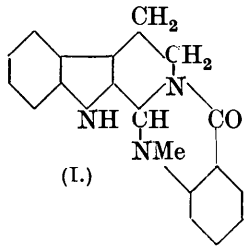
CCXX.—*A Synthesis of Rutœcarpine.*

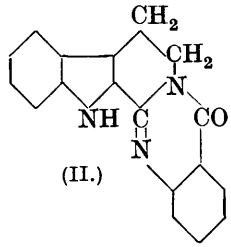
By YASUHIKO ASAHINA, RICHARD HELMUTH FRED MANSKE, and ROBERT ROBINSON.

FOLLOWING the analytical investigations (Asahina and Mayeda, *J. Pharm. Soc. Japan*, 1916, No. 416; Asahina and Fujita, *ibid.*, 1921, 863; Asahina, *ibid.*, 1924, No. 503, 1) which clearly proved that evodiamine and rutæcarpine, the alkaloids of *Evodia rutœcarpa*, Benth. and Hook., have the constitutions (I) and (II), respectively,

synthetical experiments were instituted by one of us in Japan,* whilst, on the other hand, the natural development of some work in progress at Manchester led in the same direction; the outcome is the present joint memoir, in which we describe an unexpectedly simple synthesis of rutæcarpine (II).



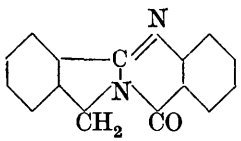
(I.)

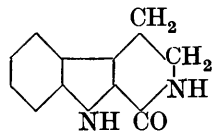


(II.)

As a preliminary we studied the preparation of a quinazolone derivative from an available cyclic amide and anthranilic acid and found that phthalimidine and methyl anthranilate readily condense in the presence of phosphorus trichloride (compare Sen and Rây, J., 1926, 646) with formation of an *iso*quinazindolone (III). The

(III.)





(IV.)

application of this process to 3-keto-3 : 4 : 5 : 6-tetrahydro-4-carboline (IV) (Manske and Robinson, this vol., p. 240) resulted in the production of rutæcarpine. The identity of the synthetical specimen with one of natural origin was proved by careful direct comparison.

EXPERIMENTAL.

iso*Quinazindol-2-one* (III).—A mixture of phthalimidine (6·7 g.), methyl anthranilate (8 g.), and phosphorus trichloride (30 g.) was heated under reflux for 3 hours, the product was decomposed by ice and hydrochloric acid, and the *base*, precipitated by addition of alkali to the solution, filtered after treatment with charcoal, was purified to some extent by redissolution in hydrochloric acid and recovery. It crystallised from ethyl alcohol in slender, colourless needles (yield, 4 g.), m. p. 205—206° (Found: C, 76·9; H, 4·5; N, 11·9. $C_{15}H_{10}ON_2$ requires C, 76·9; H, 4·3; N, 12·0%). This

* The degradative fission of rutæcarpine yields 3-β-aminoethylindole-2-carboxylic acid, and recently this acid has been reconverted into rutæcarpine. Its *o*-nitrobenzoyl derivative was reduced and then dehydrated. A brief account of the experiment will be found in the May (1927) issue of the *Journal of the Pharmaceutical Society of Japan*. Y. A.

weak base is soluble in moderately concentrated hydrochloric acid and is sparingly soluble in most neutral organic solvents.

Rutœcarpine (II).—A mixture of the ketotetrahydrocarboline (4 g.), methyl anthranilate (5 g.), and phosphorus trichloride (20 g.) was heated under reflux for 4 hours and the excess of the trichloride was then removed by distillation under diminished pressure. The residue was decomposed with ice, the solid collected and boiled with concentrated hydrochloric acid (200 c.c.), and the solution filtered hot. Unchanged lactam was recovered from the solution; the insoluble, pale brown residue crystallised from boiling ethyl alcohol in colourless needles (yield about 1·5 g.), m. p. 257—258° (Found: C, 75·3; H, 4·7; N, 14·7. Calc. for $C_{18}H_{13}ON_3$: C, 75·2; H, 4·5; N, 14·6%), which also melted at 257—258° when mixed with a specimen of rutæcarpine from *Evodia rutœcarpa*. The experiments involved in the following observations were carried out side by side with both specimens and with identical results in every case. The substance is sparingly soluble in most organic solvents and crystallises from ethyl acetate in characteristic, very slender needles; it is very stable and may be distilled in small quantities in a high vacuum without decomposition. The bright yellow solution in sulphuric acid becomes deep brown on the addition of Mandelin's reagent or colourless on dilution with water. On boiling with dilute hydrochloric acid, the substance does not dissolve but is coloured yellow. The colourless solution in acetic acid exhibits a bluish-green fluorescence after the introduction of a few drops of sulphuric acid. The hot alcoholic solution becomes yellow on the addition of solid potassium hydroxide, but after dilution with water the colour is discharged and the unchanged substance separates in needles, m. p. 257°.

THE UNIVERSITIES OF TOKYO
AND MANCHESTER.

[*Received, June 1st*, 1927.]