Studies of Pyrazines. I. Pyrolyses of Substituted Pyrazines and Their Thermal Stabilities

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The pyrolyses and thermal stabilities of 2,5-dialkylpyrazines (**1a**—**e**), 2,5-diethoxypyrazine (**2**), chloropyrazine (**3**), alkoxypyrazines (**4a**—**c**), alkylthiopyrazines (**5a**, **b**), and alkylaminopyrazines (**6a**—**d**) were studied by means of a mass spectrometer, by which the pyrolysates in the sample reservoir were analyzed. The temperature dependence of the molecular ions and/or fragment ions was also discussed. The thermal dehydrogenation from two α-methine groups makes the **1d** molecule thermally sensitive. The other 2,5-dibutylpyrazines were more stable than it, except for the *t*-butyl derivative, **1e**. Hydroxy- and aminopyrazine, **4a** and **6a**, were very stable. The alkoxypyrazines, **4b** and **4c**, and alkylthiopyrazines, **5**, underwent the thermal elimination of olefine to yield hydroxy- and mercaptopyrazine respectively. The latter disproportionated to form dipyrazinyl sulfide (**11**). At 280 °C, no analogous reactions of alkylaminopyrazines **6b**—**d** could be observed. The relative thermal stabilities of the compounds were as follows:

2, 4a, 6a, 4b>1c>1e>1b>6c, 5a>3>6b>1d>1a>6d, 5b>4c

The chemistry of pyrazine derivatives has been investigated in various kinds of fields.[1] Recently, several new synthetic methods of the pyrazine ring have been reported. Azirines undergo both acid-catalyzed and photochemical dimerization to give pyrazines.[2,3] Many kinds of pyrazines have been prepared from diaminomaleonitrile and its derivatives.[4,5] Both thermal and photochemical transformations of perfluoroalkyl pyridazines to perfluoroalkylpyrazines have been reported.[6,7] On the other hand, it is well known that the pyrazine ring is isomerized to other diazine rings under both photolytic and pyrolytic conditions.[1] Although many kinds of reactions of substituted pyrazines have been reported, it is difficult to find intramolecular γ-hydrogen abstruction reactions analogous to the Norrish Type II reaction of ketones except for a photoreaction of 2-alkylquinolines.[1,6b,8]

In this paper, we wish to report our findings on the thermal behavior of substituted pyrazines (**1**—**6**), which can be expected to undergo thermal elimination reactions analogous to those of acetates and of *S*-methyl xantates.[9-11] Indeed, pyrazines (**4c**, **5b**) eliminated propylene at a temperature (250 °C) lower than acetates.[9] Some of the others, (**1b**—**d**, **4b**, and **5a**), were confirmed to eliminate olefines at higher temperatures. The mercaptopyrazine (**10**) produced by thermal decomposition dispropotionates to give dipyrazinyl sulfide (**11**). The thermal stabilities of these compounds were also discussed.

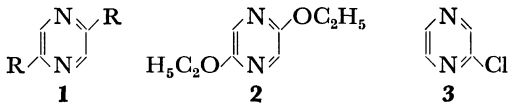
Results and Discussion

Pyrolysis was carried out in an indirect-inlet system of a mass spectrometer under reduced pressure (see Experimental section). In order to minimize the mass-spectral fragmentations of the thermal decomposition products, the low-energy ionization technique was used. The substituted pyrazines, **1**—**6**, were heated in the vapor phase at 150—280 °C for a constant period (3—5 min), and then the pyrolysates were transferred into an ionization chamber without fractionation. The total ion current was approximately constant throughout the period. The temperature dependence on the molecular ion abundances (Σ_{26} values) are shown in Figs. 1, 3, 4, and 7, and the relative total ion current $I_r^+(t)$, in Table 1. $I_r^+(t)$ was calculated by means of the following Equation (1):

$$I^+(t) = \sum_{i=26}^{n} I_i^+(t)$$

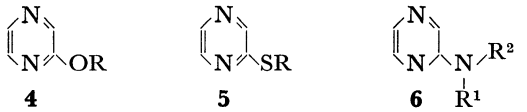
$$I_r^+(t) = I^+(t)/I^+(150) \qquad (1)$$

where $I_r^+(t)$ is the relative abundance of a "*m/e i*" ion in a 16 eV spectrum at *t* °C and where *n* is the highest mass number in the spectrum. If all of the spectra are obtained under the same operating conditions except for the temperature of the sample reservoir, it is obvious that the changes in the spectra (for example, a change in the ion abundance, and the appearance of a new peak) are attributable to a change in the temperature. The operating conditions are shown in the Experimental section. For that reason, the temperature dependence of the molecular ion intensity and of the relative total ion current $I_r^+(t)$ give us information about the thermal reaction and stability of a compound.



1 **2** **3**

a: R=CH_3
b: R=*n*-C_4H_9
c: R=*i*-C_4H_9
d: R=*s*-C_4H_9
e: R=*t*-C_4H_9



4 **5** **6**

a: R=H
b: R=C_2H_5
c: R=*i*-C_3H_7

a: R=C_2H_5
b: R=*i*-C_3H_7

a: $R^1=R^2=H$
b: $R^1=C_2H_5$, $R^2=H$
c: $R^1=R^2=C_2H_5$
d: R^1=*i*-C_3H_7, $R^2=H$

Pyrolyses of 2,5-Dialkylpyrazines **1**. Figure 1 shows the following facts: (i) the molecular ion abundances of the butyl and isobutyl derivatives, **1b** and **1c**,

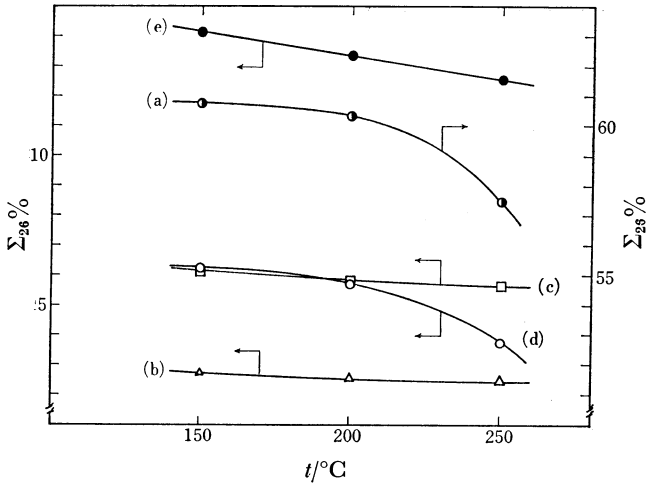


Fig. 1. Temperature dependence of M^+ of 2,5-dialkylpyrazines (**1**) at 16 eV: (a) 2,5-dimethylpyrazine(**1a**), (b) 2,5-dibutylpyrazine (**1b**), (c) 2,5-diisobutylpyrazine (**1c**), (d) 2,5-di-*s*-butylpyrazine (**1d**), (e) 2,5-di-*t*-butylpyrazine (**1e**).

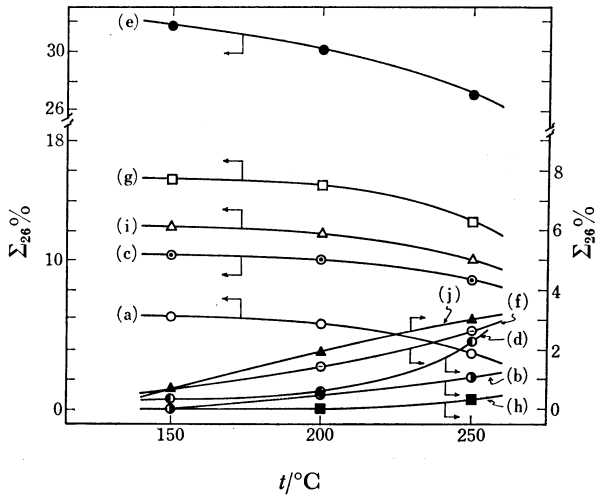
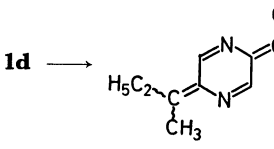


Fig. 2. Temperature dependence of fragment ion abundances of 2,5-di-*s*-butylpyrazine (**1d**): (a) M^+, *m/e* 192.1597 (error −2.8); (b) M−2, 190.1469 (0.0); (c) $M-CH_3$, 177.1391 (0.0); (d) $(M-CH_3)$ −2, 175.1232 (−0.2); (e) $M-C_2H_4$, 164.1306 (−0.6); (f) $(M-C_2H_4)$ −2, 162.1180 (2.4); (g) $(M-C_2H_4)-C_2H_5$, 135.0913 (−0.7); (h) $M-(C_2H_4+C_2H_5)$ −2, 133.0761 (−0.3), (i) $M-C_3H_6$, 150.1142 (−1.3); (j) $(M-C_3H_6)$ −2, 148.0987 mu (−1.2 mmu).

are almost independent of the temperature (150—250 °C), (ii) that of the *t*-butyl derivative (**1e**) decreases slowly with the rise in the temperature, and (iii) those of methyl and *s*-butyl derivatives (**1a**) and **1d**, show a strong temperature dependence at 200—250 °C. These results suggest the thermal unstability of **1a** and **1d**. In order to explain the unstability of **1d**, the temperature dependence of the fragment ions was examined (Fig. 2) and the elemental composition of each ion was determined by means of a high-resolution mass spectrometer. Although the intensity of the molecular ion ($C_{12}H_{20}N_2$, *m/e* 192.1597, error −2.8 mmu) decreases with the rise in the temperature, that of the dehydrogenated ion ($C_{12}H_{18}N_2$, *m/e* 190.1469, error 0.0 mmu) increases. The relative total ion current $I_r^+(t)$ also increases (see Table 1). This suggests that the thermal reaction, Eq. 2, occurs in the sample reservoir before the ionization by electron impact. No thermally induced elimination of ethylene from this compound was



(2)

7

observed at 250 °C (*cf.* Compounds (**4**) and **5**).[13c] In the case of **1a**, however, no increasing ion like (**7**) could be found in spite of the strong temperature dependence of its molecular ion abundance. Therfore, the decrease in the intensity of the molecular ion appears to result from a lack of stabilizing ability of the methyl group.

Pyrolyses of Chloropyrazine (3), Hydroxypyrazine (4a), and Aminopyrazine (6a). The temperature dependence of the molecular ions for these compounds is

Table 1. Temperature dependence of the relative total ion current $I_r^+(t)$ and $\Delta I(250)$ at 16 eV

	$I_r^+(t)$				$\Delta I(t)$
t/°C	150	200	250	280	250
1a	1.00	1.01	1.06	—	0.06
1b	1.00	1.00	1.07	—	0.07
1c	1.00	1.03	1.05	—	0.05
1d	1.00	1.05	1.17	—	0.17
1e	1.00	1.03	1.09	—	0.09
2	1.00	0.98	1.02	—	0.02
3	1.00	1.01	1.05	1.07	0.05
4a	—	1.00	0.99	0.98	−0.01
4b	1.00	1.02	1.03	1.08	0.03
4c	1.00	1.15	1.67	1.62	0.67
5a	1.00	1.02	1.08	1.13	0.08
5b	1.00	1.03	1.24	1.36	0.24
6a	1.00	0.99	1.01	0.99	0.01
6b	1.00	1.04	1.13	1.33	0.13
6c	1.00	1.01	1.10	1.17	0.10
6d	1.00	1.05	1.10	1.31	0.10

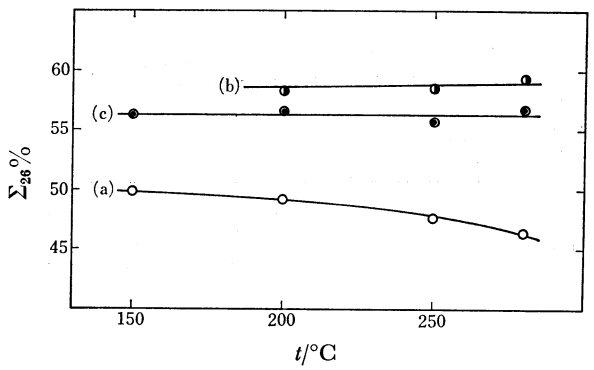


Fig. 3. Temperature dependence of M^+ of (a) chloropyrazine (**3**), (b) hydroxypyrazine (**4a**), and (c) aminopyrazine (**6a**) at 16 eV.

TABLE 2. YIELDS AND PHYSICAL PROPERTIES FOR PYRAZINES (**1**)—(**6**)

Compd No.	Yield (%)	Bp (°C/mmHg)	UV in EtOH λ(nm) (ε)	IR (cm^{-1})	MS m/e	NMR in CCl_4 δ value[o]	Found (Calcd) C%	Found (Calcd) H%
1b	26	95/11.5	274(7100) 279(7200) 312 (840)	3070 1360	192	0.95(t,6H),[a] 1.57(m,8H), 2.74(t,4H),[b] 8.20(s,2H)	74.02 $C_{12}H_{20}N_2$ (74.95)	10.41 (10.48)
1c	48	103/13	275(7000) 278(7100) 312(1000)	3075 1365 1155	192	0.93(d,12H),[c] 2.12(m,2H), 2.62(d,4H),[a] 8.26(s,2H)		
1d	45 lit,[m] 60	112/13 lit,[m] 114/13	273(7100) 279(6800) 310(760)	3070 1375 1160	192	0.83(t,6H),[b] 1.28(d,6H),[d] 1.70(q-d,4H),[b,d] 2.78(se,2H),[d] 8.25(s,2H)	192.1597 mu $C_{12}H_{20}N_2$ error −2.8 mmu	
4b	65 lit,[n] 56	58/13 lit,[n] 73/30	211(11200) 279(5500) 295(sh)	3070 1590 1390	124	1.37(t,3H),[b,l] 4.33(q,2H),[b] 8.05(m,2H), 8.18(d,1H)[e]		
4c	51	74.5/22	212(11400) 280(4680) 295(sh)	3050 1585 1170	138	1.33(d,6H),[d,l] 5.28(h,1H),[d] 8.01(d,1H),[f] 8.03(d,1H),[f] 8.13(s, 1H)	60.03 $C_7H_{10}ON_2$ (60.85)	7.19 (7.30)
5a	81	87/10.5	252(9700) 300(sh) 322(4900)	3040 1560	140	1.33(t,3H),[b] 3.12(q,2H),[b] 8.08(d,1H),[q] 8.23(d-d,6H),[g,h] 8.34(d,1H)[h]	51.11 $C_6H_8SN_2$ (51.40)	5.87 (5.75)
5b	59	79/6	253(9910) 300(sh) 322(5030)	3050 1565 1175	154	1.36(d,6H),[a] 3.94(h,1H),[a] 8.08(d,1H),[i] 8.25(d-d,1H),[h,i] 8.32(d,1H),[h]	54.59 $C_7H_{10}SN_2$ (54.51)	6.62 (6.54)
6b	88	90.5/2.5	247(15800) 290(1300) 334(4460)	3270 1600 1530	123	1.19(t,3H),[j] 3.33(q,2H),[j] 5.83(bs,1H), 7.63(d,1H),[i] 7.79(d,1H),[h] 7.87(d-d,1H)[h,i]	57.69 $C_6H_9N_3$ (58.51)	7.50 (7.37)
6c	78	125/26	255(18000) 295(990) 345(4400)	1603	151	1.15(t,6H),[a] 3.45(q,4H),[a] 7.62(m,1H),7.85(m,2H)	63.30 $C_8H_{13}N_3$ (63.54)	8.80 (8.67)
6d	60	82.5/2.0	247(16300) 290(sh) 335(4340)	3270 1600	137	1.18(d,6H),[c] 4.01(h-d,1H)[b,c] 5.64(bd,1H),[b] 7.62(d,1H),[i] 7.77(d,1H),[k] 7.87(d-d,1H)[i,k]	60.81 $C_7H_{11}N_3$ (61.28)	7.82 (8.08)

a) J=7 Hz. b) J=7.5 Hz. c) J=6 Hz. d) 6.5 Hz. e) J=1.35 Hz. f) J=1.9 Hz. g) J=3 Hz. h) J=2 Hz. i) J=2.5 Hz. j) 8 Hz. k) J=1.5 Hz. l) in $CDCl_3$. m) Ref. 22. n) Ref. 25. o) (**1**): at 60 MHz; (**4**)—(**6**): at 100 MHz.

shown in Fig. 3. Hydroxy- and aminopyrazine, **4a** and **6a**, are independent of the temperature. They are stabilized by the electron-donating substituents, while the electron-withdrawing chloro group makes its molecular ion thermally sensitive. This conclusion is also supported by the data in Tables 1 and 3.

*Pyrolyses of Alkoxypyrazines **4b**, **4c** and Alkylthiopyrazines **5a**, **5b**.* Except for **4b**, the pyrazines, **4c**, **5a**, and **5b**, are more thermally sensitive than the others. The molecular ion abundances of both **4c** and **5b** are especially strikingly decreased at 200—250 °C (Fig. 4). The details are shown in Figs. 5 and 6. In Fig. 5, a molecular ion (*m/e* 138) decreases with the rise in the temperature and almost disappears at 280 °C. On the other hand, the *m/e* 96 ion decreases at 150—250 °C and becomes constant at 250—280 °C. The abundance of the *m/e* 42 ion increases with the rise in the temperature and is constricted to a constant value. The behavior

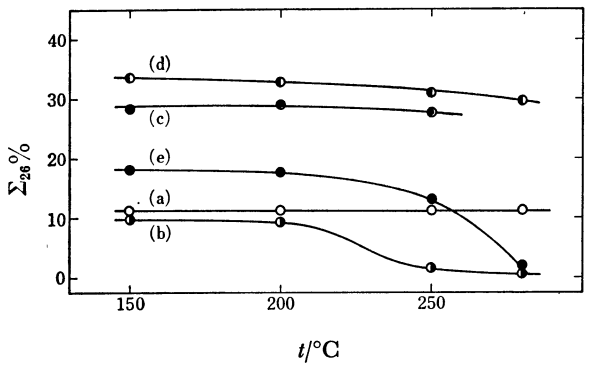


Fig. 4. Temperature dependence of M^+ of (a) ethoxypyrazine (**4b**), (b) isopropoxypyrazine (**4c**), (c) 2,5-diethoxypyrazine (**2**), (d) ethylthiopyrazine (**5a**), and (e) isopropylthiopyrazine (**5b**) at 16 eV.

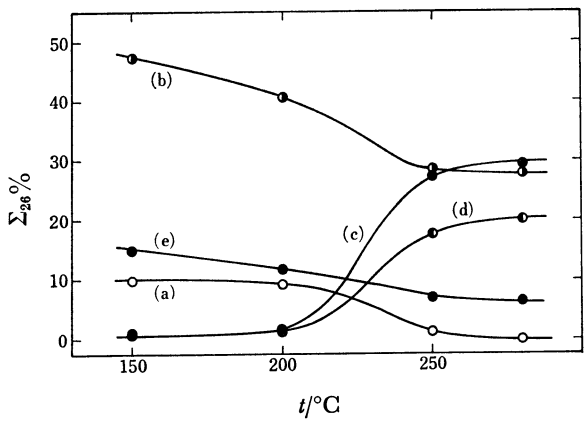
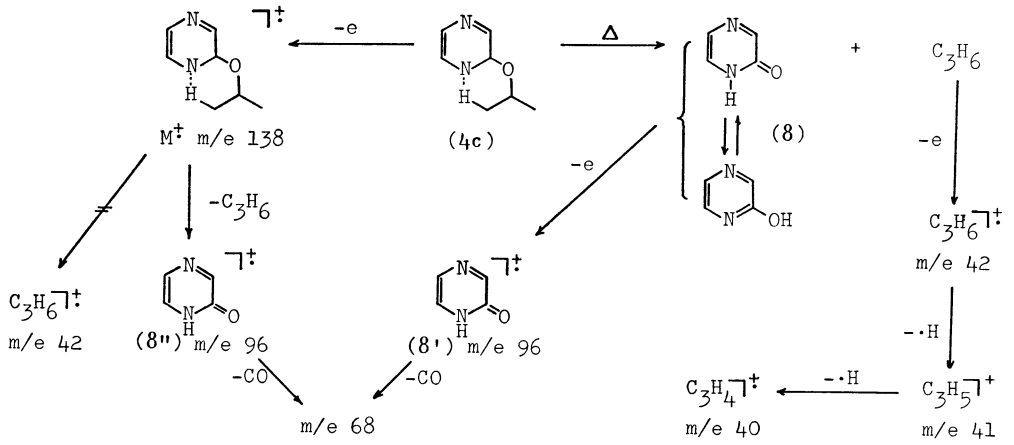


Fig. 5. Temperature dependence of fragment ion abundances of isopropoxypyrazine (**4c**): (a) M^+, *m/e* 138; (b) $M-C_3H_6$, 96; (c) $C_3H_6^+$, 42; (d) $C_3H_5^+$, 41; (e) $M-(C_3H_6+CO)$, 68.



Scheme 1.

of the ions shown in Fig. 5 is explained by means of Scheme 1. In an electron-impact reaction, the abundances of the competing ion products generally reflect their relative ionization potentials (I_p). As the I_p of hydroxypyrazine is smaller than that of propylene, the formation of the ion (**8″**) (charge retention) is more favored than that of propylene ($CH_3CH=CH_2^+$/$C_4H_3N_2OH^+=0.023$ at 150 °C).[12] Moreover, hydroxypyrazine is independent of the temperature (Fig. 3). From these facts, it is obvious: (i) that isoproxypyrazine **4c** is thermally decomposed to give hydroxypyrazine **8** and propylene, and (ii) that curve (b) in Fig. 5 is composed of both **8′** and **8″** at 200—250 °C. That is, the low-temperature region is due to **8″** and the high-temperature region, to **8′**. In a kinetic study of the pyrolysis of alkoxypyrazines, it was found that ethoxypyrazine **4b** was decomposed in the same way as **4c**.[13a] Although a similar reaction of 2,5-diethoxypyrazine, **2**, which had two reaction sites, was not observed at these temperatures, it was expected to occur at more elevated temperatures.

A reaction analogous to that of **4c** was also observed in the pyrolysis of isopropylthiopyrazine, **5b**; it is illustrated in Fig. 6 and Scheme 2. Compared with **4c**, this compound showed more drastic changes in the abundances of the ion products, especially in a mass region higher than that of the molecular ion. At 200—250 °C, a new *m/e* 190 peak, the abundance of which was increased by the elevation of the temperature, appeared. It corresponds to the ionized dipyrazinyl sulfide, **11**, produced by the thermal disproportionation reaction of mercaptopyrazine, **10**. This disproportionation reaction was reported by Cheeseman in the pyrolysis of mercaptopyrazine at 220 °C.[14] Curve (b) in Fig. 6 suggests that, in the sample reservoir, most of the molecule of mercaptopyrazine, **10**, is disproportionated so easily that there is no molecule to give the ion radical (**9**) upon electron impact. Ethylthiopyrazine, **5a**, may also be expected to decompose similarly at temperatures higher than 280 °C.

*Pyrolyses of Alkylamino- and Dialkylaminopyrazines (**6b**—**d**).* As has previously been mentioned, amino-

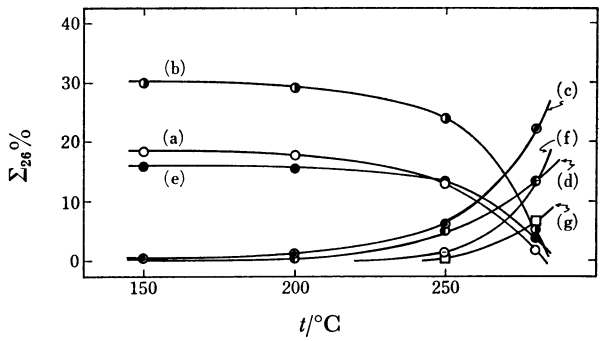
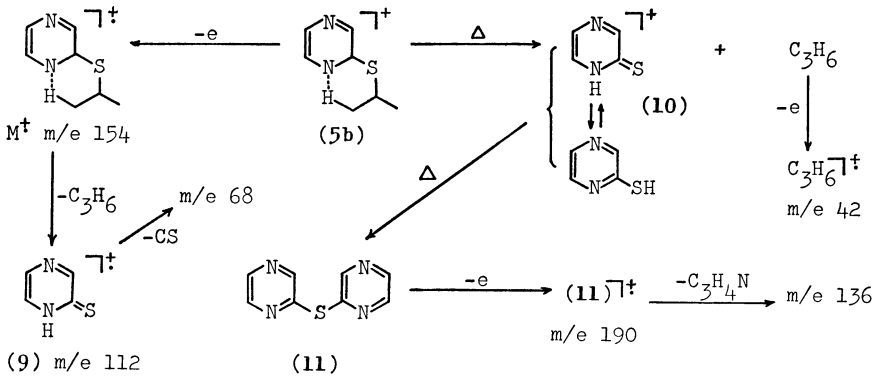


Fig. 6. Temperature dependence of fragment ion abundances of isopropylthiopyrazine (**5b**): (a) M^+, *m/e* 154; (b) $M-C_3H_6$, 112; (c) $C_3H_6^+$, 42; (d) $C_3H_5^+$, 41; (e) $M-(C_3H_6+CO)$, 68; (f) dipyrazinyl sulfide (**11**), 190; (g) (**11**)$-C_3H_4N$, 136.



Scheme 2.

pyrazine, **6a**, is thermally stable. Its alkyl derivatives (**6b**—**d**), however, show interesting behavior. Monoalkylation on the amino group destabilizes the molecule more strikingly than dialkylation (see Figs. 3 and 7). This destabilization may be caused by dehydrogenation from the imino and/or alkyl group. The molecular ion abundance of isopropylaminopyrazine (**6d**) is more strongly suppressed at 280 °C than the others. Details of the thermal dehydrogenation from the **6b** and **6d** molecules are shown in Figs. 8 and 9 respectively. The isopropylamino derivative **6d** behaved much like **6b**. Reactions of **6b**, **6c**, and **6d** analogous to that of **4c** were observed at temperatures higher than 280 °C.[13b]

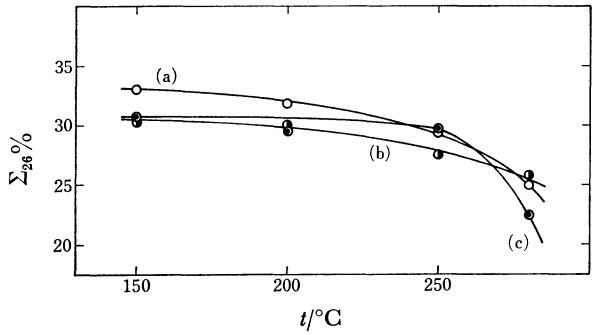


Fig. 7. Temperature dependence of M^+ of (a) ethylaminopyrazine (**6b**), (b) diethylaminopyrazine (**6c**), and (c) isopropylaminopyrazine (**6d**) at 16 eV.

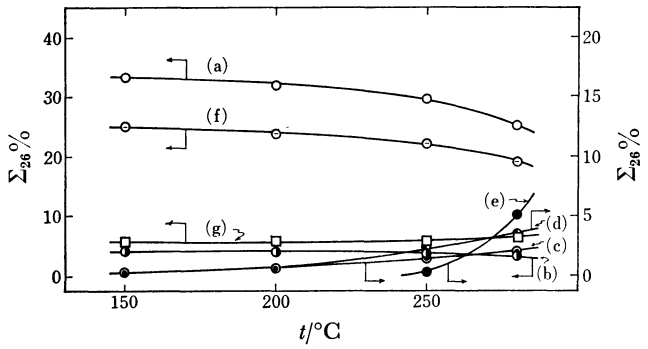


Fig. 8. Temperature dependence of fragment ion abundances of ethylaminopyrazine (**6b**): (a) M^+, *m/e* 123; (b) M−1, 122; (c) M−2, 121; (d) M−3, 120; (e) M−4, 119; (f) $M-CH_3$, 108; (g) $M-C_3H_6$, 95.

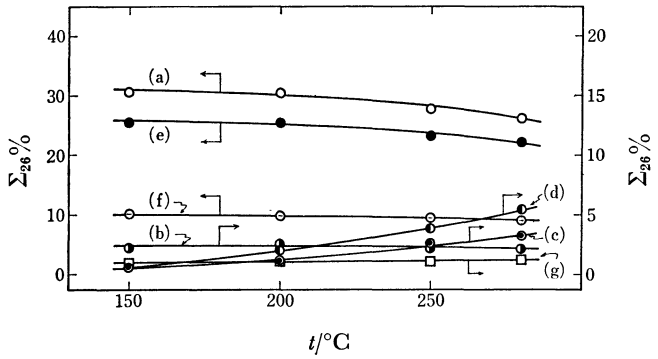


Fig. 9. Temperature dependence of fragment ion abundances of diethylaminopyrazine (**6c**): (a) M^+, *m/e* 151; (b) M−1, 150; (c) M−2, 149; (d) M−3, 148; (e) $M-CH_3$, 136; (f) $M-C_2H_5$, 122; (g) $M-C_2H_4$, 121.

Thermal Stability of Compounds 1—6. Generally, changes in the thermal stability of a series of compounds have been determined by a comparison of half-lives,[15] the amount of evoluted volatile products,[16] the temperatures of the beginning of the evolution of volatile products,[17] and the thermogravimetric curves.[18] From the discussion above, the changes in the ion abundances have proved to be attributable to thermal decomposition reactions. If it is correlated to the reaction temperature, the thermal stability of the compound can be clarified. However, a complete treatment of this subject involves a detailed study of the kinetics of the thermal decomposition reactions, followed by electron-impact reactions, and is very complicated. Therefore, a qualitative treatment was employed in this work. A conversion, α, at a certain temperature is obtained from the following Eq. 3:

$$\alpha = \frac{M(T_0)-M(T)}{M(T_0)} \tag{3}$$

where $M(T)$ is a molecular ion abundance of the pyrazine derivative at T K (see Figs. 1, 3, 4, and 7). When T_0 was 423.15 K, a plot of ln α *vs.* $1/T$ gave a straight line with a negative slope, s. The s values are summarized in Table 3. The most unstable compound, **4c**, showed a small s value (−14.7 kK), and **1c**, more stable than **4c**, a large one (−1.4 kK) (Fig. 10). That is to say, the more unstable a compound is, the smaller the s value is, and *vice versa*. Accordingly, it can be adopted as one of the measures of the thermal stability for the compound. From the data in Table 3, the following order of the thermal stability of the pyrazines **1**—**6** is given:

$$\mathbf{2, 4a, 6a, 4b} > \mathbf{1c} > \mathbf{1e} > \mathbf{1b} > \mathbf{6c},$$
$$\mathbf{5a} > \mathbf{3} > \mathbf{6b} > \mathbf{1d} > \mathbf{1a} > \mathbf{6d}, \ \mathbf{5b} > \mathbf{4c} \tag{4}$$

As the molecular ion peaks of **2**, **4a**, **4b**, and **6a** were not affected by the temperature, they were classified into the group of the most stable compound. However,

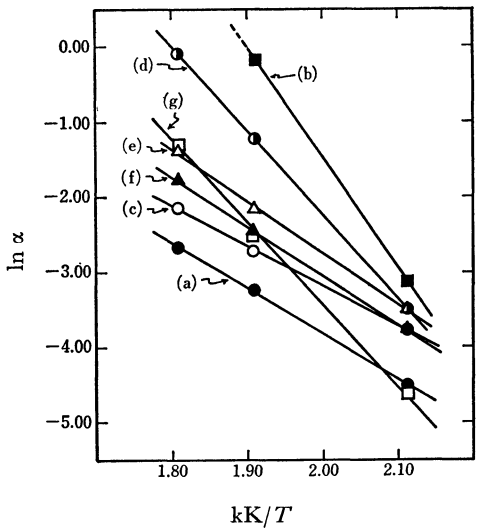
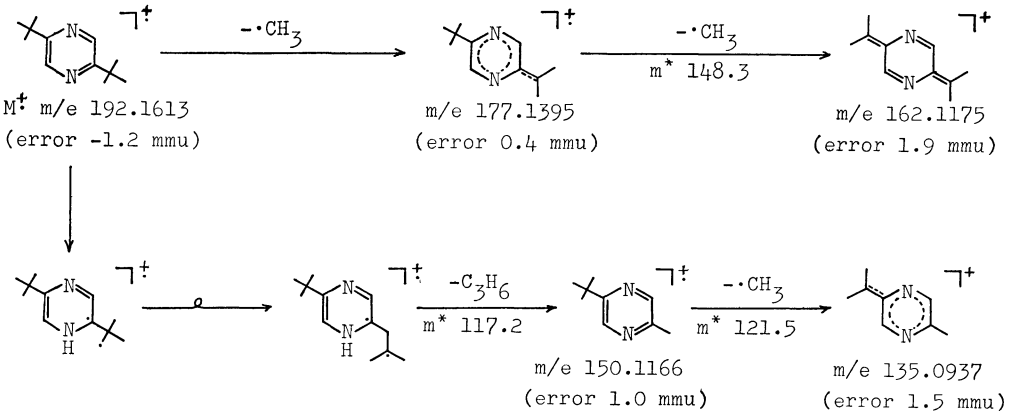


Fig. 10. A plot of ln α *vs.* $1/T$: (a) chloropyrazine (**3**), (b) isopropyrazine (**4c**), (c) ethylthiopyrazine (**5a**), (d) isopropylthiopyrazine (**5b**), (e) ethylaminopyrazine (**6b**), (f) diethylaminopyrazine (**6c**), (g) isopropylaminopyrazine (**6d**). The plot of ln α *vs.* $1/T$ for (**1a**)—(**1e**) was omitted in the Figure.

Table 3. Thermal stability of the pyrazines (**1**)—(**6**)

Compds	**1a**	**1b**	**1c**	**1d**	**1e**	**2**	**3**	**4a**	**4b**	**4c**	**5a**	**5b**	**6a**	**6b**	**6c**	**6d**
s/kK[a)]	−9.8	−3.9	−1.4	−8.0	—	−5.7	—	—	—	−14.7	−5.1	−11.2	—	−6.8	−5.0	−11.0

a) s: the slope obtained from $\ln \alpha$ *vs.* $1/T$.



Scheme 3.

4b was decomposed in the same way as **4c**. On the other hand, an attempt to compare the thermal stability of the pyrazines on the basis of the temperature dependence on the $I_r^+(t)$ values in Table 1 was also successful. Although neither $\ln I_r^+(t)$ nor $\ln(I_r^+(t)-1)$ yielded a linear relationship with $1/T$, the order of the thermal stability was obtained by a comparison of $\Delta I(t)$, which was calculated by means of the following Eq. 5.

$$\Delta I(t) = I_r^+(t) - 1 \quad (5)$$

The $\Delta I(250)$ values in Table 1 gave the following order:

2, 4a, 6a, 4b > **1c, 3, 1a, 1b, 5a,**
1e, 6c, 6d > **6b** > **1d** > **5b** > **4c** (6)

This is in agreement with the order of (4) except for the cases of **1a** and **6d**. The s value appears to be more suitable for a comparison of the thermal stability of the **1**—**6** pyrazines than $\Delta I(t)$. No theoretical interpretation of the linear relationship between $\ln \alpha$ and $1/T$ can be offered at the present time.

Mass-spectral Reaction. In the mass-spectral fragmentation of **6c**, the McLafferty rearrangement was scarcely observed; this is in contrast with the other cases (except for **1a**, **1e**, **3**, **4a**, and **6a**).[19] This appears to result from a steric effect of the diethylamino group. 2,5-Di-*t*-butylpyrazine, **1e**, produces the rearranged ion ($C_9H_{14}N_2$; *m/e* 150.116; error, 1.0 mmu), which is responsible for the base peak in low-energy spectra at various temperatures. At 70 eV, **1e** loses a methyl radical from one of the *t*-butyl groups to give a base peak.[20] The fragmentation pattern is shown in Scheme 3.

Experimental

All the melting points and boiling points are uncorrected. The melting points were measured with a Meiho micro-melting point apparatus or with a sealed capillary in silicon oil. The ultraviolet spectra were recorded on a Hitachi EPS-3T spectrophotometer. The infrared spectra were recorded on a Hitachi EPI-G2 type spectrometer. The NMR spectra were recorded with either a JNM 4H-100 or a Varian A-60 spectrometer for solutions in deuteriochloroform, carbon tetrachrolide, or deuterium oxide. The chemical shifts are reported in δ(internal tetramethylsilane). The unpublished UV and NMR data are summarized in Table 3. The analitycal GLC determinations were carried out with a Shimadzu GC-4APF apparatus using a 2 m by 4 mm glass column of 10% Silicon GE SE-30 liquid phase on Shimalite W support (60—80 mesh). Elemental analyses were performed at the Institute of Physical and Chemical Research.

Mass Spectra and Pyrolyses of the Compounds. Both normal and high-resolution mass spectra were recorded with a Hitachi RMU-7M double-focusing mass spectrometer at 70 eV. The pyrolyses of the compounds were performed in the indirect inlet system of this instrument. Both a liquid and a solid sample were vaporized at 100 °C under a highly reduced pressure and were transferred into a sample reservior heated previously, in which the gaseous sample was then heated at 150, 200, 250, and 280 °C at 10^{-4}—10^{-5} mmHg for a constant period (3—5 min). An equilibrium mixture of the pyrolysate was introduced into an ionizing chamber through a transfer line heated at the same temperature as the reservior. All of the inlet system was made of Pyrex glass, and a gold orifice (Q_o=0.3 ml/s, molecular leak) was used as the gas leak. The operating conditions in this experiment were fixed as follows: ionizing voltage, 16 eV; chamber temperature, 170 or 200 °C; target current, 10 or 13 μA; total emission current, 10, 12, or 13 μA.

Materials. 2,5-Dimethylpyrazine (**1a**),[21] 2,5-di-*s*-butylpyrazine (**1d**),[22] 2,5-di-*t*-butylpyrazine (**1e**),[20] 2,5-diethoxypyrazine (**2**),[23] and chloropyrazine (**3**)[24] were prepared by known methods.

Hydroxypyrazine (4a): The direct synthetic method devised by Karmas and Spoerri was employed.[24] Both the effect of the reaction temperature and of the addition velocity of alkali on the yield were examined.[25] In consequence, it was found that the following procedure gave the highest yield (the technique was substantially that of Karmas and Spoerri).[24] A solution of glycine amide hydrochloride (22.2 g, 0.2 mol) and water (40 ml) in methanol (400 ml) was stirred at −30—−40 °C while a 40% glyoxal solution (34.8 g, 0.24 mol) was added rapidly. The mixture was then cooled at −50——60

°C, and 12.5 M sodium hydroxide (0.50 mol) was added, drop by drop, over a period of 55—60 min. After an additional stirring for 1 h at this temperature, the mixture was stirred at room temperature for 4 h. Then it was treated by the same way as before.[24] The lower the temperature, the higher the yield, unless the reaction mixture was solidified. It was solidified at a temperature lower than −60 °C. On the other hand, the maximum yield was obtained when alkali was added over a period of 55—60 min. Recrystallzation from ethanol using activated carbon was employed instead of purification with silver acetate. The purity of the product, determined by means of its UV spectrum, was 96% (corrected yield, 61%; mp 180 °C; lit,[24] 51%, 188—190 °C). This was used without further purification to prepare chloropyrazine **3**.

*2,5-Dibutylpyrazines (**1b**, **c**)*: The method of Newbold and Spring was applied.[22] The yields and physical properties are shown in Table 2.

*Alkoxypyrazines (**4b**, **c**)*: The following general procedure was used.[26] Chloropyrazine **3** (4 g, 0.035 mol) was added, drop by drop, into a stirred alcoholic solution of sodium alkoxide RONa (R=C_2H_5, *i*-C_3H_7) (from 1.6 g of sodium and 32 ml of the corresponding absolute alcohol), after which the mixture was heated under reflux for 1 h. After cooling, the mixture was poured into a saturated aq sodium chloride solution (200 ml) and then completely extracted with ether. The dried (Na_2SO_4) and evaporated extract was then distilled under reduced pressure (see Table 2).

*Alkylthiopyrazines (**5a**, **b**)*: The following general procedure was used. A solution of 0.045 mol of alkyl thiol RSH (R=C_2H_5, *i*-C_3H_7) and sodium hydroxide (1.9 g, 0.045 mol) in absolute ethanol (20 ml) was heated to boiling and then cooled. Chloropyrazine **3** (5.1 g, 0.045 mol) was subsequently added cautiously with stirring. The mixture was then refluxed for an additional 30 min. After cooling, the mixture was poured into a satulated aq sodium chloride solution (150 ml) and then extracted completely with ether. The dried (Na_2SO_4) and evaporated extract was distilled under reduced pressure (see Table 2).

*Aminopyrazine (**6a**)*: This was prepared by Erickson and Spoerri's method.[26] The crude product was purified by sublimation under reduced pressure (75—80 °C at 1.5 mmHg). Yield, 81%; mp 119 °C (lit,[26] 80%, 118—120 °C).

*Ethylaminopyrazine (**6b**) and Isopropylaminopyrazine (**6d**)*: These substances were prepared by an application of Cheeseman's method.[14] Chloropyrazine **3** (2 g, 0.017 mol), 70% aq ethylamine (or isopropylamine) (0.096 mol), and ethanol (10 ml) were used (see Table 2).

*Diethylaminopyrazine (**6c**)*: Diethylamine (7 g, 0.096 mol) and chloropyrazine **3** (2 g, 0.017 mol) in ethanol (15 ml) were heated in a sealed tube at 150 °C for 7 h. The cooled reaction mixture was then poured into 10 ml of *ca.* 8 M NaOH, extracted with chloroform, and washed with water. The dried (Na_2SO_4) and evaporated extract was then distilled under reduced pressure (see Table 2).

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