CROATICA CHEMICA ACTA CCACAA **49** (3) 415—424 (1977)

YU ISSN 0011-1643
CCA-1013 547.7
Original Scientific Paper

A Mass Spectral Study of Substituent Effects in Some Substituted *N*,*N*-Dimethyl-*N*′-Phenyl- and *N*′-Pyridyl-Formamidines

*M. Medved, S. Stavber, V. Kramer, L. Benčić, and J. Marsel**

J. Stefan Institute, University of Ljubljana, Yugoslavia
*and *Faculty for Natural Sciences and Technology, Department of Chemistry,*
University of Ljubljana, 61000 Ljubljana, Slovenia, Yugoslavia

Received August 30, 1976

Several competing fragmentation reactions, initiating directly from the molecular ion, which are common to *p*- and *m*- substituted *N*,*N*-dimethyl-*N*′- phenyl-formamidine, were examined. IP, AP and daughter/parent ion ratio measurements were made to provide some insight into the substituent effects on reaction mechanisms. The results obtained were compared with those found for the compounds *N*,*N*-dimethyl-*N*′-pyridyl-4-formamidine and isomeric 3-formamidine. The substituent constant σ_p^+ for the nitrogen in the pyridine ring was determined.

INTRODUCTION

A considerable number of attempts have been made to study substituent effects by means of mass spectrometry since the initial suggestion of the simplified steady-state kinetic approach was given[1]. Mass spectral studies of meta and para substituted benzene derivatives show in many instances a clear correlation between the relative ionic abundance of the daughter ion and the Hammet constant for the substituent[2]. The steady-state kinetic approach was to equate $\log Z/Z_0$ with k/k_0, where k is the rate constant for the reaction $M^{+\cdot} \rightarrow A^+$, and Z the relative abundance of ion A^+, i. e. ($[A^+]/[M^{+\cdot}]$). Thus the basic equation (1) becomes

$$\log Z/Z_0 = \varrho\sigma \tag{1}$$

It has been shown over the last few years that this kinetic approach can rarely give reliable enough information about the structure and the reaction mechanisms. Attention has been drawn to many complex defects which can influence the ratio Z/Z_0[3–5]. Briefly stated, the introduction of a substituent may considerably affect the internal energy distribution of molecular ion, and further, the substituent may influence the secondary fragmentation reactions. For this reason, ionization (*IP*) and appearance potential (*AP*) measurements[6,7], low electron voltage spectra[8] and metastable ion studies[9] are now frequently employed in substituent effect studies, in order to extract mechanistic information.

---

* To whom correspondence should be addressed

The activation energies obtained from *AP* — *IP* measurements may provide a more reliable and practical kinetic measure of the substituent effect on the reaction rate in spite of the approximation due to the kinetic shifts, to excess energy problems,[4] and to experimental errors in the determination of *IP* and *AP*. The relationship between the rate constant and activation energy (eq 2) can be derived from Hammett's equation[10] (eq 3) and from the simplified QET equation[4] assuming equal frequency factors and an equal number of effective oscillators in the decomposing ion.

$$\log k/k_o = \left(\frac{S-1}{E}\right)(E_a^{\,o} - E_a) \tag{2}$$

$$\log k/k_o = \varrho\sigma \tag{3}$$

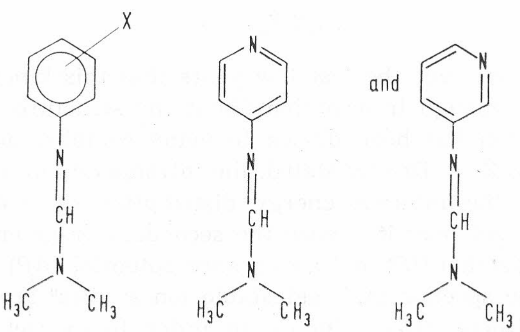
$$k(E) = \nu\left(\frac{E - E_a}{E}\right)^{S-1} \tag{4}$$

A linear correlation of (*AP* — *IP*) with σ or σ^+ is not demanded for every reaction, but in several more complex aromatic systems it is possible to draw conclusions as to whether a fragment ion arises by simple cleavage or through a rearrangement prior to, or during, the fragmentation reaction. An interesting system for studying substituent effects on decomposition behaviour is *N,N*-dimethyl-*N'*-phenyl-formamidine (I). Its fragmentation as well as the effects of some substituents on the loss of hydrogen or halogen from the molecular ion have been studied[11]. This prompted us to report our observations on para and meta substituted formamidines together with the σ^+ constant for *N,N*-dimethyl-*N'*-pyridyl-4-formamidine (II) and for its isomeric 3-formamidine (III), by correlating (*AP* — *IP*) differences and log Z/Z_0 vs. substituent constant σ^+.

RESULTS AND DISCUSSION

IP, *AP* and (*AP* — *IP*) values in eV for the reactions $M^{+\cdot} \rightarrow (M-H)^+$, $M^{+\cdot} \rightarrow (M-CH_3)^+$ and $M^{+\cdot} \rightarrow (M-N(CH_3)_2)^+$ of para and meta substituted compounds I—III are given in Table I. The blanks in the Table indicate that for the relevant ions it was impossible to determine the appearance potentials because of the extremely low signal to noise ratio at the threshold.

I II III



X(m,p) = H, CH_3, OCH_3, CF_3, F, NO_2, and X = p-CO_2CH_3

$M^{+\cdot} \rightarrow (M - H)^+$: A previous labelling study by Grützmacher[11] showed that molecular ions of substituted *N,N*-dimethyl-*N'*-phenyl-formamidine lose hydrogen from the *ortho* position in the reaction $M^{+\cdot} \rightarrow (M - H)^+$. An electrophilic aromatic substitution mechanism was suggested for these compounds and, by analogy, also for their halogen o-substituted derivatives. The same conclusion was also drawn for formanilide, thioformanilide as well for their *o*-chloro derivatives. This conclusion was drawn from the relative intensity measurements (Z/Z_0), as well as using *IP* and *AP* data, i. e., differences between the ionization and appearance potentials of substituted and unsubstituted compounds. The results reported show much smaller dependence of the *IP* of M^+ and *AP* of the $(M - H)^+$ ions on substitution at the phenyl ring then data presented in this work (Table I). The diferences could be explained in terms of techniques used for the measurements.

TABLE I

IP, AP *and Approximate Activation Energy* (E_a) *Values for Reactions* $M^{+\cdot}$, $M^{+\cdot}$*—H*, $M^{+\cdot}$*—*CH_3 *and* $M^{+\cdot}$*—*$N(CH_3)_2$ *in Compounds I—III*

	$M^{+\cdot}$	$(M-1)^+$		$(M-15)^+$		$(M-44)^+$	
X	*IP*	*AP*	E_a	*AP*	E_a	*AP*	E_a
H	8.5	10.7	2.2	10.6	2.1	13.5	5.0
p-CH_3	7.7	10.0	2.3	10.0	2.3	11.9	4.2
m-CH_3	7.9	9.8	1.9	10.4	2.5		
p-OCH_3	6.5			8.7	2.2	10.4	3.9
m-OCH_3	8.3	10.3	2.0	10.0	1.7		
p-Cl	8.9	11.0	2.1	11.3	2.4	13.4	4.5
m-Cl	8.4	10.1	1.7	10.5	2.1		
p-CF_3	8.3	10.1	1.8	10.5	2.2	14.2	5.9
m-CF_3	10.1	11.6	1.5	12.5	2.4		
p-F	8.4	10.6	2.2	10.4	2.0	12.5	4.1
m-F	10.0	11.8	1.8	11.4	1.4		
p-NO_2	8.5	10.2	1.7	11.0	2.5		
m-NO_2	7.5	9.0	1.5	8.9	1.4		
p-$COOCH_3$	10.3	12.0	1.7	12.8	2.5		
II	8.2	9.2	1.0	10.4	2.2	12.5	4.3
III	8.7	9.3	0.6	10.5	1.8		

In Figure 1, the correlation curve *IP* vs. σ_p^+ for para substituted compounds shows fair linearity, but for CF_3 and NO_2 groups the ionization potentials are lower than would be expected. A similar break in the correlation curve at *para* — CF_3 and NO_2-substituted compounds can be observed by plotting the appearance potentials of $(M - H)^+$ ions versus σ_p^+. The data *IP* vs. σ_m^+ for meta substituents show more scattering than for para isomers; the ionization potential of the nitro compound is extremely low and the *IP* of the chloro substituted compound is very similar to that of the methoxy compound. In contradistinction, the curves (*AP* — *IP*) vs. σ^+ show a satisfactory linearity for both para and meta substituted compounds (Figure 2). These observations indicate a different ionization process for the molecules substituted with strongly electron withdrawing groups compared to the others.

The (*AP* — *IP*) values for the loss of a hydrogen atom from the molecular ions, when plotted versus corresponding substituent constants, exhibit a negative slope for both *p*- and *m*-substituted isomers. The slope of the correlation curve

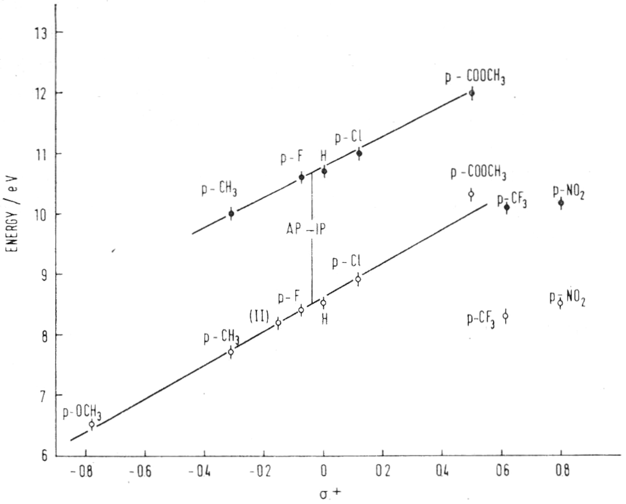


Figure 1. *IP* of p-substituted *N,N*-dimethyl-*N'*-phenyl-formamidines (○) and AP for the formation of the (M—1)$^+$ ion (●) plotted vs σ_p^+. Slopes are + 2.91 for *IP* vs. σ_p^+ and + 2.53 for AP vs. σ_p. II means IP of pyridiyl-formamidine.

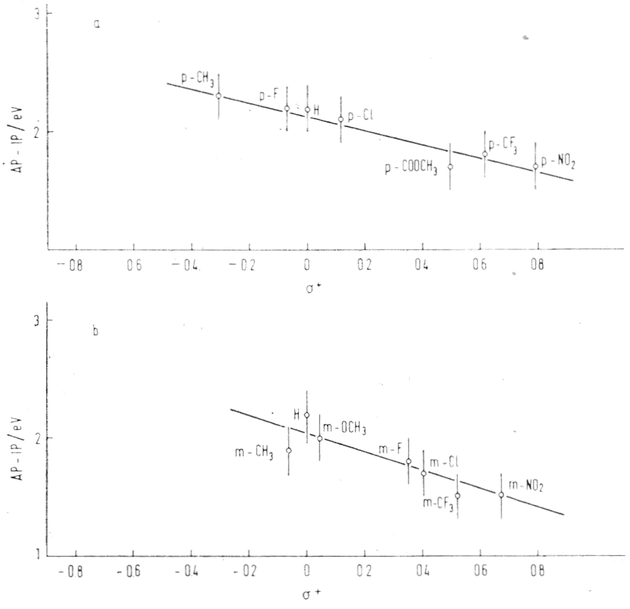


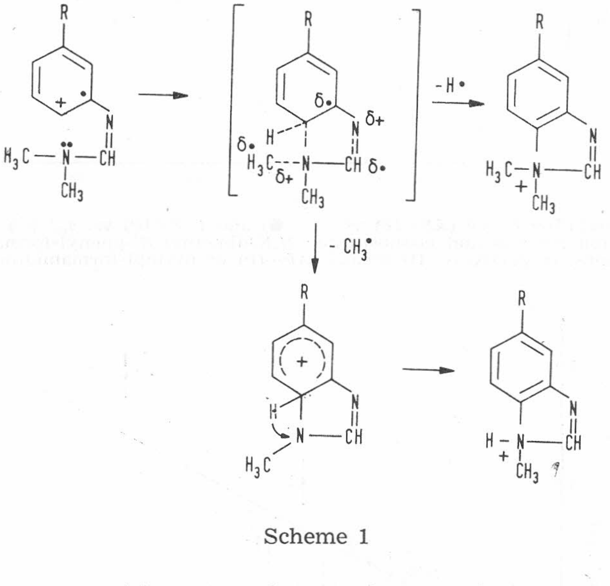
Figure 2. a) The correlation curve (*AP—IP*) vs. σ_p^+ for the formation of the (M—1)$^+$ ion from *p*-substituted. *N,N*-dimethyl-*N'*-phenyl-formamidine molecular ions. Slope is — **0.64.**

b) The correlation curve (*AP—IP*) vs. σ_m^+ for the formation of the (M—1)$^+$ ion from *m*-substituted *N,N*-dimethyl-*N'*-phenyl-formamidine molecular ions. Slope is — **0.80.**

for meta substituted compounds is slightly more negative (— 0.80) than for para compounds (—0.64). It is noteworthy that the approximate activation energy for the reaction $M^{+\cdot}$ — H has higher values for the para than for meta substituted compounds.

Assuming the ionization of the ring electrons[12] and the localization of the charge-radical site in the benzene ring of the *p*-substituted compounds, only the inductive effect has an influence on the *o*-position, lowering the electron density. The positive charge located at the *o*-position promotes a nucleophilic attack by the electron lone-pair located on the dimethylamino group forming a bicyclic transition state. The unpaired electron density located in the ring can reduce the energy requirement for hydrogen expulsion from the transition state[13]. Nucleophilic attack seems to be the driving force for the reaction of hydrogen loss.

A similar reaction mechanism is probably operating in *m*-substituted compounds. Electron-donating groups lessen the charge localization at *ortho* and *para* positions. Electron withdrawing groups make these sites more positive than in the case of *p*-substituted compounds, i. e. they enable the easier formation of the transition state, lowering the activation energy for the complete reaction (Scheme 1). Besides this, in the case of *m*-substituted compounds, the influence of a substituent on the electron lone-pair of the dimethylamino group is small.



Scheme 1

The more pronounced lowering of approximate activation energy (*AP* — *IP*) with increasing electron demand by the substituent in the *m*-substituted compounds compared to that in *p*-substituted compounds can be explained as a plausible concerted reaction mechanism, i. e., nucleophilic attack of the electron lone-pair of the dimethylamino group to the ortho site followed by hydrogen loss.

$M^{+\cdot} \rightarrow (M - CH_3)^+$: The slope (— 0.77) of the correlation curve (*AP* — *IP*) vs. σ_m^+ is similar to that observed for the reaction $M^+ \rightarrow (M - 1)^+$ in *m*-substituted compounds (Figure 3), indicating a similar reaction mechanism for both reactions. It seems that methyl group and hydrogen expulsion take place in a competitive fragmentation reaction, i. e., from a common transition state leading to the bicyclic product ion (Scheme 1). The last stabilization step to form the product ion might occur by hydrogen rearrangement.

The correlation curve (*AP* — *IP*) vs σ_p^+ for the loss of a methyl group from the *p*-substituted molecular ions (Figure 3) exhibits a weak increase of approximate activation energy with electron withdrawing substituents (slope = = + 0.18). We are probably dealing with a simple cleavage reaction without the formation of the cyclic transition state if the charge at the reaction site increases. We suppose that here the positive charge is initially located on the nitrogen of the dimethylamino group.

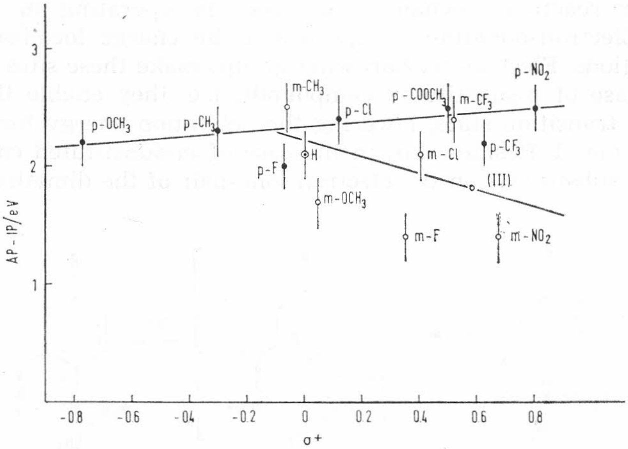


Figure 3. The correlation curve (*AP—IP*) vs. σ_p^+ (●) and (*AP—IP*) vs. σ_m^+ (○) for the formation of the $(M—CH_3)^+$ ion from *p*- and *m*-substituted *N,N*-dimethyl-*N'*-phenyl-formamidine molecular ions, respectively. III means (*AP—IP*) of pyridyl-formamidine.

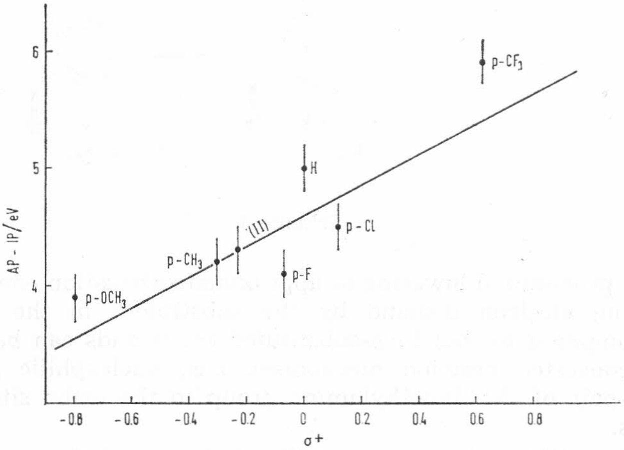
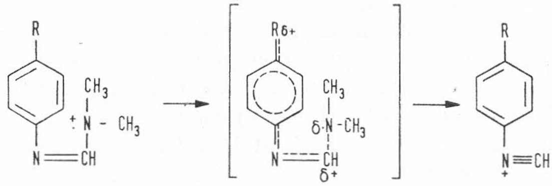


Figure 4. The correlation curve (*AP—IP*) vs. σ_p^+ for the formation of the $(M—N(CH_3)_2)^+$ ion from the *p*-substituted *N,N*-dimethyl-*N'*-phenyl-formamidine molecular ion. II means (*AP—IP*) of pyridylformamidine.

$M^+ \rightarrow (M - N(CH_3)_2^+$: The loss of the dimethylamino radical from the molecular ion of *p*-substituted compounds occurs most likely by simple cleavage. In the transition state the substituents can have a direct influence on the positive charge developed at the reaction site. Therefore, the activation energy increases with increasing electron demand (Figure 4). After the loss of the dimethylamino group, the positive charge located on the —N≡CH group of the product ion (Scheme 2) is stabilized more effectively by an electron-donating group, because it increases the electron density, particularly at the *ortho* and *para* positions.



Scheme 2

The Nitrogen Effect on Reaction Mechanisms in N*-Pyridyl-Formamidineh*

It is known from solution chemistry[14] that the nitrogen atom in the pyridine ring causes a similar effect on reactivity to that of the NO_2 group in nitrobenzene in terms of nucleophilic and electrophilic substitution reactions. To examine the influence of the pyridine nitrogen on the decomposition rate of molecular ions in order to determine its approximate σ^+ constant, the ionization potential and approximate activation energy, have been measured for *N,N*-dimethyl-N'-pyridyl-4-formamidine (II) and for its isomer 3-formamidine (III). The results on 4-formamidine reported in Table II were obtained from the correlation curves of *IP, AP* and *(AP — IP)* vs. σ_p^+ para substituted compounds.

TABLE II

	Reaction	σ_p^+ (pyridine nitrogen)
IP vs. σ_p^+	$M + e \rightarrow M^{+\cdot} + 2e$	—0.16
AP vs. σ_p^+	$M^{+\cdot} \rightarrow [M - CH_3]^+$	—0.18
AP vs. σ_p^+	$M^{+\cdot} \rightarrow [M - N(CH_3)_2]^+$	—0.16
AP — IP vs. σ_p^+	$M^{+\cdot} \rightarrow [M - N(CH_3)_2]^+$	—0.22

σ_p^+ pyridine nitrogen = —0.18 ± 0.03

When ionization and/or appearance potentials are plotted versus σ_m^+ for meta substituted compounds, the data show so much scatter that no correlation curve can be drawn. The only σ_m^+ value for the pyridine nitrogen could be obtained from the correlation curve (*AP — IP*) vs. σ_m^+ for the loss of a methyl radical from the meta substituted molecular ions (see Figure 3); therefore the reliability of the substituent constant ($\sigma_m^+ = + 0.59$) is still open to question.

Substituent Effects on Ion Relative Intensities

Some variation of log Z/Z_0 with σ^+ in the mass spectra of *p*- and *m*-substituted compounds are represented in Figures 5 and 6 for 18 eV and 13 eV, respectively. From these plots it is noticeable that only reaction $M^+ \rightarrow (M - 1)^+$ correlates reasonably with σ^+ values. However, there a certain scattering of data is also present. Particularly, the value for *p*-NO_2 fails at all electron energies, similarly to the result found on plotting *IP* vs. σ_p^+ (Figure 1). The slope of the correlation curve is positive and the substituent effects on log Z/Z_0 would suggest that reaction $M^{+\cdot} \rightarrow (M - H)^+$ is enhanced by electron withdrawing substituents, in agreement with (*AP* — *IP*) measurements. On the other hand, a satisfactory correlation is found for the loss of hydrogen in meta substituted compounds, but the negative slope indicates that this reaction should be enhanced by electron donating substituents. This is opposite to the conclusion reached from the corresponding (*AP* — *IP*) measurements.

Comparing the values 1 + log Z/Z_0 at 18 eV electron energy for *N*,*N*-dimethyl-*N*'-pyridyl-4-formamidine (1.19) and for its 3-isomer (1.21) with the plots in Figure 5, it becomes apparent that no coincidence exists, which is similar to the behaviour observed for the *AP* and (*AP* — *IP*) measurements for the corresponding reaction. The ratios Z/Z_0 for the formation of the $(M - H)^+$ ion for both compounds are unexpectedly high, but in agrement with the extremely low activation energy (see Table I).

The correlation curve for the formation of $(M—N(CH_3)_2^+$ for the p-substituted compounds (Figure 6) shows two slopes, having the highest Z/Z_0 ratio for the unsubstituted compound. This anomalous behaviour is not surprising since the more the substituent is electron withdrawing, the more it favours charge stabilization on the side chain, reducing to a considerable extent the production of the $(M—N(CH_3)_2)^+$ ions (see Scheme 2). The correlation curve is only in partial agreement with that from the (*AP* — *IP*) measurements for the same reaction.

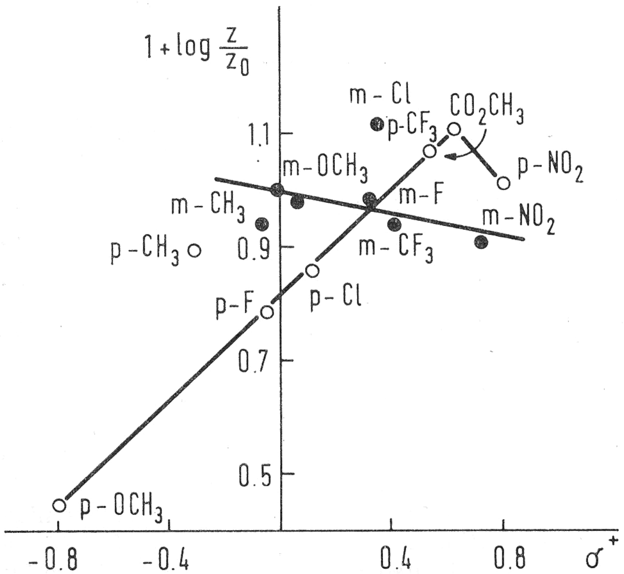


Figure 5. 1 + log Z/Z_0 vs. σ^+ for the formation of the $(M—H)^+$ ion from the *m*- and *p*-substituted *N*,*N*-dimethyl-*N*'-phenyl-formamidine molecular ion at 18 eV.

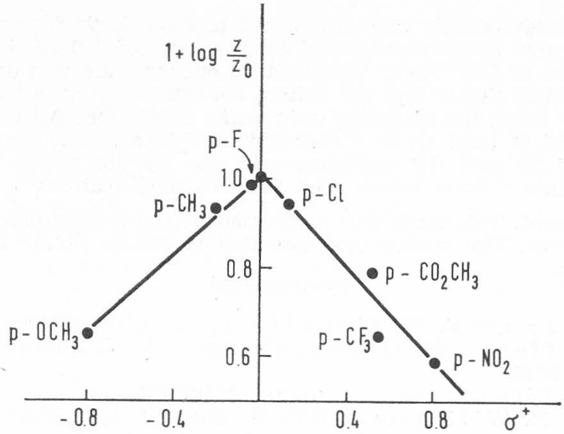


Figure 6. 1 + log Z/Z_0 vs. σ^+ for the formation of the $(M—N(CH_3)_2)^+$ ion from the *p*-substituted *N,N*-dimethyl-*N'*-phenyl-formamidine molecular ion at 13 eV.

For all other measurements, 1 + log Z/Z_0 values plotted versus σ^+ showed considerable scattering and it was not possible to determine the slope of the corelation curves reliably.

CONCLUSIONS

The correlations of approximate activation energy with substituent constants were found to be better than the corresponding correlations of daughter/parent ion ratios vs. σ^+, where considerable scattering of data was observed in most cases. Although in some cases, using both methods, satisfactory correlation curves are obtained, the mechanistic interpretation of the results derived from these slopes can be either in contradiction or in agreement. Our results agree with previous observations.[6,7] The interpretation of the negative slope of the correlation curve ($AP — IP$) vs. σ_p^+ for the reaction of *p*-substituted compounds $M^+ \rightarrow (M —1)^+$ and that of the positive slope found for 1 — log Z/Z_0 plotted vs. σ_p^+ agree, but they disagree with the corresponding measurements for *m*-substituted isomers. Also, for the loss of the dimethyl-amino radical from the *p*-substituted molecular ions the results obtained by both methods agree to some extent.

An experiment to determine the substituent effect of the nitrogen in the pyridine ring using the correlation curves from *IP*, *AP* and ($AP — IP$) measurements of correspondingly substituted compounds was partly successful for *N,N*-dimethyl-*N'*-pyridyl-4-formamidine. Only one result was obtained for 3-formamidine. Isotopic labelling, kinetic energy release and collision induced dissociation studies should be performed to explain the extremely low ($AP — IP$) value for the loss of hydrogen from the molecular ions of pyridyl-3- and 4-formamidines. Such studies will be the next step in the further investigation of the systems examined here.

EXPERIMENTAL

All the mass spectra were recorded on a Du Pont double focussing mass spectrometer (CEC 21—110C) at 6 kV accelerating voltage, 150 μA ionizing current and various electron energies (70-, 40-, 18- and 13 eV*). The samples were introduced via a glass inlet system at a temperature of about 150 °C.

---

* 1 eV = 1.60219×10^{-19} J.

IP and *AP* measurements were performed using a single focussing mass spectrometer. The molecular beam was ionized by electrons of 100 μA ionizing current at the source pressure of 1.10^{-6} torr.* The electron energy scale was calibrated using Ne as standard. To obtain the *IP* and *AP* values, ion efficiency curves were evaluated by the EDD method[15] using the statistical subroutine STATJOB. All the results reported are the average of at least three values obtained in separate experiments and the reproducibility of *IP* and *AP* measurements was in the range of ± 0.1 eV. The substituent constants σ^+ were taken from Brown's modifications[16].

Acknowlegement. This work was performed by the final support of the Research Community Slovenia. The authors are indebted to Dr. A. Pollak and M. Zupan for useful discussions.

REFERENCES

1. M. M. Bursey and F. W. McLafferty, *J. Amer. Chem. Soc.* **88** (1966) 529.
2. F. W. McLafferty, M. M. Bursey, and S. M. Kimball, *J. Amer. Chem. Soc.* **88** (1966) 5022.
3. F. W. McLafferty, *Chem. Commun.* (1968) 956.
4. I. Howe, D. H. Williams, and R. G. Cooks, *Org. Mass Spectrom.* **2** (1969) 137.
5. F. W. McLafferty, T. Wachs, Ch. Lifshitz, G. Innorta, and Irving, *J. Amer. Chem. Soc.*, **92** (1970) 6867.
6. P. Brown, *Org. Mass Spectrom.* **4** (1970) 519.
7. P. Brown, *Org. Mass Spectrom.* **4** (1970) 533.
8. M. M. Bursey, *Org. Mass Spectrom.* **1** (1968) 31.
9. R. G. Cooks, J. H. Beynon, R. M. Caprioli, and G. R. Lester, *Metastable Ions,* Elsevier, Amsterdam, 1973, p. 196.
10. a) L. P. Hammet, *Chem. Rev.* **17** (1953) 125; b) H. M. Jaffe, *Chem. Rev.* **53** (1953) 191.
11. a) H. F. Grützmacher and H. Kuschel, *Org. Mass Spectrom.* **3** (1970) 605.
    b) H. Kuschel and H. F. Grützmacher, *ibid.*, **9** (1974) 395.
    c) H. Kuschel and H. F. Grützmacher, *ibid.*, **9** (1974) 408.
12. A. D. Baker, D. P. May and D. W. Turner, *J. Chem. Soc.* (B) (1968) 22.
13. D. H. Williams and J. H. Beynon, *Org. Mass Spectrom.* **11** (1976) 103.
14. J. D. Roberts and M. C. Caserio, *Basic Principles of Organic Chemistry,* W. A. Benjamin, Inc., New York (1965), p. 991.
15. R. E. Winters, J. H. Collins, and W. L. Chourchene, *J. Chem. Phys.* **45** (1966) 1931.
16. H. C. Brown and Y. Okomoto, *J. Amer. Chem. Soc.* **80** (1958) 4979.

IZVLEČEK

Študij substituentnih efektov v nekaterih substituiranih *N,N*-dimetil-*N'*-fenil- in *N'*-piridil-formamidinih s pomočjo masnospektrometričnih meritev

M. Medved, S. Stavber, V. Kramer, L. Benčić in J. Marsel

V tem delu smo raziskali nekaj konkurenčnih razgradnih reakcij, ki potekajo neposredno iz molekulskega iona in so skupne *p-* in *m-* substituiranim *N,N*-dimetil-*N'*-fenilformamidinom. Izmerili smo tudi IP, AP in razmerja intenzitet produktnih in reaktantnih ionov, da smo lahko opazovali vpliv substituent na reakcijske mehanizme. Dobljene rezultate smo primerjali z ustreznimi rezultati pri spojinah: pri *N,N*-dimetil-*N'*-piridil-4-formamidinu in izomernem 3-formamidinu. Določili smo tudi konstanto substituente σ_p^+ za dušik v piridinovem obroču.

INSTITUT JOŽEF STEFAN,
UNIVERZA V LJUBLJANI
in
FAKULTETA ZA NARAVOSLOVJE IN
TEHNOLOGIJO, ODDELEK ZA KEMIJO,
UNIVERZA V LJUBLJANI
61000 LJUBLJANA

Prispjelo 30. kolovoza 1976.

---

* 1 torr = 133.322 Pa