STUDIES OF PYRAZINES. V. PYROLYSIS OF 2-ALKOXYPYRAZINES

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Abstract — A pyrolysis of 2-alkoxypyrazine (1) has been performed to give 2-pyrazinol (2) and alkene (3) and to obey first-order kinetics. The reaction proceeds through a 6-membered cyclic transition state analogous to that of ester pyrolysis. The activation parameters, log(\(A/s^{-1}\)) and \(E_a/(\text{kcal mol}^{-1})\), and the relative rate constants were determined in the pyrolysis of eight 2-alkoxypyrazines \(1\) (R = \(\text{C}_2\text{H}_5\), \(\text{n}-\text{C}_3\text{H}_7\), \(\text{i}-\text{C}_3\text{H}_7\), \(\text{i}-\text{C}_4\text{H}_9\), \(\text{s}-\text{C}_4\text{H}_9\), \(\text{t}-\text{C}_4\text{H}_9\), \(\text{T}-\text{C}_5\text{H}_{11}\), and \(\text{1,2-dimethylpropyl}\)). Substitution effects on the reaction rate at the \(\alpha\)- and \(\beta\)-position in the alkoxyl group were discussed on the basis of the kinetic data.

Previously, the pyrolysis of isopropoxypyrazine was reported to give 2-pyrazinol and propene.\(^1\) This was the first reaction which was a nitrogen analogue of ester pyrolysis, and an analogous reaction has also been observed in the mass spectra of 2-alkoxypyrazines.\(^2\) In the progress of the kinetic study on the reaction by us,\(^3\) Taylor has independently reported a kinetics in an analogous type of reaction of 2-ethoxypyrazine.\(^4\) In his report, he proposed that the reaction proceeded through a semi-concerted 6-centered cyclic transition state. However, the detailed nature of the transition state has not been described.

In this communication, we wish to report our findings on the pyrolysis of the 2-alkoxypyrazines \(1\). As mentioned above, \(1\) was decomposed to 2-pyrazinol (2) and alkene (3) (Eq. 1).

\[\text{Pyrolysis of 2-alkoxypyrazine (1)} \rightarrow \text{2-pyrazinol (2)} + \text{alkene (3)} \]

\(a)\) R = \(\text{C}_2\text{H}_5\) \(b)\) R = \(\text{n}-\text{C}_3\text{H}_7\) \(c)\) R = \(\text{i}-\text{C}_3\text{H}_7\) \(d)\) R = \(\text{i}-\text{C}_4\text{H}_9\) \(e)\) R = \(\text{s}-\text{C}_4\text{H}_9\) \(f)\) R = \(\text{t}-\text{C}_4\text{H}_9\) \(g)\) R = \(\text{t}-\text{C}_5\text{H}_{11}\) \(h)\) R = 1,2-dimethylpropyl \(i)\) R = \(\text{C}_9\text{H}_{17}\) \(j)\) R = \(\text{neo-C}_5\text{H}_{11}\)
and alkene (1) at 360 to 585 °C (Eq. 1). The reaction was performed in a silver-tubular reactor coupled with a gas chromatograph apparatus in series. The decrease of 1 obeyed good first-order kinetics. The activation parameters (ln A and E_a) in the pyrolysis of eight 2-alkoxypyrazines (1_a ~ 1_h) were determined and shown in Table. The values change drastically with substituents at the α- or β-position in the alkoxyl group. 2-Octyloxypyrazine (1_a) did not yield isomers except for 1-octene, and 2-neopentyloxypyrazine (1_d) resisted stubbornly to the pyrolysis. These facts imply that the reaction (1) proceeds through the 6-membered cyclic transition state analogous to that of ester pyrolysis. The activation energy in the pyrolysis of 1_a is 63.8 kcal mol⁻¹ and larger than that of 2-ethoxypyridine reported by Taylor (46.8 kcal mol⁻¹). The rate of the former is about 2.3 times slower than that of the later. The deactivation effect results from the decrease in the electron density on the pyrazine-ring nitrogen, which shows lower pK_a values than that of pyridine ring. This is the first observation on the electronic effect at the trigger atom which abstracts 6-hydrogen in the unimolecular thermal elimination of alkene analogous to ester pyrolysis.

If the compound 1_a is selected as a logical standard, the relative rate constants, k_rel, are calculated as shown in Table 1. The reactivity order in each compounds studied is tertiary > secondary > primary. This is the same order as Taylor has previously reported in a pyrolysis of acetates. The k_rel values for isoproxy- and t-butoxypyrazine, (1_c) and (1_f), are 18.8 and 758, respectively.

Table. Activation Parameters and Relative Rate Constants in Pyrolysis of 2-Alkoxypyrazines (1_a ~ 1_h)

<table>
<thead>
<tr>
<th>Compd.</th>
<th>log(A/s⁻¹)</th>
<th>E_a/(kcal mol⁻¹)</th>
<th>Temp. range t/°C</th>
<th>k_rel a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1_a</td>
<td>16.55</td>
<td>63.8</td>
<td>550 ~ 585</td>
<td>1.00</td>
</tr>
<tr>
<td>1_b</td>
<td>14.60</td>
<td>56.3</td>
<td>533 ~ 571</td>
<td>1.3</td>
</tr>
<tr>
<td>1_c</td>
<td>13.22</td>
<td>47.1</td>
<td>465 ~ 525</td>
<td>18.8</td>
</tr>
<tr>
<td>1_d</td>
<td>27.79</td>
<td>106.4</td>
<td>527 ~ 553</td>
<td>0.32</td>
</tr>
<tr>
<td>1_e</td>
<td>12.91</td>
<td>45.3</td>
<td>468 ~ 495</td>
<td>22.3</td>
</tr>
<tr>
<td>1_f</td>
<td>12.65</td>
<td>39.2</td>
<td>357 ~ 387</td>
<td>758</td>
</tr>
<tr>
<td>1_g</td>
<td>13.70</td>
<td>41.6</td>
<td>357 ~ 389</td>
<td>1850</td>
</tr>
<tr>
<td>1_h</td>
<td>14.07</td>
<td>49.8</td>
<td>459 ~ 487</td>
<td>24.3</td>
</tr>
</tbody>
</table>

a) At 520 °C. b) Relative rate method.
In comparison with relative rate constant in a pyrolysis of the corresponding acetate at the same temperature, a plot of $\log(k_{rel})_{acetate}$ vs. $\log(k_{rel})_{2-alkoxy-pyrazine}$ gives a straight line (Figure). The fact suggests that the transition state in the pyrolysis of 2-alkoxy-pyrazine is similar to that of acetate.

![Figure. Correlation of relative rates of 2-alkoxy-pyrazine and ester pyrolysis at 520 °C.](image)

The effects on the rate by methyl branching at the $\alpha$-position in the pyrolysis of a compound at 520 °C were clarified by a comparison of $k_{rel}$ for $\lambda_a$ with that for $\lambda_d$; or that for $\lambda_e$ with that for $\lambda_g$. The accelerating effects in $\lambda_c$ and $\lambda_f$ are 18.8 and 40.3; and those in $\lambda_e$ and $\lambda_g$ are 17.1 and 83.0, respectively. These results imply that the electronic effect is important in the pyrolysis of the $\alpha$-substituted and that the $\alpha$-carbon in $\lambda_a$ possesses the same carbonium ion character in the transition state of the pyrolysis as proposed in a pyrolysis of esters.

On the other hand, the effects at the $\beta$-position is very different from those at the $\alpha$-position. The reaction rates were accelerated by the factors of 1.2 to 2.4 when the $\beta$-position in each of the primary, secondary and tertiary alkoxy groups was substituted with one methyl group. Although an pronounced accelerating effect was not observed in the pyrolysis of $\lambda_h$ (1.1 times relative to $\lambda_c$), the reaction of isobutoxypyrine ($\lambda_d$) was suppressed (0.25 times relative to $\lambda_h$). These deaccelerating effects in the pyrolysis of $\lambda_d$ and $\lambda_h$ result from a steric hindrance between the 2-pyrazinyl group and the bulky isopropyl one attached to
the α-carbon. 10

The tublar reactor used in this work was made in our laboratory and coupled with a Shimadzu GC-4CPF gas chromatograph apparatus in series. In a typical procedure, a mixture of 1 and an appropriate internal standard (quinoline, o-xylene or mesitylene) was injected with a micro injector into the reactor. The 2-alkoxy-pyrazines 1 were prepared by the method reported previously. 1

References
5. When 1 was heated at 555.6 °C for 3.68 s, most of 1 was recovered (>98%).
6. The pKₐ values of pyrazine itself are 0.65 and -5.8, and that of pyridine is 5.17. 7
10. Most of the hydrogen abstraction in the reaction of 1 may occur at the 1-methyl group in the 1,2-dimethylpropyl one.

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