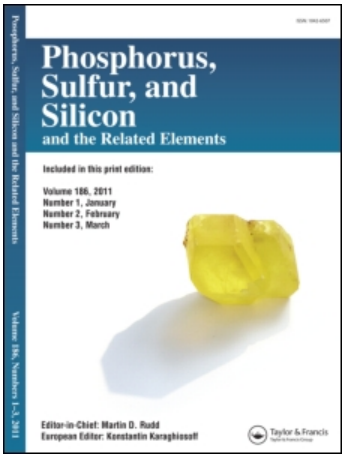

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MASS SPECTRAL STUDIES ON SYNTHETIC ANALOGUES OF ORGANOPHOSPHORUS TOXIN ISOLATED FROM *PTYCHODISCUS BREVIS*

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MASS SPECTRAL STUDIES ON SYNTHETIC ANALOGUES OF ORGANOPHOSPHORUS TOXIN ISOLATED FROM *PTYCHODISCUS BREVIS*

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A series of structurally related organophosphorus oximes analogous to O,O-dipropyl-(E)-2-(1-methyl-2-oxopropylidene)phosphorahydrazidothioate-(E)-oxime, isolated from *Ptychodiscus brevis*, have been synthesised and subjected to electron impact (EI) mass spectral studies. These studies, though aimed at total identification of these compounds, resulted in certain interesting observations and hence are being reported. In order to confirm the observations under electron impact and to support the mechanism of fragmentation we have also performed tandem mass spectrometry experiments in some cases.

Keywords: Organophosphorus oximes; phosphorahydrazidothioateoxime; *Ptychodiscus brevis*; electron impact; mass spectrometry; tandem mass spectrometry; fragmentation; parent ion; daughter ion; neutral loss

INTRODUCTION

The natural toxins produced by dinoflagellates, have been a matter of concern for the last thirty years and have caused massive damage to the marine life[1]. Although most of the species of dinoflagellate are non-toxic, there are a few exceptions such as *Gonyaulax spp.* producing Saxitoxin, one of the most toxic chemical toxin and *Ptychodiscus brevis* which gives brevetoxins[2]. The toxin isolated from *Ptychodiscus brevis* was characterised as O,O-Dipropyl-(E)-2-(1-methyl-2-oxopropylidene) phosphorahydrazidothioate-(E)-oxime (III)[3]. This toxin was synthesised for the first time in our laboratory and tested for its cardiorespiratory effects on anaes-

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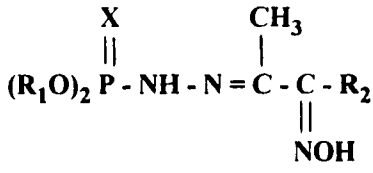
thesised cats[4]. In an attempt to obtain more insight into the structure-activity relationship of this toxin we synthesised a series of analogues of the fish toxin (III) and here we report the electron impact mass spectral behaviour of a series of structurally related organophosphorus oximes shown in Figure 1.



	X	R_1	R_2		X	R_1	R_2
(I)	S	C_2H_5	CH_3	**(VI)**	O	i-C_3H_7	CH_3
(II)	S	n-C_3H_7	CH_3	**(VII)**	O	C_6H_5	CH_3
(III)	S	i-C_3H_7	CH_3	**(VIII)**	O	i-C_3H_7	C_6H_5
(IV)	S	i-C_4H_9	CH_3	**(IX)**	O	C_6H_5	C_6H_5
(V)	S	n-C_3H_7	C_6H_5				

FIGURE 1 Structures of Organophosphorus Compounds Subjected to EIMS Studies

RESULTS AND DISCUSSION

The mass spectra of the compounds **I – IX** are shown in Table I. All these compounds showed prominent molecular (M^+)/pseudomolecular ($M+H^+$) ion peaks in addition to some of the very characteristic fragment ions which may be considered to be of diagnostic value for the total identification of these classes of compounds.

O, O-Dialkyl-(E)-2-(1-methyl-2-oxopropylidene) phosphorahydrazidothioate-(E)-oximes (I-IV)

The EI mass spectrum of O,O-Dipropyl-(E)-2-(1-methyl-2-oxopropylidene) phosphorahydrazidothioate-(E)-oxime **(II)** is shown in Figure 2. The oxime **II** showed an abundant molecular ion at m/z 295 and prominent fragment ions at m/z 278, 253, 236, 220, 211, 194, 178, 140, 115, 114 and 98. In order to get an insight into the genesis of the formation of these

fragment ions we carried out the parent ion scans of almost all the significant ions formed from **II**. These experiments showed interesting results summerised in Table II. From the spectrum it is evident that compound **II** gives a number of ions due to the loss of 42 mass units. This loss can be accounted for by the ejection of a neutral moiety C_3H_6 and to confirm this we performed Neutral Loss Scans under MS/MS which supported the proposed losses. The mechanism for the formation of various ions has been discussed in the following based on the parent ion scans.

TABLE I EI Mass Spectral Data for Organophosphorus Compounds

Compd. No.	*Molecular Weight*	*m/z (Relative intensity)*
I	267	268($M+H^{+\cdot}$, 100), 267($M^{+\cdot}$, 7.4), 250(6.2), 209(4.6), 184(4.2), 153 (2.7,125(5.8), 121(5.6), 114(5.3) 98(2.8, 97(10.3).
II	295	296($M+H^{+\cdot}$, 71.7), 295($M^{+\cdot}$, 82.8), 278(16.2), 253(22.6), 236(11.6), 220(10.7), 211(55.8), 194(19.7), 178(24.7), 153(22.3), 139(34.7), 116(40.7), 115(78.1), 114(96.3), 98(100), 97(42.9).
III	295	296($M+H^{+\cdot}$, 3.8), 295($M^{+\cdot}$, 50.9), 278(46.9), 236(6.5), 220(54.0), 211(8.9), 194(27.3), 178(86.3), 153(12.5), 139(33.7), 116(10.1), 115(88.7), 114(85.2), 98(100), 97(28.8).
IV	323	323($M^{+\cdot}$, 12.9), 321(16.8), 306(26.9), 209(12.0), 181(20.7), 170 (14.6), 164(55.7), 153(26.3), 114(43.1), 102(14.0), 98(27.5), 97(4.9), 85(100).
V	357	357($M^{+\cdot}$,36.1), 340(3.3), 298(2.6), 273(2.1), 240(3.1), 202(5.6), 178(13.5), 177(22.1), 160(33.9), 77(40.9).
VI	279	280($M+H^{+\cdot}$, 4.4), 279($M^{+\cdot}$, 23.9), 264(2.0), 262(1.0), 237(14.6), 220(6.4), 195(38.4), 178(27.8), 137(11.8), 115(13.2), 114(11.1), 99(11.4), 98(100).
VII	347	348($M+H^{+\cdot}$, 24.6), 347($M^{+\cdot}$, 17.1), 330(24.3), 254(14.6), 233(10.0), 215(14.4), 173(15.0), 132(15.2), 114(8.2). 98(28.2), 94(100), 77(13.9).
VIII	341	342($M+H^{+\cdot}$, 17.9), 341($M^{+\cdot}$, 28.5), 299(11.5), 257(23.9), 256(24.1), 240(11.1), 178(4.7), 177(12.7), 176(20.9), 160(100), 130(28.9), 125(17.5), 105(16.6), 99(25.6), 77(7.9).
IX	409	409($M^{+\cdot}$,1.6), 392(1.3), 250(2.1), 249(3.9), 248(2.3), 235(1.8), 178 (1.1), 177(3.2), 176(2.5), 170(5.9), 160(25.9), 159(62.8), 130(16.9), 118(21.7), 106(2.9), 105(21.9), 104(18.9), 103(27.4), 94(100), 77(28.9)

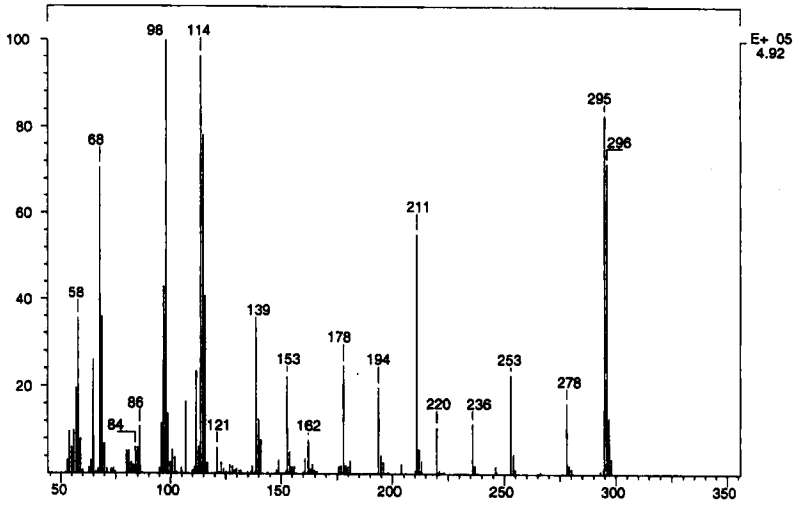
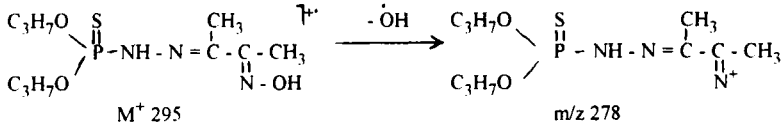


FIGURE 2 EI Mass Spectrum of O,O-Dipropyl-(E)-2-(1-methyl-2-oxopropylidene) phosphorahydrazidothioate-(E)-oximes (II)

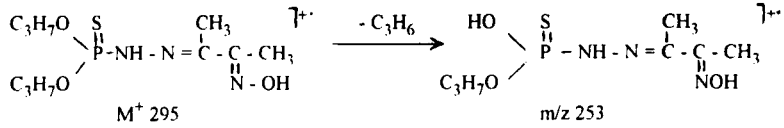
TABLE II Parent Ions of Various Daughter Ions in II

Daughter Ions	*Parent Ions*
278	295
253	295
236	278
220	278
211	295 & 253
194	278
178	220
115	211
98	115

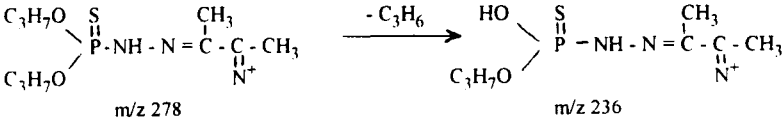
m/z 278: This ion arises directly from the parent ion and can be accounted for by the loss of a hydroxyl radical from the parent ion.



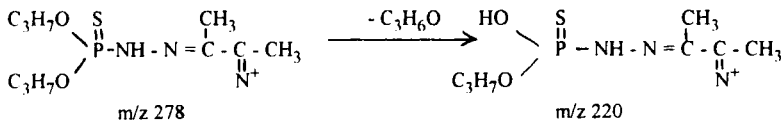
m/z 253: This ion also arise directly from the molecular ion most probably due to the loss of C_3H_6, a neutral moiety supported also by the neutral loss scan under MS/MS.



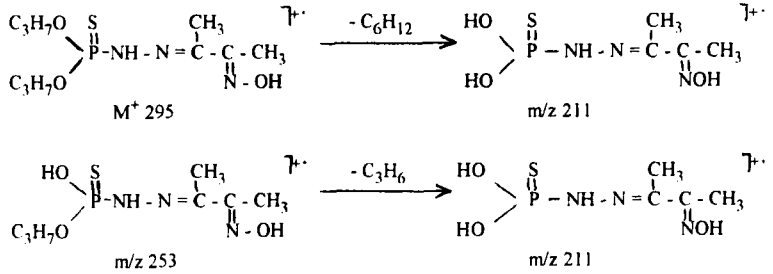
m/z 236 : This ion arises from the ion m/z 278 by the loss of C_3H_6 as shown below.



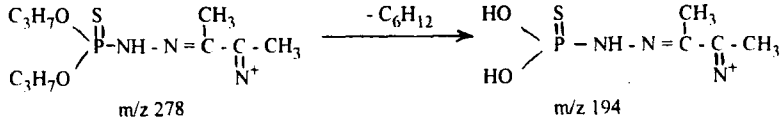
m/z 220: This ion shows only one parent ion, m/z 278 and can be accounted for by the loss of 58 mass units (C_3H_6O) as shown below.



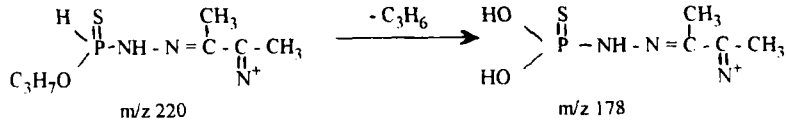
m/z 211: This ion shows two parent ions namely m/z 295 (the molecular ion) and m/z 253 and arises by the loss of 84 (C_6H_{12}) and 42 (C_3H_6) mass units respectively.



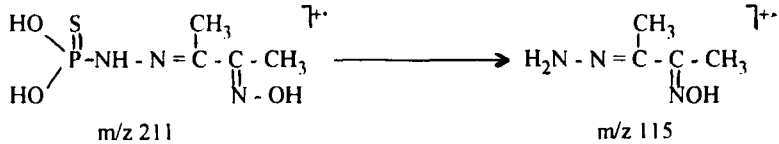
m/z 194: The ion m/z 194 arises from m/z 278 by the loss of mass units 84 (C_6H_{12}).



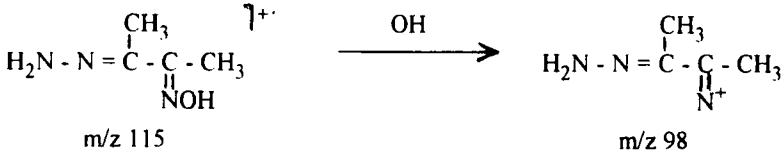
m/z 178: This ion is shown to arise from the ion m/z 220 by the loss of C_3H_6.



m/z 115: The ion m/z 115 arises from m/z 211 as shown below. This ion involves the loss of phosphorus moiety with some hydrogen scrambling which is difficult to predict in the absence of deuterated analogues.



m/z 98: This ion arises from the ion m/z 115 due to the loss of a hydroxyl radical.

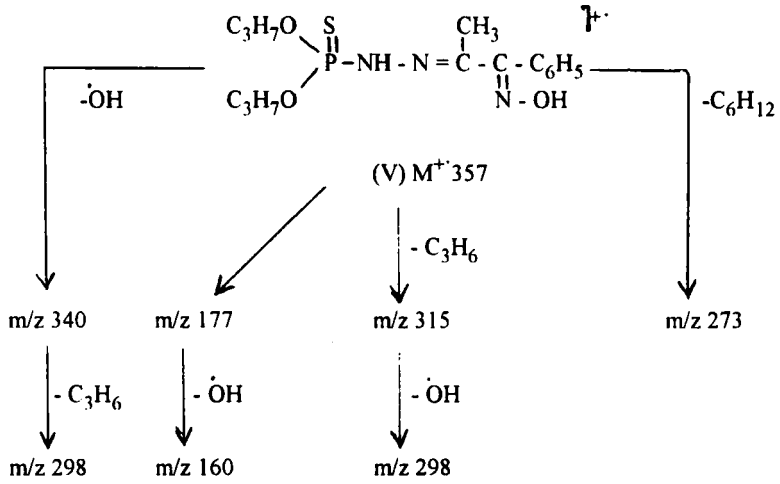


O,O-Dialkyl-(E)-2-(1-phenyl-2-oxopropylidene) phosphorahydrazidothioate-(E)-oxime (V)

In an attempt to see how fragmentation is effected by the changes in substituents, we have selected O,O-Dialkyl-(E)-2-(1-phenyl-2-oxopropylidene) phosphorahydrazidothioate-(E)-oxime (V). In this compound the propylidene group has a phenyl group in place of methyl as in compounds **I – IV**. The EI mass spectrum of **V** showed a strong molecular ion peak at m/z 357. The fragment ions were observed at m/z 340 (base peak), 315, 298, 273, 240, 202, 178, 177, 160, 104 and 77. The genesis of the fragmentation of these ions is shown in Scheme 1. The parent ion and neutral loss experiments performed in MS/MS mode confirmed the proposed mechanism (Table III).

O,O – Dialkyl/aryl – (E) – 2-(1- methyl/phenyl –2- oxopropylidene) phosphorahydrazido-(E)-oxime (VI-IX)

The electron impact mass spectra of compounds VI – IX were selected for these studies in order to see the difference in the fragmentation patterns between the oxo analogues. The mass spectrum of compound (VI), as a representative of the oxo analogue showed a prominent molecular ion peak at m/z 279 besides the fragment ions at m/z 264, 262, 237, 220, 195, 178, 115, 114, 99 and 98 (base peak). It is evident from these ions that most of the fragment ions are exactly same as those observed in II discussed above. The aprent ion experiments (Table IV) confirmed the fragmentation mechanism proposed in Scheme 2.



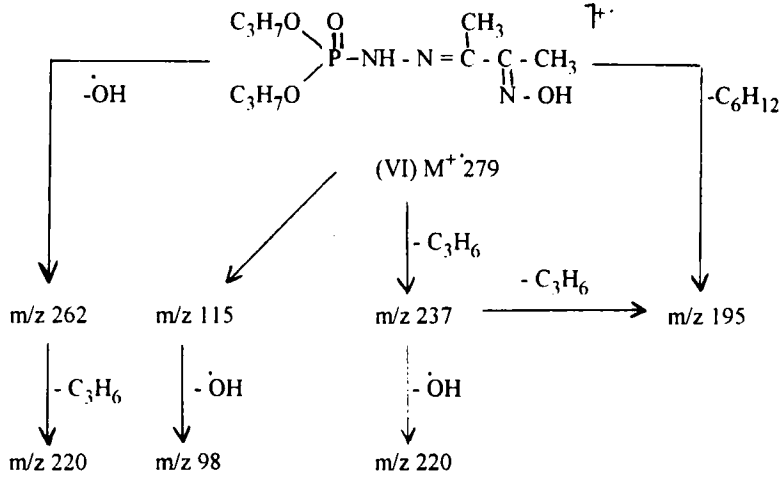
SCHEME 1 Probable Fragmentation Mechanism from V

TABLE III Parent Ions of Various Daughter ions in V

Daughter Ions	*Parent Ions*
340	357
315	357
298	340 & 315
273	357
177	357
160	177

TABLE IV Parent ions of Various Daughter Ions in VI

Parent Ions	*Daughter Ions*
262	279
237	279
220	279 & 237
195	279 & 237
115	279
98	115



SCHEME 2 Probable Fragmentation Mechanism from VI

EXPERIMENTAL

Instruments

The mass spectra were recorded under EI using TSQ 7000 Mass Spectrometer (Finnigan Mat, USA). The EI mass spectrometric operating conditions were as follows: ion source pressure 1.5×10^{-6} torr; source temperature 150°C; electron energy 70 eV; and emission current 400 μA The tandem mass spectrometry experiments were performed by using Argon as the collision gas at a pressure of 2 torr.

Synthesis of Compounds

The oximes studied in this paper were synthesised in our laboratory[5] as a part of the project on the synthsesis and biological evaluation of synthetic analogues of organophosphorus toxin isolated from *Ptychodiscus brevis*.

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