabadani [a,b], Davood Ashrafi [b], Seyyed Sajjad Mousavi Faraz [b]

[a] Department of Science, Payame Noor University (PNU), P.O Box 19395-4697, Tehran, Iran
[b] Defense Chemical Research Lab (DCRL), P.O. Box 31585-1461, Karaj, Iran
[c] Department of Chemistry, Science and Research Branch Islamic Azad University, Tehran, Iran

ARTICLE INFO

Article history:
Received 23 February 2014
Received in revised form 25 May 2014
Accepted 2 June 2014
Available online 5 June 2014

Keywords:
Mass spectrometry
Spiro alkylphoshonates
McLafferty rearrangements
Cycloaddition
Microsynthesis
Chemical Weapons Convention

ABSTRACT

The availability of mass spectra and interpretation skills are essential for unambiguous identification of the Chemical Weapons Convention (CWC)-related compounds. This paper examines electron ionization (EI) and electrospray ionization (ESI) mass spectral fragmentation routes of spiro alkylphosphonates I and 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II as compounds which are covered under CWC schedule 2.B.4. Mass spectrometric studies revealed some fragmentation pathways, such as elimination of alkyl(oxo)phosphane oxide (RPO_2), chlorine, chloromethylene, alkene, HCl, and H_2O, α-cleavage and McLafferty-type and hydrogen rearrangements. The proposed fragmentation processes include some new fragmentation patterns, such as isomerization of cations to stabilized carbocations and oxocarbocations, and elimination of formaldehyde and alkoxy through concerted retro [2+2] cycloaddition reaction and 1,2 P—O alkyl shift. Structures of fragments were confirmed using EI-MS and MS/MS analysis of the deuterated analogs. The results will make a contribution to the Organization for the Prohibition of Chemical Weapons (OPCW) Central Analytical Database (OCAD) which may be used for the detection and identification of CWC-related compounds during on-site inspection and OPCW proficiency tests.

1. Introduction

All activities related to the production, development, stockpiling and use of chemical weapons are forbidden by the Chemical Weapons Convention (CWC), which came into force on 29 April 1997. Chemical warfare agents (CWAs) were used during World War I, the Iran–Iraq war and subsequently in some terrorist attacks in Japan. Recently sarin, as nerve agent, was used during the Syria conflict. These tragic events show that monitoring and analysis of CWAs, their precursors and degradation/reaction products is an important part of verification activities in support of CWC. The state parties to CWC have established the Organization for the Prohibition of Chemical Weapons (OPCW) to achieve the objective and purpose of CWC. It is interesting to note that OPCW received the Nobel peace prize for its extensive efforts to eliminate chemical weapons in 2013. Mass spectrometry coupled with gas chromatography (GC/MS) provides a key analytical technique for the unambiguous identification of scheduled chemicals during proficiency tests (PTs) and off- and/or on-site analyses [1]. For unequivocal identification of CWC-related compounds in real samples or PTs, the availability of mass spectra and interpretation skills are essential requirements. Due to the extreme toxicity of CWC-related compounds, there is limited number of research on such compounds. In recent years, some research results have been reported which contains microsynthesis and interpretation of mass spectra of CWC-related compounds [2–7], but to our knowledge there is no mass spectral fragmentation study for spiro alkylphosphonate compounds I and 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II. These compounds are covered under CWC schedule 2.B.4 as well as all compounds with phosphorus bonded to a methyl, ethyl, isopropyl, or propyl moieties. The studied compounds are the reaction products of alkylphosphonic dichlorides with pentaerythritol. Mass spectra of such compounds might be of interest to OPCW. It should be mentioned that pentaerythritol is a versatile building block for the

* Corresponding authors at: Department of Science, Payame Noor University (PNU), P.O. Box 19395-4697, Tehran, Iran.
E-mail address: h_porkaleh@yahoo.com (H. Saeidian).

http://dx.doi.org/10.1016/j.ijms.2014.06.003
1387-3806/

preparation of many polyfunctionalized compounds such as the explosive pentaerythritol tetranitrate and pentaerythritol tetraacrylate [8]. As continuation of our mass spectral fragmentations studies on CWC-related compounds [9–12], it was concluded that detailed studies on a class of spiro alkylphosphonate I and 5,5-bis (chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II were necessary. This paper describes a study on a general microsynthesis procedure for a few title compounds (Scheme 1). Subsequently, electron ionization (EI) and electrospray ionization (ESI) mass spectra of these compounds, with possible fragmentation routes, were investigated via analysis of fragment ions of deuterated analogs and MS–MS experiments.

2. Experimental

2.1. Reagents and chemicals

All chemicals required for the microsynthesis of spiro alkylphosphonates were purchased from Sigma–Aldrich (St. Louis, MO, USA), Fluka (Neu-Ulm, Germany), and Merck (Darmstadt, Germany), and were used as received. Alkylphosphonic dichlorides were synthesized by use of a method described elsewhere [13,14].

2.2. GC/MS and GC/MS–MS analysis

GC/MS analyses were performed using an Agilent 6890 N gas chromatograph equipped with a 5973 quadrupole mass selective detector, MSD, (Agilent Technologies, Inc., Santa Clara, CA, USA), a HP-5MS (5% phenyl, 95% dimethylpolysiloxane, Agilent's J&W Scientific) capillary column of (30 m, 320 μm i.d. and 0.25 μm film thickness), and helium as carrier gas at constant flow of 1.8 mL min^{-1}. The oven temperature was set at 40 °C for 3 min and then was increased to 280 °C with ramp of 10 °C/min and held at 280 °C for 6 min. The samples were injected in splitless mode at an injection temperature of 250 °C. The temperatures of the EI source and analyzer were kept at 230 and 150 °C, respectively. The scan range was m/z > 35–500. GC/MS–MS analyses were performed using an Agilent 7890 N gas chromatograph interfaced to a 7000 A triple quadruple mass spectrometer (Agilent Technologies, Inc., Wilmington, DE, USA). GC conditions were as noted above. The ionization energy was set at 70 eV in both MS spectrometers. MS–MS analyses were carried out using nitrogen as collision gas, at collision energy of 10 eV and source temperature of 230 °C. CI-MS experiments also were done on 5973 MSD using isobutane as reagent gas. The scan range was set at m/z > 70–500. Other instrumental conditions were as EI experiments. Automated mass spectral deconvolution and identification system (AMDIS) software (NIST, Gaithersburg, MD, USA) were used to calculate retention indices of the synthesized compounds. An alkane mixture [octane (C_8) to tetracosane (C_{24})] was used for retention indices calculations.

2.3. ESI-MS and ESI-MS–MS analysis

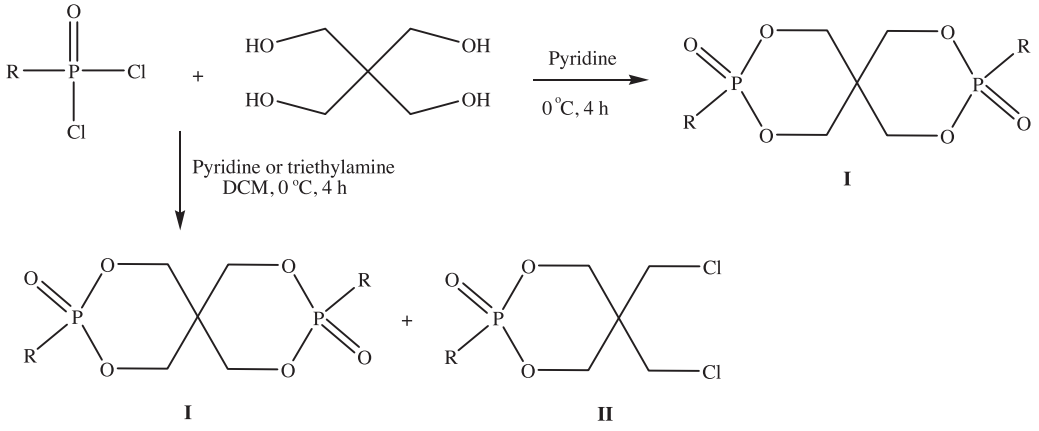
LC/MS analysis was performed on an Agilent 1200 LC system (Agilent Technologies, Inc., Waldbronn, Germany) equipped with Agilent 6410 triple quadrupole tandem mass spectrometer and managed by a Mass Hunter workstation (Agilent Technologies Inc., CA, Santa Clara, USA). The column used for separation was an Agilent rapid resolution HT zorbax SB-C18 (3 × 150 mm, 3.5 μm) (Agilent Technologies Inc., Santa Clara, CA, USA). The column temperature was set at 25 °C. A gradient mobile phase of (A) water plus 20 mM formic acid and (B) acetonitrile plus 20 mM formic acid was used. The initial condition was set at 5% of B. The following solvent gradient was applied: from 95% A and 5% B to 5% A and 95% B within 20 min, hold for 10 min. Flow rate was set at 0.25 mL $min^{-1}$and 4 μL of samples were injected using ALS autosampler (Agilent Technologies, Inc., Waldbronn, Germany). The electrospray ionization (ESI) and fragmentor voltages were set at 4000 and 60 V, respectively. The ultra-high pure nitrogen was used as the nebulizer, drying and collision gas. The heated capillary temperature was maintained at 300 °C. The drying gas flow rate and nebulizer gas pressure were 10 L min^{-1} and 40 psi, respectively. Mass spectra were obtained by scanning from m/z > 80 to 1000 with 0.5 s scan time.

2.4. NMR analysis

A Bruker (Avance DRX-250 MHz, Germany) NMR instrument was employed for ^{1}H, ^{31}P and ^{13}C NMR experiments. All spectra were recorded at ambient temperature using $CDCl_3$ as a solvent.

2. 5. General procedure for microsynthesis of spiro alkylphosphonates *I*

Pentaerythritol (0.30 mmol) and triethylamine or pyridine (0.65 mmol) in 500 μL CH_2Cl_2 or pyridine were added dropwise, with stirring, to a solution of 0.60 mmol alkylphosphonic dichloride, in 500 μL CH_2Cl_2 at 0–5 °C. The reaction mixture was stirred for 4 h. The resulting precipitate was removed by filtration and the solution analyzed by GC/MS or GC/MS–MS as required. For separation of spiro methylphosphonate 1a (entry 1a, Table 1) from mixture, after completion of the reaction, the mixture was poured into ice cold H_2O and stirred for 15 min, then the mixture was saturated with brine. Subsequently, extraction



Scheme 1. Microsynthesis route of spiro alkylphosphonates I and 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II.