LII. THE SYNTHESIS OF 3:4-DIHYDROXY-PHENYLALANINE.

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IN a note recently published in this *Journal* by the author together with W. McCartney [1927] on a modification of the Erlenmeyer amino-acid synthesis, a description was given of the synthesis of 3:4-dihydroxyphenylalanine from vanillin. My attention has since been called, by other workers, to certain difficulties which they have encountered in the preparation of the ethyl benzoylamino-3-methoxy-4-hydroxycinnamate from the azlactone resulting from the condensation of vanillin with hippuric acid. Although, in our hands, the method originally described gave satisfactory results, the preparation was admittedly tedious. The reaction was therefore re-investigated, and a much more rapid method of working up the ester has been devised. In view of the fact that the series of reactions under consideration appears to constitute the simplest available synthesis of 3:4-dihydroxyphenylalanine, it is thought worth while to record the following improved method of preparation of the ester.

10 g. of the azlactone, obtained by the condensation of vanillin with hippuric acid, were dissolved in 100 cc. of alcohol to which were added 10 cc. of concentrated sulphuric acid; the solution was boiled under a reflux condenser for 20 minutes. About 75 % of the alcohol was distilled off under diminished pressure, the bath temperature being kept below 40°; with this precaution, no discoloration should occur at this stage. The residual yellowish syrup was poured into a dish and rubbed up with cold water to which was added sufficient sodium bicarbonate to neutralise the sulphuric acid present and to leave the solution slightly alkaline. The oily ester was separated with the aid of ethyl acetate, the aqueous solution was again extracted with this solvent, and the combined ethyl acetate extracts were dried and evaporated. The residue was dissolved in warm alcohol and the ester precipitated by the cautious addition of water; it separated first as an oil which crystallised on rubbing; this crystallisation is almost immediate if a trace of the substance be available for seeding. After standing in the ice-chest for some hours, the precipitate was filtered off and recrystallised from dilute (60 %–65 %) alcohol. There was thus obtained 55 %–60 % of the theoretical yield of the pure ester, m.p. 129°.

REFERENCE.

Harington and McCartney (1927). *Biochem. J.* 21, 852.