

The present results are in agreement with previous findings where no detectable amounts of free Δ^1 -THC-7-oic acids could be found after administration of Δ^1 -THC⁷. To be eliminated, it appears that the free acids need further hydroxylation (IVa, b) and/or conjugation.

The results presented in this paper in conjunction with those in the literature, particularly the recent observations by BURSTEIN et al.³, make possible a tentative partial delineation of the overall THC metabolism. In the case of Δ^1 -THC, the initial conversion^{1,2} is oxygenation, mainly at C-7, but also at C-6, and as an epoxide^{12,13} on C-1, C-2. With Δ^6 -THC, oxygenation takes place on C-7, on C-5^{12,13} and on the side chain (1'' and 3''-hydroxy- Δ^6 -THC). Some of the mono oxygenated THC's are biologically active and may represent the actual active species in the body^{1,2,14}. Others, such as 1''hydroxy- Δ^6 -THC and 6-keto- Δ^1 -THC, show no activity (rhesus monkey). It should be pointed out that the various metabolites have been isolated in studies with different animal species or animal organ homogenates and may not all be relevant to human metabolism. However, 7-OH- Δ^1 -THC, 6 β and 6 α -hydroxy- Δ^1 -THC have been identified as metabolites of Δ^1 -THC in man^{15,16}. The THC-7-oic acids, on the basis of the present report, are formed by further metabolism of the respective 7-hydroxy-THC's. The 7-aldehyde compounds are possible intermediates¹⁷. The acids are excreted mainly as water-soluble 'conjugates', the nature of which is as yet unknown. All the THC-7-oic acids, including those hydroxylated on the side chain, on the basis of the present report, are probably inactive and represent the final, or one of the final, detoxification stages. Very little, if any, unchanged THC's, or mono oxygenated THC's are excreted as such¹⁸.

Zusammenfassung. 7-Hydroxy- Δ^6 -tetrahydrocannabinol (7-hydroxy- Δ^6 -THC), ein psychotomimetisch aktiver Metabolit des Δ^6 -THC, wird von Kaninchen in inaktive Δ^6 -THC-7 Säure metabolisiert. Die Synthese dieser Säure wird beschrieben.

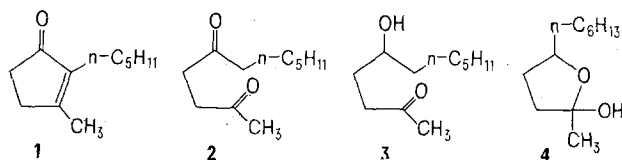
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- ¹² O. GURNY, D. E. MAYNARD, R. G. PITCHER and R. W. KIERSTEAD, J. Am. chem. Soc. 94, 7928 (1972).
- ¹³ R. MECHOULAM, H. VARCONI, Z. BEN-ZVI, H. EDERY and Y. GRUNFELD, J. Am. chem. Soc. 94, 7930 (1972).
- ¹⁴ E. W. GILL, G. JONES and D. K. LAWRENCE, Biochem. pharmac. 22, 175 (1973).
- ¹⁵ L. LEMBERGER, J. AXELROD and I. J. KOPIN, Ann. N.Y. Acad. Sci. 191, 142 (1971).
- ¹⁶ M. E. WALL, D. R. BRINE, C. G. PITT and M. PEREZ-REYES, J. Am. chem. Soc. 94, 8579 (1972).
- ¹⁷ S. BURSTEIN and J. ROSENFELD, Acta pharmac. Suecica 8, 699 (1971).
- ¹⁸ The work in Jerusalem was supported by the US National Institute of Mental Health and in Stockholm by the Swedish Medical Research Council.

A Facile Approach to Dihydrojasmane

Our continued interest¹ in the fragrant components of *Jasminum grandifolium* and related species has led to the development of a simple synthesis of dihydrojasmane (1). The present approach involves, as in our previous syntheses and a number of others, undecan-2,5-dione (2) as the penultimate precursor.



The HAUSER method² is a convenient procedure for the synthesis of methyl alkyl ketones. However, its extension to building up the γ -ketol system via alkylation of an oxirane or a derivative thereof was hitherto unexplored. An analysis of various synthetic possibilities toward dihydrojasmane prompted us to investigate such a reaction, since upon procurement of 5-hydroxyundecan-2-one (3) by a simple alkylation, one is assured of a three-step synthesis of the target molecule from readily accessible and inexpensive materials.

Alkylation of pentan-2,4-dione with 1,2-epoxyoctane in refluxing absolute ethanol in the presence of sodium iodide and anhydrous potassium carbonate for 20 h followed by distillation off most of the solvent, dissolution of the residue in water and extraction into ether and final isolation by Girard T separation³, furnished in 28% yield. (Bp. 81° (oven temp.)/0.75 Torr; Anal. Found: C, 71.11; H, 11.84; ν (CH₂Cl₂) 3605, 1710 cm⁻¹). Judging from the

spectral characteristics, especially the methyl ketone absorption region in the PMR-spectrum, this alkylation product exists in a dynamic equilibrium between the ketol 3 and the hemiacetal 4 forms.

JONES⁴ oxidation was then carried out by dropwise introduction of chromic acid to a stirred acetone solution of the 3, 4 mixture until an orange-brown tinge persisted. Water was added and the diketone 2 was obtained by ether extraction and distillation (74% yield).

Since 2 has been previously converted to dihydrojasmane, our synthesis is completed. The success of producing 3 indicates a rapid and general way for the synthesis of γ -ketols.

Résumé. La dihydrojasmane a été synthétisée en trois étapes à partir du pentanedione-2, 4.

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6 February 1973.

- ¹ H. C. Ho, T. L. Ho and C. M. WONG, Can. J. Chem. 50, 2718 (1972); T. L. Ho, H. C. Ho and C. M. WONG, Can. J. Chem. 51, 153 (1973).
- ² S. BOATMAN, T. M. HARRIS and C. R. HAUSER, J. org. Chem. 30, 3321 (1965).
- ³ A. I. VOGEL, A Textbook of Practical Organic Chemistry, 3rd edn, (Longman-Green, London 1962), p. 976.
- ⁴ K. BOWDEN, I. M. HEILBRON, E. R. H. JONES and B. C. L. WEEDON, J. chem. Soc., 39 (1946).
- ⁵ This research was supported by NRCC, Ottawa.