CLXXXIV.—*A New Synthesis of* dl-*Pilopic Acid.*

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IT was stated in a previous paper (J., 1930, 258) that an attempt would be made to utilise the reaction of malonic esters with formaldehyde in the presence of dilute sodium hydroxide solution for the preparation of 2-keto-3-ethyltetrahydrofuran-4-carboxylic acid. This has been successful, but in the meantime Tschitschibabin and Preobraschenski (*Ber.*, 1930, **63**, 460) have synthesised this acid by a different method and proved the identity of one of its active forms with the acid derived from pilocarpine. The acid prepared by the successive action of formaldehyde and hydrochloric acid on ethyl butane-ααβ-tricarboxylate seems to be identical with the stable form of Tschitschibabin and Preobraschenski's acid.

Ethyl butane-ααβ-tricarboxylate (from ethyl α-bromobutyrate and ethyl sodiomalonate) (10 g.) was kept with formalin in aqueous alcoholic solution at p_H 6—9 for 1 week at room temperature, water then being added. The separated ester was mixed with 50 c.c. of concentrated hydrochloric acid and saturated with hydrogen chloride, and the solution thus obtained was kept at room temperature for 10 days with occasional addition of a little water. An equal volume of water was then added, and the whole boiled under reflux for 5 hours. (An attempt to carry out the hydrolysis, ring closure, and loss of carbon dioxide in one stage by boiling the separated ester with dilute hydrochloric acid gave a very poor yield, much loss of formaldehyde having occurred.) When, after evaporation of the water, the residue was distilled under reduced pressure, water was evolved, ethylsuccinic anhydride passed over at 115—120°/18 mm., and 2-keto-3-ethyltetrahydrofuran-4-carboxylic acid (3 g.) was collected at 210—215°/18 mm. After crystallisation from water, the acid had m. p. 86—87° (Found : C, 53·0; H, 6·2; equiv., 155; equiv. after boiling with excess of sodium hydroxide solution, 80. Calc. : C, 53·2; H, 6·3%; equiv., 158; equiv. after boiling, 79). The intermediate products in the reaction could not be isolated.

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