appeared after precipitation of the S-RNA as quaternary ammonium salt and regeneration. This precipitation would thus constitute a method of purification of S-RNA, which is equivalent, so far as the elimination of inactive oligonucleotides is concerned, to chromatography on 'Ecteola'-cellulose.

In summary, after treatment with a quaternary ammonium salt, S-RNA can be dissolved in an organic solvent and regenerated from this solution as the sodium salt, without loss of its biological activity.

Experiments are in progress to take advantage of this dissolution in an organic solvent and attempt a fractionation of S-RNA.

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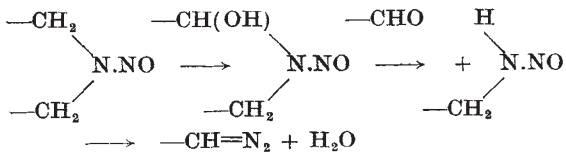
Mechanism of the Hepatoxic Action of Dialkylnitrosamines

Dimethylnitrosamine[1] and some other dialkylnitrosamines[2,3] cause centrilobular necrosis in rats. Schoental and Rose[4] suggested independently that centrilobular necrosis was caused by diazo-alkanes formed by the metabolic oxidation of the nitrosamines in the liver *in vivo*[5,6]. The sequence of reactions is presumed to be :



On this sequence (*n*-butyl)(methyl)nitrosamine (BuMeN.NO) should cause centrilobular necrosis, but (*tert*-butyl)(methyl)nitrosamine ($Me_3C.MeN.NO$) should not. α-Oxidation of the *n*-butyl compound can give either diazomethane or diazobutane, according to which alkyl group is attacked. In the *tert*-butyl compound the *tert*-butyl group cannot be attacked in the α position, and oxidation of the methyl group leaves a compound with no α-hydrogen atom, which cannot, therefore, yield a diazo-alkane.

The two compounds were synthesized and tested on female rats (Porton Wistar strain). Both compounds were given intraperitoneally as solutions in normal saline.

The *n*-butyl compound caused acute centrilobular necrosis in doses of 100–120 mgm./kgm. in 1–2 days. Doses of 60 mgm./kgm. were without obvious effect. This compound is about one-quarter as toxic as dimethylnitrosamine, and affects the liver in a very similar way.

Twenty rats were treated with the *tert*-butyl compound. Four died from the treatment they received, so the doses given were near the maximum tolerable. Three survived 1,600 mgm./kgm. given in divided doses over 4 days, and three others survived 1,400 mgm./kgm. given over the same period. The rest survived smaller doses given over shorter periods. The survivors were killed at various times after the last dose—from the highest doses at 1, 3 or 10 days after. Various lesions were observed on histological examination, but no centrilobular necrosis in any case. Thus the *n*-butyl compound caused the typical lesion, but the *tert*-butyl compound did not, in accordance with the diazo-alkane theory.

This evidence for the diazo-alkane theory is not, of course, conclusive. It is possible that still higher doses of the *tert*-butyl compound might cause centrilobular necrosis. Alternatively, perhaps the *tert*-butyl compound does not reach the sites in the liver at which metabolism takes place. This last possibility is being investigated with nitrosamines labelled with carbon-14.

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PHYSIOLOGY

Cytotoxic Effect of Aminoacetonitrile on Fibroblast Cultures and its Prevention by Histidine

The understanding of the ætiological factors involved in the curious poisoning arising from the ingestion of *Lathyrus odoratus* seeds has been greatly advanced by the identification of β-amino-propionitrile as the active moiety of the toxic principle and the recognition of the even more potent lathyrogenic property of aminoacetonitrile (AAN)[1,2]. However, the site and nature of the primary metabolic disturbance responsible for the characteristic mesenchymal lesions produced by aminonitriles have not yet been elucidated. The present investigation was designed primarily to explore the possibility of using tissue cultures as a prospective tool for studying under *in vitro* conditions the biochemical mechanism underlying the toxic action of AAN.

The experiments were performed regularly with chick embryo fibroblasts grown in a modified *M*–150 medium of Morgan *et al.*[3] consisting of Hanks's salt solution, a mixture of amino-acids and vitamins and fortified with 2 per cent calf serum. In most experiments 3–4 days-old cultures were used and AAN was added with fresh medium following the removal of the initial culture fluid. Under such conditions