

(1971 crop): *Bracts*  $\Delta^1$ -THC: 13.9; CBD: 6.4. *Bracteoles*  $\Delta^1$ -THC: 57.9; CBD: 35.0.

2. *Turkish strain* (1971 crop): *Leaf* (no gl. hairs). CBD: 3.0. *Small bracts*, upper part (very few gl. hairs) CBD: 4.9. Lower part of *same bracts* (numerous gl. hairs) CBD: 16.7.

3. *Thailand strain* (1971 crop): Vegetative stage; leaf. Of particular interest as no typical gl. h. present but numerous large spherical sessile glands.  $\Delta^1$ -THC: 11.6; CBD: 0.8.

TLC examination of all samples showed that the cannabinoids always occurred as the corresponding acids.

We conclude that the cannabinoids are probably formed in many parts of the plant, but stored mainly in the glandular hairs of the floral parts or in the sessile glands just referred to. Workers on biosynthesis should take this into account as well as legislators, whose definition of cannabis often omits reference to the vegetative leaves which may have significant activity.

Pure  $\Delta^1$ -THC in petroleum spirit was stable in the dark at 4°C (no measureable loss after 7 months) and at room temperature. However, in bright light, room temperature, 20 % was destroyed in 2 days and the remainder after 6 days. In carefully air dried herb, little loss occurred after 2 months storage in the dark (4°C and room temperature) or even when exposed to bright light. Microscopical examination showed that the glands were still intact and possibly function as excellent storage containers. In contrast, in Hashish samples ("Cannabis resin"), much resinous fluid lies free in the sample and is obviously liable to oxidation.

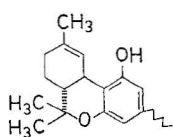
"Stabilised" herb is also being examined to determine if enzyme activity is a factor.

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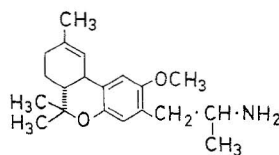
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### Preliminary studies of the synthesis of nitrogen analogs of $\Delta^1$ -THC

Heretofore, nitrogen analogs of tetrahydrocannabinol (THC) have been designed starting with the carbon skeleton of the parent cannabinoid and replacing one or another carbon atom with its nitrogen counterpart.



$\Delta^1$ -THC

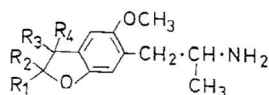


Amphetamine analog

Razdan and co-workers have prepared three of these analogs, with a nitrogen in the 1-position (terpene nomenclature), the 5 position (as the quinuclidine heterocycle) and the  $\gamma$ -position in the amyl side chain (as the dimethylaminoethyl analog). Anker and Cook have reported the N-methyl piperidine analog with the nitrogen found in the 6-position. Hoops *et al.* have described the analog wherein the pyran oxygen is replaced with an N-methyl. Cushman has developed a synthetic route to the 2-aza analog. In all these compounds except the last, the double bond is found in the unnatural 3,4-position.

The approach considered here is to construct an analog by starting with known active compounds that already contain nitrogen, and modifying their structures to imitate THC. The DOM family of psychotomimatics are 2,5-dimethoxy-4-alkyl phenylisopropylamines, and the most active of the methoxy methylenedioxy analogs carries a heterocyclic ring in the 4,5-position and still shows the *para*-oxygen substitution pattern. The extension of these features into the THC carbon skeleton dictates the structure of the analog shown above.

A preliminary study to this end has been the synthesis of a number of benzofuran and benzopyren counterparts. The synthesis of several methyl substituted furan compounds of the general formula:



have been completed and some chemical problems associated with these syntheses will be discussed.

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#### TLC, GLC and MS of cannabidivarin, tetrahydrocannabivarin and cannabivarin

Many constituents of hashish have been found in the past years and their chemical structures have been elucidated.

Recently, we isolated a new constituent of hashish: cannabivarin [1, 2] and we published [2] the isolation, identification and quantification of cannabidivarin [3], cannabivarin and tetrahydrocannabivarin [4] in