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-hydroxymandelic acid[1]. In the white rat, however, a major metabolite of this catecholamine has been shown to be 3-methoxy-4-hydroxyphenylglycol[2]. 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 oxidase[3]. 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 deamination[4].

The postulated metabolite of tryptamine, tryptophol (indolylethyl alcohol), was synthesized by reduction of indole-3-acetic acid with $LiAlH_4$ (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° and the picrate melted over a range of 93–96° (*cf.* ref. 6: m.p., 59°; m.p. picrate, 94–96°).

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 1 with HCl, heated to 100° 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. 1 filter paper. After development in isopropanol–NH_3, 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[7]. 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–NH_3 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 NH_3 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 scheme[2] 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 β-substituted acetaldehydes as well as acetaldehyde.

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