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The Use of Radioactive Element. III.[*1] Decarboxylative Acylation of Phenylacetic Acid.

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The preparation of benzyl methyl ketone by heating a mixture of phenylacetic acid and acetic anhydride in the presence of pyridine was orginally described by Dakin and West.1) This reaction was re-investigated by King and McMillan.2) They showed that dibenzyl ketone was also formed and proposed the following mechanism : From phenylacetic acid and acetic anhydride (A), phenylacetic anhydride (B) and phenylacetic-acetic anhydride (C) are formed. Three anhydrides (A, B, and C) are in a state of equilibrium and the reaction is a base-catalyzed condensation reaction of two acid anhydride molecules, involving a quasi-six-membered ring, as shown in Chart 1.

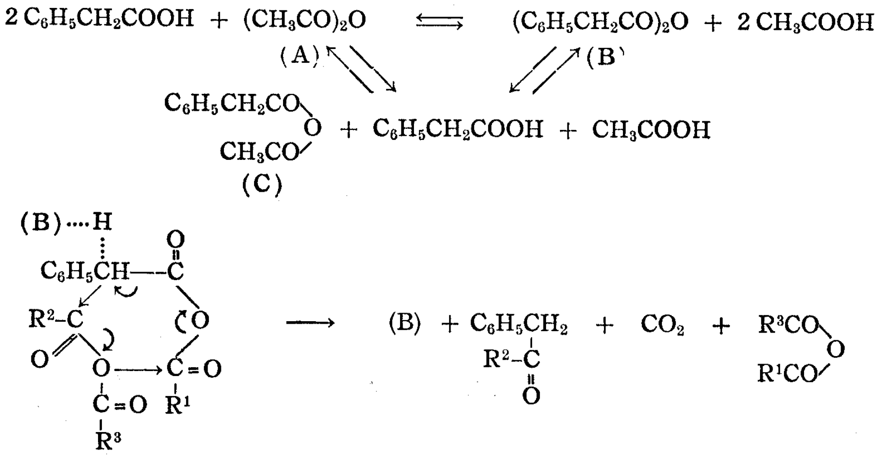

Chart 1.

To examine this hypothesis, similar study was carried out using a mixture of phenylacetic acid[*carboxyl*-^{14}C] and acetic anhydride in the presence of pyridine. If the reaction is a condensation reaction as shown in Chart 1, the carbon dioxide should be liberated from the carboxyl group of phenylacetic acid[*carboxyl*-^{14}C].

Table J. Radioactivity of Barium Carbonate and 2,4-Dinitrophenylhydrazones

Reactants	Compound	Specific activity[μc/mM.]
Phenylacetic acid[*carboxyl*-^{14}C]		11.41±0.23
Acetic anhydride		——
	$BaCO_3$	11.18±0.14
	$\begin{matrix}C_6H_5CH_2\\CH_3\end{matrix}\!\!>C{=}NNHC_6H_3(NO_2)_2$	inactive
	$\begin{matrix}C_6H_5CH_2\\C_6H_5CH_2\end{matrix}\!\!>C{=}NNHC_6H_3(NO_2)_2$	11.21±0.38

[*1] Part II : This Bulletin, **5**, 576(1957).
[*2] Takatsuki, Osaka-fu (中井利三郎, 杉井通泰).
[*3] Matsubara, Osaka-fu (田中千秋).
1) H.D. Dakin, R. West : J. Biol. Chem., **78**, 91(1928).
2) J.A. King, F.H. McMillan : J. Am. Chem. Soc., **73**, 4911(1951).

The reaction was performed under a slow stream of carbon dioxide-free air and the evolved carbon dioxide was precipitated as barium carbonate. The ketones produced were converted to corresponding 2,4-dinitrophenylhydrazones. The crude mixture of hydrazones was separated into its components by means of column chromatography and the radioactivity was determined. The results are shown in Table I.

The results indicated that the specific activity of barium carbonate and dibenzyl ketone is equal to that of phenylacetic acid[*carboxyl*-^{14}C] and benzyl methyl ketone is inactive. These facts show that the carbon dioxide originates from the carboxyl group of phenylacetic acid[*carboxyl*-^{14}C]. From the experimental results, King and McMillan's hypothesis is probable so far as the evolution of carbon dioxide is concerned. Method of isotopic assay was the same as that described in the previous paper.*1

Experimental

Action of Acetic Anhydride and Pyridine on Phenylacetic Acid[*carboxyl*-^{14}C]—A mixture of phenylacetic acid [*carboxyl*-^{14}C] (0.7 g., 11.41±0.23 μc/mM.), Ac_2O(2.5 cc.), and pyridine (2.5 cc.) was refluxed for 4 hr. While heating, a slow stream of dry CO_2-free air was passed through the reaction mixture by means of water aspiration and CO_2 evolved was precipitated as $BaCO_3$ by 0.2*N* $Ba(OH)_2$. Yield of $BaCO_3$ was 0.51 g. and the radioactivity was 11.18±0.14 μc/mM. The reaction mixture was poured into a saturated solution of 2,4-dinitrophenylhydrazine in 2*N* HCl. The weight of precipitated hydrazone was 0.7 g. The crude mixture of hydrazones was dissolved in benzene and adsorbed on a silicic acid-Super Cel (4 : 1) column (3×70 cm.). It was developed by washing with the same solvent. After development the column consisted of two bands. The zones were cut into sections, eluted with EtOH, and EtOH evaporated to dryness. The residues were recrystallized from EtOH. From the upper orange band 0.42 g. of benzyl methyl ketone was obtained as 2,4-dinitrophenylhydrazone. It formed orange plates, melting at 152~154°, and possessed no observable radioactivity. The lower yellow band yielded 0.1 g. of dibenzyl ketone as 2,4-dinitrophenylhydrazone of yellow needles, m.p. 105~107°. The radioactivity was 11.21±0.38 μc/mM.

Summary

The reaction between phenylacetic acid and acetic anhydride in the presence of pyridine was studied by using carboxyl-labeled (with ^{14}C) phenylacetic acid. It was found that the carbon dioxide was liberated from the carboxyl group of phenylacetic acid.

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