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A novel rearrangement in ESI-MS^n of spirocyclic pentaerythritol di(phosphate monoamides)

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ABSTRACT

Several spirocyclic pentaerythritol di(phosphate monoamides) as intumescent flame retardants were synthesized and analyzed by electrospray ionization multistage tandem mass spectrometry. A novel amino group migration from the phosphoryl group to the two methylenes was observed. This migration is believed to be a general pathway for ions with the small size and electronic donating alkyl groups of spirocyclic pentaerythritol di(phosphate monoamides), which is assisted by twice nucleophilic substitutions. Steric and electronic effects of alkyl groups might be a key factor responsible for this migration.

1. Introduction

Traditionally, halogen containing compounds were as the main flame retardants, which would produce large amounts of smoke and toxic gas on burning, thus their use was restricted in some occasions [1–3]. As a low-toxicity flame retardant system, the phosphorus–nitrogen combination has been extensively studied and reviewed in the literature [4,5], which mainly act as intumescent flame retardants resulting in a char layer in the condensed phase which can produce less toxic gas and smoke [6–9], and the effect depends on the type of phosphorus and nitrogen products used [10]. An effective intumescent flame retardant should comprise three basic elements, which are called dehydrating agent, char forming agent and foaming agent. In order to obtain the halogen-free, low-toxicity and intumescent flame retardant that concentrates all of the three elements in itself, a series of spirocyclic pentaerythritol di(phosphate monoamides) have been synthesized recently.

Electrospray ionization multistage tandem mass spectrometry (ESI-MS^n) is a very powerful tool for structural determination and has been widely used in chemistry, biochemistry, pharmaceutical research and the study of degradation mechanism [11–14]. In several cases previously, this technique was used to study the organophosphorus derivatives of phosphoramidates in our laboratory. Novel rearrangement reactions, e.g., carbonyl oxygen migration [15], benzyl migration [16], P–N to P–O rearrangement [17], formamide extrusion [18] and methoxy group migration [19] have been observed. In this paper, we report our investigations on several spirocyclic pentaerythritol di(phosphate primary monoamides) (in Scheme 1) by ESI-MS combined with tandem techniques, in which a novel rearrangement of amino group migration was discovered.

2. Experimental

All compounds synthesized were identified by FTIR, ^{31}P NMR, ^{1}H NMR, ^{13}C NMR, and ESI-MS.

2.1. 3,9-Dichloro-2,4,8,10-tetraoxa-3,9-diphospha-spiro-[5,5]undecane (DDP)

DDP was prepared by the method described previously [20,21].

2.2. Spirocyclic pentaerythritol di(phosphate monoamide) [22]

To DDP (5 mmol) in dry acetonitrile (40 ml) was dispersed, the solution of amine (10 mmol) and triethylamine (10 mmol) in dry acetonitrile (10 ml) and added dropwise to the suspension below 10 °C under stirring. After 40 min, the solution was warmed to room temperature for 6 h. The crude product was filtrated and washed

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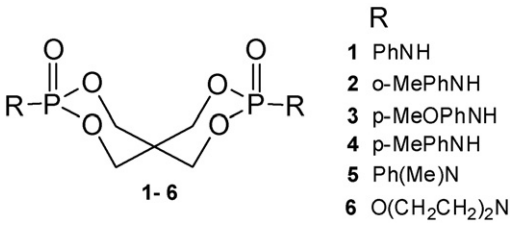


Scheme 1. Structures of compounds **1**–**6**.

three times with water. The residue was then purified by recrystallization technology from anhydrous ether. The final product was obtained in moderate yield.

2.3. MS measurements

Mass spectra were acquired in positive ion mode using a Bruker ESQUIRE 3000 ion trap spectrometer equipped with a gas nebulizer probe, capable of analyzing ions up to *m*/*z* 6000. Nitrogen was used as drying gas at a flow rate of 4.5 L/min. The nebulizer pressure was 7.5 psi. The capillary was typically held at 4 kV and the source temperature was maintained at 300 °C. The instrument was operated at unit-mass resolution, calibration of *m*/*z* was performed using a standard ES-tuning-mix. The samples were continuously infused into the ESI chamber by a Cole-Parmer 74900 syringe pump (Cole Parmer Instrument Company, Vernon Hills, IL).

The high-resolution mass spectral data for compound **1** was recorded on a Bruker APEXII Fourier transform ion cyclotron resonance (FTICR) MS instrument with an external ion source and analyzed using liquid secondary ion (LSI) MS with a Cs ion gun in the positive ion mode. The accelerating voltage was 10 kV and the full scan was from *m*/*z* 100 to 600. The sample was analyzed as a solution in methanol.

3. Results and discussion

Compounds **1**–**4** display similar fragmentation patterns, the ESI-MS^2 and ESI-MS^3 data of which are showed in Table 1. As a representative, the ESI-MS^n positive ion mass spectral fragmentation pattern of spirocyclic pentaerythritol di(phosphate primary monoanilines) (**1**) is discussed in detail. Its ESI-MS, ESI-MS^2 and ESI-MS^3 spectra are shown in Fig. 1.

In ESI-MS, $[M+H]^+$ is predominant, followed by $[M+Na]^+$. In ESI-MS^2, however, there were two unexpected ions at *m*/*z* 331 and 158,

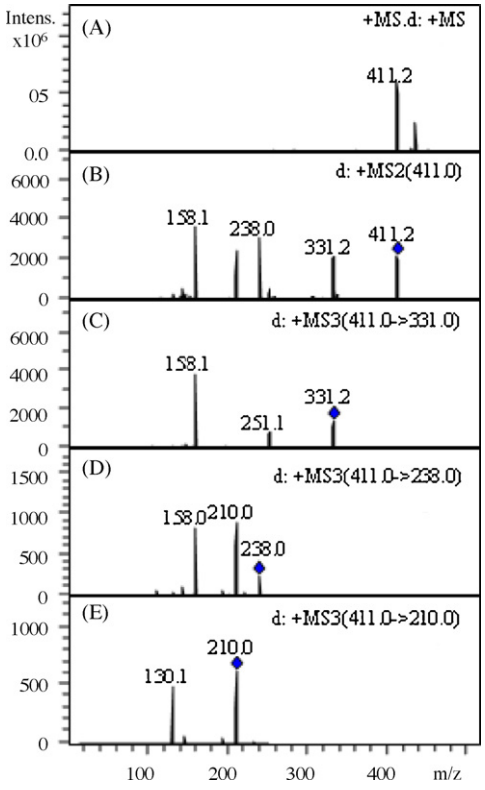


Fig. 1. MS of (**1**). (A) Full MS; (B) MS^2 of $[M+H]^+$ at *m*/*z* 411; (C) MS^3 of the ion at *m*/*z* 331; (D) MS^3 of the ion at *m*/*z* 238;(E) MS^3 of the ion at *m*/*z* 210.

which were found not only in ESI-MS^2 (Fig. 1(B)), but also in ESI-MS^3 (Fig. 1(C and D)). According to ESI-MS^n, the fragment ion at *m*/*z* 331 derived from the precursor ion at *m*/*z* 411, can be further fragmented into the ions at *m*/*z* 158 and 251. High-resolution FTICR-MS indicated that the exactmass of the ions at *m*/*z* 331, 251 and 158 is 331.1201, 251.1539 and 158.0961, respectively, corresponding to the formula $C_{17}H_{20}N_2O_3P$, $C_{17}H_{19}N_2$ and $C_{11}H_{12}N$ (calculated 331.1206, 251.1543 and 158.0964; relative error 1.5, 1.6 and 1.9 ppm) (Table 2). Apparently, the ions at *m*/*z* 331 and 251 were both produced by loss of HPO_3 from their precursor ions, respectively.

The formation of the ion at *m*/*z* 331 is shown in Scheme 2. Which could possibly involve twice nucleophilic reactions mediated rearrangement pathway. Starting from the hydrogen adduct ion **I** at *m*/*z* 411, the nucleophilic PhNH group attacks the methylene of the

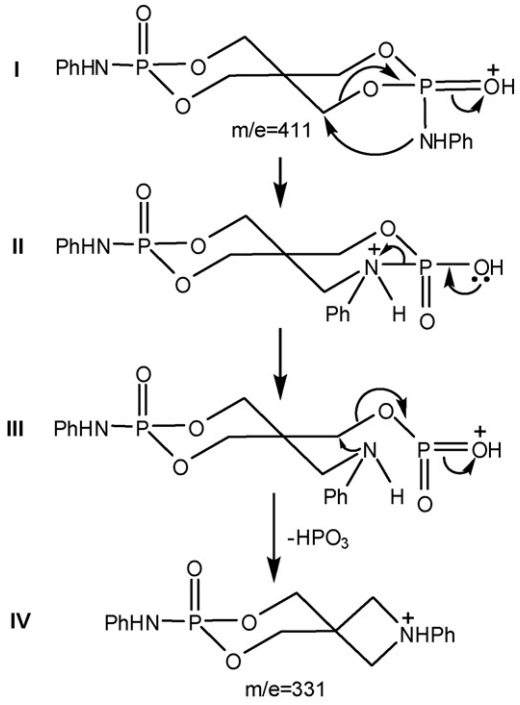
Table 1
MS^2 and MS^3 spectra data of the compounds **1**–**4** $[M+H]^+$

No.	Precursor Ions, *m*/*z*	Fragment ions, *m*/*z* (relative abundance (%))		
		Rearrangement ions	$[M+H-RPO_3H_2]^+$	$[M+H-RPO_3C_2H_6]^+$
1	411(39)	331(54) 158(100)	238(77)	210(61)
	331(37)	251(23) 158(100)		
	238(27)	158(97)		210(100)
	210(100)	130(78)		
2	439(33)	359(43) 172(100)	252(76)	224(58)
	359(41)	279(13) 172(100)		
	252(14)	172(100)		224(95)
	224(100)	144(90)		
3	471(10)	391(48) 188(50)	268(28)	240(100)
	391(100)	311(32) 188(39)		
	240(100)	160(72)		
4	439(40)	359(51) 172(100)	252(47)	224(75)
	359(50)	279(32) 172(100)		
	252(36)	172(100)		224(82)
	224(100)	144(80)		

Table 2
High-resolution mass spectral data for the main ions of **1**[a]

Ions species	Theoretical mass (*m*/*z*)	Measured mass (*m*/*z*)	Relative error (ppm)
$[M+H]^+$	411.0869	411.0875	1.4
$[M+H-HPO_3]^+$	331.1206	331.1201	1.5
$[M+H-2HPO_3]^+$	251.1543	251.1539	1.6
$[M+H-PhNHPO_3H_2]^+$	238.0628	238.0625	1.2
$[M+H-PhNHPO_3C_2H_6]^+$	210.0315	210.0323	3.8
$[M+H-HPO_3-PhNHPO_3H_2]^+$	158.0964	158.0961	1.9

[a] Obtained with LSI-MS in the positive ion mode.



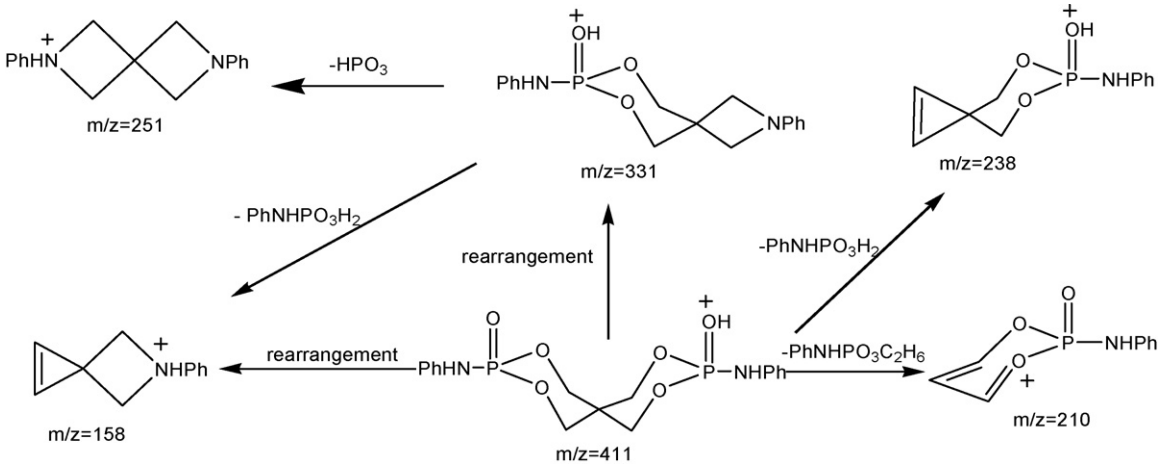
Scheme 2. Proposed rearrangement mechanism of the ion at *m*/*z* 331.

phosphonate group and causes the C—O bond to break. In this step, the positive charge on the hydroxy group transfers to the N atom of the PhNH group, and a quaternary ammonium cation is formed. The adduct ion **I** is converted into the intermediate **II**. Electrons on the oxygen are then used to aid the cleavage of the P—N bond. The positive charge on the quaternary ammonium cation is shiftted to the O atom of the hydroxy group, and reforms the bond of the phosphoryl group. This converts the intermediate **II** into the intermediate **III**. Followed by the same nucleophilic reaction, the positive charge on the hydroxy group is diverted to the N atom of the PhNH group again, then losing a molecule of HPO_3 and producing the observed rearrangement ion **IV** at *m*/*z* 331. In this process, the amino group migrates from the phosphoryl group to the two methylenes. Successively, elimination of $PhNHPO_3H_2$ and HPO_3 from the ion at *m*/*z* 331 formed the fragment ions at *m*/*z* 158 and 251, respectively (Scheme 3).

To further test the hypothesis, spirocyclic pentaerythritol di(phosphate secondary monoamides) (**5** and **6** in Scheme 1) were synthesized and analyzed by ESI-MS^2 (Fig. 2). It is very interesting that the rearrangement ion $[M+H-80]^+$ at *m*/*z* 319 is observed for the compound **6**, that at *m*/*z* 359 not for the compound **5**, which revealed the need to reduce the steric hindrance and increase electron donating capacity to facilitate the migration of the amino group in spirocyclic pentaerythritol di(phosphate monoamides). Therefore, we rationalized that the amino group migration is assisted by twice nucleophilic reactions, and the steric and electronic effects of the alkyl group, play an important role in the rearrangement.

In ESI-MS^2, the other fragment ions at *m*/*z* 238 and 210 were observed by losing $PhNHPO_3H_2$ and $PhNHPO_3C_2H_6$ from the precursor ions, respectively. They were also as expected and were further identified by ESI-MS^3 (Fig. 1 (D and E)). Their exact mass are 238.0625 and 210.0323 (Table 2), corresponding to $C_{11}H_{13}NO_3P$ and $C_9H_9NO_3P$. A possible fragmentation pathway of $[M+H]^+$ is shown in Scheme 3.

Organophosphorus flame retardants mostly perform their flame retardant function in the condensed phase. Phosphorus can act in the condensed phase promoting char formation on the surface, which acts as a barrier to inhibit gaseous products from diffusing to the flame and to shield the polymer surface from heat and air. Here, the tandem mass spectra of compound 1–5 show characteristic $[M+H-80]^+$ ion. It means a molecule of HPO_3 easy to lose. The



Scheme 3. ESI-MS^2 fragmentation pathway of hydrogen adduct of compound **1**.

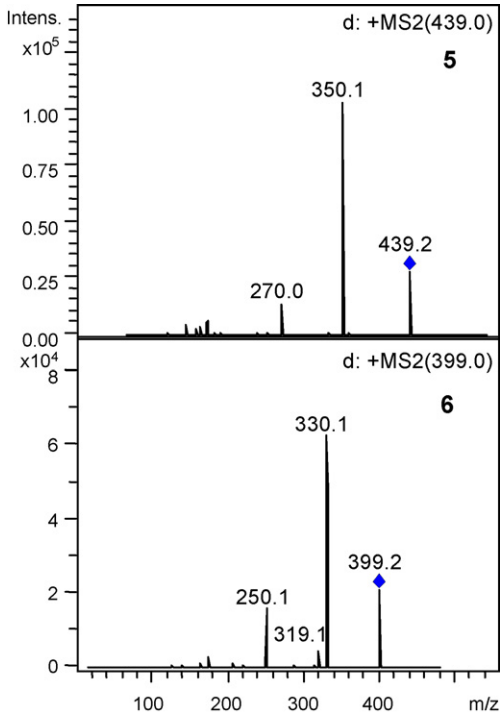


Fig. 2. MS/MS of (**5**) and (**6**).

acid catalyses accumulation of char and formation of a surface layer of protective char. Our results give a strong evidence for an effective, strong physical flame retardance mechanism (formation of barrier).

4. Conclusions

In conclusion, a novel amino group migration from the phosphoryl group to the two methylenes was observed in the ESI-MS^n of spirocyclic pentaerythritol di(phosphate monoamides). This migration is believed to be a general pathway for ions with the small size and electronic donating alkyl groups of spirocyclic pentaerythritol di(phosphate monoamides). If the tandem mass spectra of a compound show characteristic $[M+H-80]^+$ ion, it means that this compound has a phosphonate group. This finding could be valuable for the structural analysis of spirocyclic pentaerythritol di(phosphate monoamides) derivatives, and useful for the study of the correlation between flame retardant properties and their structures, too.

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