

NEW COMPOUNDS FROM AVOCADO PEAR

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Abstract—Eight new compounds have been isolated and identified from avocado fruit and seeds. Their structures were determined by chemical as well as by spectroscopic means. All compounds have been interconverted and shown to belong to the same group of long chain aliphatic compounds, constituting four pairs. Each pair contains two compounds which differ only in having a double or triple bond at the end of the chain.

IN THE last decade, several compounds have been isolated from the avocado pear, an octulose,¹ a nonulose,² various paraffins and alcohols,³ and some branched fatty acids.⁴ It seems evident, however, that the wealth of natural products in the avocado has not yet been fully explored.

In an earlier communication,⁵ we reported the discovery of six oxygenated n-heptadecanes and n-heptadecaynes. We now wish to present the full spectral and chemical evidence for the structure of these and several other compounds isolated by us from avocados.

Avocado seed (variety Nabal or Ettinger) was extracted with boiling hexane. The solution was left at 5° overnight and the precipitate formed was recrystallized from hexane several times until it migrated as a single spot on TLC. This substance, however, proved to be a mixture of two compounds, as shown by various spectroscopic methods.

Since the IR spectrum of the crystalline product showed absorptions at 3320 and 2080 cm^{-1} , indicative of a terminal acetylenic group, AgNO_3 was added to its solution in ethanol in order to precipitate the acetylenic component as an acetylide. From the precipitate, after freeing it from the silver, the acetylenic compound Ib was isolated and from the supernatant solution the olefinic compound IIb was crystallized. In the IR spectrum of the latter (IIb), the presence of absorptions characteristic for a terminal double bond were clearly visible (Table 1). The relationship between these two compounds could be easily established, since the acetylenic Ib yielded, upon partial hydrogenation over Pd/BaSO_4 in pyridine, the olefinic compound IIb. Complete hydrogenation of Ib and of IIb over Pd/C in ethanol solution afforded the same product III (Scheme 1).

Compound Ib $\text{C}_{19}\text{H}_{34}\text{O}_4$ ($M^+ 326$) shows in the IR spectrum (Table 1) the presence of three functional groups: acetylene, hydroxyl and acetate. The NMR spectrum (Table 2) of this compound confirms the existence of these three functional groups and indicates also the presence of a long aliphatic chain. When the NMR spectrum of Ib was examined after the addition *in situ* of trichloroacetyl isocyanate,⁶ it showed that the compound contains two hydroxyls. Two singlets appeared at $\delta - 8.18$ (1H)

TABLE I. DATA OF THE NATURAL COMPOUNDS

Ia	$C_{17}H_{32}O_3$ (M^+ , 284) m.p. 76° $[\alpha]_D^{25} -4.9^\circ$; ν_{max}^{KBr} 3400, 1130, 1100, 1075, 1060, 1040, 1020 cm^{-1} (C—OH) 3320, 2080 cm^{-1} (—C≡CH)
Ib	$C_{19}H_{34}O_4$ (M^+ , 326) m.p. 73° $[\alpha]_D^{25} -4.6^\circ$; ν_{max}^{KBr} 3400, 1135, 1090, 1040 cm^{-1} (C—OH) 3270, 2100 cm^{-1} (—C≡CH) 1730, 1255 cm^{-1} (OCOCH ₃)
IIa	$C_{17}H_{34}O_3$ (M^+ , 286) m.p. 68° $[\alpha]_D^{25} -6.7^\circ$; ν_{max}^{KBr} 3400, 1120, 1095, 1055, 1020 cm^{-1} (C—OH) 3050, 1630, 990, 900 cm^{-1} (—CH=CH ₂)
IIb	$C_{19}H_{36}O_4$ (M^+ , 328) m.p. $58-59^\circ$ $[\alpha]_D^{25} -4.6^\circ$; ν_{max}^{KBr} 3400, 1185, 1135, 1040 cm^{-1} (C—OH) 3050, 1635, 985, 905 cm^{-1} (—CH=CH ₂) 1730, 1255 cm^{-1} (OCOCH ₃)
IV	$C_{19}H_{32}O_4$ (M^+ , 324) m.p. 47° $[\alpha]_D^{25} +26^\circ$; ν_{max}^{KBr} 3460, 1125, 1110, 1075, 1035 cm^{-1} (C—OH) 3270, 2100 cm^{-1} (—C≡CH) 1720, 1260 cm^{-1} (CO, OCOCH ₃)
V	$C_{19}H_{34}O_4$ (M^+ , 326) m.p. 47° $[\alpha]_D^{25} +20^\circ$; ν_{max}^{KBr} 3400, 1130, 1080, 1040 cm^{-1} (C—OH) 3050, 1635, 990, 910 cm^{-1} (—CH=CH ₂) 1735, 1260 (OAc) 1710 (CO)
IX	$C_{17}H_{26}O$ (M^+ , 246) Low m.p. crystals; $\nu_{max}^{CHCl_3}$ 3280, 2100 cm^{-1} (—C≡CH) 1590, 1500, 1260, 1145, 1050, 915, 880 cm^{-1} (furan ring)
X	$C_{17}H_{28}O$ (M^+ , 248) oil; $\nu_{max}^{CHCl_3}$ 3050, 1630, 910 (—CH=CH ₂) 1590, 1500, 1260, 1145, 1070, 1005, 880 cm^{-1} (furan ring)

* All $[\alpha]_D^{25}$ were examined at 1% concentration in $CHCl_3$.

and $\delta -8.19$ (1H) which are attributed to the two N-protons of the carbamates resulting from the interaction of the two OH groups of compound Ib with the reagent.

Presence of two OH and one acetate groups accounts for the four O atoms of the molecule as required by the elemental and mass spectrum analyses. The number of H atoms found by the elemental and mass spectrum analyses accounts for the above-mentioned functional groups and indicates that no other unsaturation exists.

Acetylation of compound Ib yielded an oily compound Ic. Fig. 1 shows the NMR

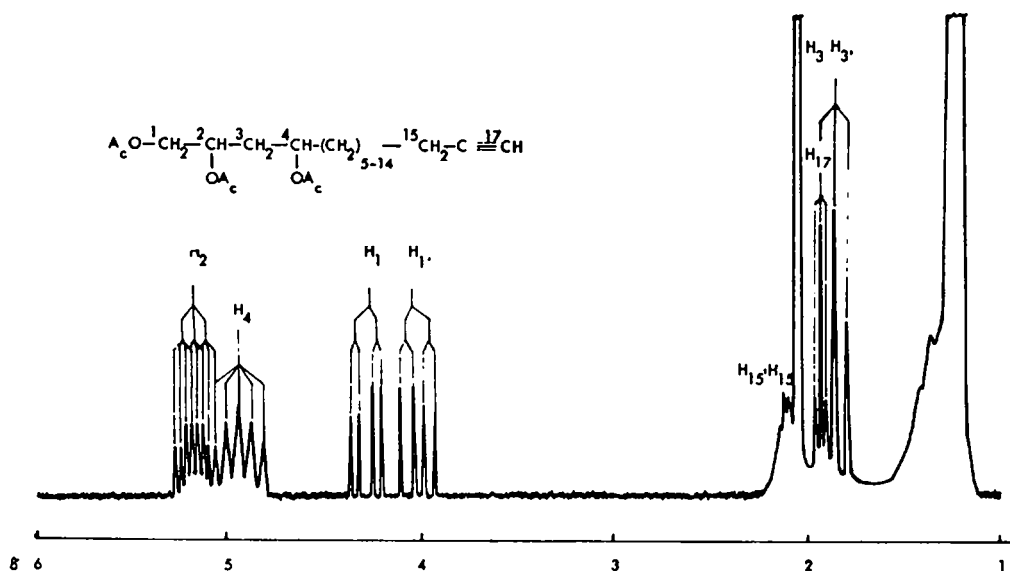


FIG. 1

spectrum of this compound dissolved in CDCl_3 . Careful examination of the spectrum enabled us to define unambiguously the relations between the functional groups, and thus reveal the exact structure of the compound.

The correlations between the adjacent protons in the functional sites were assigned with the aid of spin decoupling experiments. Protons H-1H-1' and H-2 constitute an ABX system; on irradiating the H-2 at $\delta - 5.13$ (the X part of the system), the C-1-protons changed into two doublets at $\delta-4.05$ and $\delta-4.27$ ($J = 12$). This pattern remains as an AB system due to the asymmetric center at C-2. This irradiation also converted the triplet at $\delta-1.86$ assigned to the C-3 protons into a doublet. Another irradiation at $\delta-4.16$, (the center of the AB part of the ABX system) changed the 8-line pattern at $\delta-5.13$ ddt of the H-2 proton into a triplet ($J = 6.5$) as expected. Irradiation at the site of the triplet at $\delta-1.86$ assigned to the H-3 protons now, changed the H-2 pattern to a double doublet ($J = 3$) and ($J = 6$), and the quintet of H-4 at $\delta-4.94$ to a triplet ($J = 6.5$). Ultimately, by a final irradiation of this site at $\delta-4.94$, a doublet at $\delta-1.86$ was observed as expected.

Irradiation at $\delta-2.12$ (H-15H-15') converted the triplet at $\delta-1.92$ attributed to H-17 into a singlet, thus ascertaining the relationship between the C-15 and C-17 protons as proposed in the structure shown (Ic).

The proximity of the two OH groups was also demonstrated by the ease of formation of the acetonide (compound XIII). Since the carbon atoms are arranged in an aliphatic chain, as will be proved later, compound Ic is 1,2,4-triacetoxy-n-heptadeca-16-yn. Comparison of the NMR spectrum of Ib with that of Ic revealed a shift of a two proton signal from the $\delta-4$ in Ib to the $\delta-5$ region in Ic. The two proton signal remaining at the original location indicates that the acetate of Ib is primary. Compound Ib is therefore the monoacetate, 1-acetoxy-2,4-dihydroxy-n-heptadeca-16-yn. Further evidence for the general structure of Ib was adduced through analysis of the mass spectrum of this compound.

Once the structure of Ib was elucidated, the structure of the closely related compound IIb, namely 1-acetoxy-2,4-dihydroxy-n-heptadeca-16-en was easily established. As previously mentioned, this compound IIb was formed when its acetylenic counterpart Ib was hydrogenated over Pd/BaSO₄, and when acetylated it gave the expected triacetate IIc. The only difference between the NMR data of the respective compounds Ib, Ic and IIb, IIc was the appearance of three vinylic protons of the terminal methylene group replacing the acetylenic protons. Ic had been selected for the elucidation of the general structure of the whole group since the low field area of the olefinic compounds was overcrowded.

After removal of the last amounts of Ib and IIb by elution of the chromatographic column with hexane-chloroform, a second pair of more polar compounds was obtained from the crude extract by elution with more polar solvents. It was separated again into an olefinic and an acetylenic component, and was found to be the 1,2,4-trihydroxy-n-heptadeca-16-yn (Ia) and 1,2,4-trihydroxy-n-heptadeca-16-en (IIa) (Tables 1,2). Their structures were established through acetylation yielding the respective triacetates Ic and IIc.

When compounds Ib and IIb were hydrolyzed in basic conditions or treated with LAH, they were converted almost quantitatively into compounds Ia and IIa respectively. When acidic conditions were applied, the same compounds resulted but in a much poorer yield.

TABLE 2

	H_1H_1	H_2	H_3H_3	H_4	H_3H_3	$(CH_2)_{6-14}$ *	$H_{15}H_{15}$ '	H_{16}	$H_{17}H_{17}$	$O=C-CH_3$
Ia	3.53 m*	3.84 m	—	3.84 m	—	1.25	2.15 dt $J = 2.5; 6.5$	—	1.96 t $J = 2.5$	—
Ib	3.97 m*	3.97 m	—	3.97 m	—	1.25	2.13 m	—	1.92 t $J = 2.5$	2.09 s
Ic	4.25 m	4.25 m	1.90 t $J = 6.5$	4.25 m	—	1.23 $\Delta W_4 = 8 \text{ cps}$	2.16 m	—	2.63 t $J = 2.5$	1.94 s C_3H_5N
	4.05 dd $J = 12; 3$	5.13 ddt $J = 6; 3; 6.5$	1.86 t $J = 6.5$	4.94 quin $J = 6.5$	—	1.25	2.12 m	—	1.92 t $J = 2.5$	2.04 s
	3.98 dd $J = 12; 3$	5.30 ddt $J = 6; 3; 6.5$	—	5.10 quin $J = 6.5$	—	1.24	1.99 m	—	1.85 t $J = 2.5$	1.71 s 1.75 s 1.775 s C_6H_6
IIa	3.53 m*	3.84 m	—	3.84 m	—	1.25	2.04 m	5.78 m	4.95 m	—
IIb	3.97 m*	3.97 m	—	3.97 m	—	1.26	2.04 m	5.78 m	4.97 m	2.08 s
IIc	4.03 dd $J = 12; 3$	4.98 m	1.84 t $J = 6.5$	4.98 m	—	1.25	—	5.80 m	4.98 m	2.04 s
III	3.97 m*	3.97 m	—	3.97 m	—	1.25	—	—	0.86 t $J = 6$	2.08 s

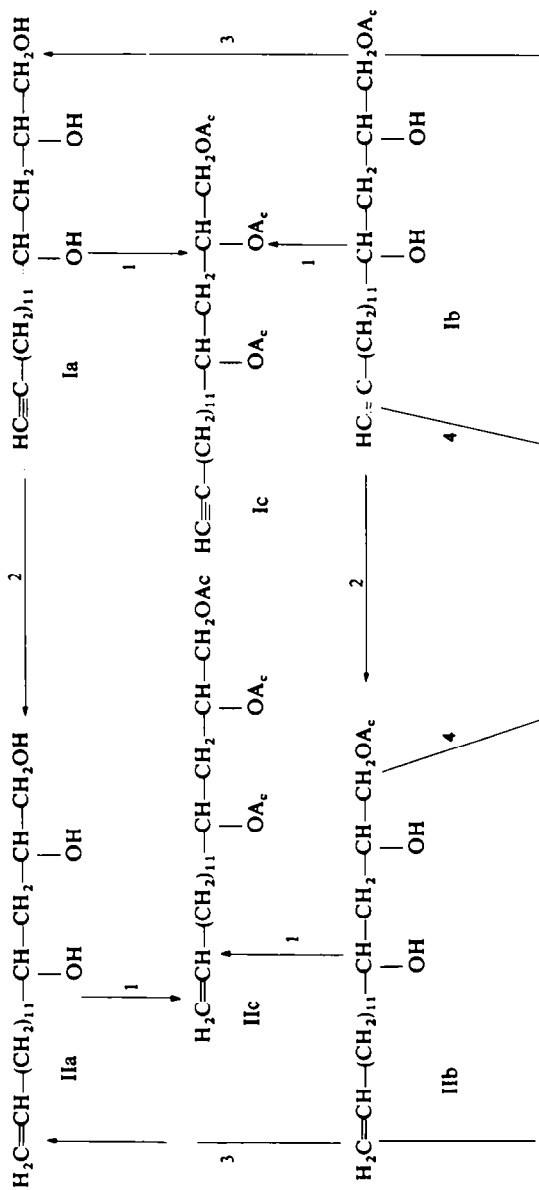
IV	4.07 m	4.16 m	2.62 d J = 6	—	2.45 t J = 7	1.25	2.15 m	—	1.92 t J = 2.5	2.10 s
V	4.07 m	4.16 m	2.62 d J = 6	—	2.45 t J = 7	1.25	—	5.75 m	4.94 m	2.10 s
Vla	4.10 m	4.23 m	2.62 d J = 6	—	2.44 t J = 7	1.25	—	—	0.89 t J = 6	2.12 s
Vlb	4.125 dd J = 12; 3	4.275 dd 12; 4.5	2.70 m	—	2.40 t J = 7	1.25	—	—	0.86 t J = 6	2.01 s
VII	4.06 d† J = 4.8	6.90 dt J = 16; 4	6.36 d J = 16	—	2.44 t J = 7	1.25	—	—	0.86 t J = 6	2.05 s
VIII	7.25 dd J = 0.7; 2	6.42 dd J = 2; 3	5.94 m	—	2.58 t† J = 7	1.25	—	—	0.87 t J = 6	—
IX	7.25 dd J = 0.7; 2	6.24 dd J = 2; 3	5.94 m	—	2.58 t† J = 7	1.25	2.12 dt J = 2.5; 6.5	—	1.92 t J = 2.5	—
X	7.25 dd J = 0.7; 2	6.24 dd J = 2; 3	5.94 m	—	2.58 t† J = 7	1.25	2.04 m	5.78 m	4.96 m	—
XIa	3.68 dd J = 10.5; 4.5	3.99 dd 10.5; 2.2	—	3.90 m	—	1.25	—	—	0.87 t J = 6	—
XIb	3.70 dd J = 10.5; 2.5	4.10 dd 10.5; 5	—	3.98 m	—	1.25	—	—	0.87 t J = 6	—
XIII	4.01 m	3.80 m	—	3.80 m	—	1.25	—	—	0.87 t J = 6	1.40 s 1.44 s (Me-Acetamide)

* 8 lines of the ABX system are seen, after addition of D₂O the pattern is usually clearer.

† This signal is a quiet sharp singlet with $\Delta W_{\frac{1}{2}} = 5$ c/s.

‡ Not sharp.

SCHEME 1



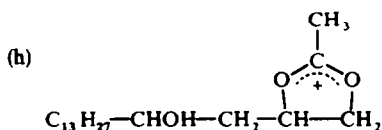
In addition to these two pairs of compounds, two other pairs were isolated in minute quantities. The first pair to be dealt with is compounds IV and V, which were found to be the keto derivatives of Ib and I Ib respectively (Table 1). The NMR spectrum of compound IV (Table 2) reveals at low field only three protons which constitute quite a complex ABC system centered at δ -4.12, while at high field a new pattern due to four protons besides the known signals could be observed: a doublet (2H) at δ -2.60 ($J = 6$), which can be attributed to the C-3 protons, and a triplet (2H) at δ -2.45 ($J = 7$) due to the C-5 protons. Compound V also showed a similar pattern (Table 2).

Compounds Ib and I Ib were converted into their respective keto derivatives IV and V by oxidation of the C4-OH group without affecting the second hydroxyl on C-2. It was clear that the ketone resulting from the oxidation of the C4-OH will be highly sensitive to acid and will easily change to an $\alpha\beta$ unsaturated ketone which possessing an allylic acetate will be equally sensitive to acid. Of the various oxidative methods attempted, only the heterogeneous oxidation by the Brown method⁷ was successful, and starting from compound III, the desired hydroxy ketone VIa was obtained. Indeed, the NMR spectrum of this compound had a pattern similar to that of IV and V for its protons adjacent to the ketone on C-4 (Table 2). That oxidation occurred only at C-4 was indicated by the signal at δ -4.16 of H-2 which was still present in the NMR spectrum of the oxidation product VIa. This hydroxy ketone was found to be highly sensitive to acid, as anticipated, and was obtained unchanged only following quick filtration through a florisil column.

Acetylation of VIa afforded the keto diacetate derivative VIb thus confirming that during the oxidation only one OH group had reacted. The ABC system, in the NMR of compound VIa, attributed to C-1C-2 protons, changed to an ABX system after the acetylation, which enabled irradiation experiments. These irradiations disclosed several coupling constants, shown in Table 2, and confirmed thereby the relationship between the various protons of this functional site. When compounds Ib and I Ib were submitted to the same oxidation procedure used for compound III, the acetylenic hydroxy acetoxy ketone IV and the olefinic V were obtained. These compounds, as previously mentioned, were also isolated from the natural extract.

The fact that only one OH group is oxidized requires further clarification. It is not likely that this phenomenon is due to the 1,3 relations of the two OH groups, since when 1,3 dihydroxypentane was submitted to Brown oxidation conditions, it was readily converted to the 1,3 diketone which gives a positive color reaction with FeCl_3 . No such reaction occurred when Brown oxidation conditions were applied to compound III, Ib or I Ib. The formation of an acetoxonium ion (h) does not seem probable, though not impossible. Such an ion should cause an inversion or even a recemization at C-2 when decomposed by water, a change which could not be detected.

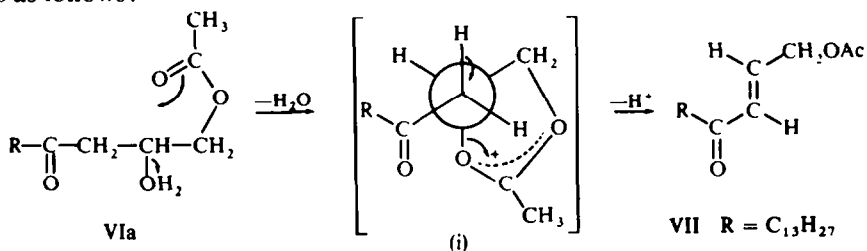
The reason for the oxidation of the C4-OH only, seems to be due to a neighboring effect of the acetate group of C-1, shielding the C-2 hydrogen and thereby disturbing



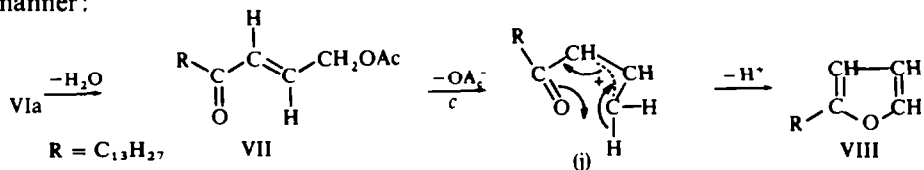
the proton abstraction. The resistance of the natural acetoxy hydroxy keto compounds IV and V to further oxidation also supports the explanation of existence of such neighboring effects. These two compounds which, like compound III, could produce an acetoxonium ion similar to (h) and undergo the same changes, remained unchanged, as far as we could observe, when left overnight in Brown oxidation conditions. Work on this problem is still in process.

When compound VIa was filtered through deactivated neutral alumina, VII was obtained. The NMR spectrum of this compound clearly shows the presence of a *trans* double bond $\alpha\beta$ to a ketone δ -6.90 dt ($J = 16$; $J = 4$); δ -6.36 d ($J = 16$).

The ease of water elimination from compound VIa can be attributed to the fact that the C2-OH group is not only β to a ketone but also vicinal to an acetate, so that VIa can, through the acetoxonium ion (i), easily lose a molecule of water in two steps as follows:



If the hydroxy ketone (VIa) is left somewhat longer on the alumina column or when purification of compound VII is attempted, a new product VIII results. This compound can best be prepared from VIa by the addition of traces of *p*-toluenesulfonic acid to its solution in ether, or even by refluxing compound VIa in hexane in the presence of anhydrous CuSO_4 as a mild Lewis acid. The NMR spectrum of compound VIII clearly shows the presence of a furan ring δ -7.25 dd ($J = 2$; 0.7), δ -6.24 dd ($J = 2$; 3), δ -5.94 m. This could also be seen from the IR absorption at 1260, 1145, 1070, 1005, 915, 880 cm^{-1} . The last transformation can be illustrated in the following manner:



This mechanism is supported by the isolation of compound VII—the keto allylic derivative, indicating that the first step of the reaction is the elimination of water followed by the departure of the acetate group and the formation of the allylic cation (j). *cis-trans* Isomerization becomes possible and the furan is formed by ring closure and proton abstraction.

Another possible mechanism for this transformation is:



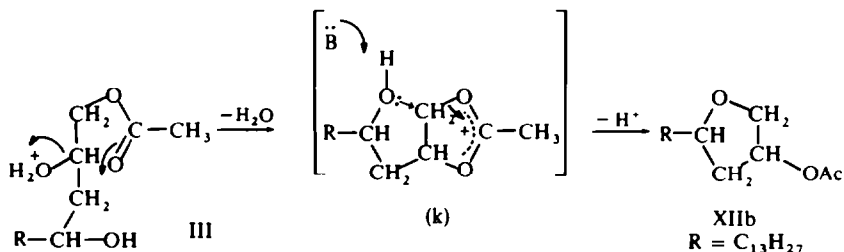
Similar acid treatment of compounds IV and V yielded the respective acetylenic and olefinic furans namely 2-(trideca-12-yn)-furan and 2-(trideca-12-en)-furan IX

and X. This pair of furans was also obtained by rapid chromatography of the crude natural hexane extract through florisol. When examining the NMR of the natural crude extract, the signals of the low field furanic protons could be observed, so that it appears that the furans described are natural substances.

Ozonolysis of both furanic compounds IX and X yielded, after oxidative treatment, the 1,13-tridecaedioic (brassicic) acid,⁸ thus supporting the proposed long aliphatic chain structure of the various members of the group described. This treatment cleaved the unsaturated bond at C-12 as well as the furan ring, converting the two end groups into carboxyls.

The various 1-acetoxy-2,4-dihydroxy compounds previously described (Ib, Ic, III) when boiled azeotropically in benzene in the presence of *p*-toluenesulfonic acid, gave rise to elimination products. From III, compound XIIb $C_{19}H_{36}O_3$ ($M^+ 312$) was obtained. Although elemental analysis and mass spectrum of XIIb indicated that only one molecule of water was eliminated by the last treatment, the presence of the second OH could not be seen in the IR of the compound. In the NMR spectrum of XIIb, again no change could be observed when trichloroacetyl isocyanate was added, indicating absence of OH groups and strangely no signal of vinylic protons was evident.

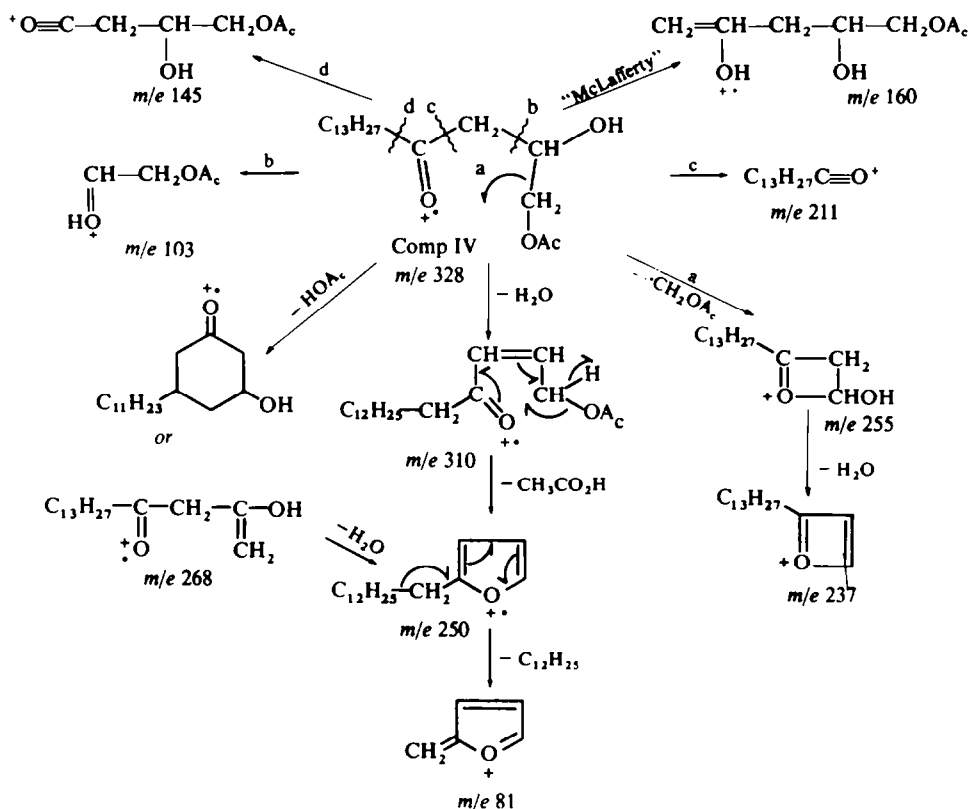
Hydrolysis of XIIb yielded XIIa, $C_{17}H_{34}O_2$ (M^+ , 270) which showed in the IR spectrum, the disappearance of the acetate and the appearance of an OH group. In the NMR spectrum of this compound XIIa, the multiplet (IH) at δ -5.26 shifted to δ -4.46, indicating that only one proton was geminal to the original acetoxy group instead of the two present in compound III. These facts can best be rationalized by the following scheme:



Following protonation the C-2 OH in compound III, a molecule of water leaves, and the acetoxonium ion (k) is formed. Subsequently, a nucleophilic attack of the C-4 OH group takes place producing a tetrahydrofuranic ring in which the acetate group previously attached to C-1 migrated to C-2. The NMR data of XIIb is in accordance with the proposed structure. Signals of four protons were observed in the low field: δ -3.70 dd ($J = 10.5$; $J = 2.5$); δ -4.10 dd ($J = 10.5$; $J = 5$); δ -5.26 m and δ -3.98 m. Spin decoupling experiments performed by irradiating these four protons established their relative positions (Table 2). Compound XIIb could also be obtained by boiling III in hexane using very mild acid conditions (anhydrous $CuSO_4$).

The compounds reported herein are unique in some respects. To the best of our knowledge, no such compounds have ever been isolated. Their structure—unsaturation at one end of the compound and an oxidative sugar-like form at the other—is quite unusual. The appearance of the compounds in pairs, each containing an acetylenic and olefinic compound is also of interest.

SCHEME 2



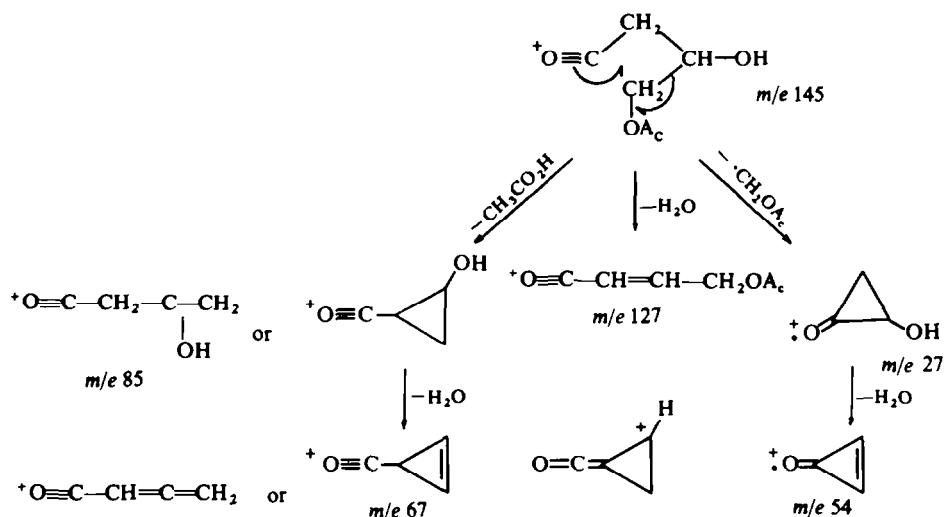
Mass spectrometry. The mass spectrum of VI is in full agreement with the given structure; this compound shows a molecular peak at m/e 328 of 0.5% intensity (the base peak being m/e 43). The fragmentation of VI which is shown in Scheme 2 is supported by comparison with the mass spectra of compounds IV and V, all the fragments which comprise the oxygenated moiety carrying functional groups are identical, while those derived from the hydrocarbon chain moiety are shifted by two or four mass units from each other respectively. Further fragmentation of the common ions m/e 145 and m/e 160 are shown in Schemes 3 and 4.

The furan fragments at m/e 250 (3%) and m/e 81 (36%) could be observed also in the mass spectrum of the furanic compound VIII, where they are the two most abundant peaks. (Similar peaks appear also in the spectra of compounds IX and X.)

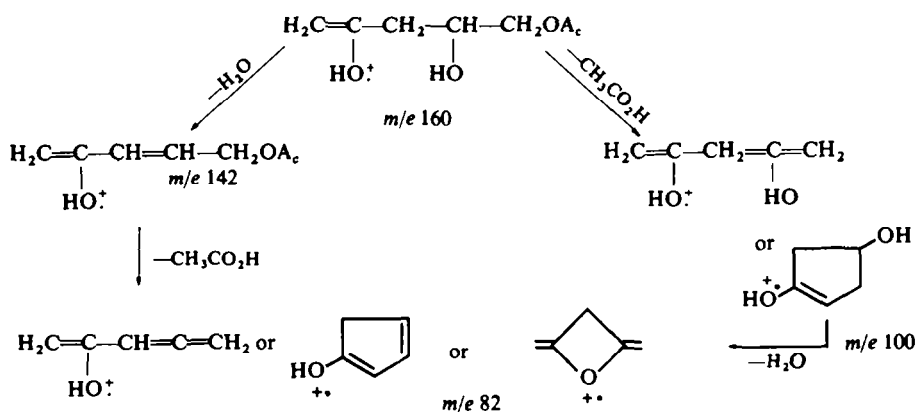
The mass spectrum of Ia shows a base peak at m/e 87 which probably arises by loss of water from $[\text{CH}(\text{OH})\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH}]^+$ m/e 105 (85%). The molecular peak m/e 284 (0.8%) is accompanied by the "M + 1" (m/e 285) (0.4%), a phenomenon which is quite known for polyhydroxy compounds *inter alia*.⁹ Other significant peaks are: m/e 266 (M - H₂O, 3.5%), 253 (M - CH₂OH, 14%), 235 (M - (CH₂OH) - H₂O, 63%), 217 (M - (CH₂OH) - 2H₂O, 9%), 209 (M - CH₂CH(OH)CH₂OH, 62%) and 191 (m/e 209 - H₂O, 9%).

The corresponding peaks, shifted to higher m/e by two mass units, appear in the spectrum of iIa.

SCHEME 3



SCHEME 4

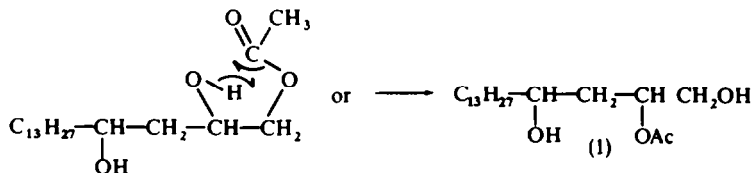


The mass spectrum of III shows the following peaks:
m/e 331 ("M + 1", 0.25%), 330 (M, 0.4%), 312 (M - H₂O, 0.4%), 299 (M - CH₂OH, 11%), 270 (M - HOAc, 5%), 257 (M - CH₂OAc, 58%), 252 (M - HOAc - H₂O, 12%), 239 (M - CH₂OAc) - H₂O, 55%), 234 (M - HOAc - 2H₂O, 7%), 221 (M - CH₂OAc - 2H₂O, 14%), 213 (M - (CH₂CH(OH)CH₂OAc), 20%), 211 (M - (CH₂OAc) - H₂O - 28, 77%).

The peak at 299 can be explained by loss of CH₂OH from (1)

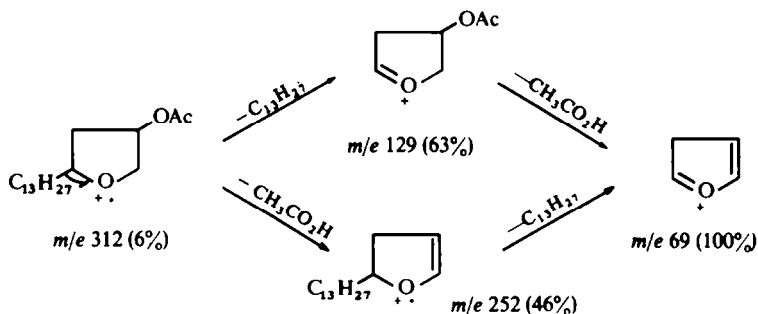
This rearrangement can be regarded as the electron impact promoted equivalent of the vicinal hydroxyacetoxy rearrangement, which are known for example in the case of the equilibration of diaxial hydroxy acetates to their diequatorial isomers.¹⁰

All the above peaks appear also in the mass spectra of Ib and IIb where they are shifted by two or four mass units correspondingly. The three compounds show a



second series of parallel peaks, derived from m/e 147 ($\text{HO}^+ = \text{CH}-\text{CH}_2 - \text{CHOH}-\text{CH}_2\text{OAc}$, 78%): m/e 129 (147- H_2O , 55%), 111 (147-2 H_2O , 26%), 87 (147- HOAc , 71%), 74 (147- CH_2OAc , 26%). The base peak is m/e 43.

The fragmentation pattern of the oxygenated moiety of Ic greatly resembles the mass spectrum of acetylated sugars,¹¹ thus the following peaks correlated to the base peak at m/e 43 appear: m/e 410 (M, 0.3%), 350 (M- HOAc , 13%), 337 (M- CH_2OAc , 40%), 290 (M-2 HOAc , 10%), 277 (M-(CH_2OAc)- HOAc , 35%), 253 (M-(CH_2OAc)-2($\text{O}=\text{C}=\text{CH}_2$), 12%), 248 (M-2 HOAc -($\text{O}=\text{C}=\text{CH}_2$), 43%), 235 (M-(CH_2OAc)- HOAc -($\text{O}=\text{C}=\text{CH}_2$), 40%), 230 (M-3 HOAc , 27%). The same fragmentation shifted up by two m.u. also appears in the spectrum of IIc. The base peak in the mass spectrum of compound XIIb is at m/e 69 which can be arrived from m/e 129 or from m/e 252 as follows:



This fragmentation which is typical for partially hydrogenated furzans lends additional support to the suggested structure of this rearranged elimination product.

EXPERIMENTAL

M.ps were taken on a Fisher-Johns apparatus and are uncorrected. Optical rotation measurements were carried out in CHCl_3 soln. IR spectra were recorded on a Perkin-Elmer Infracord model 337 spectrophotometer equipped with a NaCl prism. NMR spectra were taken on a Varian HA-100 spectrometer for 5-10% solns in CDCl_3 containing TMS as an internal standard. Mass spectra were taken with an Atlas CH_4 instrument, the samples being introduced directly into the ion source through a vacuum-lock, electron energy 70 ev. electron current 20 μA source temp $< 120^\circ$, secondary electron multiplier as the detector. Elemental analyses were performed by the microanalytical laboratory of the Weizman Institute of Science.

Isolation procedure. Dried seeds (100 g) of avocado pear were extracted for 24 hr with boiling hexane. The cooled soln was evaporated and the residue obtained (ca. 2.5 g) chromatographed on a florasil column (60-100 mesh). The first eluted compounds with hexane were the two furans IX and X (ca. 200 mg), further elution with hexane- CHCl_3 95:5 gave compounds IV and V (ca. 250 mg). With hexane- CHCl_3 4:1 compounds Ib and IIb (ca. 800 mg) were eluted and pure CHCl_3 eluted compounds Ia and IIa (ca. 300 mg).

When dried fruit was used instead of seed the yield from 100 g was ca. 200 mg of compound Ib and IIb and 10 mg of compounds Ia and IIa.

Each pair of an acetylenic and olefinic compounds was separated as follows: A pair (500 mg) in EtOH (abs, 60 ml) was stirred for 2 hr with AgNO₃ (400 mg) dissolved in water (10 ml). The ppt obtained was separated by centrifugation, and was washed several times with EtOH. The wet acetylide was suspended and stirred in 5% ammoniumthiocyanate (20 ml) for 48 hr after which it was extracted with ether. The ethereal extract was washed with a sat NaCl aq dried (Na₂SO₄) and evaporated, yielding the acetylenic component (ca. 200 mg).

The ethanolic mother liquor was neutralized with dil NaHCO₃ aq evaporated, taken into ether, washed with saturated salt soln, dried and evaporated. The yield of the olefinic component was ca. 150 mg.

The above mentioned natural compounds whose spectral data is given in Tables 1 and 2 gave the following results on elemental analysis:

(Ia) Found: C, 71.67; H, 11.50. C₁₇H₃₂O₃ Requires: C, 71.79; H, 11.34%;

(Ib) Found: C, 69.76; H, 10.86. C₁₉H₃₄O₄ Requires: C, 69.90; H, 10.50%;

(IIa) Found: C, 71.03; H, 12.00. C₁₇H₃₄O₃ Requires: C, 71.28; H, 11.96%;

(IIb) Found: C, 69.56; H, 10.96. C₁₉H₃₆O₄ Requires: C, 69.47; H, 11.05%;

(IV) Found: C, 70.19; H, 10.20. C₁₉H₃₂O₄ Requires: C, 70.33; H, 9.94%;

(V) Found: C, 70.05; H, 10.30. C₁₉H₃₄O₄ Requires: C, 69.90; H, 10.50%.

As the furans IX and X do not crystallize and were available only in minute quantities, elemental analysis was not carried out on them, and only their mass spectra were examined.

Partial hydrogenation of Ib to IIb. Compound Ib (50 mg) in dry pyridine (5 ml) was hydrogenated over 5% Pd on BaSO₄ at room temp and atm press. After one mole H₂ was absorbed (30 min) the reaction was discontinued. The product which was obtained following the work-up crystallized from hexane (30 mg) m.p. 56–58° identical with IIb.

Partial hydrogenation of Ia to IIa. The procedure described for the conversion of Ib to IIb was followed.

Full hydrogenation of Ib to III. Compound Ib (100 mg) in abs EtOH (20 ml) was hydrogenated over 10% Pd on charcoal at atm press and room temp for 2 hr. The product III obtained following the work-up, crystallized from hexane, (80 mg) m.p. 68° [α]_D²⁵ – 6.8 (c, 1.0 CHCl₃); ν_{\max}^{KBr} 3400, 1720, 1260, 1135, 1118, 1090, 1065, 1040 cm⁻¹, (Found: M⁺ 330; C, 68.84; H, 11.57. C₁₉H₃₈O₄. Requires: MW 330. C, 69.04; H, 11.59%).

Full hydrogenation of IIb to III. Compound IIb (100 mg) hydrogenated as Ib gave the same product (III).

Acetylation of Ib to Ic. Compound Ic was prepared by treating Ib in the usual way with Ac₂O and pyridine. The oily product could not be crystallized, $\nu_{\max}^{\text{CHCl}_3}$ 3280, 2100, 1780, 1250 cm⁻¹. (Found: M⁺ 410. C₂₃H₃₈O₆. Requires: MW 410).

Acetylation of Ia to Ic. The procedure described for the acetylation of Ib to Ic was followed. The product was identical in all respects.

Acetylation of IIb to IIc. The procedure described for the acetylation of Ib to Ic was followed. The oily product could not be crystallized; $\nu_{\max}^{\text{CHCl}_3}$ 3050, 1730, 1630, 1250 cm⁻¹ (Found: M⁺ 412 C₂₃H₄₀O₆. Requires: MW. M⁺ 412).

Acetylation of IIa to IIc. The procedure described for the acetylation of IIb to IIc was followed. The product was identical in all respects.

Preparation of the acetone XIII from III. A soln of III (100 mg) was refluxed with anhyd CuSO₄ (1 gr) in acetone (50 ml) for 36 hr. The soln was filtered and the acetone evaporated. The crude product was chromatographed through silica-gel and then crystallized from hexane, m.p. 44–45° (MeOH) [α]_D²⁵ – 40° (c, 1.0 CHCl₃); ν_{\max}^{KBr} 1740, 1240, 1195, 1160, 1040 cm⁻¹, (Found: C, 71.26; H, 11.26. C₂₂H₄₂O₄. Requires: C, 71.30; H, 11.42%).

Conversion of Ib to Ia. a. Comp Ib (50 mg) was left overnight in the presence of methanolic KOH (2%; 5 ml). The soln was neutralized by the dropwise addition of 5% HCl aq and most of the solvent was removed under reduced press. The residue was diluted with ether washed with water, dried (Na₂SO₄), and the solvent removed. The product (Ia), after crystallization (30 mg) was found to be identical with the natural product.

b. A soln of Ib (100 mg) in ether (20 ml) was added dropwise to an ethereal slurry (50 ml) of LAH (150 mg). The mixture was refluxed for 2 hr and the excess reagent destroyed by the dropwise addition of EtOAc and sat Na₂SO₄ aq soln. After filtration the soln was washed with water, dried and the solvent was removed under press to give Ia.

c. An ethereal soln (20 ml) of Ib (100 mg) was left overnight in the presence of toluene-*p*-sulphonic acid

(10 mg). The ether was washed with water dried and evaporated. The crude product was chromatographed on a silica-gel column, and from the fraction eluted with CHCl_3 , Ia (30 mg) was crystallized.

Conversion of IIb to IIa. The procedure described for conversion of Ib to IIb was followed.

*Oxidation of III to VIa.*⁷ To a stirred soln of III (50 mg) in ether (5 ml) chromic acid (1.2 equiv) was added in 5 min. After 2 hr, the upper ether layer was separated and the aqueous phase extracted with three 10 ml portions ether. The combined extracts were washed with sat NaHCO_3 aq, then with water, and dried. The product (VIa), which was obtained following evaporation, was filtered through a florisil column and crystallized from hexane, m.p. 57–58° $[\alpha]_D^{25} + 20$ (c, 1.0 CHCl_3); $\nu_{\text{max}}^{\text{KBr}}$ 3400, 1735, 1705, 1260, 1125, 1080, 1040 cm^{-1} , (Found: C, 69.22; H, 10.92. $\text{C}_{19}\text{H}_{36}\text{O}_4$. Requires: C, 69.47; H, 11.05%).

Oxidation of Ib to IV. The procedure described for the oxidation of III to VIa was followed.

Oxidation of IIb to V. The procedure described for the oxidation of III to VIa was followed.

Conversion of IV to IX. Compound IX (100 mg) was left for 48 hr in ether (50 ml) in the presence of toluene-*p*-sulphonic acid (10 mg). The ether was washed with water, dried and evaporated, to yield IX (80 mg).

Conversion of V to X. The procedure described for the conversion of IV to IX was followed.

Ozonolysis of IX to XI. Compound IX (200 mg) in a soln of EtOAc: AcOH 2:1 (20 ml) was ozonized at 0°. When ca. 3 equivs O_3 were introduced the reaction was discontinued and water (4 ml) and H_2O_2 (30%, 0.5 ml) were added. After 24 hr more water was added and the product was extracted with EtOAc and washed several times with water until pH 6 was obtained. Evaporation of the solvent left a residue which was crystallized twice from EtOH–water, m.p. 105–110° (lit. 110°).⁸ The NMR spectrum showed a triplet at $\delta - 2.36$ ($J = 7$) and a singlet at $\delta - 1.28$ $\Delta W_{\frac{1}{2}} = 6$ c/s.

Ozonolysis of X to XI. The procedure described for the conversion of IX to XI was followed.

Elimination of III to XIIb. a. Compound III (100 mg) in hexane (25 ml) was boiled for 24 hr in the presence of anhyd CuSO_4 (1 g). After cooling, the soln was filtered and evaporated. The residue was crystallized from hexane to give XIIb (70 mg), m.p. 32–33° $[\alpha]_D^{25} - 17^\circ$ (c, 1.0 CHCl_3); $\nu_{\text{max}}^{\text{KBr}}$ 1730, 1240, 1040, 1010 cm^{-1} , (Found: C, 73.09; H, 11.35. $\text{C}_{19}\text{H}_{36}\text{O}_3$. Requires: C, 73.03; H, 11.61%).

b. A soln of III (100 mg) in benzene (25 ml) was heated azeotropically under reflux for 6 hr in the presence of toluene-*p*-sulphonic acid (20 mg). The residue was washed with 5% NaHCO_3 aq and with water, dried, and evaporated. Following crystallization XIIb (70 mg) was obtained.

Hydrolysis of XIIb to XIIa. The procedure described for hydrolysis of Ib to Ia was followed. XIIa was crystallized from hexane m.p. 48° (hexane); $\nu_{\text{max}}^{\text{KBr}}$ 3380, 1095, 1070, 1040, 1025, 970 cm^{-1} , (Found: C, 75.80; H, 12.71. $\text{C}_{17}\text{H}_{34}\text{O}_2$. Requires: C, 75.50; H, 12.67%).

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