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The Structure of Bisabolangelone, a Sesquiterpenic Ketoalcohol from *Angelica silvestris L.* Seeds

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The constituents of *Angelica silvestris L.* seeds were investigated by Khadzhai and Sokolova[1] and by Hörhammer, Wagner and Eyrich[2] few years ago. The authors named at last isolated a series of furocumarine derivatives and reported also a compound of m.p. 145-148°C ("Compound 4") declared as an unknown furocumarine which after isolation very quickly became yellow under decomposition and liberated products of aromatic odour. Besides ultra-violet spectrum, neither the composition nor other informations about the structure of the compound in question have been reported.

Recently, we studied also the constituents of *Angelica silvestris L.* seeds and isolated a compound of m.p. 148-149°C which probably was identical with the substance of Hörhammer and co-workers. In this paper we wish to report the structure of this compound which we named bisabolangelone because it belonged to the bisabolane series.

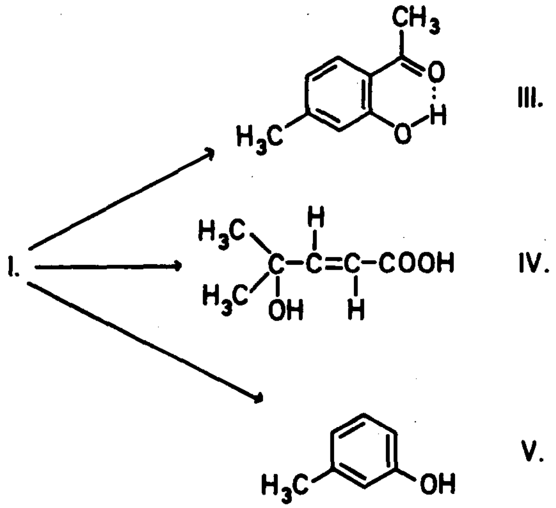
Bisabolangelone I was isolated from crystalline material after concentration of light petroleum extracts of freshly ripened *Angelica silvestris L.* seeds by chromatography on silica gel (15 % water; benzene-ether 95:5) and crystallization from benzene.

The molecular formula $C_{15}H_{20}O_3$ (found: 72.75 % C, 8.20 % H; requires 72.55 % C, 8.12 % H) was verified by mass spectrometry (Mass number 248). The infra-red spectrum exhibited only a very strong and broad band at 1668-1680 cm^{-1} (α,β-unsaturated ketone) and a maximum at 3600 cm^{-1} (hydroxyl group); UV spectrum: λ_{max}^{EtOH} 254 mμ (log ε 4.56); ORD in dioxane (c = 0.073), 28°C: $[\alpha]_{589}$ + 49.3°; $[\alpha]_{400}$ + 202°; $[\alpha]_{368}$ + 504°; $[\alpha]_{360}$ + 471° (shoulder); $[\alpha]_{352}$ + 561°.

On hydrogenation in ethyl acetate in the presence of 5% Pd/$SrCO_3$, the compound I afforded hexahydro derivative II, m.p. 142-143°C of molecular formula $C_{15}H_{26}O_3$ (Found: 70.68 % C, 10.12 % H, 0.46 % H^+; requires 70.83 % C, 10.30 % H, 0.40 $\%^+$, mass number 254); ORD in methanol (c = 0.1765), 26°C; $[\alpha]_{589}$ + + 65.2°; $[\alpha]_{450}$ + 195°; $[\alpha]_{350}$ + 603°; $[\alpha]_{312}$ + 1515°; $[\alpha]_{300}$ + 749°; $[\alpha]_{272}$ − 978°; $[\alpha]_{250}$ − 489°.

Information about structure of bisabolangelone I has been obtained mainly by isolation and identification of main products of its autooxidative degradation together with the result of ozonization and pyrolysis and a degradation of hexahydro derivative II in alkaline medium. All the reactions named are summarised in Scheme 1. The products of autooxidation of bisabolangelone I (obtained by keeping compound I exposed to day light and air for several weeks) were chromatographed on silica gel. The main product was a substance III of molecular formula $C_9H_{10}O_2$ (Found: 71.98 % C, 6.71 % H; requires 71.98 % C, 6.71 % H; mass number 150) identified by ultra-violet, infra-red and NMR[x/] as 2-hydroxy-4-methylacetophenone. Further, hydroxy-acid IV, m.p. 99°C, of molecular formula $C_6H_{10}O_3$ has been isolated (Found: 55.58 % C, 7.67 % H; requires 55.37 % C, 7.75 % H; mass number 130). Infra-red spectrum exhibited bands at 3600 cm^{-1} (hydroxyl group), 1699, 1667 and 2400-3400 (difuse) cm^{-1} (-C-C-COOH). The NMR spectrum of this compound corroborated its structure as 4-methyl-4-hydroxypenten-2-oic acid (IV).

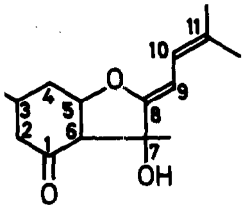
The configuration for $H_{(2)}$, $H_{(3)}$ is trans as follows also from the fact that the cis-acid has been known in the form of its lactone only. Besides the above named two main products, the eluates contained also a small amount of m-cresol (V).



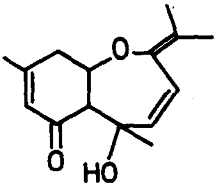
[x/] NMR spectra of all compounds have been measured on 40 and 80 Mc spectrometer constructed in NMR Department of the Institute of Instrumentation, Czechoslovak Academy of Sciences, Brno.

The m-cresol was identified as the main product of degradation of hexahydro derivative II in alkaline medium (10 min. reflux in 5% NaOH) and as main product (besides lesser amount of 2-hydroxy-4-methylacetophenone III) after pyrolysis of compound I ($200^{\circ}C$, 20 min., under nitrogen). Further information was obtained after ozonolysis of substance I which afforded acetone (identified as 2,4-dinitrophenylhydrazone, m.p. $128^{\circ}C$) and after oxidation with hydrogen peroxide also oxalic acid.

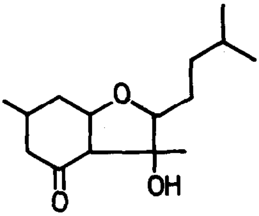
From the above experimental results and NMR spectra of compounds I and II, two structures Ia and Ib come into account.



Ia



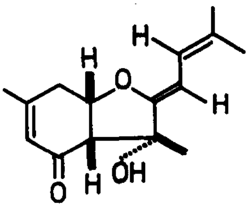
Ib



II.

A decision between both structures on behalf of formula Ia together with determination of cis-junction of rings has been made on the basis of detailed study of NMR spectra of compounds I and II. Using solvent effect in C_6D_6 and field-swept decoupling experiments (at 80 Mc in $CDCl_3$) it was possible to identify unambiguously the signals in the spectrum of compound I. From the characteristic long-range couplings between olefinic protons and methyl groups and from vicinal interaction of olefinic protons (J ~ 11.2 c.p.s.) it was possible to judge on the presence of conjugated fragment $-CH{=}CH{-}CH{=}C(CH_3)_2$ with trans-configuration of double bonds in the sense of structure Ia. Further, from comparison of NMR spectra I and II followed that configuration of both angular protons on cetra of asymmetry $C_{(5)}$ and $C_{(6)}$ most probably was cis. The found coupling constant ($J_{5,6}$ ~ 6.5 c.p.s.) in Ia was rather low but after hydrogenation was ~ 9.5 c.p.s. in substance II. Other features of the NMR spectra of both compounds I and II were in good agreement with the structure Ia. The configuration on $C_{(7)}$ in compound I was inferred on the basis of evidence following from a formation of hydrogen bridges in compounds I and II. The compound I showed free allylic ν(OH) at 3601 cm^{-1}, ν(OH) bound probably to ethereal oxygen at 3576 cm^{-1} (weak) and $OH....O{=}C<$ at 3432 cm^{-1} (very strong). The compound II showed ν(OH) free at 3615 cm^{-1} and ν(OH) bound weakly probably to ethereal oxygen at 3579 cm^{-1}. Investigation of molecular models showed that hydrogen bridge in compound I cannot be formed in cis-fused system and (probable) boat-conformation of six-membered ring unless hydroxyl group is transtowards hydrogen on $C_{(6)}$. The relative configuration of bisabolangelone may be thus expressed by formula I.

I.



The paper will be published in full detail in Collection of Czechoslovak Chemical Communications.

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