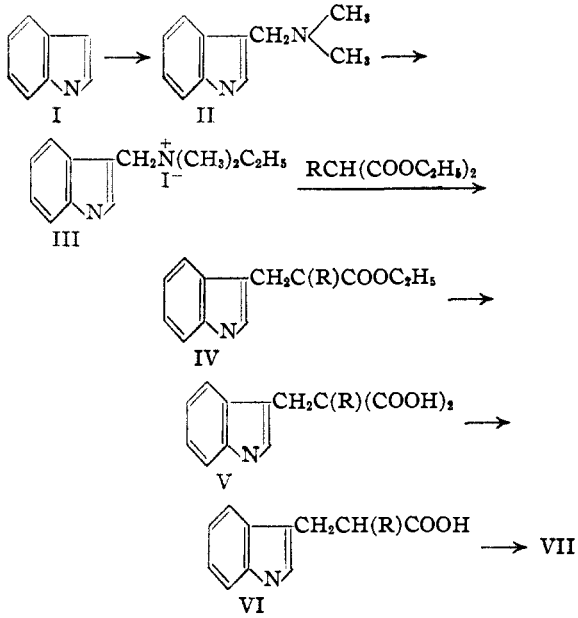
COMMUNICATIONS TO THE EDITOR

A NEW SYNTHESIS OF TRYPTOPHAN

Sirs:

In view of the recent communication of Snyder, *et al.*,[1] on the use of gramine methiodide as an alkylating agent, we wish at this time to record our experience in this field.

Tryptophan (VII) was synthesized by the procedure outlined in the following equations



The condensation was carried out successfully when R = H, $HNCOCH_3$ or $HNCOC_6H_5$. The ethyl α-carbethoxy-β-(3-indolyl)-propionate, (R = H), was hydrolyzed to the malonic acid which melted at 187–189° when pure.[2] The free acid was easily converted to β-(3-indolyl)-propionic acid, which melted at 128–130°.[2]

Ethyl α-carbethoxy-α-acetamido-β-(3-indolyl)-propionate, (R = $HNCOCH_3$), melted at 157° (Calcd. N, 8.09. Found: N, 8.27). Ethyl α-carbethoxy - α - benzamido - β - (3 - indolyl) - propionate, (R = $HNCOC_6H_5$), melted at 142° (Calcd. N, 6.86. Found: N, 7.20).

Hydrolysis of IV in sodium hydroxide solution proceeded quite smoothly. The free acetamido and benzamidomalonic acids (V), m. p. 135–137° (dec.), 85–90° (dec.), respectively, were used inthe crude form since some decarboxylation accompanied purification, thus rendering the preparation of analytical samples difficult. Complete decarboxylation was effected by heating at 180–200° until the evolution of carbon dioxide ceased.[2] The structures of the acetyl and benzoyltryptophan so prepared were confirmed by direct comparison with authentic specimens. The free amino acid was obtained from the above derivatives by hydrolysis according to procedures described in the literature. The over-all yield of tryptophan based on indole as the starting material was as high as 35% of the theoretical. Details of the procedure will be published at some future date.

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(1) Snyder, Smith and Stewart, This Journal, **66**, 200 (1944).

(2) Maurer and Moser, *Z. physiol. Chem.*, **161**, 131 (1926). The authors report 188° as the m. p. for the malonic acid and 134° for the decarboxylated product.

LOW ANGLE X-RAY SCATTERING FROM CHRYSOTILES

Sir:

It is becoming increasingly evident that studies of low angle scattering of monochromatic X-rays will prove valuable in the study of sub-optical–microscopic structures. Bernal and Fankuchen in their virus studies,[1] Bear in his collagen studies,[2] Warren for carbon black[3] and Kratky in studies of proteins and of fibers,[4,5] found such significant small angle scattering. We have now studied various chrysotiles with X-rays using a standard technique for the wide angle scattering and the apparatus and technique employed in the study of dry gels of tobacco mosaic virus[1] for the low angle work. Copper characteristic radiation filtered through nickel foil was used. In the low angle work a fine slit system to define the X-ray beam and a 30 cm. specimen to film distance permitted the study of the small angle scattering down to angles corresponding to 500 Å. The specimens were stationary thin slabs of chrysotile mounted so that the X-rays passed through the thin direction of the specimen. The wide angle diagrams are substantially alike and all showed an undifferentiated low angle equatorial scattering. The use of a fine slit system[1] resolved this scattering into clearly differentiated lines. In each of the four samples studied to date, at least two lines were always visible, the ratio of their Bragg spacings being $\sqrt{3}$. This suggests strongly that these chrysotiles are composed of parallel fundamental fibrils—hexagonally packed in cross section. The diameters of the fibrils can be computed from the Bragg spacings (on the hypothesis

(1) Bernal and Fankuchen, *J. Gen. Physiol.*, **25**, 111–165 (1941).

(2) Bear, This Journal, **64**, 727 (1942).

(3) Biscoe and Warren, *J. Applied Phys.*, **13**, 364–371 (1942).

(4) Kratky, Sekora and Treer, *Z. Elektrochem.*, **48**, 587–601 (1942).

(5) Kratky and Sekora, *Naturwissenschaften*, **31**, 46–47 (1943).

of hexagonal packing) and prove to be significantly different.

TABLE I

	Diam. of fibrils in Å.
Canadian chrysotile	195
"harsh" chrysotile (U. S. A.)	250
"soft" chrysotile (U. S. A.)	226
Chrysotile (Italy)	218

It seems possible that the explanation of the variations in mechanical properties of the chrysotiles can be explained on the basis of the differences in their low angle scattering (and consequently on differing fundamental fibril diameter). An extensive survey of asbestos-like materials is now in progress.

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GLIOTOXIN, THE ANTIBIOTIC PRINCIPLE OF *GLIOCLADIUM FIMBRIATUM*[1]

Sir:

We find that the antibiotic substance gliotoxin is produced by at least three different organisms.

Professor Harold Raistrick of the London School of Hygiene and Tropical Medicine has isolated from a species of *Penicillium* (as yet not completely identified) a crystalline substance which appeared to be identical with gliotoxin from *Gliocladium fimbriatum*.[1] He had independently reached the conclusion that it should be represented by the formula $C_{13}H_{14}N_2O_4S_2$ (private communication to J. R. J., London, October 11, 1943). Professor Raistrick has kindly furnished us a sample of his crystalline material and a comparison with our gliotoxin has shown that the two substances are identical.

The sample from Professor Raistrick on examination with a polarizing microscope was monoclinic hemimorphic, crystallizing as flattened rods elongated parallel to the "b" axis. It showed the forms: basal pinacoid, 001; orthopinacoid, 100; hemiclinodomes, 011 and $01\bar{1}$, and hemiprisms, $\bar{1}10$ and 110. The crystallographic angle β is 79° with the interfacial angle, $011:01\bar{1}$, equal to 109°. The optic axial plane is perpendicular to 010 with α, the obtuse bisectrix, 34° from "a" in the obtuse angle β. The optic axial angles are $2V = 53°$ and $2E = 90°$. The refractive indices are α, 1.644 ± 0.001; β, 1.658 ± 0.001; β' (component of β in the plane 100), 1.655 ± 0.002; and γ, 1.708 ± 0.001. This description agrees in every respect with the previously published crystal structure of gliotoxin[1]; hence Professor Raistrick's material is identical with gliotoxin.

Determination of the decomposition point[2] showed 218° (uncor.), and a mixed decomposition point with gliotoxin, melting with decomposition at 219°, was 218°. In a determination of specific rotation, a very characteristic constant of gliotoxin, 6.1 mg. of the sample in 1 ml. of chloroform gave $\alpha = -1.71 \pm 0.06°$, $[\alpha]^{20}D$ $-280 \pm 10°$. This is in reasonably good agreement with the values previously found for gliotoxin: $[\alpha]^{19}D$ -239 (C, 0.51 in $CHCl_3$)[2]; $[\alpha]^{26}D$ $-255 \pm 15°$ (C, 0.103 in $CHCl_3$).

Furthermore, identification of gliotoxin as a product of the fungus *Aspergillus fumigatus* has been accomplished by Dr. O. Wintersteiner.[3]

Since gliotoxin has been isolated from cultures of *Gliocladium fimbriatum*, *Aspergillus fumigatus* and a species of *Penicillium* not yet identified, it may prove to be an antibiotic product of still other fungi.

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ITHACA, NEW YORK WILLIAM F. BRUCE

RECEIVED FEBRUARY 9, 1944

(1) Johnson, Bruce and Dutcher, THIS JOURNAL, **65**, 2005 (1943).

(2) Weindling and Emerson, *Phytopathology*, **26**, 1069 (1936).

(3) In press; private communication to W. F. B., March, 1943.