Technical Papers

Biosynthesis of Penicillin. I. Role of Phenylacetic Acid

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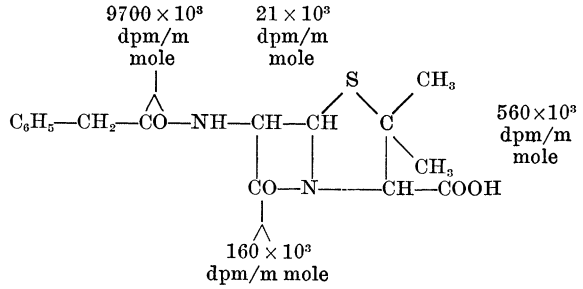
In view of the long period that penicillin has been under investigation it is somewhat surprising that comparatively little is known about the biosynthesis of this antibiotic. The only tracer studies that have come to our attention are those utilizing deuterophenylacetyl-N^{15}-valine (*1*), phenylacetic acid-1-C^{13} (*2*), and S^{35} (*3*). The apparently clear-cut results obtained in the incorporation of the benzyl residue from phenylacetic acid into benzylpenicillin have perhaps discouraged further investigations with this precursor.

Behrens *et al.* (*1*) found that 92.5% of the benzylpenicillin obtained was derived from the deuterium-labeled phenylacetic acid. Craig *et al.* (*2*) similarly found excellent incorporation of phenylacetic acid-1-C^{13} into benzylpenicillin, although quantitative data are not given.

We have studied the incorporation of phenylacetic acid-1-C^{14} into benzylpenicillin by *Penicillium chrysogenum* Wis 49-133 and have found that the specific activity of the phenylacetic acid isolated by chemical degradation of the penicillin (*4*) was about 82% of the activity of the precursor phenylacetic acid. Decarboxylation (*5*) of the phenylacetic acid isolated by hydrolysis of the penicillin showed all of the radioactivity to be in the carboxyl group. We have also investigated other major fragments of the penicillin molecule by chemical degradation (*4*) and the results are summarized below:



The starting phenylacetic acid had an activity of $11{,}500 \times 10^3$ disintegrations/min/m mole. The specific activity of the penicillin was approximately $12{,}000 \times 10^3$ disintegrations/min/m mole. All activity values have a standard deviation of 5% or less, except for the figure given for the glycine moiety (21×10^3) which has an S.D. of about 10%.

A rough correspondence has been observed between the average specific activity of the respiratory CO_2 from the fungus and that of the CO_2 from the β-lactam carbonyl, and this similarity points to the possibility of CO_2 fixation playing a role in penicillin biosynthesis (*6*). These results are apparently not in agreement with those of Godzesky, Martin, and Stone (*7*), who report no significant fixation of $C^{14}O_2$ from bicarbonate into the penicillin molecule by *P. chrysogenum* (Q-176). Work on determination of the individual specific activities of all the carbons in this biosynthetic penicillin is in progress. Fermentation details will be described separately.

References

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The Reaction Occurring in CO_2–H_2O Mixtures in a High-Frequency Electric Arc[1]

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This study was initiated in the hope of isolating 1, and possibly 2, carbon-atom compounds formed by the reduction of carbon dioxide by water vapor in a high-frequency arc. It forms a part of a series of studies of the chemical effects of high-frequency discharges on gaseous systems. The action of radiation on these 2 gases is of special interest in relation to the basic photosynthetic process, and also carries implications with respect to the origin of living matter on earth. A typical flow system was employed, with an army aircraft 150-w transmitter supplying the necessary power to the discharge tube.

Exhaustive examination has failed, however, to definitely establish the presence of any interesting reduction products in a reproducible way. Most of the parameters affecting the process were investigated, including current, pressure, flow rate, and H_2O/CO_2

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