Mass Spectra of 7H-Thiazolo[3,2-a]Pyridine Derivatives

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Mass spectra of 7H-thiazolo[3,2-a] pyridine derivatives were measured by electron-impact ionization mass spectrometry. The substituents on the phenyl group were H, p-CH₃, p-OCH₃, p-Cl, p-NO₂. The methyl or ethyl esters were also examined. The fragmentation patterns were deduced with the aid of the shift of the peaks by substituted groups and by deuterated derivatives. And they were confirmed by metastable peaks. Substituent effect of the phenyl groups on the fragmentation was only observed in the change of intensity of fragment ions, but not observed as the change of fragmentation pathway. On the other hand, fragmentation pathway was changed by the ester groups.

1. Introduction

We have previously reported on the one-step synthesis of 7H-thiazolo[3,2-a] pyridine derivatives (5) from α-cyano-cinnamic esters and thioglycol esters. These compounds contain substituted groups of H, p-CH₃, p-OCH₃, p-Cl, p-NO₂ on the 2-benzylidene group and on the 7-phenyl group, which are varied in electronic property from electron attracting (p-NO₂) to electron donating (p-CH₃). From mass spectrometric point of view, the effect of these substituent groups on the fragmentation mechanism is interesting. This report deals with the fragmentation mechanism of these compounds and the substituent effect on the fragmentation.

2. Experimental

Samples tested are listed in Table 1., and illustrated in Fig. 1. Most of the samples were prepared by the method previously reported.

![Structure of Compound 5](image)

Fig. 1. Structure of Compound 5

In order to elucidate the fragmentation mechanism, compounds 5k, 5l, 5m, 5n, and 5o were prepared by two-step reactions through intermediates. Compounds 5k and
Table 1. List of Samples Tested

<table>
<thead>
<tr>
<th>Compound</th>
<th>5a</th>
<th>5b</th>
<th>5c</th>
<th>5d</th>
<th>5e</th>
<th>5f</th>
<th>5g</th>
<th>5h</th>
<th>5i</th>
<th>5j</th>
</tr>
</thead>
<tbody>
<tr>
<td>R&lt;sub&gt;1&lt;/sub&gt;</td>
<td>H</td>
<td>p-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>p-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>p-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>H</td>
<td>p-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>p-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>H</td>
<td>p-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>p-NO&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td>R&lt;sub&gt;2&lt;/sub&gt;</td>
<td>H</td>
<td>p-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>p-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>p-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>H</td>
<td>p-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>p-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>p-NO&lt;sub&gt;2&lt;/sub&gt;</td>
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<tr>
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<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
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</tr>
<tr>
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<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td></td>
</tr>
</tbody>
</table>

(⁎) In compound 5p, 5r, hydrogen atoms of 5-amino group were deuterium labeled.
(‡) In compound 5q, 7-hydrogen were deuterium labeled.

Scheme 1. Synthesis of Compound 5q

5<sub>1</sub> contain different alkyl groups on 6-, and 8-alkoxycarbonyls. Compounds 5m, 5n, and 5o contain different substituent groups on 2-benzylidene and on 7-phenyl groups. Other samples(5a–5j; 5p–5r) contain the same alkyl group in 6-, and 8-alkoxycarbonyls, and also, contain the same substituent group on 2-benzylidene and on 7-phenyl groups.

The 5-amino-D-labeled compounds (5p, 5r) were synthesized through substitution of H atom in the 5-NH<sub>2</sub> group of compounds 5a and 5f, by D<sub>2</sub>O in CD<sub>3</sub>C<sub>1</sub>. Percentages of substitution were calculated from isotope
peaks of the molecular ions. In 5p, they were 3.0% for d₀, 24.5% for d₁, and 72.5% for d₂. In 5r, 4.5% for d₀, 20.7% for d₁, and 74.8% for d₂. Synthesis of 7-hydrogen-D-labeled compound (5q) were carried out from benzaldehyde-d₁², as shown in the Scheme 1.

Percentages of substitution of 5q were 8.4% for d₀, 65.0% for d₁, 21.2% for d₂, and 5.4% for d₃.

Mass spectra were measured with a Hitachi M-52 GC-MS by introducing samples through a direct inlet system. The samples were usually vaporized at 120°C. Then, they were ionized by 70 eV electrons and the ions were accelerated by an electric field of 3.0 kV and recorded by a 056-type pen recorder.

3. Results and Discussion

In order to determine the fragmentation pathway, the peak shifts by the substituted groups of the compounds (5a-5o) and by the deuterium labeling(5p-5r) were compared. Their spectra are illustrated graphically in Fig. 2, and in Fig. 3.

Metastable peaks observed in their spectra are listed in Table 2.

(1) The molecular ion decomposes by releasing the substituted phenyl group to give the (M-(76+R))+ ion. Where, R is the mass number of the substituent group on 8-phenyl and on 2-benzylidene groups. This process is the most predominant path for the degradation of the M⁺ ion. These fragment ions were base peaks in their all derivatives. This process is ascertained by its metastable peaks.(Table 2).

The mass spectra of compound 5m shows (M-77)+ peak instead of (M-(76+15))+, and compound 5n and 5o show (M-(76+15))+ and (M-(76+35))+ peaks respectively, instead of (M-77)+ peak. From these facts, the phenyl groups are thought to be eliminated from 7-position, not from 2-benzylidene group.

(2) The molecular ion decomposes also by releasing alkoxy carbonyl group to give (M-(44+R'))+ peak. Where, R' is the mass number of alkyl group in 6, or 8-alkoxy-carbonyls. These alkoxy carbonyl groups are mainly eliminated from 6-position instead of 8-position. Because, mass spectrum of 5k shows (M-59)+ peak stronger than (M-73)+, and 5l shows (M-73)+ peak instead of (M-59)+. Metastable peaks of this process were not found. (Table 2).

These fragment ions did not decompose further by releasing another alkoxy carbonyl group to give (M-2(44+R'))+ ion.

(3) The (M-(76+R))+ ion decomposes further, releasing alkoxy carbonyl + H, in rearrangement process, to give (M-(76+R)-(45+R'))+ ion. Most of this process is ascertained by metastable peaks.(Table 2). The alkoxy carbonyl group are also eliminated mainly from 6-position instead of 8-position, similarly to the process(2). This is shown in the spectrum of 5k, which shows (M-77-60)+ peak instead of M-(77-74)+, and in 5l, (M-77-74)+ peak instead of (M-77-60)+.

These (M-(76+R)-(45+R'))+ ions may be derived from (M-(76+R)-(17+R'))+ ions by elimination of CO. In R' = ethyl derivatives (5f-5l, 5n), these (M-(76+R)-(45+R'))+ ions may be derived from (M-(76+R)-28)+ ions, by elimination of C₂H₅OH. Weak metastable peaks of these processes are observed for few
Fig. 2 (1) Mass Spectra of Compounds 5a-5e
Mass Spectra of 7H-Thiazolo [3,2-a] Pyridine Derivatives

![Mass Spectra of Compounds 5f-5j](image)

Fig. 2 (2)  Mass Spectra of Compounds 5f-5j
Fig. 2 (3) Mass Spectra of Compounds 5k-5o
Fig. 3. Mass Spectra of D-labeled Compounds 5p-5r

derivatives (5f, 5o, 5k). (Table 2).

The origine of H atom in this rearrangement process is perhaps from 5-amino group. Because, in the spectrum of D-labeled compound (5p), (M-77-60)+ peak shifted to (M-77-61)+. In 7-hydrogen-D-labeled compound (5q), (M-77-60)+ did not shift to (M-77-61)+. Also, in 5r, (M-77-74)+ shifted to (M-77-75)+. So, this H atom rearranged not from 7-hydrogen, but from 5-amino group.

(4) The (M-(76+R))+ ion decomposes in another path of releasing alcohol, to give (M-(76+R)-(17+R'))+ ion. This process is ascertained by its metastable peaks (Table 2). By the same reason as (3), this alcohol may be derived from 6-, and not from 8-aloxycarbonyl group.

The origine of H atom in this process is not from 7-hydrogen but from 5-amino group. This is seen in the spectrum of 5p, 5q, and 5r. In 5p, (M-77-32)+ peak shifted to (M-77-33)+. In 5r, (M-77-46)+ peak shifted to (M-77-47)+. And in
Table 2. List of Metastable Peaks

<table>
<thead>
<tr>
<th>Compound Metastable Process (**)</th>
<th>5a</th>
<th>5b</th>
<th>5c</th>
<th>5d</th>
<th>5e</th>
<th>5f</th>
<th>5g</th>
<th>5h</th>
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<th>5j</th>
<th>5k</th>
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<th>5m</th>
<th>5n</th>
<th>5o</th>
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<tr>
<td>(1)→(2) 307.0</td>
<td>311.5</td>
<td>316.5</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>334.0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>320.5</td>
<td>320.5</td>
<td>321.0</td>
<td>320.5</td>
<td>285.5 (obs.)</td>
</tr>
<tr>
<td>(1)→(5) 307.2</td>
<td>311.4</td>
<td>316.5</td>
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<td>321.7</td>
<td>334.5</td>
<td>338.4</td>
<td>343.4</td>
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<td>348.3</td>
<td>320.8</td>
<td>320.8</td>
<td>320.8</td>
<td>320.8</td>
<td>324.9</td>
<td>285.6 (calc.)</td>
</tr>
<tr>
<td>(2)→(3) 260.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>+</td>
<td>298.0</td>
<td>308.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>260.0 (obs.)</td>
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<tr>
<td>(2)→(6) 310.0</td>
<td>323.5</td>
<td>—</td>
<td>—</td>
<td>354.5</td>
<td>312.0</td>
<td>326.0</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>298.0</td>
<td>+</td>
<td>—</td>
<td>309.5 (obs.)</td>
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<tr>
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<td>231.6</td>
<td>235.4</td>
<td>304.7</td>
<td>—</td>
<td>—</td>
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<td>—</td>
<td>—</td>
<td>193.9</td>
<td>202.6</td>
<td>216.1</td>
<td>—</td>
<td>202.6 (calc.)</td>
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<tr>
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<td>—</td>
<td>—</td>
<td>—</td>
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<td>271.0</td>
<td>285.0</td>
<td>+</td>
<td>—</td>
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<td>+</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(obs.)</td>
</tr>
<tr>
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<td>284.0</td>
<td>294.9</td>
<td>239.5</td>
<td>253.2</td>
<td>269.0</td>
<td>272.9</td>
<td>383.7</td>
<td>239.5</td>
<td>250.3</td>
<td>264.2</td>
<td>239.5</td>
<td>250.3 (calc.)</td>
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<tr>
<td>(4)→(3) 285.3</td>
<td>299.2</td>
<td>315.1</td>
<td>319.1</td>
<td>330.0</td>
<td>299.2</td>
<td>313.1</td>
<td>329.1</td>
<td>333.0</td>
<td>344.0</td>
<td>299.2</td>
<td>285.3</td>
<td>299.2</td>
<td>285.3</td>
<td>(calc.)</td>
<td></td>
</tr>
<tr>
<td>(9)→(3) 284.7</td>
<td>298.5</td>
<td>314.3</td>
<td>318.2</td>
<td>329.1</td>
<td>295.9</td>
<td>270.9</td>
<td>—</td>
<td>284.7</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(calc.)</td>
</tr>
</tbody>
</table>

(**) Numbers in the parentheses are referred to those of Fig. 4 or Fig. 5.
(obs.): observed value, (calc.): calculated value.
—: not detected, +: barely detected.
5r, (M−77−32)+ did not to shift (M−77−33)+.

(5) In R′ = ethyl derivatives (5f−5j), the (M−(76+R))+ ion further decomposes in another process, which release CO to give (M−(76+R)−28)+ ion. Metastable peaks of this process are observed. (Table 2).

In R′ = methyl derivatives (5a−5e), this process were not observed.

(6) In R′ = methyl derivatives (5a−5e), the ion (M−(76+R)−(45+R′))+ decomposes further by releasing COOCH3 + H to give (M−(76+R)−2(45+R′))+ ion. The origine of rearranged H atom in this process is not from 5-amino group. In the spectrum of 5p, (M−77−61−60)+ peak did not shift to (M−77−61−61)+.

In R′ = ethyl derivatives (5f−5j), this process were not found.

(7) Decarbonylation process of (M−(76+R)−(45+R′))+ ion to give (M−(76+R)(45+R′)−28)+ ion were found in R′ = ethyl derivatives (5f−5j), but not found in R′ = methyl derivatives (5a−5e).

(8) From (M−(76+R)−(45+R′))+ ion, by releasing R′O + H, (M−(76+R)−(45 +R′)−(17+R′))+ ion were formed in the compounds of 5a−5d and 5f−5i. But in R=NO2 (5e and 5j), this peak was not observed.

(9) By thiazolo-ring opening. (R−C6H4 CH = C = (S)+ ion were observed in all derivatives.

(10) m/e 241 peak were observed in all derivatives. But the component of elements of this ion is uncertain.

In summary, the above interpreted fragmentation mechanism of 7H-thiazolo [3,2-a] pyridine derivatives are shown in Fig. 4 for methyl derivatives, and in Fig. 5 for ethyl derivatives.

In conclusion, substituent effect, by the groups on 2-benzyldene and on 7-phenyl, was only observed in the intensity change of fragment peaks. But not observed in the change of fragmentation mechanism, excepting NO2 group.

Ester groups changed fragmentation mechanism.

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Fig. 4. Fragmentation Pathway of Methyl Derivatives
Fig. 5. Fragmentation Pathway of Ethyl Derivatives

References

Keywords
7H-Thiazolo [3,2-a] Pyridine Derivatives
Mass Spectra
Fragmentation
Substituent Effect
Electron Impact