


 Very Important Paper

# Low-Temperature Thermal Formation of the Cyclic Methylphosphonic Acid Trimer [c-(CH<sub>3</sub>PO<sub>2</sub>)<sub>3</sub>]

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We report the formation of the cyclic methylphosphonic acid trimer [c-(CH<sub>3</sub>PO<sub>2</sub>)<sub>3</sub>] through condensation reactions during thermal processing of low-temperature methylphosphonic acid samples exploiting photoionization reflectron time-of-flight mass spectrometry (PI-ReTOF-MS) along with electronic structure calculations. Cyclic methylphosphonic acid trimers are

formed in the solid state and detected together with its protonated species in the gas phase upon single photon ionization. Our studies provide an understanding of the preparation of phosphorus-bearing potentially prebiotic molecules and the fundamental knowledge of low-temperature phosphorus chemistry in extraterrestrial environments.

## Introduction

Phosphorus represents a key element in the origin and evolution of life.<sup>[1–3]</sup> The phosphate group (PO<sub>4</sub><sup>3–</sup>) along with its P(+V) derivatives are contemplated as critical reactants in the prebiotic synthesis of phosphorus-bearing molecules such as deoxyribonucleic acid/ribonucleic acid (DNA/RNA), adenosine diphosphate/triphosphate (ADP/ATP), and phospholipids.<sup>[4–7]</sup> The hypothesis that the molecular precursors related to the origins of life were synthesized in deep space on ice-coated interstellar nanoparticles containing, e.g., phosphine (PH<sub>3</sub>), methane (CH<sub>4</sub>), and water (H<sub>2</sub>O) with phosphine detected in the carbon star envelopes IRC + 10216.<sup>[8]</sup> Processed by ultraviolet radiation (UV) and energetic galactic cosmic rays (GCRs), those matters could have been delivered to early Earth thus presenting an alternative route to the terrestrial *in situ* formation of prebiotic molecules.<sup>[9,10]</sup> Besides the interstellar medium, phosphorus was also detected in comet 67P/Churyumov-Gerasimenko even its parent molecule has not been identified<sup>[11,12]</sup> and exists as phosphide (P<sup>3–</sup>) and phosphate (PO<sub>4</sub><sup>3–</sup>) minerals in the Murchison meteorite.<sup>[13]</sup> Upon impact on Earth, schreibersite, a meteoritic iron-nickel phosphide [(Fe,

Ni)<sub>3</sub>P] mineral may react with water to produce phosphorus-containing organic molecules like glycerol-phosphate (C<sub>3</sub>H<sub>9</sub>PO<sub>6</sub>) possibly relevant to prebiotic biochemistry.<sup>[14–16]</sup> Alternatively as the only organic compounds of extraterrestrial origin identified thus far, the simplest alkylphosphonic acids RH<sub>2</sub>PO<sub>3</sub> (R = methyl (–CH<sub>3</sub>), ethyl (–C<sub>2</sub>H<sub>5</sub>), propyl (–C<sub>3</sub>H<sub>7</sub>)), which have been prepared in laboratory simulation experiments exposing phosphine (PH<sub>3</sub>), water (H<sub>2</sub>O), and methane (CH<sub>4</sub>) ice mixtures to proxies of GCRs. These studies provided compelling evidence that phosphorus-containing organics can form in extraterrestrial environments on ice-coated interstellar nanoparticles and be delivered to Earth.<sup>[17–23]</sup>

The di- and trimerization of alkylphosphonic acids such as methylphosphonic acid (Scheme 1) in deep space may not only supply previously elusive pathways to more complex phosphorus-carrying molecules but also has promising applications for material sciences such as proton conductors for polymer electrolyte membrane fuel cells.<sup>[24–26]</sup> Due to this relevance, phosphonic acid anhydrides consisting of a six-membered (PO)<sub>3</sub> ring with alkyl and phenyl groups were synthesized preparatively.<sup>[27–30]</sup> However, the condensation reactions of phosphorus-bearing molecules at low temperatures in the deep space environment have not yet been reported. Thus, the study of the condensation reactions of phosphorus-bearing organics in interstellar and in early solar system analog ices may provide important insight into the inventory of phosphorus-carrying organics along with their di- and trimers available for prebiotic phosphorylation reactions.


Here, we report the formation of the cyclic methylphosphonic acid trimer (CMPAT) – 2,4,6-trimethyl-2,4,6-trioxide-1,3,5-trioxo-2,4,6-triphosphorinane – formed via the condensation reaction of solid methylphosphonic acid (MPA) (Scheme 1). The condensation reactions were triggered by warming up MPA samples from 5 K to 320 K at 1 Kmin<sup>–1</sup>. Our studies present the first discovery of CMPAT in thermally processed biorelevant phosphorus-bearing molecules demonstrating that those molecules can be synthesized once the cold molecular cloud (10 K) transits to star-forming regions (up to 320 K) abiotically thus providing evidence for condensation

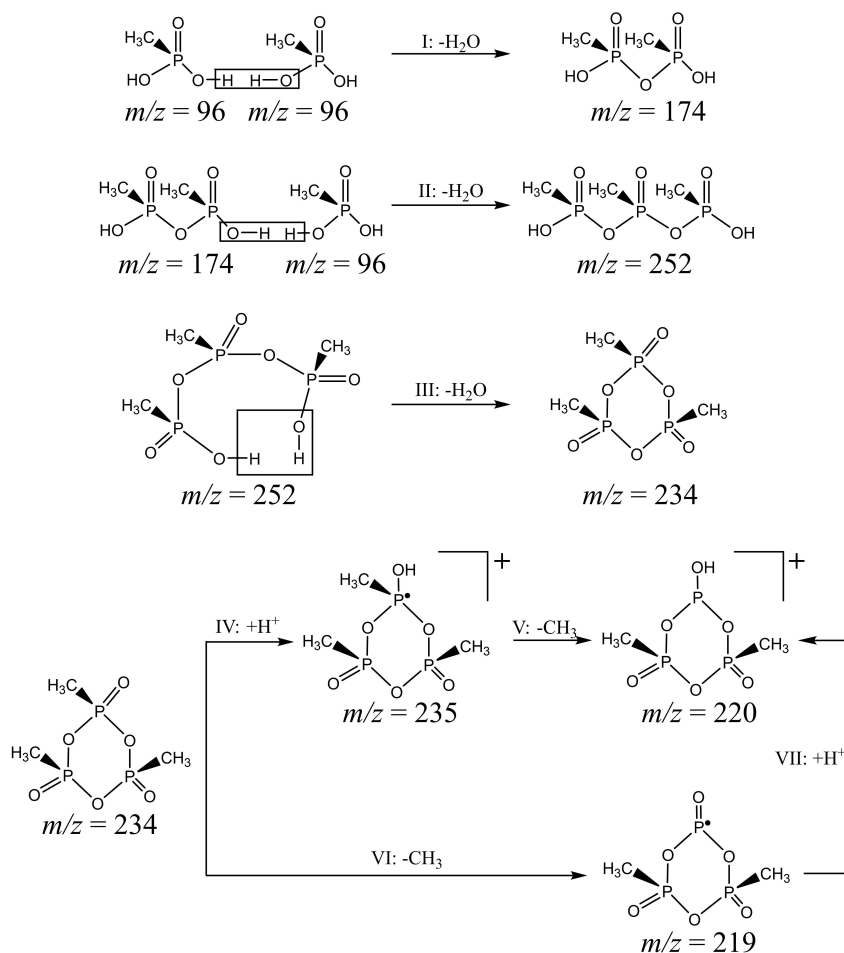
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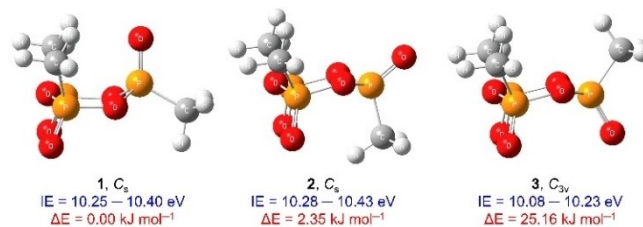
**Scheme 1.** Schematic presentation of condensation reactions of methylphosphonic acid (top) along with potential gas phase fragmentation upon photoionization.

reactions of phosphorus-bearing precursors to prebiotic, bio-relevant molecules under extraterrestrial conditions.

## Results and Discussion

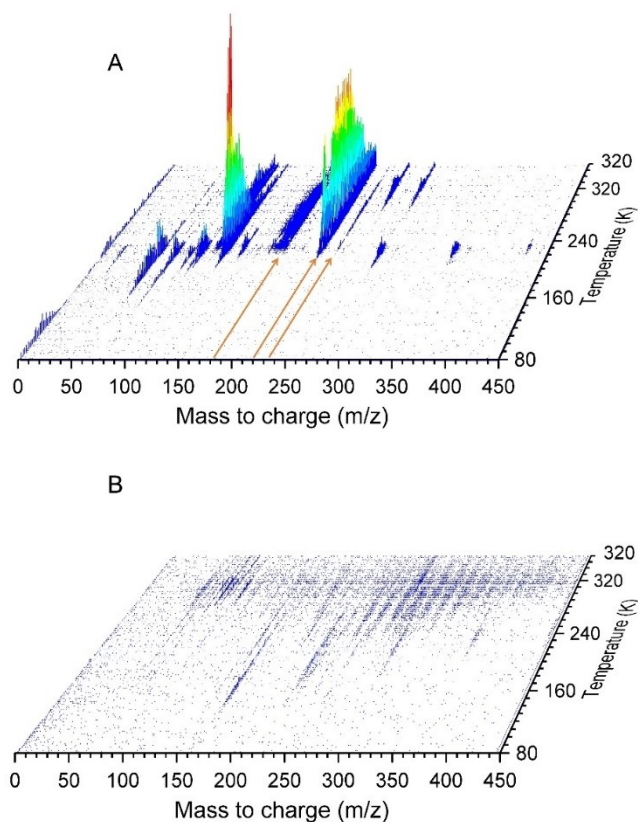
The computed molecular structures of distinct CMPAT conformers 1–3 are depicted in Figure 1 along with their adiabatic ionization energies (IEs), relative energies, and geometrical parameters. It is important to stress here that the calculated IEs of the isomers can be lower by 0.08 eV or higher by 0.07 eV based on a comparison of experimental and calculated IEs of molecular benchmark systems (Table S2). Further, ReTOF-MS calibration experiments revealed that the electric field of the ion optics lowers the IE by 0.03 eV.<sup>[31]</sup> The energies, Cartesian coordinates, and normal modes of distinct CMPAT isomers calculated at the CCSD(T)-F12b/cc-pVTZ//B3LYP/aug-cc-pVTZ level of theory with B3LYP/aug-cc-pVTZ zero-point vibrational energy corrections are provided in Table S3.

The photoionization reflectron time-of-flight mass spectra (PI-ReTOF-MS) of subliming molecules released from the thermally processed methylphosphonic acid are shown as a



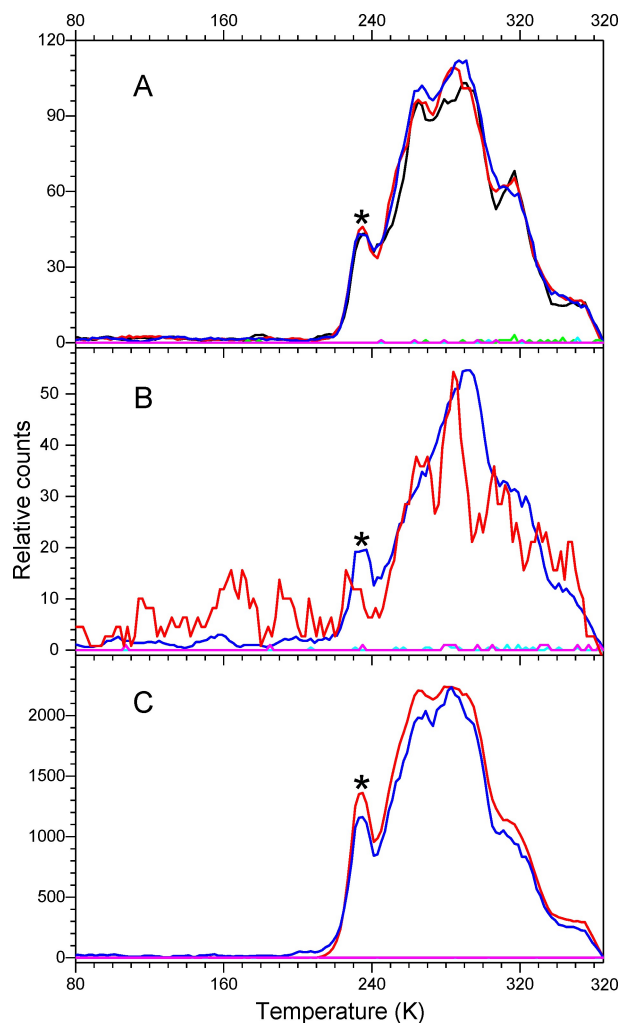
**Figure 1.** Molecular structures of distinct conformers of cyclic methylphosphonic acid trimer [c-(CH<sub>3</sub>PO<sub>2</sub>)<sub>3</sub>]. Point group, computed adiabatic ionization energies corrected for the electric field effect (IE, blue), and relative energies ( $\Delta E$ , red) are also shown. The energies were computed at the CCSD(T)-F12b/cc-pVTZ//B3LYP/aug-cc-pVTZ level and corrected by zero-point vibrational energies obtained at the B3LYP/aug-cc-pVTZ level. The atoms are color-coded in white (hydrogen), gray (carbon), red (oxygen), and orange (phosphorus). Coordinates and normal modes are provided in Table S3.

function of temperature after photoionization at 10.35 and 9.50 eV in Figure 2. The TPD profiles of the species generated via condensation reactions are presented in Figure 3. Based on the calculated IEs of the CMPAT conformers, at 10.35 eV, conformer 3 (IE=10.08–10.23) can be ionized. In addition,



**Figure 2.** Photoionization reflectron time-of-flight mass spectra (PI-ReTOF-MS) as a function of temperature for the subliming molecules from the methylphosphonic acid samples. The data were recorded at photon energies of (A) 10.35 eV and (B) 9.50 eV. The ion signal collected at 10.35 eV for  $m/z = 174$  (methylphosphonic acid dimer, MPAD), 219 (cyclic methylphosphonic acid trimer minus one methyl, CMPAT-CH<sub>3</sub>), and 235 (protonated cyclic methylphosphonic acid trimer, HCMPAT) are marked with orange arrows.

conformers **1** (IE = 10.25–10.40) and **2** (IE = 10.28–10.43) are also detectable at the photon energy of 10.35 eV. All conformers **1–3** cannot be ionized at a photon energy of 9.50 eV. The search for ion signal linked to polymeric methylphosphonic acid focus first on cations associated with the methylphosphonic acid dimer (MPAD,  $m/z = 174$ ) along with MPAD minus one hydrogen (MPAD-H,  $m/z = 173$ ) and protonated MPAD (MPAD+H,  $m/z = 175$ ); these TPD profiles are presented in Figure 3A. Ion counts connected to the cyclic methylphosphonic acid trimer (CMPAT) arose at  $m/z = 234$  (Figure 3B), whereas high-intensity signals at  $m/z = 235$  are assigned to the protonated cyclic methylphosphonic acid trimer (HCMPAT). These findings support the production of cyclic methylphosphonic acid trimer (CMPAT) during the warm-up process of methylphosphonic acid samples. In addition, ion signals at  $m/z = 219$  and  $m/z = 220$ , i.e. CMPAT and HCMPAT minus one methyl group (-CH<sub>3</sub>), were also observed and presented in Figure 3C. These fragment products are generated from their parent ions CMPAT and HCMPAT through route V and VI (Scheme 1). From Figure 3, the counts of CMPAT and HCMPAT minus one methyl group are much more than that of MPAD suggesting CMPAT is the dominant species during the thermal process, which agrees



**Figure 3.** Temperature programmed desorption (TPD) profiles of species related to Scheme 1 collected at photon energies of 10.35 and 9.50 eV. (A) Methylphosphonic acid dimer (MPAD,  $m/z = 174$ , 10.35 eV in red and 9.50 eV in cyan) along with MPAD minus one hydrogen (MPAD-H,  $m/z = 173$ , 10.35 eV in black and 9.50 eV in green) and protonated MPAD (MPAD+H,  $m/z = 175$ , 10.35 eV in blue and 9.50 eV in magenta), (B) cyclic methylphosphonic acid trimer (CMPAT,  $m/z = 234$ , 10.35 eV in red and 9.50 eV in cyan) and protonated CMPAT (HCMPAT,  $m/z = 235$ , 10.35 eV in blue and 9.50 eV in magenta), and (C) CMPAT minus one methyl (CMPAT-CH<sub>3</sub>,  $m/z = 219$ , 10.35 eV in red and 9.50 eV in cyan) and HCMPAT minus one methyl (HCMPAT-CH<sub>3</sub>,  $m/z = 220$ , 10.35 eV in blue and 9.50 eV in magenta). At 10.35 eV, the relative counts of CMPAT are multiplied by 8 and those of HCMPAT-CH<sub>3</sub> are multiplied by 12. Peaks marked with an asterisk origin from dissociative photoionization of subliming molecules with a molecular weight of 428 amu (Figure 4A).

with the finding in the literature on the trimer of methylphosphonic acid synthesized via conventional methods.<sup>[27]</sup> It is possibly because that the reaction energy for the formation of CMPAT is much lower than that of MPAD and MPAT in low-temperature conditions. Additionally, the energy of the combined CMPAT cation minus one methyl radical and the separated methyl group is lower in energy than full CMPAT cation by 18.9 kJ mol<sup>-1</sup> for conformers **1** and **2** since they share a common cation isomer and 9.5 kJ mol<sup>-1</sup> for conformer **3** due to the formation of a secondary O<sub>2</sub>P<sub>2</sub> ring. These values can also

be interpreted as the appearance energies of the  $m/z = 219$  ion signals. Besides the broad sublimation events of the methylphosphonic acid dimer (MPAD) and cyclic methylphosphonic acid trimer (CMPAT) covering 240 to 320 K, the TPD profiles reveal a sharp peak starting from 220 K and reaching a maximum of 235 K. The sharp peak is assigned to the fragments from photodissociation of  $m/z = 428$  species (Figure 4A). Note that, in the mass spectrum (Figure S1), the signals at  $m/z = 428$  are overlapped by a broad band from  $m/z = 427$  and if it is from  $m/z = 427$  then it can be assigned to a molecular cluster composed of one HCMPAT and two MPA molecules. Considering the root-mean-square velocity of  $143 \text{ m s}^{-1}$  of a dimer and trimer subliming at 290 K and the distance between the sample and the photoionization laser of  $2.0 \pm 0.1 \text{ mm}$ , we determined a lifetime of the subliming HCMPAT molecules of at least  $14 \pm 2 \mu\text{s}$ . The findings suggest the formation of the cyclic methylphosphonic acid trimer  $[\text{c}-(\text{CH}_3\text{PO}_2)_3]$  during the warm-up of low-temperature biorelevant phosphorus-bearing molecules.

After having provided experimental evidence on the formation of cyclic methylphosphonic acid trimer  $[\text{c}-(\text{CH}_3\text{PO}_2)_3]$ , we would like to now address the potential formation pathways in the warm-up process of the methylphosphonic acid samples. Condensation reactions are fundamental in biochemistry<sup>[32,33]</sup> and may be triggered by thermally heating, e.g. one pathway is the formation of peptides from amino acids through condensation reactions.<sup>[21]</sup> Methylphosphonic acid contains one

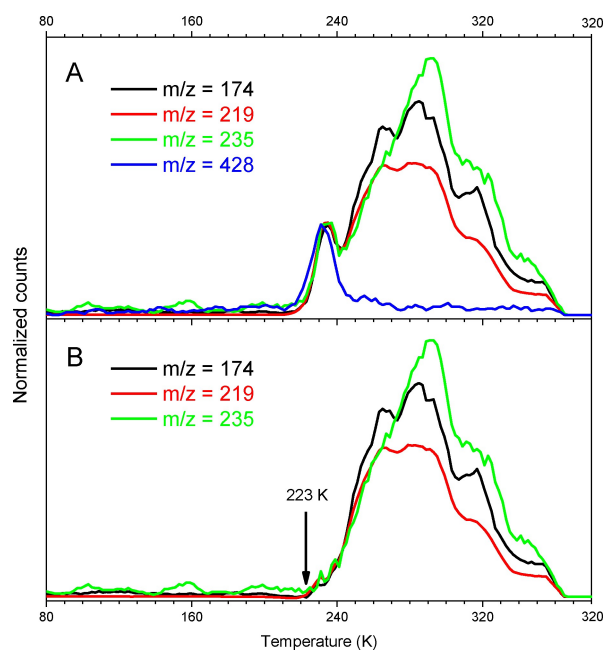
phosphorus atom that connects to a functional group (methyl,  $-\text{CH}_3$ ), one oxygen atom ( $=\text{O}$ ), and two hydroxyl groups ( $-\text{OH}$ ). The electronegativity of phosphorus ( $\chi = 2.19$  on the Pauling scale)<sup>[34]</sup> suggests that methylphosphonic acid may undergo a process similar to the condensation reaction of amino acids to form polymeric methylphosphonic acid (Scheme 1). Two hydroxyl ( $-\text{OH}$ ) groups from distinct MPA molecules can initially bridge via hydrogen bonding and then lose one water (route I). The MPAD can react with another MPA to form MPAT (route II). Two hydroxyl groups at both ends can be dehydrated to produce CMPAT (route III).<sup>[24]</sup> The oxygen in the CMPAT can be protonated generating protonated CMPAT as detected though  $m/z = 235$  (route IV). According to the TPD profiles of the corresponding ions, the triggering temperature of these condensation reactions should be lower than 223 K under ultra-high vacuum conditions (Figure 4B). The detection of fragments from CMPAT at  $m/z = 219$  provides further evidence for the formation of the cyclic methylphosphonic acid trimer. Theoretically, the initial barrier in forming MPAD in (Scheme 1, route I) from MPA is computed here to be  $72.8 \text{ kJ mol}^{-1}$  estimated from a similar transition state geometry as that reported in Ref. [24]. First, the dimer goes through a  $C_i$  van der Waals minimum  $100.8 \text{ kJ mol}^{-1}$  below the energy of two, separated MPA molecules. This then climbs to be  $72.8 \text{ kJ mol}^{-1}$ , as previously stated, above the starting materials before dropping to  $-106.0 \text{ kJ mol}^{-1}$  after a water molecule is released and a new P–O bond forms between the dimers. A similar process continues for the addition of a third MPA in (Scheme 1, route II) and then ring closure (Scheme 1, route III). Formation of a CMPAT is not thermodynamically favored, however.

## Conclusions

Overall, our work proposes that phosphorus-bearing compounds containing hydroxyl ( $-\text{OH}$ ) groups, for example, methylphosphonic acid ( $\text{CH}_3\text{PO}_3$ ), can form precursors of phosphorus-bearing biochemicals through condensation reactions in the star-forming regions. Our study presents the beginning of a systematic understanding of the formation of polymeric phosphorus-bearing biochemicals under low-temperature interstellar conditions and the fundamental knowledge of phosphorus chemistry in extraterrestrial environments.

## Experimental Methods

The experiments were carried out in an ultra-high vacuum chamber (UHV) pumped to a base pressure of  $7 \times 10^{-11}$  Torr utilizing turbomolecular pumps (Osaka, TG1300MUCWB, and TG420MCAB) backed with oil-free scroll pumps (Edwards GVSP30). In the chamber, a polished silver wafer is interfaced to a closed-cycle helium refrigerator (Sumitomo Heavy Industries, RDK-415E) capable of achieving temperatures of  $5.0 \pm 0.1 \text{ K}$ . The cold head can be translated vertically and rotated in the horizontal plane with a linear translator (McAllister, BLT106) and rotational feed through (Thermionics Vacuum Products, RNN-600/FA/MCO). A thin layer of methylphosphonic acid ( $(\text{CH}_3\text{P}(\text{O})(\text{OH})_2$ , Sigma-Aldrich, 98 %) was prepared on a silver wafer. Samples of solid methylphosphonic acid



**Figure 4.** Temperature-programmed desorption (TPD) profiles at  $m/z = 174$  (black), 219 (red), 235 (green), and 428 (blue). (A) The sharp peaks of TPD profiles at  $m/z = 174$ , 219, and 235 matches the signals at  $m/z = 428$  (blue) very well suggesting those peaks are from dissociative photoionization of subliming species with a molecular weight of 428 amu. (B) Difference TPD profiles at  $m/z = 174$  (black), 219 (red), 235 (green), by subtracting signals at  $m/z = 428$ . The start point at 223 K suggests the subliming event start at 223 K and the triggering temperature of the methylphosphonic acid condensation reaction should be lower than 223 K under our experimental conditions.



were directly placed onto a polished silver wafer and kept it in a dry box for several hours to remove water. The thin film of methylphosphonic acid sample covers about 1 cm<sup>2</sup> zone of that silver wafer. Then, the wafer with methylphosphonic acid was warmed up to 320 K at 1 K min<sup>-1</sup> (temperature-programmed desorption, TPD) exploiting a programmable temperature controller (Lakeshore 336). During the TPD phase, the subliming molecules were examined using a reflectron time-of-flight (ReTOF) mass spectrometer (Jordon TOF Products, Inc.) coupled with tunable vacuum ultraviolet (VUV) photoionization with photon energies of 10.35 and 9.50 eV. To produce 10.35 eV (119.792 nm) and 9.50 eV (130.510 nm) lights, a second harmonic (532 nm) of a pulsed neodymium-doped yttrium aluminum garnet laser (Nd:YAG, Spectra Physics, PRO-270, 30 Hz) was used to pump a Rhodamine 610/640 dye mixture (0.17/0.04 g L<sup>-1</sup> ethanol) and obtain 606.948 nm (2.04 eV) (Sirah, Cobra-Stretch), which underwent a frequency tripling process to achieve  $\omega_1 = 202.316$  nm (6.13 eV) ( $\beta$ -BaB<sub>2</sub>O<sub>4</sub> (BBO) crystals, 44°, and 77°). Another Nd:YAG laser with second harmonic of 532 nm and triple harmonic of 355 nm pumped DCM dye (0.30 g L<sup>-1</sup> dimethyl sulfoxide) and Coumarin 450 dye mixture (0.20 g L<sup>-1</sup> ethanol) to obtain  $\omega_2 = 650.3$  nm (1.91 eV) and  $\omega_2 = 449.8$  nm (2.76 eV), and then combined with  $2\omega_1$  generating  $\omega_{\text{VUV}} = 10.35$  eV (119.792 nm) and 9.50 eV (130.510 nm) at 10<sup>12</sup> photons per pulse via difference four-wave mixing ( $\omega_{\text{VUV}} = 2\omega_1 - \omega_2$ ) in pulsed gas jets of krypton (Kr) (Table S1). The VUV photons were spatially separated from the incident lasers ( $2\omega_1$  and  $\omega_2$ ) and other wavelengths generated via multiple resonant and non-resonant processes ( $2\omega_1 + \omega_2$ ;  $3\omega_1$ ;  $3\omega_2$ ) utilizing a biconvex lens made with lithium fluoride (LiF) (ISP Optics) and directed 2 mm above the surface of the sample for ionizing the sublimed species. The ionized molecules were examined with the ReTOF mass spectrometer based on their arrival time to a multichannel plate (MCP), which is correlated with mass-to-charge ratios ( $m/z$ ). The MCP signal was first amplified by a fast preamplifier (ORTEC 9305) and then recorded using a multichannel scalar (MCS) (FAST ComTec, P7888 – 1 E). The MCS is triggered by a pulse generator (Quantum Composers 9518) at 30 Hz. Each final mass spectrum is the average of 3600 sweeps of the flight time in 4 ns bin width and correlates to a 2 K increase in the sample temperature.

### Computational Details

The neutral and radical cation geometries are optimized with B3LYP and the aug-cc-pVTZ basis set within *Gaussian16*.<sup>[35–39]</sup> The harmonic vibrational energies and zero-point vibrational energies (ZPVEs) are also computed at this same level of theory. Single-point energies are obtained with explicitly correlated coupled-cluster singles, doubles, and perturbative triples (CCSD(T)-F12b) and the cc-pVTZ-F12 basis set with the *MOLPRO 2020.1* program<sup>[40–44]</sup> at the optimized B3LYP/aug-cc-pVTZ geometries. The relative energies and adiabatic ionization potentials are computed from the CCSD(T)-F12b/cc-pVTZ//B3LYP/aug-cc-pVTZ and corrected by zero-point vibrational energies obtained at B3LYP/aug-cc-pVTZ level with the latter involving the difference between that of the neutrals and the radical cations.

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### Conflict of Interest

The authors declare no conflict of interest.

### Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

**Keywords:** extraterrestrial phosphorus · condensation reaction · mass spectrometry · *ab initio* calculations · cyclic methylphosphonic acid trimer

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