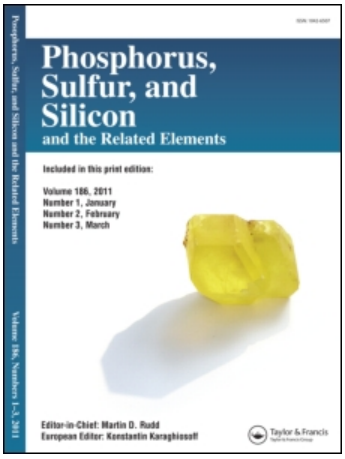

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STUDIES ON ORGANOPHOSPHORUS COMPOUNDS 98. SPECTROSCOPIC INVESTIGATIONS OF 1-SUBSTITUTED 5-TRIFLUOROMETHYL IMIDAZOLE-4-PHOSPHONATE AND 1-SUBSTITUTED-5-TRIFLUOROMETHYL IMIDAZOLE-4-CARBOXYLATE

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Dedicated to my good friend Professor John G. Verkade on the occasion of his sixtieth birthday

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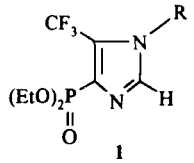
Based on electron impact and high resolution mass spectroscopic data and metastable ions measurements, fragmentation pathways of title compounds are postulated. The investigation of ^{13}C NMR data indicates a highly hindered interannular delocalization over the imidazole and phenyl rings of these compounds. An excellent correlation are found between the logarithm values of ^{31}P NMR chemical shifts and σ parameters of the nuclear substituents on the phenyl ring.

Key words: Mass spectroscopy, metastable ion, ^{13}C NMR, interannular delocalization, ^{31}P NMR, correlation analysis.

INTRODUCTION

We have reported the synthesis of 1-substituted 5-trifluoromethylimidazole-4-phosphonate **1** and 1-substituted 5-trifluoromethylimidazole-4-carboxylate **2** via base-induced cycloaddition of isocyanomethylphosphonate or isocyanoacetate to N-substituted trifluoroacetimidoyl chlorides.[1,2] Herein some interesting spectroscopic properties of these compounds are described.



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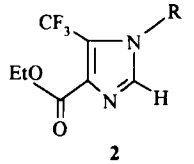


2

Compound	R	Compound	R
1a,2a	C_6H_5	**1e,2e**	p-ClC_6H_4
1b,2b	p-MeC_6H_4	**1f,2f**	p-$NO_2C_6H_4$
1c,2c	o,p-$Me_2C_6H_3$	**1g,2g**	n-C_8H_{17}
1d,2d	p-$MeOC_6H_4$		

RESULTS AND DISCUSSION

1. Mass Spectroscopic Studies[3]

Electron impact mass spectra (EIMS) data of compounds **1** are compiled in Table I. As shown in the table, these compounds exhibit molecular ion peaks and/or M+1 peaks in low intensity and the base peaks are of species at m/z M-109. Another common feature is that fragment ion peaks with m/z M-73, M-136 and M-244 were observed in moderate to high relative abundance. These indicate the existence of a regular fragmentation of compounds **1**. In order to understand the fragmentation behavior of compounds **1** high resolution mass spectroscopy (HRMS) techniques were used and metastable ion measurements were taken. As evidenced by metastable ions, the molecular ion of compound **1a** decomposed to daughter ions at m/z 320, 319, 304, 275, 268, 240 and 239, among them the former three fragment ions were formed respectively with mass losses of ethylene, ethyl and oxyethylene from the ethoxy of the phosphonate moiety. The m/z 275 ion was produced by simultaneous elimination of ethyl and oxyethylene. The m/z 268 ion could be rationalized by rearrangement involving ethyl and ethylene transfer from oxygen atoms to N-3 and C-4 of the imidazole nucleus accompanied with cleavage of the C—P bond and the m/z 240 ion was generated analogously with only ethyl transfer from oxygen to N-3. The m/z 239 ion appeared as the base peak in the EI spectrum and its fused bicyclic structure with formula $C_{12}H_{10}N_2F_3$ was supported by HRMS data (see Table II). The accurate masses and formula of m/z 240 and 239 ions verify rearrangement

TABLE I

The EIMS data of compounds **1**

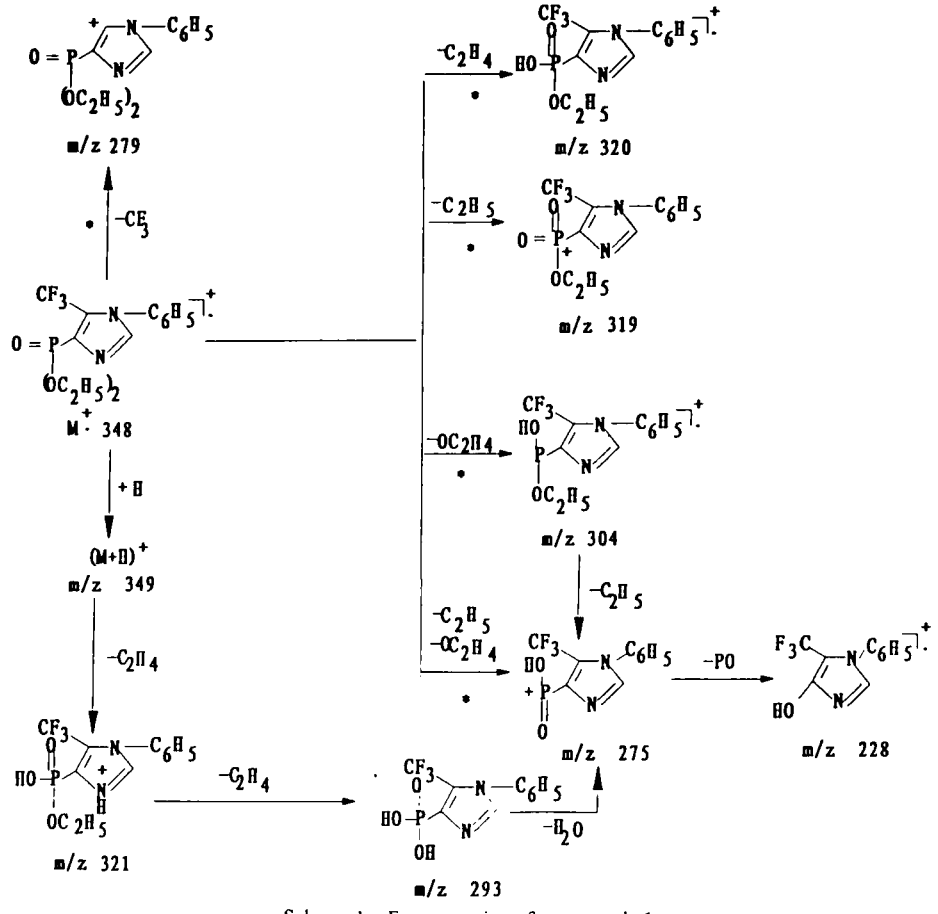
main fragment ions	**1a**	**1b**	**1c**	**1d**	**1e**	**1f**
$[M+1]^+$	349(33.6)[a]	363(20.6)	377(1.2)	379(1.5)	383(5.8)	394(-)
M^+	348(-)	362(2.7)	376(2.1)	378(2.6)	382(2.2)	393(2.9)
$[M+1-2C_2H_4]^+$	293(4.3)	307(2.4)	321(1.6)	323(1.2)	327(5.2)	338(11.1)
$[M-CF_3]^+$	279(5.4)	293(3.4)	307(2.5)	309(1.6)	313(5.4)	324(10.4)
$[M-Et-OC_2H_4]^+$	275(35.7)	289(27.8)	303(21.9)	305(25.2)	309(31.8)	320(27.5)
$[M-HPO_3]^+$	268(6.0)	282(3.3)	296(2.1)	298(1.4)	302(5.9)	313(14.2)
$[M-EtOPO_2]^+$	240(39.8)	254(37.5)	268(36.1)	270(33.4)	274(43.4)	285(43.4)
$[M-EtOPO_2H]^+$	239(100)	253(100)	267(100)	269(100)	273(100)	284(100)
$[M-Et-C_2H_4O-PO]^+$	228(11.2)	242(6.4)	256(3.7)	258(0.9)	262(8.4)	273(16.2)
$[M-EtOPO_2H-HF]^+$	219(4.7)	233(4.2)	247(2.9)	249(3.3)	253(3.3)	264(-)
$[M-(EtO)_2PO+H]^+$	212(67.5)	226(49.9)	240(35.7)	242(37.2)	246(53.3)	257(80.5)
$[HCNR]^+$	104(27.4)	118(22.5)	132(13.5)	134(20.5)	138(29.4)	149(35.6)

[a] *m/z* (relative abundance, %)

TABLE II

HRMS data of compound **1a**

exact mass	mass deviation(mmu)	composition
104.0499	-0.1	C_7H_6N
185.0469	1.7	$C_9H_6NF_3$
212.0599	-0.2	$C_{10}H_7N_2F_3$
239.0792	-0.4	$C_{12}H_{10}N_2F_3$
240.0881	0.7	$C_{12}H_{11}N_2F_3$
275.0203	0.6	$C_{10}H_7N_2O_2PF_3$
348.0865	1.5	$C_{14}H_{16}N_2O_3PF_3$

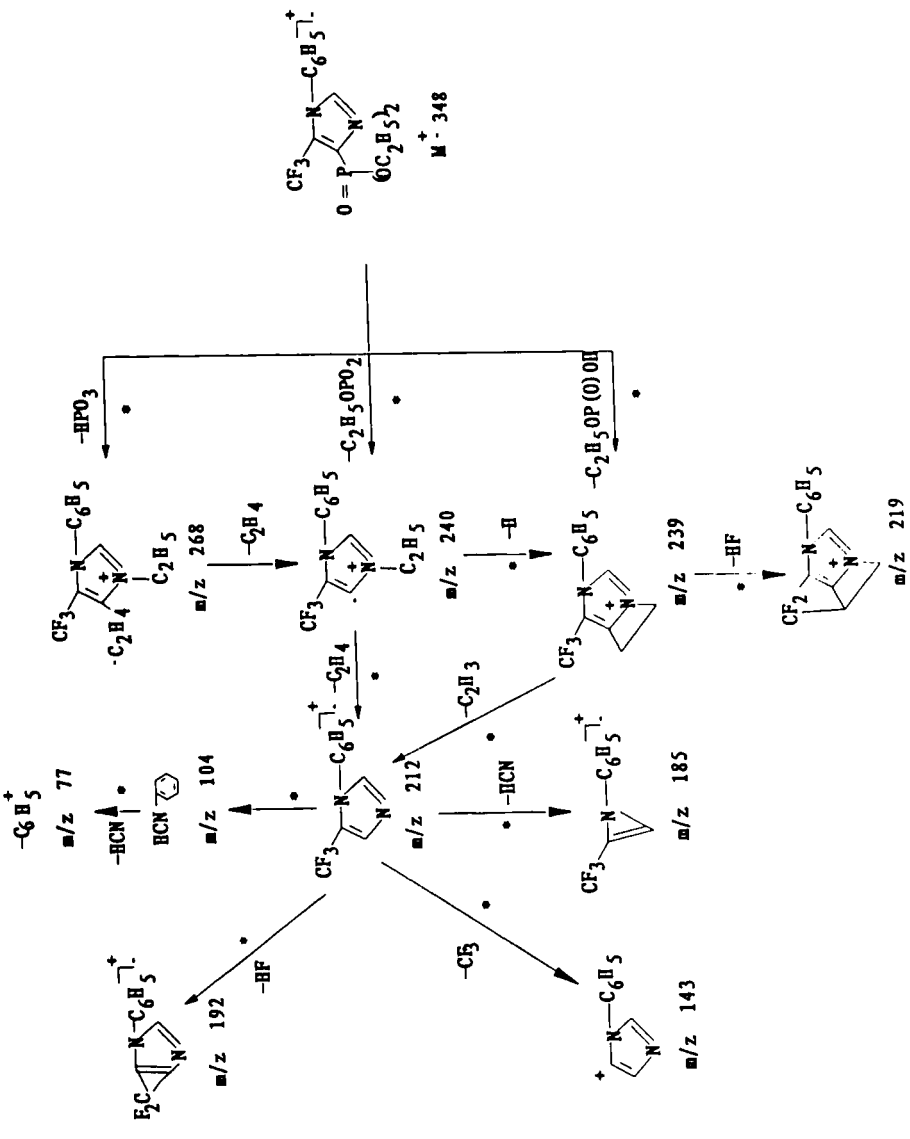


Scheme 1 Fragmentation of compounds 1

of ethyl and cleavage of the C—P bond. The m/z 240 ion derived its daughter ion at m/z 212 by a loss of ethylene. This daughter ion upon imidazole ring-opening forms the fragment ions m/z 104 and 185; their HRMS data confirms the ring-opening. These fragmentation pathways of compounds **1** are summarized in Scheme 1 and Scheme 2.

The EIMS data of compounds **2** are collected in Table III. The molecular ion peaks of these compounds appear in higher intensity than that of compounds **1** and the electron-withdrawing substituents on the phenyl ring decrease the intensity of the molecular ions. The fragmentation pathways are depicted in Scheme 3 and we describe them using compound **2a** as a typical example. Three daughter ions of the molecular ion of **2a** were observed at m/z 256, 240 and 212, among them the ion with m/z 240 lost a hydrogen to form the base peak ion m/z 239. The latter generated six daughter ions, among them the ions at m/z 212 and 184 were produced upon splitting of the imidazole-ring. As shown in Table IV, the elemental composition of these two fragment ions are $C_{10}H_5NOF_3$ and $C_9H_5NF_3$ respectively, which definitely reveal the cleavage of the imidazole nucleus.

In summary, upon electron impact the main fragmentation of compounds **1** and **2** are the partial and gradual cleavage of diethoxyphosphoryl or ethoxycarbonyl located



Scheme 2 Fragmentation of compounds 1

TABLE III

EIMS data of compound **2**

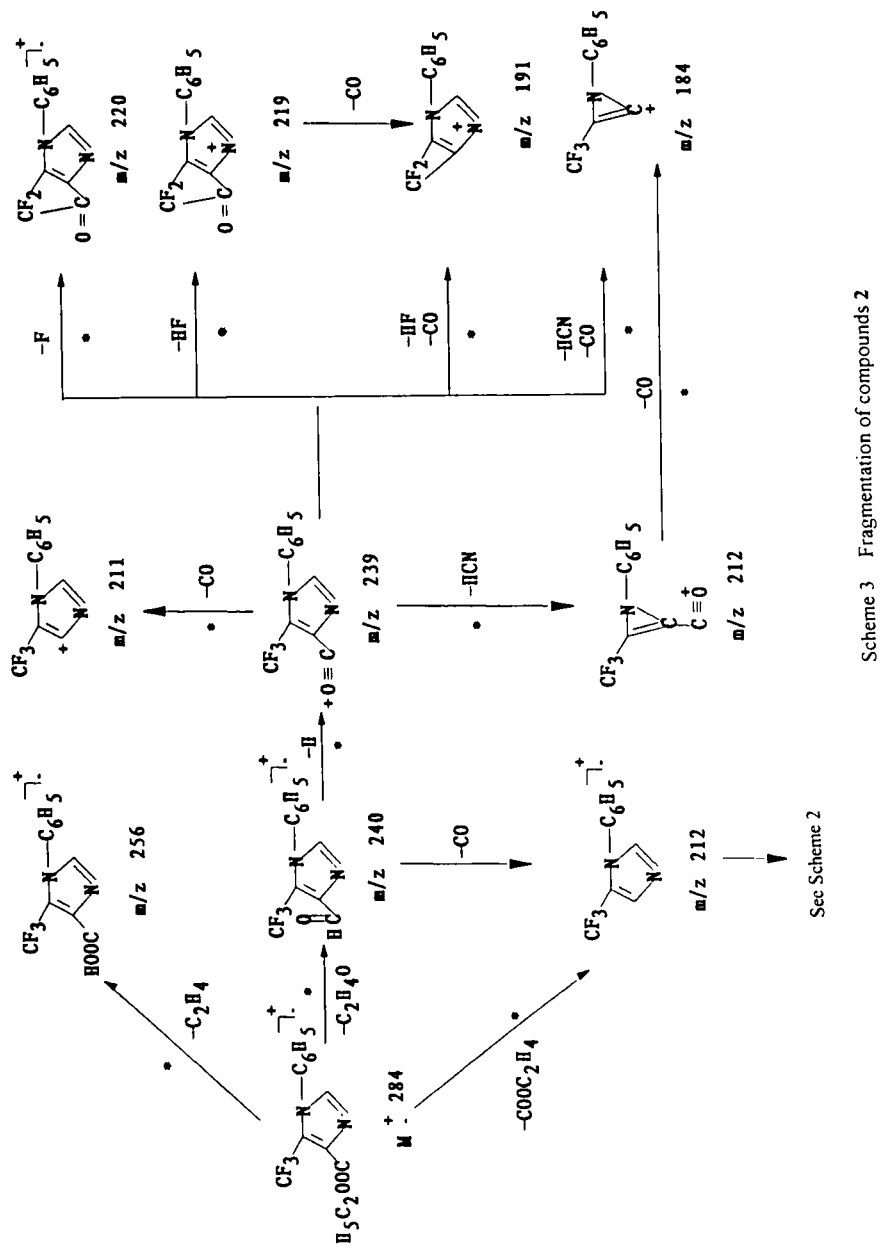
main fragment ions	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**
$[M+1]^+$	285(55.8)	299(23.3)	313(9.9)	315(14.5)	319(2.7)	330(3.4)
M^+	284(11.7)	298(16.0)	312(21.1)	314(32.8)	318(9.9)	329(5.7)
$[M-C_2H_4]^+$	256(1.4)	270(2.8)	284(2.4)	286(2.9)	290(3.2)	301(1.9)
$[M-C_2H_4O]^+$	240(27.2)	254(22.9)	268(15.3)	270(10.9)	274(24.6)	285(31.7)
$[M-EtO]^+$	239(100)	253(89.6)	267(62.9)	269(63.7)	273(90.9)	284(74.0)
$[M-EtO-HF]^+$	219(6.8)	233(11.5)	247(11.2)	249(8.4)	253(6.2)	264(-)
$[M-EtO-HCN]^+$	212(55.6)	226(100)	240(100)	242(100)	246(100)	257(100)
$[M-COOC_2H_4]^+$						
$[M-EtO-HF-CO]^+$	191(9.3)	205(13.0)	219(7.7)	221(5.5)	225(5.8)	236(-)
$[M-EtO-HCN-CO]^+$	184(4.3)	198(3.7)	212(2.6)	214(3.9)	218(4.5)	229(-)
$[HCNR]^+$	104(14.2)	118(26.5)	132(21.0)	134(29.7)	138(30.9)	149(22.5)
R^+	77(21.8)	91(26.8)	105(12.4)	107(5.7)	111(25.4)	122(1.6)

at C-4. The ring-opening of the imidazole nucleus were both observed during their decomposition. However, the rearrangement of ethyl from oxygen to N-3 was only observed in the fragmentation of compounds **1**. It should be noted that although both compound **1a** and **2a** generated the base peak ion at m/z 239 and the fragment ion at m/z 240, the different elemental compositions for each account for the different fragmentation mechanisms of compounds **1** and **2**.

2. *^{13}C NMR Spectroscopic Studies*

1-Arylimidazole, as other N-phenyl-substituted azoles, exhibits electron delocalization over the two rings which tend to be coplanar. The extension of this delocalization and the degree of planarity depend on both the electronic and steric effects of the substituents in the phenyl and imidazole rings. According to Begtrup,[4] the ^{13}C NMR chemical shifts of C-2′ and C-4′ in N-phenylazoles are most affected by steric hindrance to full interannular delocalization, in such a way that the values of $\delta_{C\text{-}2'}$ and $\delta_{C\text{-}3'} - \delta_{C\text{-}2'}$ can be diagnostic of the amount of the hindrance: the delocalization is extensive if $\delta_{C\text{-}2'}$ is ~118–121 and $\delta_{C\text{-}3'} - \delta_{C\text{-}2'}$ ~9.0–10.6 and it is hindered if $\delta_{C\text{-}2'}$ ~124.5–125.5 and $\delta_{C\text{-}3'} - \delta_{C\text{-}2'}$ ~3.3–4.6. Gomez-Sanchez concluded that Begtrup's rule could also be applied to N-phenyl azoles having a substituent attached to the phenyl ring, provided that the electronic effect of the substituent was taken into account.[5] They reported that N-(*p*-substituted)-phenylimidazole-4-carboxylate exhibited full interannular delocalization and introduction of a methyl group at C-2 or C-5, or in both carbons of imidazole increased the hindrance to delocalization. In order to investigate the influence of trifluoromethyl on the planarity of the phenyl and imidazole rings of compounds **1** and **2**, a series of ^{13}C NMR data of these compounds were examined.

Since the ^{13}C NMR spectra of compounds **1** and **2** in the upfield is easy to understand, only the assignments of the downfield signals are described here. For each compound **1**, two doublets(d) were assigned to C-2 and C-4 due to the coupling of phosphorus with carbon. The doublet with greater coupling constant($^1J_{C-P}$) was assigned to C-4, the other to C-2. The carbon of CF_3 was observed as a quartet(q) owing to its coupling with three fluorine atoms and C-5 appeared as a dq signal because of its coupling with phosphorus and fluorine. The assignments of phenyl carbons were based on the following: (1) they appeared as four singlets; (2) the peak



Scheme 3 Fragmentation of compounds 2

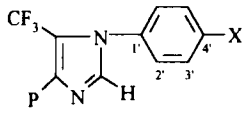
TABLE IV

HRMS data of compound **2a**

exact mass	mass deviation(mmu)	composition
104.0520	2.0	C_7H_6N
184.0405	3.1	$C_9H_5NF_3$
191.0468	4.7	$C_{10}H_5N_2F_2$
211.0516	3.3	$C_{10}H_6N_2F_3$
212.0516	2.0	$C_{10}H_5NOF_3$
239.0432	0.0	$C_{11}H_6N_2OF_3$
240.0560	5.0	$C_{11}H_7N_2OF_3$
284.0785	1.2	$C_{13}H_{11}N_2O_2F_3$

TABLE V

^{13}C NMR chemical shifts of compounds **1** and **2** (downfield section)



P=$(EtO)_2P(O)$- (**1**); EtOC(O)- (**2**).

compound	C-2	C-4	C-5	CF_3	C-1'	C-2'	C-3'	C-4'
1a	141.1	134.2	127.6	119.7	134.7	126.4	130.2	129.6
1d	141.4	133.9	127.3	119.7	127.2	127.7	114.7	160.8
1f	140.9	135.5	127.1	119.6	139.7	127.6	125.1	148.7
1g	140.3	133.2	125.4	119.7				
2a	140.0	135.3	124.6	119.8	135.2	126.3	130.2	129.6
2d	140.3	135.0	124.7	119.8	127.7	127.5	114.7	160.9
2f	139.4	136.3	124.9	119.5	140.0	127.4	125.1	148.6
2g	139.7	135.2	123.2	120.4				

TABLE VI

Incremental shifts of the phenyl carbon atoms caused by *para*-substituents X

X	C-1'	C-2'	C-3'	C-4'
OMe	-7.7	1.0	-14.4	31.4
NO_2	6.0	0.9	-5.3	19.6

heights and widths of C-2′ and C-3′ signals are greater than that of C-1′ and C-4′ because both C-2′ and C-3′ represent two tertiary carbons respectively; (3) incremental shifts caused by *para*-substituents.

The two quartets in ^{13}C NMR spectra of every compound **2** are assigned to C-5 and the carbon of CF_3; and C-5 has a smaller coupling constant($^2J_{C-F}$). The two singlets are assigned to C-2 and C-4; C-2 resonates more downfield than C-4 as a consequence of lower π-electron density of C-2.[6] Another difference is that C-2 has a greater peak height than C-4 since C-2 attaches to a proton. The C-2 and C-4

TABLE VII

"Corrected" ^{13}C NMR chemical shifts of compounds **1** and **2**

compound	X	C-1'	C-2'	C-3'	C-4'	$\delta_{C-3'} - \delta_{C-2'}$
1a	H	134.7	126.4	130.2	129.6	3.8
1d	OMe	134.9	126.7	129.1	129.4	2.4
1f	NO_2	133.7	126.7	130.4	129.1	3.7
2a	H	135.2	126.3	130.2	129.6	3.9
2d	OMe	135.4	126.5	129.1	129.5	2.6
2f	NO_2	134.0	126.5	130.4	129.0	3.9

TABLE VIII

Correlation analysis of ^{31}P NMR chemical shifts of compounds **1**

substituent	4'-MeO	3',4'-Me_2	Me	H	4'-Cl	4'-NO_2
δ	8.1315	8.1392	8.1178	7.9884	7.6421	7.1055
logδ	0.9102	0.9106	0.9094	0.9024	0.8832	0.8516
σ	-0.27	-0.23	-0.17	0	0.23	0.78

$\log\delta = -0.0584\sigma + 0.898$ (n = 6, r = 0.993, s = 0.0553, CL > 99.9%)

signals are distinguished from phenyl carbon signals by comparison with the data of compound **2g**. The assignments of the remaining four singlets of the phenyl carbons is analogous to that of compounds **1**. Table V summarizes the results of the above assignments.

The evaluation of interannular delocalization over the imidazole and phenyl rings using Begtrup's rule requires elimination of the contribution of the *para*-substituent X to the chemical shifts of the phenyl carbons. Table VI lists the incremental shifts caused by the methoxyl and nitro groups.[7] Thus, a set of "corrected" ^{13}C NMR chemical shifts was obtained upon consideration of the incremental shifts, shown in Table VII.

As shown in Table VII, the value of $\delta_{C-3'} - \delta_{C-2'}$ varies from 2.4 to 3.9. This means the interannular delocalization over the phenyl and imidazole rings of compounds **1** and **2** is highly hindered due to the steric effect of the trifluoromethyl group attached to C-5 of the imidazole ring.

3. ^{31}P NMR Spectroscopic Studies

Although the ^{13}C NMR spectra data indicate no apparent delocalization exists over the imidazole and phenyl rings of 1-substituted 5-trifluoromethylimidazole-4-phosphonates **1**, the substituents of the phenyl ring influences markedly the ^{31}P NMR chemical shifts. Regression analysis indicates that the logarithm value of the ^{31}P NMR chemical shifts correlate linearly with the σ parameters[8] of the nuclear substituents with an excellent correlation coefficient (r) and standard deviation of the estimate (s). The calculated F value is 290.62, much greater than $F_{0.001}(1,4)$, 74.14. Thus, the confidence level (CL) is greater than 99.9%. As shown in Table VIII and Figure 1, electron-withdrawing substituents resonate the ^{31}P nucleus upfield, which is inconsistent with the theory of ^{1}H and ^{13}C NMR and needs further investigation.

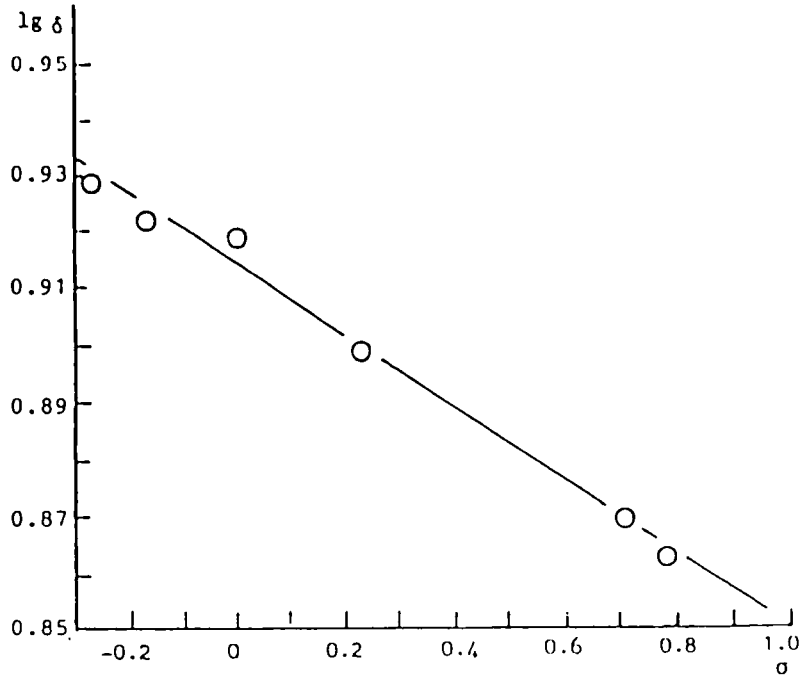


FIGURE 1 Plot ^{31}P NMR chemical shifts versus σ constant in compounds **1**.

EXPERIMENTAL

The low resolution EI mass spectra were obtained with HP 5989A mass spectrometer operating at 70 eV with an ion source temperature of 300°C. Samples were introduced by means of a direct insertion probe with temperature between 50 and 300°C. High resolution mass spectra were recorded on a Finnigan MAT 8430 mass spectrometer at 70 eV with a resolution of 8000; the ion source temperature was 150°C and the temperature for the direct insertion probe varied from 50 to 300°C. Metastable ions measurements were taken on a Finnigan MAT 95 high resolution mass spectrometer. Proton-decoupled ^{13}C and ^{31}P NMR spectra were recorded on a Bruker AM-300 spectrometer in $CDCl_3$. Chemical shifts were reported in ppm downfield from Me_4Si for ^{13}C NMR spectra and 85% H_3PO_4 for ^{31}P NMR spectra.

ACKNOWLEDGEMENT

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REFERENCES AND NOTES

1. W. S. Huang, C. Y. Yuan and Z. Q. Wang, *J. Fluorine Chem.*, **74,** 279 (1995).
2. W. S. Huang and C. Y. Yuan, *Synthesis*, in press (1996).
3. Metastable ions and HRMS measurements were done by Prof. Gui-Xiang Fu of this Institute. Many thanks due to her valuable discussion about the fragmentation mechanisms.
4. M. Begtrup, *Acta Chem. Scand.*, **27,** 3101 (1973) and references cited therein.
5. A. Gomez-Sanchez, F. J. Hidalgo and J. L. Chiara, *J. Heterocyclic Chem.*, **24,** 1757 (1987).
6. M. R. Grimmett, in "Comprehensive Heterocyclic Chemistry," A. R. Katritzky and C. W. Rees, (eds.), Pergamon Press Ltd., 1984, Vol. 5, pp. 354.
7. D. E. Ewing, *Org. Magn. Reson.*, **12,** 499 (1979).
8. C. Hansch, A. Leo, S. Unger, K. H. Kim, D. Nikaitani and E. J. Liem, *J. Med. Chem.*, **16,** 1207 (1973).