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THE ABSOLUTE CONFIGURATIONS OF ATHAMANTIN AND EDULTIN

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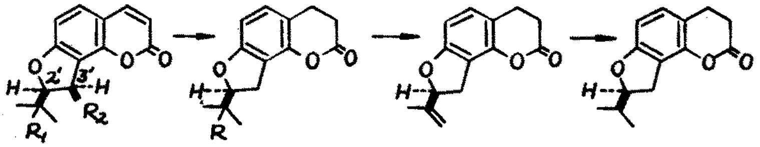
A thin layer chromatogram of the ethanolic extract of the seeds of Selinum Monnieri L. reveals the presence of several coumarins. From the extract, we isolated, beside osthol$^{1)}$ and oroselone$^{2)}$, a new coumarin compound, $C_{21}H_{22}O_7$, m.p.144-146°, $[\alpha]_D^{23}$+106.7°(c 1.71 in benzene), $[\alpha]_D^{25}$+84.8°(c 1.76 in pyridine). The close examination of its chemical behavior, however, disclosed the distinct similarity with edultin (I)a, m.p.136-142°, $[\alpha]_D^{11}$+41.5°(c 26.8 in pyridine), which was recently isolated by Mitsuhashi and Ito$^{3)}$ from the root of Angelica edulis Miyabe. And the identity was established by the comparison of both samples.



(I)a $R_1=OAc$
$R_2=O_2C-C(Me)=C(H)Me$
b $R_1=R_2$
$=O_2CCH_2CH(Me)_2$

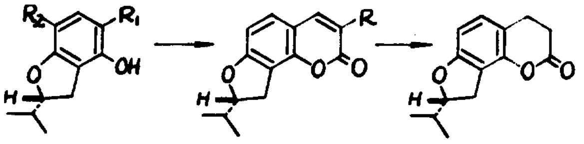
(II)a $R=OAc$
b $R=OH$

(III)

(+)-(IV)

It will be noted that athamantin (I)b and edultin (I)a share a similar structural feature and, from the biogenetical point of view[4], it is of interest to know their relative as well as absolute configurations.

Hydrogenolysis of edultin (I)a in acetic acid with palladium oxide afforded (+)-tetrahydrooroselol acetate (II)a which was hydrolyzed to (+)-tetrahydrooroselol (II)b, m.p. 113.5-114.2°, $[\alpha]_D^{26}$+68.0°(*c* 1.11 in chloroform), identical with the one obtained by Schmid et al.[2] upon the same treatment of athamantin, indicating the same configuration at $C_{2'}$ in both compounds.



(V)a $R_1=R_2=H$
b $R_1=CHO$, $R_2=H$
c $R_1=H$, $R_2=CHO$

(VI)a $R=CO_2H$
b $R=H$

(–)-(IV)

When the acetate (II)a prepared from the purified (II)b was pyrolyzed (300°, 5 min.), there was obtained a mixture of unsaturated compounds, b.p.130-145°/0.01 mm, $[\alpha]_D^{23}$+43.6°(*c* 1.44 in chloroform) whose n.m.r. spectrum[5] showed the presence of the compound (III) with isopropenyl side chain at least in 60%. The mixture was then hydrogenated with palladium in ethanol to give (+)-hexahydrooroselone (IV), a semisolid with $[\alpha]_D^{25}$+25.4°(*c* 1.02 in ethanol) after purification by chromatography on alumina.

We next attempted to secure (IV) with known absolute configuration. Gattermann's formylation of (-)-(R)-dihydrotubanol (V)a[6] prepared from rotenone,[7,8] gave the *o*-aldehyde (V)b, b.p.95-107°/0.1 mm, $[\alpha]_D^{23}$-149°(*c* 1.04 in ethanol)(semicarbazone, m.p.219-220°), together with *p*-isomer (V)c, m.p.132-133°.

The former was heated with malonic acid, pyridine and aniline to yield (VI)a, m.p.188°, which was then decarboxylated by heating with copper chromite and quinoline to give the coumarin (VI)b, m.p.110-111°, $[\alpha]_D^{22}$ -97.8° (*c* 1.22 in ethanol).

The final step was the facile hydrogenation of (VI)b to (-)-(IV), m.p.106°, $[\alpha]_D^{20}$ -72.0° (*c* 1.23 in ethanol), whose infrared spectrum was superimposable on that of (+)-(IV) from edultin. Since (+)-(IV) from edultin was appearently optically impure (minimum optical purity: 35%), the enantiomeric relationship of (+)-(IV) with (-)-(IV) was further confirmed as follows. From an optically inactive solution prepared by adding 7.8 mg. of (-)-(IV) to a solution of 22.2 mg. of (+)-(IV) in petroleum ether, there were isolated 13.5 mg. of racemic (IV), m.p.97.5-99°, which was found identical with the racemic (IV)2) prepared by catalytic hydrogenation of oroselone.

Schmid et al.2) suggested the *cis*-configuration of two hydrogens at $C_{2'}$ and $C_{3'}$ of athamantin (I)b, because (I)b is thermally stable, and this was found also to be the case with edultin (I)a. The *cis*-configuration was further supported from the observation of the n.m.r. spectrum of edultin which indicated the coupling constant of 7 c.p.s. between these hydrogens. These findings established the (R)-configuration at $C_{2'}$ and the (R)-configuration at $C_{3'}$ in both edultin and athamantin.

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