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243. Yoshiro Kobayashi,[*1,2] Fumio Nakano, and Eitatsu Chinen[*1] : Studies on Organic Fluorine Compounds. II.[*3] Mass Spectrometry of Trifluoromethylated Pyridines.[*4]

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Fragmentation behavior of trifluoromethylated pyridines was investigated. The results given were as follows : 1) α-cleavage of the substituent is well correlated to the inductive effect of the nitrogen atom of the aromatic ring; 2) β-cleavage of the substituent is strongly dependent upon the π-electron density on the carbon atom of the ring at the substituted position.

(Recieved February 17, 1967)

The studies on mass spectral fragmentation behaviors of substituted pyridines have not been reported except one by Biemann.[1] Biemann first pointed out that the extent to which simple β-cleavage[*5] of an alkyl chain in alkyl pyridine occurs is dependent on the position of the chain relative to the heteroatom.

This behavior, quite different from that of C-alkylpyrroles[2] or xylene[3,4] in which little positional selectivity was exhibited, is exemplified by the spectra of 2-ethyl, 3-ethyl, and 4-ethylpyridines, showing small, large, and medium peaks respectively, due

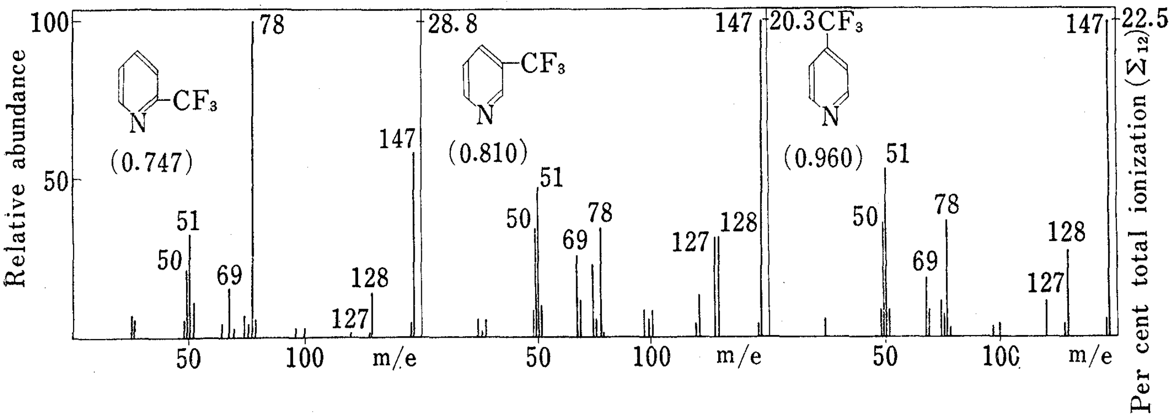

Fig. 1. Mass Spectra of Trifluoromethylpyridines

m/e	ions	m/e	ions
147	molecular ion (M^+)	128	$[M-(F)]^+$
127	$[M-(H+F)]^+$	78	$[M-(CF_3)]^+$
69	CF_3^+	51	CHF_2^+
50	CF_2^+		

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[*3] Part I. Y. Kobayashi, E. Chinen : This Bulletin, **15**, 1896 (1967).

[*4] Most part of this work was presented at the Annual Meeting of the Chemical Society of Japan, Kyoto, April 1965.

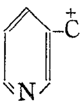
[*5] In the present paper, α(or β)-cleavage is denoted as cleavage of the bond at the α(or β)-position with respect to the aromatic ring.

1) K. Biemann : "Mass Spectrometry," 134 (1962). McGrow Hill, New York.

2) H. Buzikiewicz, C. Djerassi, D.H. Williams : "Interpretation of Mass Spectra of Organic Compounds," 240 (1960). Holden Day, San Francisco.

3) H.M. Grubb, S. Meyerson : "Mass Spectrometry of Organic Ions" (F.W. McLafferty, ed.) Chap. 10 (1963). Academic Press, New York.

4) "Catalog of Mass Spectral Data, American Petroleum Institute Research Project 44," Spectra No. 178, 179, 180. Carnegie Institute of Technology, Pittsburgh, Pa.



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to the loss of a methyl group. He suggested the dependency can be understood in terms of the view that π-electron density is relatively high at the 3-position but low at the 2- and 4-positions, thus making I the most favorable ion.

In the present work, in addition to α-cleavage, β-cleavage of some trifluoromethylated pyridines was investigated, and it was found that in the α-cleavage of these compounds high selectivity is exhibited at the ortho-position and this selectivity can be closely related with an inductive effect due to the nitrogen atom rather than π-electron densities on carbon atoms to which the substituent (or substituents) is attached.

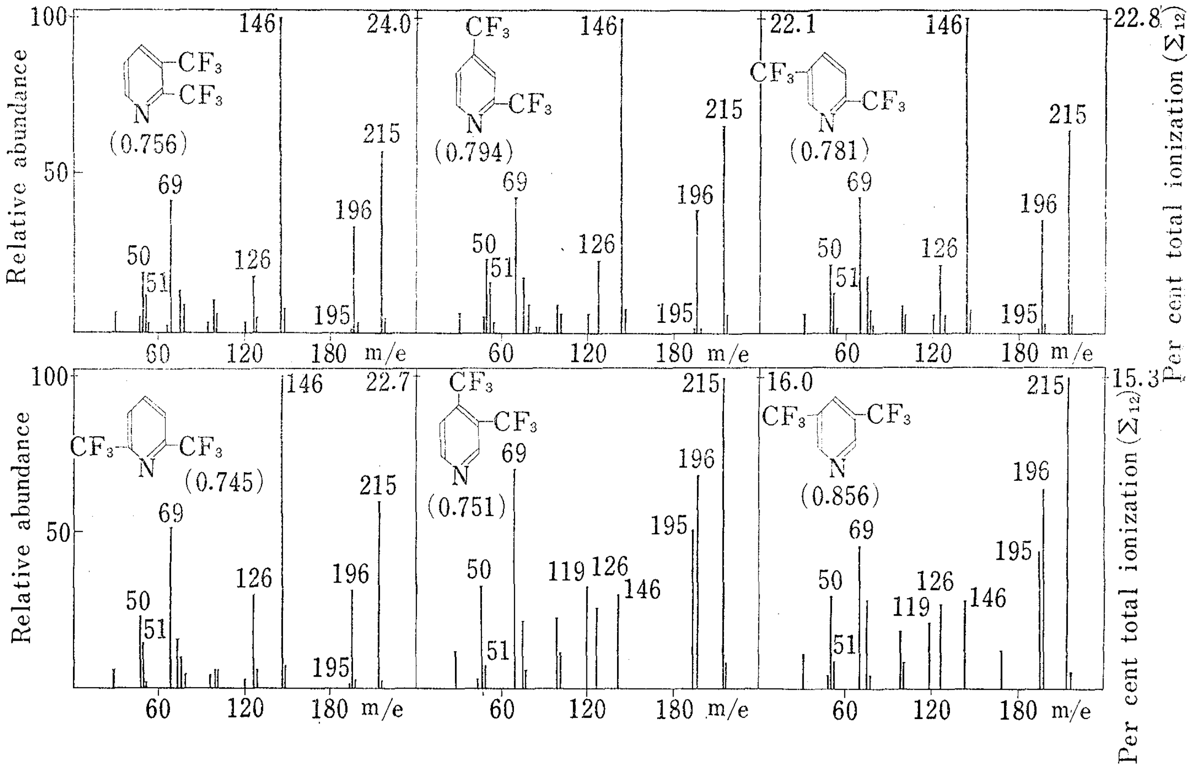


Fig. 2. Mass Spectra of Bis(trifluoromethyl)pyridines

m/e ions							
215	molecular ion (M^+)	196	$[M-(F)]^+$	195	$[M-(H+F)]^+$	146	$[M-(CF_3)]^+$
126	$[M-(CF_3+F+H)]^+$	69	CF_3^+	51	CHF_2^+	50	CF_2^+

Experimental

1) **Spectrometer**——CEC Model 21～103C.

2) **Ionization Voltage**——70 eV.
Ionizing Current——10 μA.

3) **Samples**——A sample was introduced to the inlet system of the spectrometer using a dipper-and-mercury-seal type device (Asahi Shoko Co.). All the liquid compounds were used in the liquid state. However, the 2,5-, 2,6-, and 3,5-isomers were dissolved in pure benzene before introduction to the spectrometer.

4) **Materials**——All of the trifluoromethylated compounds were synthesized*3 and finally purified with a preparative gas chromatograph (Megachrom) in our laboratory. All the pyridine derivatives used as standards were of more than 99% purity based on gas chromatographic analysis.

5) **Mass Spectra**——Mass spectra obtained are shown in Fig. 1, 2, 4, and 5. The normalized sensitivities of the parent ions (sensitivity of parent ion/sensitivity of *n*-butane (m/e =43)) are shown in parentheses for each compound in these figures.

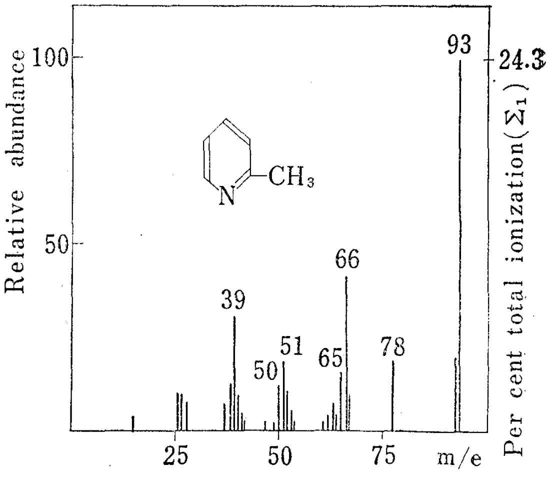


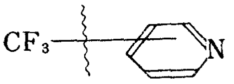
Fig. 3. Mass Spectrum of 2-Methylpyridine (From A. P. I. Data book[5])

m/e=78 : $[M-(CH_3)]^+$

Discussion

(1) Trifluoromethylpyridines

i) Cleavage of exocyclic C–C bond.

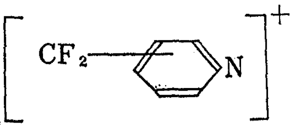


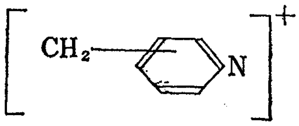
Owing to high electronegativity of F-atoms, the exocyclic C–C bond may become more electron deficient and more susceptible to cleavage than in the case of a CH_3-substituents, where CH_3-group has electron donating properties and, hence, strengthens the exocyclic C–C bond.

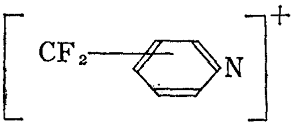
This can be understood if we compare m/e=78 in Fig. 1 and 3. Abundance of m/e=78 varies greatly depending upon the position of the substituent. This pattern of cleavage can very well be correlated with the inductive effect of N-atom of the ring.

In fact, Bernstein, *et al.*⁶⁾ measured NMR of methyl and deuterium substituted pyridines, and from the position of the methyl group signals as well as the overlapping of the *meta*- and *para*-proton signals, they suggested that *meta*- and *para*-protons are more nearly magnetically equivalent than *ortho*- and *para*-, contrary to the expectation suggested by the molecular orbital treatment of the π-electrons of the pyridine skeleton. They interpreted the pyridine spectra on the basis of inductive effect due to the N-atom which is transmitted primarily through σ-bonds. More recently, Adam and Grimison⁷⁾ applied the Extended Hückel Method for pyridine and showed σ-electron densities for the *ortho*-, *meta*-, and *para*-positions as 2.86, 3.11, and 3.09, respectively. These results correspond very well to our experimental data in which relative intensity of m/e=78 ion is highest on the 2-isomer and almost the same on the 3- and 4-isomers.

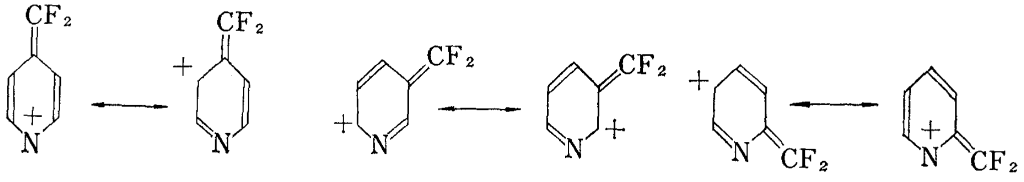
Therefore, it may be said that α-cleavage of trifluoromethylpyridines in the fragmentation process is influenced mainly by inductive effect due to the N-atom, and minorly, if any, by π-electron density over carbon atoms of the skeleton.

ii) M−(F) ions (*i.e.* )

As mentioned before, Biemann found the abundance of 

formed by β-cleavage of ethylpyridine decreases in the order of 3-, 4-, and 2-isomers, and explained this behavior in terms of the stability of ions formed in connection with π-electron density on carbon atoms of the skeleton. Similar idea can be applied to the behavior of M-(F) ions. Resonance structure (III) is preferable to others (II or IV), and hence, is more stable, making the 

(III) ion formed from the 3-isomer most abundant.



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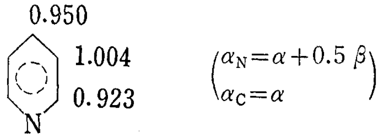
5) Ref. 4), Spectra N. 1535.

6) H. J. Bernstein, W. G. Schneider : J. Chem. Phys., **24**, 469 (1956).

7) W. Adam, A. Grimison : Tetrahedron, **21**, 3417 (1965).

π-electron density calculated by Brown is shown below.[8]

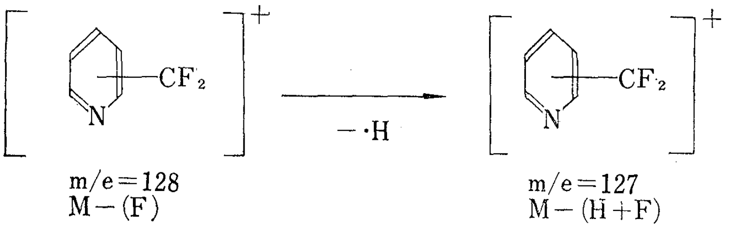


$$\left(\begin{array}{l}\alpha_N=\alpha+0.5\,\beta\\ \alpha_C=\alpha\end{array}\right)$$

A good correlation is exhibited between the π-electron densities and relative intensities of M−(F) ions shown in Fig. 1.

iii) M−(F+H) ions.

It can be assumed that M−(F+H) ions are formed by homolytic cleavage of C–H bond of M−(F) ions as shown below.



As in the case of α-cleavage of exocyclic C–C bond discussed before, a C–H σ-bond may not be much influenced by π-electron distribution on the skeleton. Thus, *ortho* positions are most favorable for the cleavage and most hydrogen eliminations at this stage may occur at *ortho* positions. The 2-isomer has only one hydrogen atom at *ortho* positions, whereas others have two. Therefore, statistically the 2-isomer will show the smallest relative intensity at m/e=127.

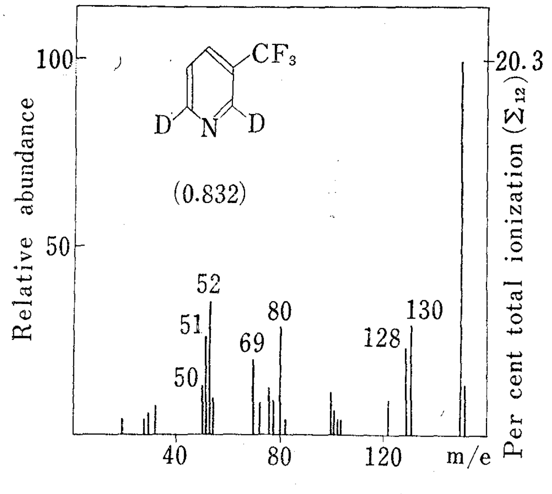


Fig. 4. Mass Spectrum of 3-Trifluoromethylpyridine-2,6-d_2

m/e	ions	m/e	ions
149	molecular ion (M^+)	128	$[M-(D+F)]^+$
130	$[M-(F)]^+$	80	$[M-(CF_3)]^+$

Resonance structures (III) of the 3-isomer have a π-electron deficiency at *ortho* positions, which makes the removal of H-atom of this isomer preferable to that of 4-isomers. Thus the relative intensities of M−(H+F) ions should be in the order of 3-, 4-, and 2-isomers.

The mechanism proposed above was verified by taking the spectrum of 3-trifluoromethylpyridine-2,6-d_2 as shown in Fig. 4.

The M−(D+F) ion is much more abundant than the M−(H+F) ion, and this behavior indicates the hydrogen elimination occurs mainly at the 2- and 6-positions and less frequently at other positions.

(2) Bis(trifluoromethyl)pyridines

The points discussed above are consistent with bis(trifluoromethyl)pyridines.

i) M−(CF_3) ions.

At m/e=146, 3,4-, 3,5-isomers have relatively low relative intensities. Removal of $-CF_3$ occurs most easily at *ortho* (2-, 6-) positions. Therefore, isomers which have a

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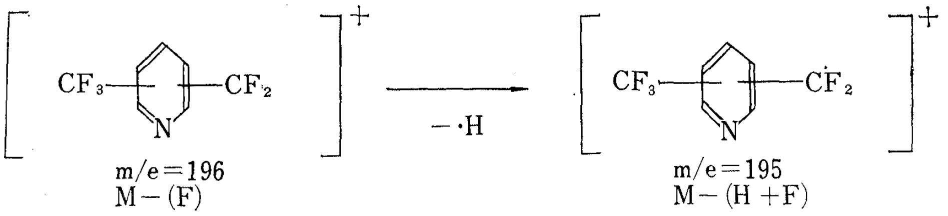
[8] R.D. Brown, M.L. Heffermann: Australian J. Chem., **9**, 83 (1956).

substituent (or substituents) at *ortho* positions should have higher relative intensities at m/e=146 than the 3,4-, 3,5-isomers, which in turn have no CF_3 group at the *ortho* positions.

ii) M−(H+F) ions, m/e=195.

This kind of ion may be formed as follows.



H-elimination is performed most easily at *ortho* positions. Therefore, contrary to the case of M−(CF_3), m/e=146, 3,4-, 3,5-isomers can form M−(H+F) ions, m/e=195, most easily, and hence have higher relative intensities.

In the preceding discussions on bis(trifluoromethyl)pyridines, we have assumed that the interaction between substituents has only a minor effect on positional selectivities in comparison with the major effect caused by the heteroatom, and put the minor effect out of consideration. This may be verified by considering the spectra of bis(trifluoromethyl)benzenes shown in Fig. 5.

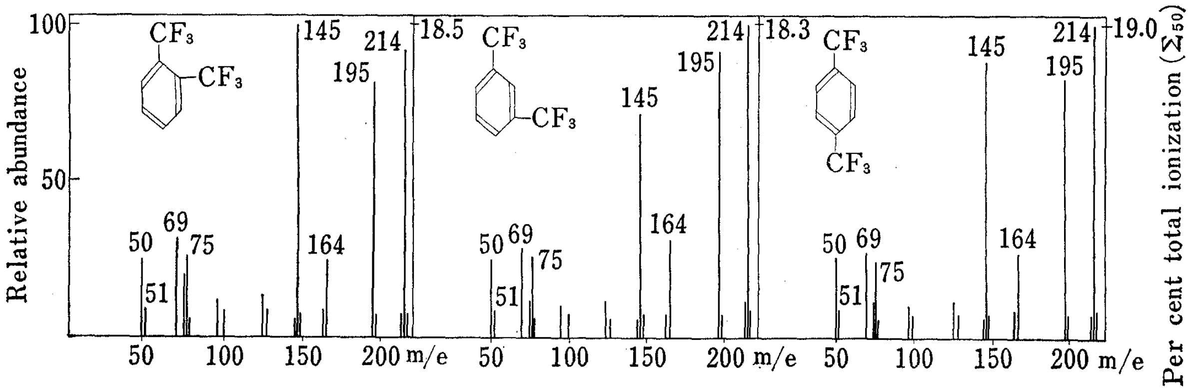


Fig. 5. Mass Spectra of Bis(trifluorometyl)benzenes

m/e	ions
214	molecular ion (M^+)
195	$[M-F]^+$
145	$[M-(CF_3)]^+$

Three isomers show little difference in mass spectral behaviors. Even at m/e=145, where the largest difference is exhibited, the difference is still small compared with the large difference exhibited at m/e=146 in the spectra of bis(trifluoromethyl)pyridines which corresponds to m/e=145 in the spectra of bis(trifluoromethyl)benzenes. This small difference means that the mutual configuration of CF_3 groups has only a minor effect on the positional selectivity of mass spectral cleavage of exocyclic C–C bond of bis(trifluoromethyl)pyridines.

We are grateful to Mr. N. Yamaguchi of Yawata Iron and Steel Co. for the measurement of mass spectra. We also wish to thank Yawata Chem. Ind. Co. for permission of publication of the work.