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OCCURRENCE OF ISOUSNIC ACID IN LICHENS
WITH REFERENCE TO "ISODIHYDROUSNIC ACID" DERIVED FROM DIHYDROUSNIC ACID

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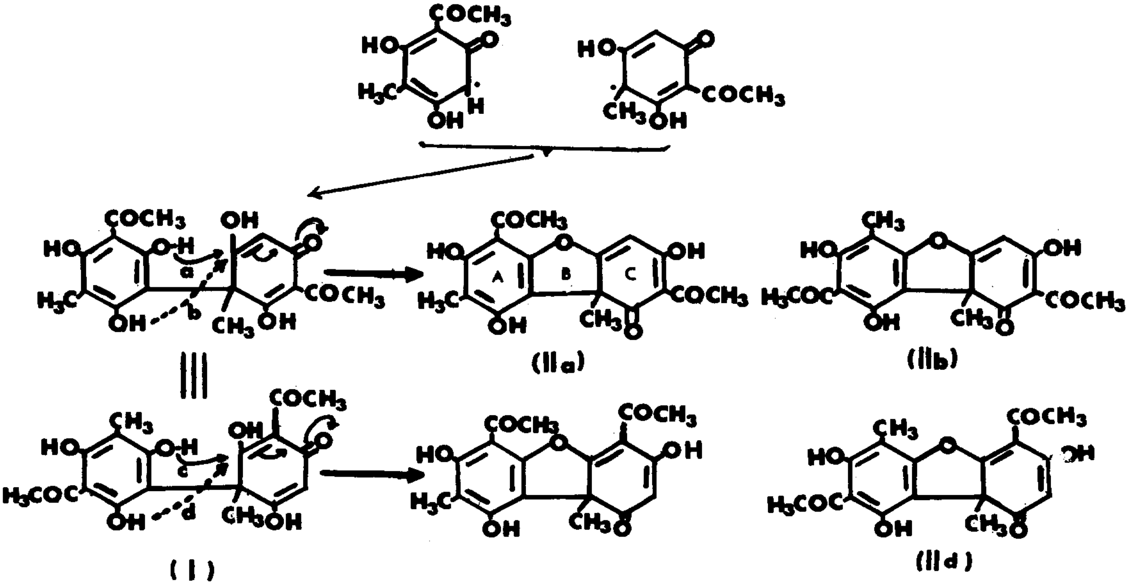
During the course of biosynthetical study of usnic acid in lichens (1), we found that the ethereal extracts of Cladonia mitis Sandst. gave an unidentified yellow spot (Rf: 0.36) being accompanied by the spot of (+)usnic acid (Rf:0.20) on the thin layer chromatogram developed on Silica gel G impregnated with oxalic acid using benzene as the solvent.

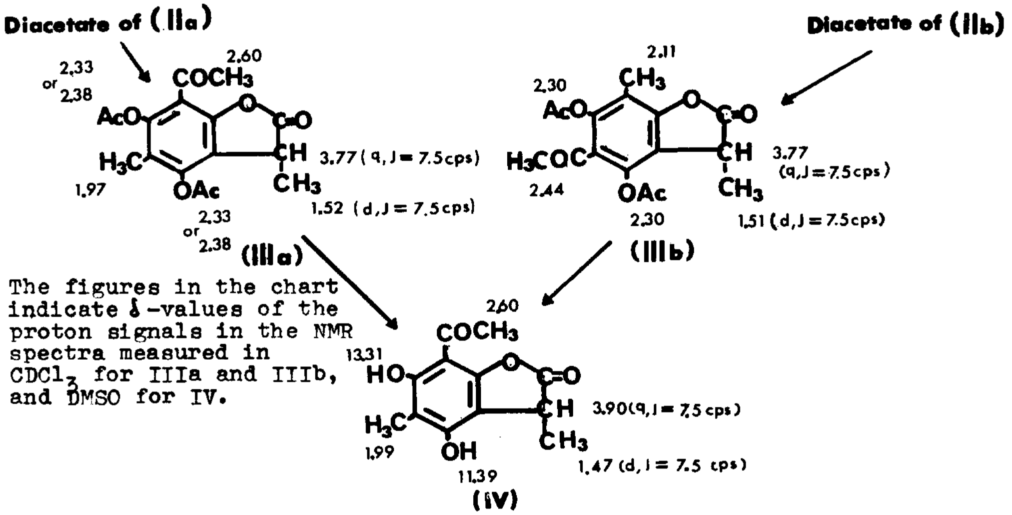
The new compound named (+)isousnic acid was isolated as yellow prisms (from benzene-methanol), $C_{18}H_{16}O_7$, m.p. 150-152°, $[\alpha]_D^{21}$ + 500°(in dioxane), showing a close similarity to (+)usnic acid, yellow prisms, $C_{18}H_{16}O_7$, m.p. 203-204°, $[\alpha]_D$ + 492°(in chloroform), in the UV and IR spectra.

The established biosynthetical pathway of usnic acid (IIa) (1,2) suggests that there are three other possibilities of ring closure after the first oxidative coupling of the two methylphloroacetophenone units.



Dehydration of the intermediates would afford usnic acid (IIa) and its structural isomers (IIb,IIc and IId), and isousnic acid should possibly be one of the latter cases (IIb~IId).

Acetylation of (+)isousnic acid afforded (+)diacetylisousnic acid,$C_{22}H_{20}O_9$, pale yellow prisms(from methanol),m.p.110-112°(resolidify at 120-122° and remelt at 181-183.5° *),$[\alpha]_D$ + 289° (in dioxane), which showed very similar UV and IR spectra to those of (+)diacetylusnic acid, $C_{22}H_{20}O_9$,m.p.202°, $[\alpha]_D$ + 200°. Ozonolysis of diacetylisousnic acid was carried out by the procedure adopted to diacetylusnic acid (3,4,5,6) which yielded 3,5-dimethyl-4,6-diacetoxy-7-acetyl-2-coumaranone (lactone A),$C_{16}H_{16}O_7$,m.p.130-132° (IIIa). The ozonolytic product,$C_{16}H_{16}O_7$,m.p.124-126°,obtained from (+)diacetylisousnic acid showed an obvious depression of melting point on admixture with lactone A, whereas it gave almost identical UV and IR spectra with those of lactone A. The NMR spectrum supported the structure (IIIb) of the ozonolytic product of diacetylisousnic acid. Deacetylation of this compound (IIIb) with conc.H_2SO_4 afforded IV, the same compound derived from IIIa. This would have been resulted by the rearrangement of lactone linkage on deacetylation of IIIb.



(IIIa) (IIIb) (IV)

The figures in the chart indicate δ-values of the proton signals in the NMR spectra measured in $CDCl_3$ for IIIa and IIIb, and DMSO for IV.

The formation of IIIb by the above ozonolysis rejected the possibility of adopting the formula (IIc) for isousnic acid.

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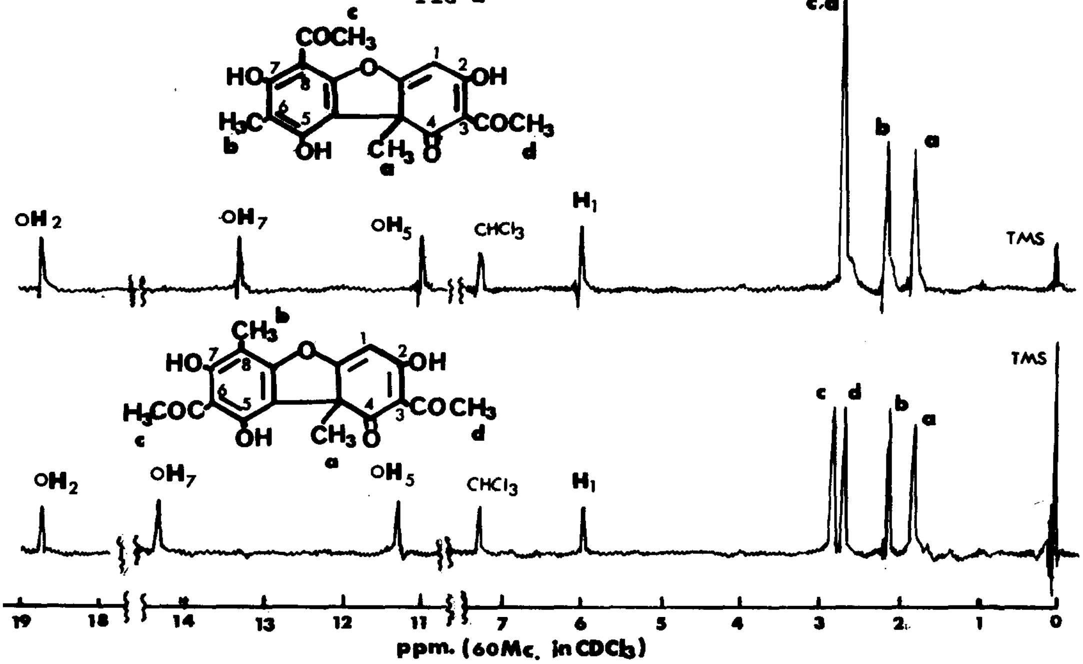
* (+)Diacetylisousnic acid is recemized readily on heating, and the racemate melts at 181-183.5°.

The NMR spectrum of isousnic acid showed a close similarity to that of usnic acid about almost all the proton signals except those of aromatic acetyl and the neighbouring hydroxyls which gave slightly lower shifts (Fig.1).

FIG 1



This would suggest the difference in location of the acetyl and methyl groupings in the ring A of both compounds without any remarkable change in the rest portion (ring C) of the molecules.

Thus the formula(IId) having a different location of acetyl groupings in the ring C is ruled out. All the evidences provided as above led to a conclusion that isousnic acid occurring in lichens should be formulated as IIb.

The microchemical investigation showed the co-occurrence of isousnic acid and usnic acid in some Cladonia spp. other than Cl. mitis, such as Cl. submitis Evans, Cl. pleurota Schaer.[**], Cl. sylvatica Harm. , whereas it has not been found so far in Usnea, Parmelia and Evernia spp. which contain usnic acid.

Catalytic hydrogenation of (+)isousnic acid with Pd-black in tetrahydrofuran afforded (+)isodihydrousnic acid, $C_{18}H_{18}O_7$, pale yellow plates (from methanol), m.p. 109-115°, $[\alpha]_D^{23}$ + 157°(in dioxane), whose UV and IR spectra resemble those of (-)dihydrousnic acid, $C_{18}H_{18}O_7$, m.p.147°, $[\alpha]_D$ -85°.

[**] Cl. pleurota contains (-)isousnic acid, m.p. 150-152°, $[\alpha]_D$ -490°(in dioxane) being accompanied by (-)usnic acid.

On the other hand, "(+)isodihydrousnic acid", $C_{18}H_{18}O_7$, m.p. 128°, $[\alpha]_D$ + 47.5°, was reported previously by us as a thermo-rearrangement product of (-)dihydrousnic acid (7). In our previous report (8), we concluded that isodihydrousnic acid exists in an equilibrium of two tautomeric forms in the solution, since the NMR spectrum showed a double shifting at every signal of proton. However, (+)isodihydrousnic acid derived from the naturally occurring (+) isousnic acid has given a well-defined single feature at every proton signal in the NMR spectrum.

As has been recognized by the present experiment and was overlooked, if not completely be excluded, in the previous study, isodihydrousnic acid is readily converted into dihydrousnic acid even by the process of recrystallization.

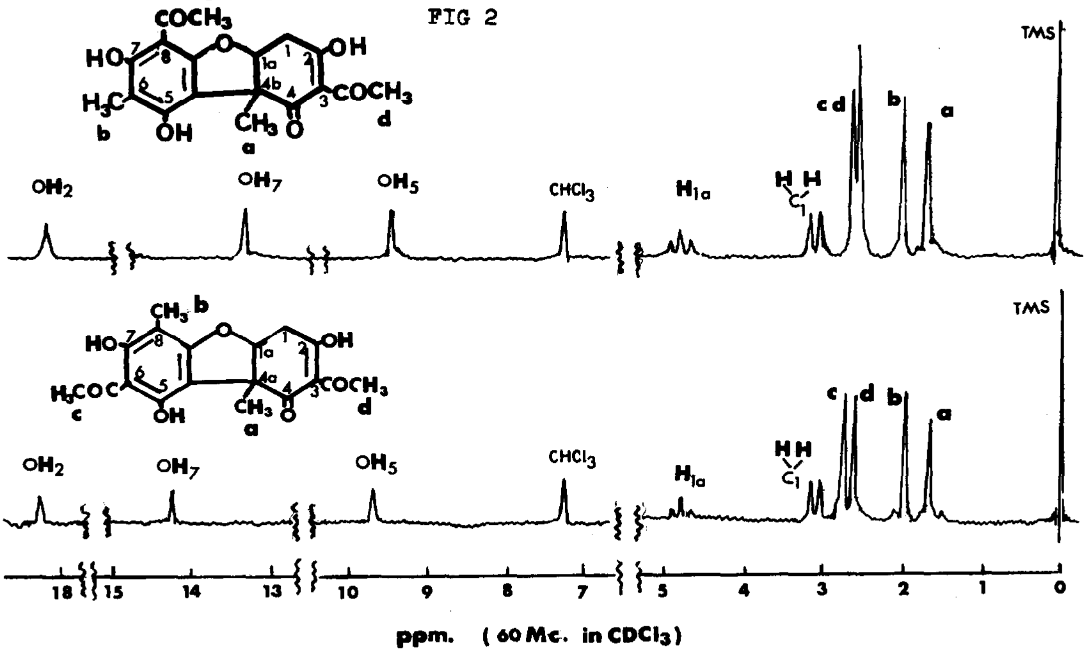


FIG 2

Thus "isodihydrousnic acid" previously reported must have been contaminated in some extent with dihydrousnic acid, and the NMR spectrum would show the state of mixture of both compounds. The thin layer chromatography which was not available at the time of our previous study has now proved the contamination of dihydrousnic acid in our former sample of "isodihydrousnic acid".

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