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THE STRUCTURE OF A NOVEL TERPENOID ACID "3ξ-HYDROXY-4ξ,9-DIMETHYL-6E,9E-DODECADIENEDIOIC ACID" ISOLATED FROM TURKISH TOBACCO.

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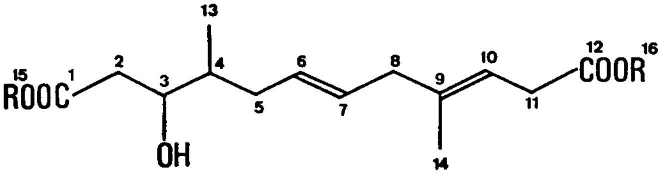
In the course of our studies on aroma constituents of Turkish tobacco,$^{1)}$ a new anomalous terpenoid acid "3ξ-hydroxy-4ξ,9-dimethyl-6E,9E-dodecadienedioic acid" (Ia) was isolated. In this communication, we wish to report the isolation and structural elucidation of this new compound.

Repeated silicic acid column chromatagraphy of the acidic part of an isopropylether extract from cured Turkish tobacco leaves and purification by preparative gas chromatography after esterification with diazomethane, furnished the dimethyl ester of the new compound (Ib, $[\alpha]_D^{23}$ -7.9(c=2.0 in CH_3OH)).

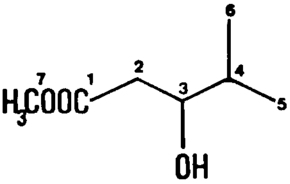
The complete decoupling ^{13}C-nmr showed the presence of fifteen lines. One of these lines (δ_C51.6(q)) was revealed as a two carbon signal by the decoupling without NOE and resolved into two lines after adding the shift reagent "Eu(fod)$_3$", indicating that this compound had sixteen carbon atoms. Precise mass determination of the highest peak at m/e 280 in the double forcus mass spectrum (found 280.1679;calcd 280.1673), caused by a loss of water from the molecular ion, established that the molecular formula was $C_{16}H_{26}O_5$, which was also confirmed by the presence of a very weak peak at m/e 298 in single forcus mass spectrum.

The five oxygen atoms in the molecule, as judged from ir, ^{13}C- and ^{1}H-nmr,$^{2)}$ were attributable to two methyl esters (1740cm^{-1}, δ_C173.5(s), 51.6(q), δ_H3.74(s); 1735cm^{-1}, δ_C172.6(s), 51.6(q), δ_H3.69(s)) and a hydroxy group (3500cm^{-1}) attached to a methine (δ_C71.2(d), δ_H3.80(m)). Four unsaturations were due to two carbonyls in the methyl esters, a trans disubstituted double bond (972cm^{-1}, δ_C129.4(d), 129.9(d), δ_H5.44(m)) and a trisubstituted double bond (840cm^{-1}, δ_C138.0(s), 116.0(d), δ_H5.35(t)). Hence, the carbon skeleton of this compound was a chain structure and had no conjugated system because of the absence of the absorption at 210-360nm in uv spectrum and non shift of the carbonyl absorption in ir spectrum.

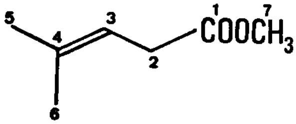
Of the two methyls revealed in ^{13}C- and ^{1}H-nmr, one (δ_C14.9(q), δ_H0.88(d)) was attached to a methine carbon (δ_C38.2(d), δ_H1.64(m), irradiation at 1.64 simplified the d. at 0.88 to a s.) and the other (δ_C16.1(q), δ_H1.63(bds)) was linked to a quartary olefinic carbon (δ_C138.0(s))



The isolated compound Ia: R=H
b: R=CH_3



Methyl 3-hydroxy-4-methyl-pentanoate (II)



Methyl 4-methyl-3-pentenoate (III)

Spectral data of the isolated compound (Ib)

Carbon No.	^{13}C-nmr δppm	^{i}H-Irradiation frequency(KHz)	^{1}H-nmr δppm	ir(cm^{-1})		ms(m/e)	
1	173.5(s)			3500(bd)	2960(s)	93(100)	105(44)
2	37.8(t)	51.2677	2.40(2H,m)	2920(m)	1740(s)	107(38)	133(36)
3	71.2(d)	51.4004	3.80(1H,m)	1735(s)	1438(m)	79(36)	74(34)
4	38.2(d)	51.1928	1.64(1H,m)	1382(m)	1367(m)	55(32)	147(32)
5	35.3(t)	51.2353	2.08(2H,m)	1316(m)	1258(m)	81(32)	130(29)
6	129.4(d)	51.5606	5.44(1H,m)	1200(m)	1165(m)	43(27)	193(22)
7	129.9(d)	51.5606	5.44(1H,m)	1050(m)	1016(m)	41(20)	135(17)
8	42.5(t)	51.2899	2.72(2H,bds)	997(w)	972(m)	125(15)	121(14)
9	138.0(s)			840(m)		103(13)	166(12)
10	116.0(d)	51.5533	5.35(1H,t,J=7.5Hz)			153(12)	206(12)
11	33.4(t)	51.3244	2.99(2H,d,J=7.5Hz)			152(10)	280(9)
12	172.6(s)					146(8)	216(7)
13	14.9(q)	51.1085	0.88(3H,d,J=7.0Hz)			266(6)	234(5)
14	16.1(q)	51.1803	1.63(3H,bds)			220(5)	248(4)
15	51.6(q)	51.3905	3.74(3H,s)				
16	51.6(q)	51.3871	3.69(3H,s)				

Spectral data of methyl 3-hydroxy-4-methyl-pentanoate (II)

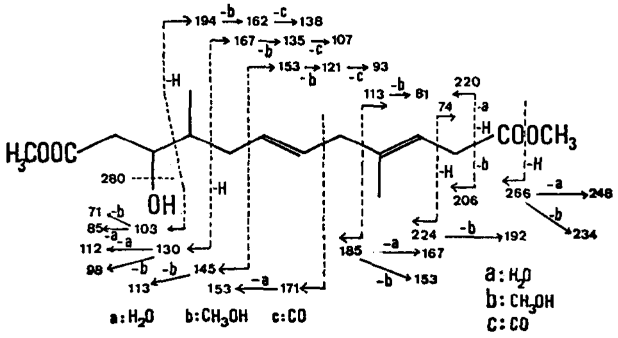
Carbon No.	^{13}C-nmr δppm	^{1}H-nmr δppm	ir(cm^{-1})		ms(m/e)		
1	173.5(s)		3500(bd)	2965(s)	103(100)	71(93)	43(62)
2	38.2(t)	2.42(2H,m)	2880(m)	1740(s)	61(36)	73(28)	74(30)
3	72.6(d)	3.80(1H,m)	1440(m)	1370(m)			
4	33.1(d)	1.66(1H,sept)	1280(m)	1173(m)			
5	17.7(q)	0.95(3H,d,J=7.0Hz)	1130(m)	1058(m)			
6	18.3(q)	0.94(3H,d,J=7.0Hz)	1015(m)	998(m)			
7	51.7(q)	3.72(3H,s)					

Spectral data of methyl 4-methyl-3-pentenoate (III)

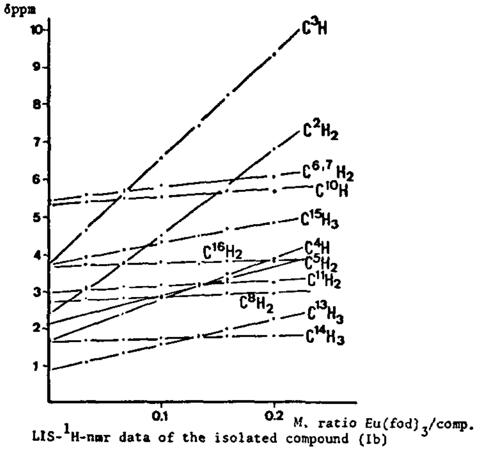
1	172.6(s)		2960(s)	2920(s)	69(100)	128(94)	68(31)
2	33.6(t)	2.97(2H,d,J=7.5Hz)	1737(s)	1436(m)	96(27)		
3	115.6(d)	5.30(1H,t,J=7.5Hz)	1378(m)	1363(m)			
4	135.4(s)		1315(m)	1260(m)			
5	25.6(q)	1.78(3H,d,J=1.2Hz)	1200(m)	1162(m)			
6	18.0(q)	1.67(3H,bds)	1032(m)	827(m)			
7	51.7(q)	3.66(3H,s)					

Off-resonance ^{13}C-nmr showed the presence of four methylenes which were assigned to be an α-carbonyl methylene ($H_3COOC-\underline{CH_2}-CH(OH)-$; δ_C37.8(t), δ_H2.40(m), irradiation at 3.80 collapsed the m. at 2.40 to a d.), an α-carbonyl methylene ($H_3COOC-\underline{CH_2}-CH=C<$; δ_C 33.4(t), δ_H2.99(d), irradiation at 5.35 simplified the d. at 2.99 to a s.), a methylene ($-CH=CH-\underline{CH_2}-C(CH_3)=CH-$; δ_C42.5(t), δ_H2.72(bds), irradiation at 5.44 sharpened the bds. at 2.72) and a methylene ($-\underline{CH_2}-CH=CH-$; δ_C35.3(t), δ_H2.08(m), irradiation at 5.44 simplified the m. at 2.08).

Consequently, the three partial structures, 2-carbomethoxy-1-hydroxy-ethyl moiety ($H_3COOC-CH_2-CH(OH)-$), 7-carbomethoxy-5-methyl-2E,5-heptadienyl moiety ($-CH_2-CH=CH-CH_2-C(CH_3)=CH-CH_2-COOCH_3$) and the methine carrying the methyl, assigned from above data, constructed the unique structure "dimethyl 3-hydroxy-4,9-dimethyl-6E,9-dodecadienedioate" for the structure of the new compound (Ib).



Examination of the precise mass determination was consistent with this structural feature. Ions at m/e 71($C_3H_3O_2$), 103($CH(OH)CH_2COOCH_3$) and a series of ions containing three oxygen atoms at m/e 224($M-CH_3COOCH_3$), 185($M-C_4H_6COOCH_3$), 171($M-C_5H_8COOCH_3$), 145($M-C_7H_{10}COOCH_3$) and 130($M-C_8H_{13}COOCH_3$) were well explainable for the terminal 2-carbomethoxy-1-hydroxy-ethyl moiety. On the other hand, ions at m/e 113($C_4H_6COOCH_3$), 153($C_7H_{10}COOCH_3$), 167($C_8H_{12}COOCH_3$) and 194($C_{10}H_{15}COOCH_3$) were explainable to be due to the other terminal 3-carbomethoxy-1-methyl-1-propenyl moiety.



LIS-^{1}H-nmr data of the isolated compound (Ib)

Relative induced shift ratio in LIS-nmr

Isolated compound (Ib) Carbon No.	r_C	r_H	Methyl 3-hydroxy-4-methyl-pentanoate (II) Carbon No.	r_C	r_H
1	3.66		1	3.74	
2	5.60	7.73	2	5.88	7.76
3	10.00	10.00	3	10.00	10.00
4	0.37	4.33	4	0.13	4.15
5	0.99	2.88	5	1.00	2.67
6	0.94	1.44			
7	0.42	1.44			
8	0.31	0.61			
9	0.26				
10	0.42	0.76			
11	0.37	0.76			
12	0.24				
13	0.99	2.56	6	1.00	2.64
14	0.21	0.40			
15	1.36	2.24	7	1.37	2.26
16	0.16	0.47			

Finally, the carbon framework of this compound was confirmed by a LIS-nmr experiment using the shift reagent "Eu(fod)$_3$". The metal was evidently co-ordinated with the hydroxy group, judged from the strongest lanthanide induced shift of the methine carrying the hydroxy group. Therefore, the strong LIS of the methylene (δ_C37.8, relative induced shift ratio[3] of the carbon=5.60; δ_H2.40, r_H=7.73), the carbonyl (δ_C173.5, r_C=3.66), the methoxy (δ_C51.6, r_C=1.36; δ_H3.74, r_H=2.24), the methyl (δ_C14.9, r_C=0.99; δ_H0.88, r_H=2.56), the methine (δ_C38.2, r_C=0.37[4]; δ_H1.64, r_H=4.33) and the methylene (δ_C35.3, r_C=0.99; δ_H2.08, r_H=2.88), which were excellently agreeable with the LIS data of methyl 3-hydroxy-4-methyl-pentanoate (II), strongly supported the presence of the 4-carbomethoxy-3-hydroxy-2-methyl-butyl moiety in the structure.

The presence of the 3-carbomethoxy-1-methyl-1-propenyl moiety as the other terminal structure was well explainable by spectral data (ir, ^{13}C- and ^{1}H-nmr) of methyl 4-methyl-3-pentenoate (III). The geometrical configuration of the trisubstituted double bond in the isolated compound was established to be trans, since the methyl (δ_C16.1, δ_H1.63 (bds)) was well consistent with the cis-methyl (δ_C18.0, δ_H1.67(bds)) rather than the trans-methyl (δ_C25.6, δ_H1.78(d,J=1.2Hz)) of methyl 4-methyl-3-pentenoate (III).[5] From the above data, 3ξ-hydroxy-4ξ,9-dimethyl-6E,9E-dodecadienedioic acid was assigned for the structure of the isolated compound (Ia).

Judging from the symmetrical structure around the trans disubstituted double bond, this anomalous terpenoid acid is considered to be derived from the central part of the carotenoid chain such as phytoene.[6]

REFERENCES

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   b) T. Chuman and M. Noguchi, ibid., 40, 1973(1976).
2. ^{13}C- and ^{1}H-nmr chemical shifts are expressed in ppm from TMS in CDCl$_3$.
   The assignments of ^{13}C-nmr signals to ^{1}H-nmr signals were carried out by the selective decoupling ^{13}C-nmr.
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4. The remarkable weak LIS of this methine carbon, which was also observed in the LIS of methyl 3-hydroxy-4-methyl-pentanoate (II), was considered to be due to the atomospheric shielding effect by the oxygen atom located between the metal and this methine carbon. The detail studies on these LIS data and on the stereochemistry of the isolated compound are in progress.
5. The assignment of two methyls was established by a LIS-nmr experiment which showed the differences between the cis-methyl (r_C=1.67; r_H=2.22) and the trans-methyl (r_C=1.39; r_H=1.11). The detail data containing ^{13}C spin lattice relaxation time (T_1) of this compound is being published elsewhere.
6. H. E. Wright, Jr., W. W. Burton and R. C. Berry, Jr., Arch. Biochem. Biophys.,82, 107(1959).