(aromatic system). The NMR spectrum of (II) showed the following signals: δ 1.40, s, 6, $-\mathrm{C}{<}^{CH_3}_{CH_3}$; 1.89, t (J=7 Hz), 2; $\geqslant$C–CH$_2$–CH_2–C–O; 2.48, t (J=7 Hz), 2, $\geqslant$C–CH_2–CH$_2$–C–O; 3.80, s, 3, –COOCH$_3$; 3.83, s, 3, –OCH$_3$; 5.63, m, 2, NH$_2$; 7.27, s, 1, aromatic proton.

Condensation of (II) with 1, 2, 3, 4-tetrahydronorharman-1-one (III) performed with POCl$_3$ in refluxing toluene[1], gave the dihydroparaensine (IV), $C_{24}H_{23}N_3O_3$ (M^+ 401), mp 305° (from isopropyl ether) which was found to be identical (mixed mp, TLC and IR spectrum) with the dihydroderivative of the natural product.

Riassunto. Dalla corteccia della *Euxylophora paraënsis* Hub. viene isolata la paraensina (I) che si rivela essere il primo alcaloide di tipo indolopiridochinazolinico a contenere una unità isoprenica.

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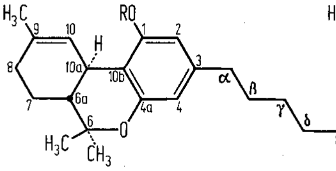
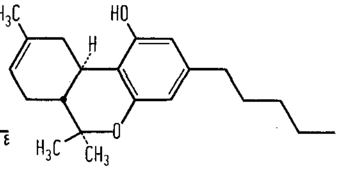
CMR Spectral Analysis of Tetrahydrocannabinol and its Isomers[1]

The biologically active constituents of *Cannabis sativa* L. (marijuana) have aroused much public and scientific interest in recent years. In view of the advent of a powerful, new tool of structure analysis, ^{13}C nuclear magnetic resonance (cmr) spectroscopy, its application to investigations of the chemical make-up of the major psychotomimetic marijuana (hashish) principle, **1**–Δ^9-tetrahydrocannabinol (Δ^9–THC) (**1a**), and related substances was undertaken.

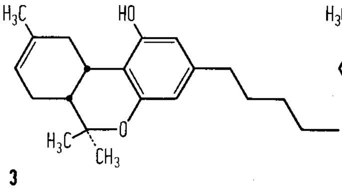
The δ values of all carbons of six tetrahydrocannabinol substances and model **5**, olivetol dimethyl ether, derived from their noise resonance decoupled and single frequency decoupled spectra[1] are listed in the Table. Assignment of the chemical shifts of the aromatic carbons is based on chemical shift theory[2] and former electron density calculations[3]. Shift data of **5** and consideration of substituent effects among alkanes[4] leads to the identification of three centers of the *n*-pentyl chain. The remaining β and γ carbons can be distinguished by inspection of the single frequency decoupled spectrum of a β, β-dideutero derivative of **5**, prepared by sodium deuteroxide-induced deuteration of *n*-butyl 3, 5-dimethoxyphenyl ketone and treatment of the product with lithium aluminum hydride and aluminum chloride[5].



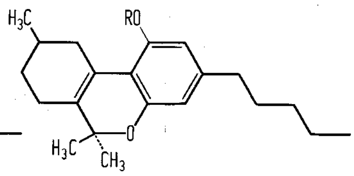
1a, R=H
b, R=Ac



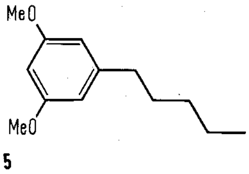
2



3



4a, R=H
b, R=Me



5

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Chemical shifts of carbon tetrachloride solutions cited in ppm upfield from carbon disulfide ($\delta_{CS_2} = \delta_{CCl_4} + 96.5$ ppm)

	1a	**1b**	**2**	**3**	**4a**	**4b**	**5**[a]
C(1)	38.5	44.3	38.3[b]	37.8[b]	40.2	36.4	34.8
C(2)	82.9	77.6	82.4	82.9	83.0	88.2	86.5
C(3)	51.1	50.9	51.0	49.6	49.8	50.5	48.5
C(4)	85.1	79.0	85.2	89.9	83.0	82.7	86.5
C(4a)	38.5	38.2	37.9[b]	37.6[b]	38.6	39.0	34.8
C(6)	115.9	115.9	116.3	116.7	115.2	115.8	
C(6a)	146.8	147.2	147.5	145.8	68.5	68.5	
C(7)	167.4	167.8	160.9	164.0	167.0	167.1	
C(8)	161.0	161.7	73.8	72.2	161.8[b]	162.0	
C(9)	60.6	59.0	58.2	58.2	163.6	163.6	
C(10)	67.8	68.9	156.4	153.4	155.7	155.8	
C(10a)	158.7	158.6	164.6	164.9	60.8	61.0	
C(10b)	83.6	77.9	82.2	76.3	81.8	88.2[c]	95.2
9-Me	169.2	169.4	169.0	168.9	170.5	170.7	
6α-Me	173.2	173.4	174.0	169.9	167.0	167.1	
6β-Me	164.9	165.3	164.9	174.2	168.6	168.8	
α-C	157.0	157.7	156.9	159.0	157.0	156.5	156.2
β-C	161.0	161.3	160.9	160.4	161.0	161.1	160.9
γ-C	162.0	162.5	161.9	161.5	162.0[b]	162.0	161.4
δ-C	170.0	170.3	169.9	169.9	170.0	170.1	169.9
ε-C	178.4	178.7	178.4	178.3	178.4	178.5	178.5
C=O		25.9					
CMe		172.0					
OMe						137.6	138.1 138.1

[a] For sake of comparison the THC numbering system is used for **5**. [b] These values within any column may be reversed. [c] Weak signal visible only in the single frequency decoupled spectrum.

JOHNSON's method of analysis of residual coupling[6] is utilized on the off-resonance proton-decoupled spectra of Δ^9-THC (**1a**) and Δ^8-THC (**2**) for the differentiation of the bridgeheads C(6a) and C(10a) in **1a**, its acetate (**1b**), **2** and its *cis* isomer (**3**). Use of the charge density data[3] facilitates distinguishing these bridgeheads from each other in compounds **4**. The expected low-field position of an oxygenated, non-protonated carbon identifies the remaining heterocyclic carbon site, –C(6).

The combination of effects of the 9-methyl group deshielding C(8) and C(10), C(1) moderately shielding C(10) and the *gem*-dimethyl function powerfully shielding C(7) makes the δ values of C(7) and C(10) of substances **2**, **3** and **4** predictably different and identifies C(7) and C(8) of Δ^9-THC (**1a**) and its acetate (**1b**). Furthermore, allylic carbons of cyclohexene rings possessing signals normally downfield of their homoallyl neighbors[7] places C(8) of **4a** and **4b** in proper shift relationship with C(7) and C(10). The assignments of chemical shifts of all other alicyclic carbons evolve from standard theory[2].

Methylcyclohexane[8] and 1-methylcyclohexene[7] serve as models for the 9-methyl group of compounds **4** and the group of substances **1**, **2** and **3**, respectively. Differentiation of the C(6) methyl groups depends on their conformation, an analysis of which has been recorded[8], and the expectation of an axial substituent to be upfield of an equatorial one[8,9].

Zusammenfassung. Die ^{13}C-NMR-Spektren des Tetrahydrocannabinols und seiner Isomeren wurden aufgenommen und vollständig analysiert.

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Indianapolis (Indiana 46206, USA), 11 October 1971.

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[6] R. A. ARCHER, R. D. G. COOPER, P. V. DEMARCO and L. F. JOHNSON, Chem. Commun. *1970*, 1291; M. TANABE, T. HAMASAKI, D. THOMAS and L. F. JOHNSON, J. Am. chem. Soc. *93*, 273 (1971).

[7] In cyclic monoterpenes (E. WENKERT and E. W. HAGAMAN, unpublished observations) and in piperideines (E. WENKERT, D. W. COCHRAN and F. M. SCHELL, unpublished observations).

[8] D. K. DALLING and D. M. GRANT, J. Am. chem. Soc. *89*, 6612 (1967).

[9] Conformational analysis of 3 indicates its 6β-methyl group to be axial.

[10] U.S. Public Health Service predoctoral fellow, 1967–1971.

[11] U.S. Public Health Service predoctoral fellow, 1969–1972.