SPECIALIA

Iso-cannabispiran, a new spiro compound isolated from Panamenian variant of *Cannabis sativa* L.[1]

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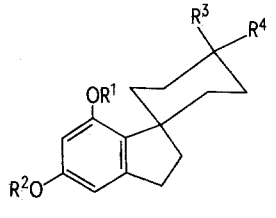
Summary. An acidic fraction of Panamenian variant of *Cannabis sativa* L., afforded upon repeated chromatography a new non-cannabinoid phenol {5′-hydroxy-7′-methoxy spiro-(cyclohexane-1,1′-indan)-4-one} **Ia**, named iso-cannabispiran.

Since the 1st report of a spiro-indan compound from *Cannabis* (**I**), a total of 6 related compounds, namely cannabispiran, (cannabispirone) (**I**), dehydrocannabispiran (cannabispirenone) (**II**)[2,3], β-cannabispiranol (cannabispirol) (**III**)[5,6], acetyl cannabispirol (**IV**)[6], cannabispirenone isomer (**V**)[7], and cannabispiradienone (**VI**)[8], have been isolated from different variants of *Cannabis sativa* L. compounds **I–IV** & **VI** were recently synthesized by Crombie et al.[9] and El-Feraly et al.[10,11].

An acidic fraction of a Panamenian variant of *Cannabis sativa* L. grown in Mississippi resulted in the isolation and characterization of 3-spiro compounds (**I–III**) and 2 dihydrostilbenes[12]. Further examination of this fraction resulted in the isolation of a new spiro compound 5′-hydroxy-7-methoxy-spiro-(cyclohexane-1,1′-indan)-4-one (**Ia**) named iso-cannabispiran. The structure of **Ia** is the subject of this report. Iso-cannabispiran (**Ia**) was isolated as optically inactive needle crystals, m.p., 222–223 °C (decomposes) (acetone/hexane). On TLC, **I** and **Ia** had R_f-value of 0.30 and 0.36 respectively using 5% EtOAc/CH_2Cl_2. Gas chromatography of **Ia** using a 2% ov-17 column showed a relative retention time of 0.39 compared to 4-androstene-3,17-dione. The IR-spectrum (KBr) showed bands at 3400 (OH) 2950, 2922 (CH), 2858 and 2840 ($-CH_2$), 1690 (c=o), 1500 and 1480 (c=c ar). The UV-spectrum showed peaks at λ_{max}^{MeOH} 213 (log ε 3.60), 227 (log ε 4.09), 280 (log ε 3.44), and 284 (log ε 3.39). The ^{1}H-NMR spectrum showed singlet at δ3.73 (3H, OCH_3), 2 aromatic protons at δ6.28 (d) 2 benzylic protons at δ2.93 (t), 2 homobenzylic protons at δ2.20 (t) and 8 methylene protons at δ1.53, 2.76 (m). The mass spectrum of **Ia** showed a M^+ at m/z 246 (10%) ($C_{15}H_{18}O_3$) and a base peak at m/z 189 (100%). The fragmentation pattern of **Ia** was similar to that of cannabispiran (**I**) except for the relative intensities of the ions. Methylation of **Ia** using diazo methane yielded a monomethyl ether **Ib** which was identical to the product obtained by methylation of cannabispiran with methyliodide/K_2CO_3 in acetone. Comparison was made by TLC, GC and GC/MS. Because of the scaricity of **Ia**, other spectral data in **Ib** could not be obtained.

However, since the methyl ethers of **I** and **Ia** were identical, this proves the structure of the new spiro-indan compound as 5′-hydroxy-7′-methoxy-spiro-(cyclohexane-1, 1′-indan)-4-one (**Ia**). Since iso-cannabispiran has a relative retention time of 0.39 and cannabigerol monomethyl ether 0.38, it is possible that iso-cannabispiran may be present in other variants and has been misidentified. *Cannabis* variants which, by gas chromatography, have been shown to contain cannabigerol monomethyl ether are being evaluated for the presence of iso-cannabispiran.



I	R^1=H, R^2=CH_3, R^3+R^4=O
Ia	R^1=CH_3, R^2=H, R^3+R^4=O
Ib	R^1=R^2=CH_3, R^3+R^4=O
II	R^1=H, R^2=CH_3, R^3+R^4=O, $\Delta\alpha,\beta$ to carbonyl
III	R^1=H, R^2=CH_3, R^3=OH, R^4=H
IV	R^1=H, R^2=CH_3, R^3=OAC, R^4=H
V	R^1=CH_3, R^2=H, R^3+R^4=O, $\Delta\alpha,\beta$ to carbonyl
VI	R^1=H, R^2=CH_3, R^3+R^4=O, $\Delta\alpha,\beta$ and $\dot{\alpha},\dot{\beta}$ to carbonyl (dienone)

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