triazole as a weed killer, but also suggest that this compound may be useful in biochemical or clinical studies relative to purine metabolism.

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## Formation of tryptophol in the disulfiram-treated rat

In man, the major deamination product of norepinephrine is 3-methoxy-4-hydroxy-mandelic acid¹. In the white rat, however, a major metabolite of this catecholamine has been shown to be 3-methoxy-4-hydroxyphenylglycol². These metabolites are presumably the oxidation and reduction products of a common intermediate, 3-methoxy-4-hydroxyphenylglycol aldehyde, which is formed *in vitro* by incubation of normetanephrine with purified monoamine oxidase³. The existence of this reduction product suggests that other biogenic amines also may be metabolized to alcohols. This possibility was considered for tryptamine which *in vivo* is largely metabolized to indole-3-acetic acid following oxidative deamination⁴.

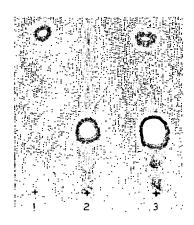
The postulated metabolite of tryptamine, tryptophol (indolylethyl alcohol), was synthesized by reduction of indole-3-acetic acid with LiAlH<sub>4</sub> (ref. 5) (this procedure appears useful for the preparation of alcohols from acidic metabolites of many biologically important amines). The leaflets obtained on crystallization from ether–petroleum ether melted at  $59^{\circ}$  and the picrate melted over a range of  $93-96^{\circ}$  (cf. ref. 6: m.p.,  $59^{\circ}$ ; m.p. picrate,  $94-96^{\circ}$ ).

After chromatography in isopropanol-7 N NH $_3$  (4:1), and in benzene-propionic acid-water (2:2:1), the papers were sprayed with 0.5% p-dimethylaminolbenzaldehyde in 50% methanol-2 N HCl. A dark blue spot quickly appeared which had the  $R_F$  of 0.9 in either solvent. In contrast with tryptophol, indole-3-acetic acid yields maximal color formation with this spray in 20-40 min.

Each of 3 adult white rats was injected intraperitoneally with 10 mg tryptamine and their urines collected in dilute acid over a 24-h period. The pooled urines were adjusted to pH I with HCl, heated to  $100^{\circ}$  for 10 min and then extracted with 4 vol. ether. The ether solution was concentrated by evaporation and a portion of the extract transferred to Whatman No. I filter paper. After development in isopropanol—NH<sub>3</sub>, the sprayed chromatogram revealed only a single blue spot which corresponded in  $R_F$ , color and rate of color development with indole-3-acetic acid.

The absence of tryptophol suggested that the presumed intermediate, indole-3-

acetaldehyde, was completely oxidized. In an attempt to inhibit the oxidation of the aldehyde and perhaps allow formation of the alcohol to take place, an inhibitor of acetaldehyde oxidation, disulfiram\*, was administered to the rats. This drug, which is used in the management of alcoholism, inhibits liver aldehyde dehydrogenase and many other oxidative enzymes?. Since disulfiram is insoluble in water, a suspension of 50 mg disulfiram/ml propylene glycol was prepared and 1 ml of this mixture injected intraperitoneally into each of 3 rats daily for 3 days. About 18 h after the last injection, each rat was injected with 10 mg tryptamine and their urines collected and processed as before. The visualized chromatogram showed indole-3-acetic acid and an additional compound. This compound had the same  $R_F$ , blue color and prompt color formation as authentic tryptophol. These results



are illustrated in a chromatogram represented by Fig. 1. Chromatography in 2 dimensions further confirmed the identity of this compound with tryptophol and also revealed the presence of another acidic metabolite of tryptamine which migrates with indole-3-acetic acid in isopropanol-NH3 but less rapidly in benzene-propionic acid-water.

Fig. 1. Paper chromatogram showing presence of tryptophol in an extract from the urines of disulfiram-treated rats injected with tryptamine. The chromatogram was developed by the ascending method in isopropanol-7 N NH3 and then sprayed with p-dimethyl-aminobenzaldehyde reagent. 1, synthetic tryptophol; 2, urine extract from untreated rats showing only indole-3-acetic acid; 3, urine extract from disulfiram-treated rats showing both indole-3-acetic acid and tryptophol.

The simultaneous occurrence of tryptophol and indole-3-acetic acid in the urines of disulfiram-treated rats suggests that they arise from a common aldehyde in accordance with the scheme2 advanced for the analogous metabolites of normetanephrine. The oxidation of the aldehyde intermediate is apparently inhibited by disulfiram which suggests that this agent inhibits the oxidation of  $\beta$ -substituted acetaldehydes as well as acetaldehyde.

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