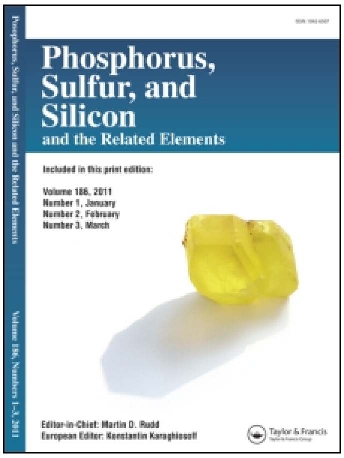

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STUDIES ON ORGANOPHOSPHORUS COMPOUNDS XLIX A MASS SPECTROSCOPIC STUDY OF PROTECTED 1-AMINO-SUBSTITUTED BENZYLPHOSPHONIC ESTERS

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STUDIES ON ORGANOPHOSPHORUS COMPOUNDS XLIX A MASS SPECTROSCOPIC STUDY OF PROTECTED 1-AMINO-SUBSTITUTED BENZYLPHOSPHONIC ESTERS

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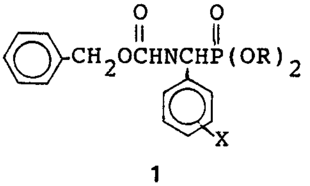
The mass spectra of diethyl and diisobutyl 1-N-benzoxycarbonylamino-substituted benzylphosphonates and diphenyl 1-N-(O,O-diethylphosphoryl)amino-substituted benzylphosphonates are recorded. Fragmentation patterns are given in detail. The nature of the nuclear substituents is found to be correlated linearly with the process of C—P bond cleavage accompanied by the loss of neutral phosphonate moieties.

Key words: Mass spectrometry; aminobenzylphosphonic esters fragmentation patterns; migratory aptitude.

INTRODUCTION

The mass spectra of aminoalkylphosphonic acid have been studied either by derivatization[1-3] or by chemical ionization (CI).[4] In the investigation of mass spectra of N-trifluoroacetyl 1-aminobenzylphosphonate, Huber[3] observed the C—P bond cleavage with subsequent loss of PO_3Et_2 giving rise to an ion at m/z 202 as the base peak.

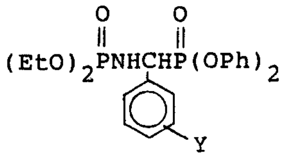
In order to evaluate the substituent effect on the process of C—P bond cleavage, a series of protected 1-amino-substituted benzylphosphonic acids of the general formula **1** and **2** was selected, namely diethyl (**1a–1j**) or diisobutyl (**1k–1n**) 1-N-benzoxycarbonylamino-substituted benzylphosphonates and diphenyl 1-N-(O,O-diethylphosphoryl) amino-substituted benzylphosphonates (**2a–2g**).



1

R=Et, X=4-Me (a); 4-MeO (b); $4\text{-}Me_2N$ (c); $3,4\text{-}(OCH_2O)\text{-}$ (d);
4-F (e); 3-Cl (f); 4-Cl (g); $3\text{-}NO_2$ (h); $4\text{-}NO_2$ (i);
$2,4\text{-}Cl_2$ (j).

R=i-Bu, X=4-MeO (k); $3,4\text{-}(OCH_2O)\text{-}$ (l); $3\text{-}NO_2$ (m); $4\text{-}NO_2$ (n).



2

Y=H (a); 4-Me (b); 4-Me_2N (c); 3-Cl (d); 3-NO_2 (e); 4-NO_2 (f); 2,4-Cl_2 (g).

RESULTS AND DISCUSSION

The mass spectra of the compounds under investigation are listed in Tables I and II.

The mass spectra of these compounds show that the M peak is observed in all cases except **2e**, which gives an discernible M + 1 peak. Apart from **1a** and **1e**, all compounds of type **1** give molecular ions with abundances greater than 6% of that of the base peak. But in the case of **2**, except for **2c** the M or M + 1 peak are less than 4% of that of the base peak which is the fragment resulting from C—P bond cleavage. It indicates that the molecular ions of these compounds are somewhat stable.

The main pathway of the fragmentation of **1** involves the cleavage of C—P bond in competition with debenzylation which is the predominant process in all cases providing the fragment m/z 91 as the base peak (Scheme I).

In contrast with Davidowitz's observation showing the P—N bond cleavage in the mass spectra of phosphoric amido esters,[5] the basic fragmentation process of **2** is only associated with the cleavage of C—P bond in addition to the breakage of P—O and C—O linkage. No P—N bond fission can be found in the mass spectra of compounds **2**. (Scheme II).

In addition to the fragments given in Scheme I, the fragment m/z 109 and 81 are also formed in all compounds of **1a**–**1j** with discernible abundance (Table I). These may be due to the following processes:

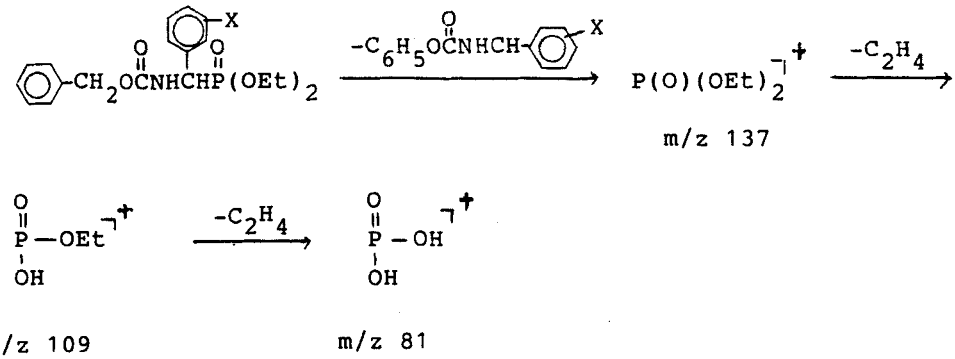


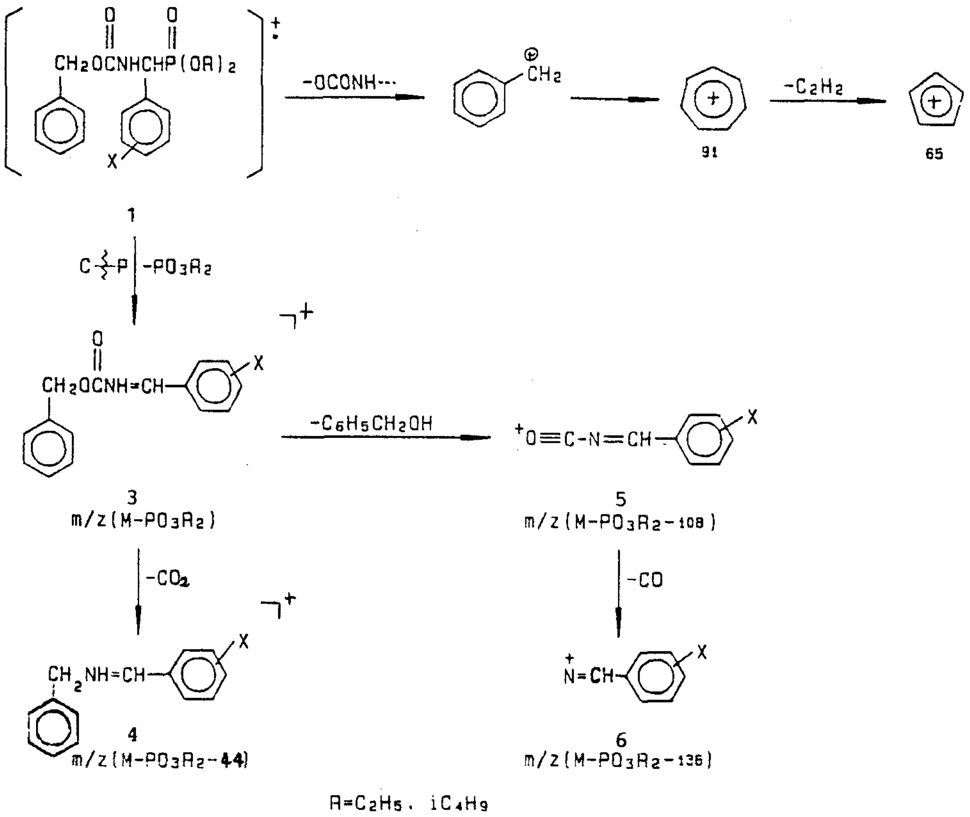
TABLE I
The mass spectra of **1**

		1(M)	3	4	5	6	91	83	81
1	R	m/z(%)	m/z(%)	m/z(%)	m/z(%)	m/z(%)	(%)	(%)	(%)
a	Et	391	254	210	146	118	100	0.00	6.15
		(2.42)	(40.40)	(32.93)	(13.80)	(9.01)			
b	Et	407	270	226	162	134	100	0.00	3.48
		(9.20)	(56.59)	(45.17)	(6.52)	(15.28)			
c	Et	420	283	239	175	147	100	0.00	4.36
		(29.59)	(88.18)	(46.96)	(9.14)	(22.51)			
d	Et	421	284	240	176	148	100	0.00	5.62
		(26.97)	(46.39)	(52.87)	(8.08)	(17.75)			
e	Et	395	258	214	150	122	100	0.00	3.19
		(1.29)	(30.98)	(23.10)	(3.43)	(4.07)			
f	Et	411	274	230	166	138	100	0.00	6.12
		(19.59)	(40.16)	(47.52)	(4.83)	(9.18)			
g	Et	411	274	230	166	138	100	0.00	4.31
		(7.46)	(26.33)	(20.28)	(2.65)	(6.99)			
h	Et	422	285	241	177	149	100	0.00	4.58
		(6.73)	(5.78)	(11.80)	(2.62)	(1.10)			
i	Et	422	285	241	177	149	100	0.00	4.28
		(10.63)	(11.07)	(10.81)	(2.33)	(0.00)			
j	Et	445	308	264	200	172	100	0.00	4.42
		(8.51)	(33.09)	(22.89)	(3.12)	(4.64)			
k	i-Bu	463	270	226	162	134	100	8.89	0.00
		(13,61)	(98.89)	(6.17)	(8.87)	(14.47)			
l	i-Bu	477	284	240	176	148	100	0.00	0.00
		(46.92)	(100.0)	(93.06)	(8.34)	(10.50)			
m	i-Bu	478	285	241	177	149	100	7.86	0.00
		(30.10)	(31.82)	(55.18)	(8.63)	(1.43)			
n	i-Bu	478	285	241	177	149	100	14.28	0.00
		(41.58)	(42.53)	(42.84)	(9.54)	(0.00)			

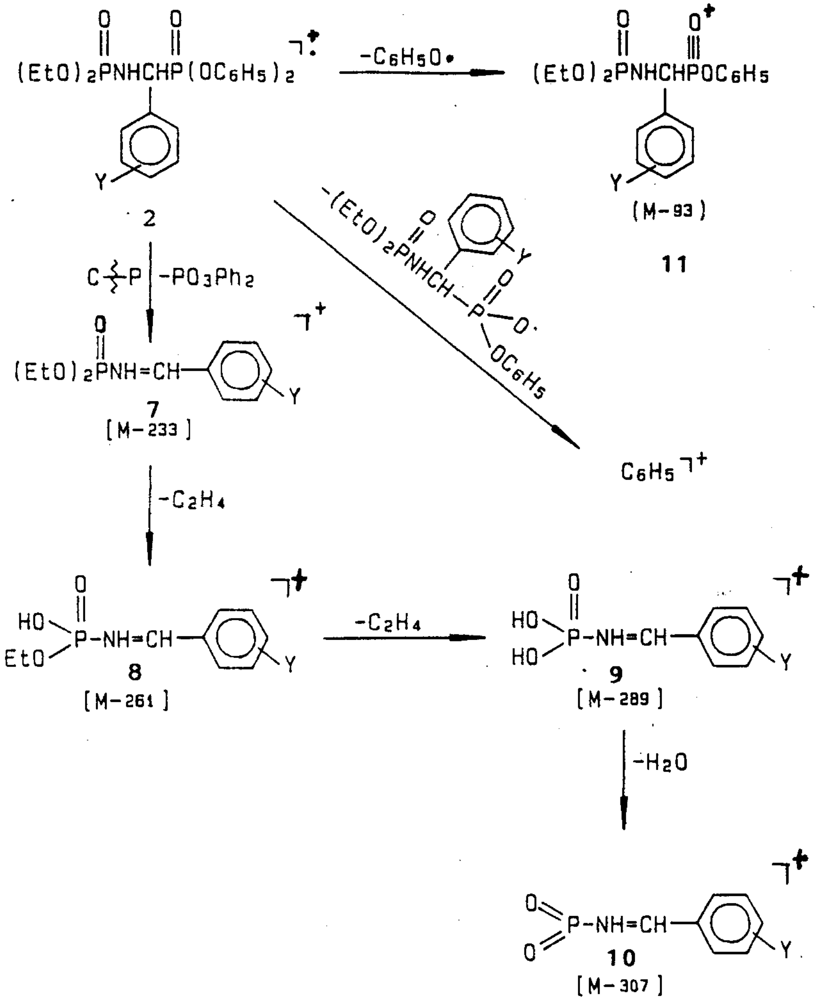
TABLE II
The mass spectra of **2**

2	2(M) m/z(%)	7 m/z(%)	8 m/z(%)	9 m/z(%)	10 m/z(%)	11 m/z(%)	140 (%)	94 (%)	77 (%)
a	475 (1.78)	242 (100)	214 (15.36)	186 (28.09)	168 (7.07)	382 (16.59)	5.63	3.69	7.85
b	489 (3.82)	256 (100)	228 (9.61)	200 (21.05)	182 (5.39)	396 (6.84)	8.14	12.11	8.29
c	518 (12.75)	285 (100)	257 (7.61)	229 (11.14)	211 (5.46)	425 (0.00)	7.39	9.80	6.11
d	509 (2.10)	276 (100)	248 (19.60)	220 (38.37)	202 (10.03)	416 (37.19)	21.31	12.11	13.38
e	521* (0.46)	287 (100)	259 (32.23)	231 (43.43)	213 (4.90)	427 (66.17)	9.95	9.12	12.46
f	520 (0.81)	287 (100)	259 (30.65)	231 (53.81)	213 (6.65)	427 (60.89)	12.11	8.30	12.19
g	543 (0.88)	310 (100)	282 (21.57)	254 (31.87)	236 (8.45)	450 (35.48)	17.69	8.27	12.94

* Corresponding M+1 peak.

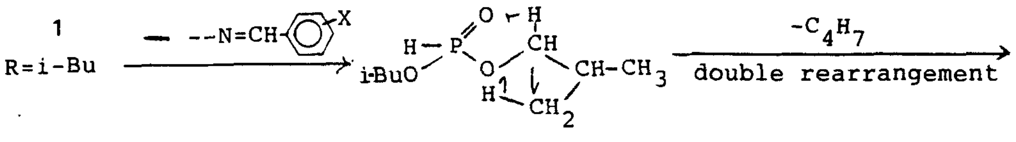


SCHEME I The fragmentation pathway of **1**



SCHEME II The fragmentation pathway of **2**

However, in corresponding diisobutyl ester series (**1k–1n**) instead of fragment m/z 81, a peak at m/z 83 was observed. This could conceivably be rationalized by the following rearrangement:



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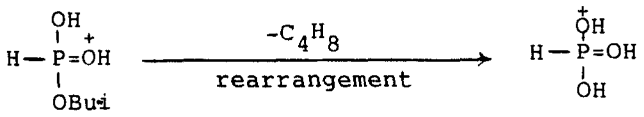
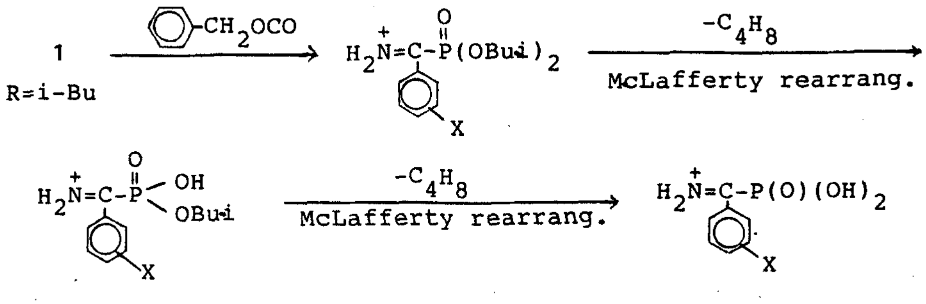


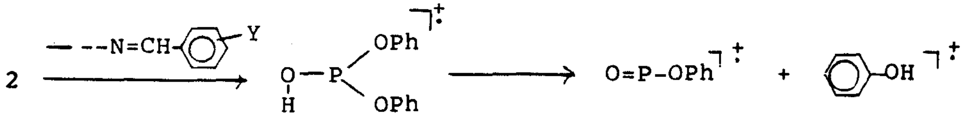
139 83

Another fragmentation pathway of compounds **1** with di-isobutyl ester underwent through two McLafferty rearrangements as shown by the following equations.



M-247

According to the Mass spectra of **2**, besides those mentioned in Scheme II, the appearance of m/z 234, 140 and 94 may be interpreted by the following process.



234 140 94

In order to evaluate the nuclear substituent effects on the process of C—P bond cleavage in **1** and **2**, we found that the electronic effect of the substituent plays an important role in the fragmentation process in Scheme I and II. Since the subsequent loss of neutral moieties from **3** or **7** are very facile reactions, the total abundance of the resultant fragments were taken as a measurement of the efficiency for the C—P bond cleavage of **1** and **2**, respectively. The total values are signed by Za, Zb and Zc for **1a–1j**, **1k–1n** and **2**, respectively.

Za = The total abundance of the fragment m/z [M_1-PO_3Et_2] and the subsequent ones by losing neutral moieties.
Zb = The total abundance of the fragment m/z [M_1-PO_3i-Bu_2] and the subsequent ones.
Zc = The total abundance of **7**, **8**, **9** and **10**.

Because the structure of the compounds discussed are very similar, the value of Za, Zb and Zc should directly relate to the degree of electrons released by the ring substituent to the positively charged nitrogen or oxygen atoms. Thus, log Za, log Zb and log Zc are correlated with substituent constants (σ) according to the following equations:

$$\log Za = 1.96 - 0.69\,\sigma \quad (r = 0.920,\ s = 0.012,\ n = 9)$$
$$\log Zb = 2.24 - 0.34\,\sigma \quad (r = 0.981,\ s = 0.030,\ n = 4)$$
$$\log Zc = 2.16 + 0.15\,\sigma \quad (r = 0.988,\ s = 0.010,\ n = 6)$$

The results are listed in Tables III, IV and V and illustrated in Figs. 1 and 2, respectively.

TABLE III
Log Za and σ values of compounds **1a–1j**[a]

1	σ	Za	log Za	1	σ	Za	log Za
a	-0.12	96.21	1.98	f	0.37	101.87	2.01
b	-0.16	123.28	2.09	g	0.27	56.32	1.75
c	-0.44	166.89	2.22	h	0.71	21.27	1.33
d	-0.16	125.95	2.10	i	0.82	24.24	1.38
e	0.17	61.60	1.79	j		63.82	1.80

[a] σ values were taken from ref. 9 and 10.

TABLE IV
Log Zb and σ values of compounds **1k–1n**[a]

1	σ	Zb	log Zb	1	σ	Zb	log Zb
k	-0.16	178.43	2.25	m	0.71	96.62	1.99
l	-0.16	211.61	2.33	n	0.82	94.80	1.98

[a] σ values were taken from ref. 9 and 10.

TABLE V

Log Zc and σ values of compounds **2a–2g**[a]

2	σ	Zc	log Zc	2	σ	Zc	log Zc
a	0.00	150.52	2.18	e	0.71	180.56	2.26
b	-0.12	136.05	2.13	f	0.82	191.11	2.28
c	-0.44	124.21	2.09	g		161.89	2.21
d	0.37	168.00	2.22				

[a] σ values were taken from ref. 9 and 10.

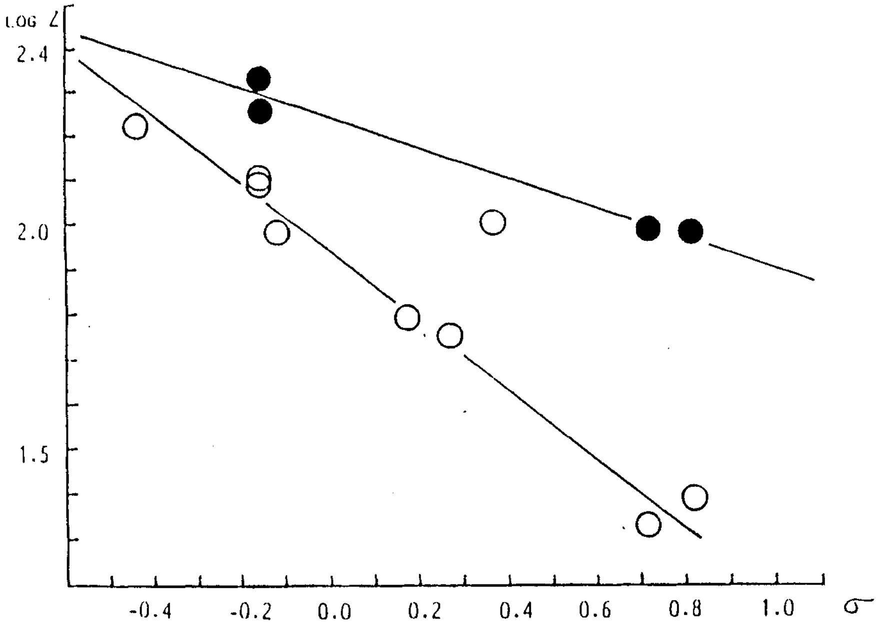


FIGURE 1 Correlation of log Za (○) and log Zb (●) with Hammett σ constants.

From the results shown above, it is obvious that the fragments **3** are comparatively unstable and the neighbouring electron-donating substituent will stabilize this fragment. In the meantime the presence of electron-donating substituent is capable to accelerate the process of C—P bond cleavage of **1**. Being a base peak, the fragment **7** is very stable due to its direct linkage with the positive charged N atom. So the nature of substituent shows no significant effect on fragment **7**. On the other hand, as the increase of the electron-withdrawing ability of the substituent, the formation of fragments **8** and **9** became easier.

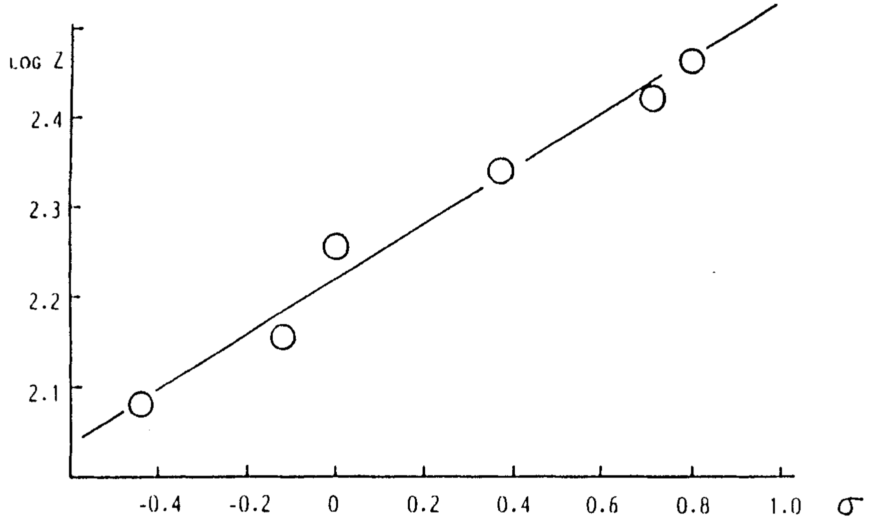


FIGURE 2 Correlation of log Zc with Hammett σ constants.

TABLE VI
Comparison of Z/[M] values of compounds of various ester alkyl group with same ring substituents

R	X			
	$4\text{-}OCH_3$	$3,4\text{-}OCH_2O\text{-}$	$3\text{-}NO_2$	$4\text{-}NO_2$
Et	13.40(**1b**)	4.67(**1d**)	3.16(**1h**)	2.28(**1i**)
i-Bu	13.11(**1k**)	4.51(**1l**)	3.21(**1m**)	2.28(**1n**)

For the evaluation of the effect of ester groups on the C—P bond cleavage, four couples of substrates were selected (see Table VI), in which each couple have the same ring substituent. The values $Z/[M_1]$ ($[M_1]$ is the abundance of the molecular ion of 1) are calculated as a measure of the structural effect of the ester alkyl groups.

Our experimental data reveal that the ester group in **1** has no significant influence on the C—P bond cleavage.

EXPERIMENTAL

Diethyl and diisobutyl 1-N-benzoxycarbonylamino-substituted benzylphosphonates were prepared by an improved method published by us recently.[6] Diphenyl 1-N-(O,O-diethylphosphoryl) amino-substituted benzylphosphonates were synthesized by the methods described by us.[7,8] The Mass spectra were obtained on a Finnigan MAT 8430 Mass Spectrometer, using 70 ev electrons for ionization and a source temperature of 50–350 °C. The samples were introduced via direct inlet.

ACKNOWLEDGEMENT

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