($^{1}/_{3}$ decrease in diameter) of the artery rings was produced by 0.2 γ of serotonin[9] per cc. When 20 γ of this analog was then applied, the effect of serotonin was completely abolished. Half maximal antagonism was observed with 5–10 γ. The corresponding 2,3-dimethyl analog[7] was slightly less active, and the corresponding 3-ethyl analog, m.p. 116–118° (calcd. C, 74.97; H, 7.55; found, C, 74.94; H, 7.57) was somewhat less than the dimethyl. The analogs by themselves did not cause relaxation of segments untreated with serotonin. The antagonism between serotonin and analog was competitive over a serotonin concentration of 0.1–2.0 γ per cc. Some antagonism could also be shown in intact guinea pigs. The toxicity of the 2,3-dimethyl-5-aminoindole for either mice or guinea pigs was low enough (150 mg. per kg. for first signs of distress) as to suggest that such antimetabolities of serotonin may be useful pharmacological agents. Further application of established principles[6] may result in even more potent compounds.

FROM THE ROCKEFELLER INSTITUTE
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(9) Serotonin was kindly supplied by the Abbott Laboratories.

(10) With the technical assistance of G. Schaffner.

THE DETECTION, ISOLATION AND IDENTIFICATION OF (−)-PIPECOLIC ACID AS A CONSTITUENT OF PLANTS

Sir:

By partition chromatography on paper an unidentified ninhydrin reacting constituent of the alcohol soluble (non-protein) nitrogen fraction of beans was detected and found to be present in the fresh fruit and dry seeds of legumes.[1] The R_F values in phenol, collidine–lutidine and butanol-acetic acid were 0.90, 0.38, and 0.21, respectively. This substance has now been isolated by the use of an ion exchange resin (Zeo-Rex). 800 mg. of pure (−)-pipecolic acid hydrochloride (piperidine-2-carboxylic acid) was isolated from approximately 10 kg. of fresh green beans (*Phaseolus vulgaris*).

A blue reaction with isatin on the chromatograms first suggested that the substance was a piperidine or pyrrolidine derivative. When the substance was finally isolated it proved to be indistinguishable in phenol, collidine–lutidine, and butanol–acetic acid chromatograms from synthetic (DL)-pipecolic acid prepared by catalytic reduction of α-picolinic acid. The two isomeric piperidine carboxylic acids were distinguishable chromatographically from the isolate in the solvents collidine-lutidine and butanol–acetic acid.

Infrared absorption spectra, obtained for us by Dr. H. Posvic,[2] of the isolated crystalline substance and of the (DL) synthetic product were similar but not identical and the X-ray diffraction patterns of the two compounds were dissimilar. The synthetic product apparently crystallized as a racemic compound; and only when the natural product was compared with the optically active (−)-enantimorph[2] did it prove to be identical as shown by matching infrared absorption spectra. The free acid and its hydrochloride are very soluble in water, sparingly so in ethanol, insoluble in benzene and petroleum ether and they are particularly insoluble in the solvents suitable for infrared absorption spectroscopy. The optically active (−) enantimorph as the free base was obtained from King[3] who prepared it by reduction of baikiain ((−)1,2,3,6-tetrahydropyridine-2-carboxylic acid), a substance isolated from a leguminous wood (Rhodesian teak). For purposes of infrared comparison with the isolate the hydrochloride was prepared in crystalline form from King's reduction product.

This evidence together with an ultimate analysis of the isolate, proves that the naturally occurring substance is (−)-pipecolic acid. (Found: C, 43.40; H, 7.30; N, 8.54; calcd. for $C_6H_{11}O_2NHCl$: C, 43.51; H, 7.30; N, 8.46). The isolate melted at 257–258° with decomposition and its rotation $[\alpha]^{23}\mathrm{D}$ was −10.3°.

Pipecolic acid is a prominent constituent of leguminous fruits and seeds and appears also to be present in a large number of other plants (*e.g.*, potato tuber, the edible mushroom) though in smaller amount. Further details will be published later.

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(1) Unknown No. 1 in Figure 2 of F. C. Steward and J. F. Thompson, *Ann. Rev. Plant Physiology*, **1**, 233–264 (1950).

(2) Chemistry Department, Cornell University, Ithaca, N. Y.

(3) F. E. King, T. J. King and A. J. Warwick, *J. Chem. Soc.*, 3590–3597 (1950).