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SUBJECT OF INVESTIGATION

EXPLORATION OF NEW CHEMOTHERAPEUTICS
FOR
INFECTIONOUS DISEASES

RESPONSIBLE INVESTIGATOR

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EXPLORATION OF NEW CHEMOTHERAPEUTICS
FOR
INFECTION DISEASES

Fundamental Studies on Protomycin, an Antiamoebic
Antibiotic and Cephalomycin, an Antiviral Antibiotic

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and
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Tokyo, Japan
1. Protomycin

In the preceding quaternary report, we have proposed the structure for protomycin.

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_2, \text{O} \\
\text{CH}_2 - \text{CH} - \text{CH} - \text{C} - \text{C} - \text{CH}_2 - \text{CH} - \text{CH} & \quad \text{CH}_2 - \text{CO} \\
\text{CH}_2 - \text{C} - \text{OH} & \\
\text{CH}_3 & , \\
\end{align*}
\]

To prove this structure, an acid obtained by the following sequence of reactions remained still to be identified:

- **Protomycin**
  - **H\textsubscript{2}O, Pd**
    - **Pyridine**
      - **NH\textsubscript{2}OH**
        - heated with H\textsubscript{2}SO\textsubscript{4} on water bath to induce Deckmann's rearrangement; distilled from dil. H\textsubscript{2}SO\textsubscript{4}.
The corresponding acid ester was synthesized by the following sequence of reactions:

\[
\text{CH}_3\text{COOC}_2\text{H}_5
\]

\[
0 = 0 - \text{CH}_3
\]

\[
\text{CH}_3\text{OH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{C} - \text{COOC}_2\text{H}_5
\]

\[
\text{CH}_3 - \text{C} = 0
\]

\[
(\text{\textcircled{5}})_{\text{CH}_3} = \text{OS}_2
\]
Although mixed melting point of the products (I) and (II) was 55-56°C at several different proportions and their infrared spectra were almost identical each other except three absorption bands, we undertook the resolution of racemate (II) into optically active components. While the experiment is still under continuous, we obtained a fraction with M.P. 62-53°C from (II) with (M.P. 72-73°C).

2. Cephalomyacin

Cephalomyacin was separated into fractions by the chromatography on DEAE-cellulose. The most active component eluted with 0.4% NaOH was assayed for amino acid constitution by DNP method. The result was as follows:

<table>
<thead>
<tr>
<th>Amino Acids</th>
<th>Malaratic</th>
<th>Amino Acids</th>
<th>Malaratic</th>
</tr>
</thead>
<tbody>
<tr>
<td>valine &amp; leucine</td>
<td>2.7</td>
<td>proline</td>
<td>4.3</td>
</tr>
<tr>
<td>alanine</td>
<td>1.45</td>
<td>arginine</td>
<td>?</td>
</tr>
<tr>
<td>serine</td>
<td>0.95</td>
<td>histidine</td>
<td>?</td>
</tr>
<tr>
<td>glutamic &amp; aspartic acid</td>
<td>4.9</td>
<td>methionine</td>
<td>?</td>
</tr>
<tr>
<td>threonine</td>
<td>0.90</td>
<td>phenylalanine</td>
<td>0.34</td>
</tr>
<tr>
<td>cystine</td>
<td>0.02</td>
<td>glycine</td>
<td>1.25</td>
</tr>
</tbody>
</table>
Protomyocin was treated with pronase, a proteolytic enzyme selectively acting on L-amino acid moiety, to evaluate liberated amino acids. Because the protomyocin is quantitatively hydrolysed with pronase, D-amino acid was supposed not to exist. Glycine, alanine, serine and threonine were detected as N-terminal groups by DNP-method.