the 3-oxime, as shown by thin layer chromatography. However, chromatography of the partially decomposed dimer on silica gel and elution with benzene–petroleum ether (1:1) gave pure nitroso dimer **12**, homogeneous by t.l.c. (benzene–petroleum ether 2:1), m.p. 192–195°, $[\alpha]_D$ +16°, $\lambda_{max}^{heptane}$ 294 mμ (ε 8500), ν_{max} 1180 cm.$^{-1}$ (*trans*-nitroso dimer).

Anal. Calcd. for $C_{54}H_{94}N_2O_2$: C, 80.73; H, 11.80; N, 3.49. Found: C, 80.31; H, 11.43; N, 3.94.

The filtrate from the original treatment of the crude reaction product with boiling acetonitrile was then concentrated, when 3β-nitro-5α-cholestane (**8**, 482 mg.) crystallized out. This material showed double m.p. 99–101° and 109–112° (lit.[23] double m.p. 98–99° and 109–110°). The analytically pure **8** obtained by recrystallization from acetonitrile showed m.p. 111.5–112.5°, $[\alpha]_D$ +24° (lit.[23] $[\alpha]_D$ +23°).

3α-Nitro-5α-cholestane (10) from 3α-Amino-5α-cholestane (9).—A solution of 3α-amino-5α-cholestane (**9**, 1.0 g.) in chloroform (15 ml.) was added dropwise (over 35 min.) to a refluxing solution of *m*-chloroperbenzoic acid (5.0 g.) in chloroform (15 ml.). After a further 10 min. (total reaction time 45 min.), the reaction mixture was cooled and worked up as described for the preparation of compound **4**. The crude reaction product was chromatographed on silica gel (30 g.) when elution with benzene–petroleum ether (1:1) gave 3α-nitro-5α-cholestane (**10**, 300 mg.). Crystallization from acetone gave **10** as plates, m.p. 159–161°, $[\alpha]_D$ +29° (lit.[23] m.p. 157–160°, $[\alpha]_D$ +26°).

Equilibration of the 20α- and 20β-Nitro Steroids 4 and 6. A. Sodium Hydrogen Carbonate in 95% Ethanol.—The nitro steroid (**4** or **6**, 1.0 mg.) was dissolved in 1.0 ml. of a saturated solution of sodium hydrogen carbonate in 95% ethanol, and the solution was refluxed for 18 hr. The reaction mixture was taken to dryness under a stream of nitrogen, the residue was extracted with chloroform, and the chloroform was washed with water and evaporated to dryness under nitrogen. The bicarbonate treatment led to hydrolysis of the 3-acetoxy group as well as equilibration at C-20. In each case, therefore, the product was dissolved in pyridine (0.1 ml.) and acetic anhydride (0.02 ml.) and kept at 25° for 18 hr. The mixture was then evaporated to dryness under a jet of nitrogen and was dissolved in benzene (1 ml.) for gas chromatographic analysis. Separate experiments, conducted with the 3α-acetoxy-20-nitro compounds **4** and **6**, showed that the pyridine–acetic anhydride treatment caused no epimerization at C-20. The areas under the curves were measured by planimetry, and the relative proportions of the isomers were calculated from the results of a series of runs with synthetic mixtures containing known quantities of the pure isomers **4** and **6**. The results are accurate to ±5%.

B. Tetramethylguanidine in Toluene.—The nitro steroid (**2** or **4**, 2 mg.) was dissolved in toluene (2 ml.) containing tetramethylguanidine (0.2 ml.), and the solution was refluxed for 1 hr. The mixture was concentrated *in vacuo*, diluted with water, and extracted with chloroform. The chloroform extract was washed with water and evaporated to dryness *in vacuo*. The residue was then dissolved in benzene (2 ml.) for gas chromatographic analysis.

The areas under the curves were determined by planimetry, and the relative proportions of the compounds were calculated from the results of a series of synthetic mixtures of the two isomers. The results are summarized in Table II and are accurate to ±5%.

TABLE II

EQUILIBRIUM DATA FOR 20α- AND 20β-NITRO COMPOUNDS

	α:β ratio	
Conditions	From 20α	From 20β
$NaHCO_3$–ethanol	41:59	42:58
Tetramethylguanidine–toluene	43:57	39:61

Acknowledgment.—We thank Mr. Bennett Lavenstein for valuable assistance with the equilibration experiments. We also thank Dr. D. P. Hollis for the n.m.r. spectra.

New Enynolic Acids from *Acanthosyris*. Structures and Chemistry[1]

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The seed oil of *Acanthosyris spinescens* contains three previously unknown hydroxyacetylenic fatty acids. These are shown to be 7-hydroxy-*trans*-10,16-heptadecadien-8-ynoic acid (Ia), 9%; 8-hydroxy-*trans*-11,17-octadecadien-9-ynoic acid, 4%; and 7-hydroxy-*trans*-10-heptadecen-8-ynoic acid, 6%. The methyl ester Ib does not dehydrate readily in acidic methanol but instead undergoes slow etherification. The hydroxyl in the grouping -CH=CHC≡CCHOH- is less readily etherified than that in the isomeric grouping -C≡CCH=CHCHOH-. Two etherification products of Ib were detected: methyl 7-methoxy-*trans*-10,16-heptadecadien-8-ynoate and a dimethoxyallene that was not fully characterized. Two other derivatives of Ib have been synthesized: methyl 7-hydroxyheptadecanoate and *trans*-8-*trans*-10,16-heptadecatriene-1,7-diol.

In an earlier report[3] we discussed the isolation of a number of new acetylenic fatty acids from *Acanthosyris spinescens* (Mart. et Eich.) Griseb. (*Santalaceae*) seed oil. The nonoxygenated acid fraction included two unique acids having normal C_{17} skeletons and a C_{18} acid having an isolated triple bond. This present paper reports the isolation and structure proof of three new hydroxyacetylenic acids from *Acanthosyris* oil and describes some of the chemistry of the grouping -CH=CHC≡CCHOH-.[4]

The hydroxy acid fraction of *Acanthosyris* oil accounted for 20% of the total fatty acids.[3] Hydrogenation of a portion of the mixed hydroxy acids and gas-liquid partition chromatographic (glpc) analyses of the product indicated that both C_{17} and C_{18} hydroxy acids were present and that these occurred in a ratio of approximately 3:1.

The mixture of hydroxy acids was resolved by countercurrent distribution of the methyl esters. This separation was accomplished with a hexane–acetonitrile system in a Craig–Post[5] apparatus. The weight distribution obtained after 1500 transfers (Figure 1) showed separation of the esters into two peaks. The slower moving peak (tubes 50–110) was shown by its infrared spectrum (strong band at 10.95 μ) to contain esters having terminal double bonds (Ib and IIb, Chart I). The faster moving peak contained

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[1] Presented in part before the American Oil Chemists' Society, Houston, Texas, April 25–28, 1965.

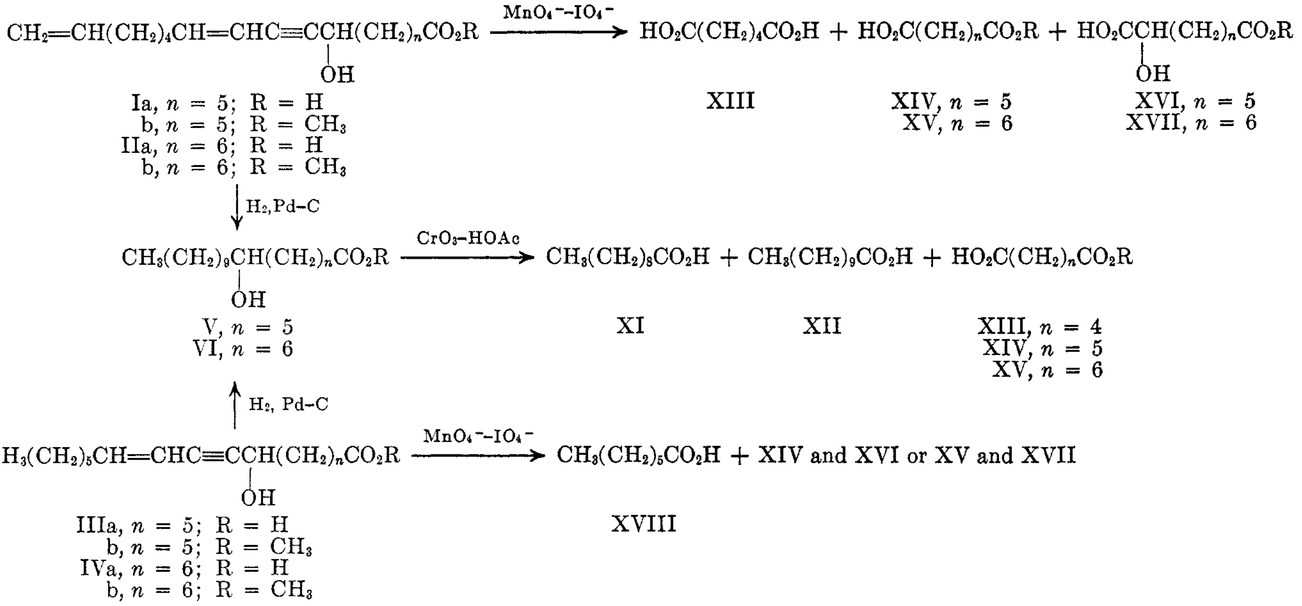
[2] One of the laboratories of the Northern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

[3] R. G. Powell and C. R. Smith, Jr., *Biochemistry*, in press.

[4] The structure of Ia was indicated in a preliminary communication: R. G. Powell and C. R. Smith, Jr., *Chem. Ind.* (London), 470 (1965).

[5] The mention of firm names or trade products does not imply that they are endorsed or recommended by the Department of Agriculture over other firms or similar products not mentioned.

CHART I



$$\mathrm{CH_2{=}CH(CH_2)_4CH{=}CHC{\equiv}C\underset{\displaystyle OH}{\underset{|}{C}}H(CH_2)_nCO_2R} \xrightarrow{\mathrm{MnO_4^-{-}IO_4^-}} \underset{\mathrm{XIII}}{\mathrm{HO_2C(CH_2)_4CO_2H}} + \underset{\mathrm{XIV},\, n = 5;\ \mathrm{XV},\, n = 6}{\mathrm{HO_2C(CH_2)_nCO_2R}} + \underset{\mathrm{XVI},\, n = 5;\ \mathrm{XVII},\, n = 6}{\mathrm{HO_2C\underset{\displaystyle OH}{\underset{|}{C}}H(CH_2)_nCO_2R}}$$

Ia, $n = 5$; R = H
b, $n = 5$; R = CH_3
IIa, $n = 6$; R = H
b, $n = 6$; R = CH_3

$$\downarrow \mathrm{H_2,Pd\text{-}C}$$

$$\mathrm{CH_3(CH_2)_9\underset{\displaystyle OH}{\underset{|}{C}}H(CH_2)_nCO_2R} \xrightarrow{\mathrm{CrO_3{-}HOAc}} \underset{\mathrm{XI}}{\mathrm{CH_3(CH_2)_8CO_2H}} + \underset{\mathrm{XII}}{\mathrm{CH_3(CH_2)_9CO_2H}} + \underset{\mathrm{XIII},\, n = 4;\ \mathrm{XIV},\, n = 5;\ \mathrm{XV},\, n = 6}{\mathrm{HO_2C(CH_2)_nCO_2R}}$$

V, $n = 5$
VI, $n = 6$

$$\uparrow \mathrm{H_2,\ Pd\text{-}C}$$

$$\mathrm{CH_3(CH_2)_5CH{=}CHC{\equiv}C\underset{\displaystyle OH}{\underset{|}{C}}H(CH_2)_nCO_2R} \xrightarrow{\mathrm{MnO_4^-{-}IO_4^-}} \underset{\mathrm{XVIII}}{\mathrm{CH_3(CH_2)_5CO_2H}} + \text{XIV and XVI or XV and XVII}$$

IIIa, $n = 5$; R = H
b, $n = 5$; R = CH_3
IVa, $n = 6$; R = H
b, $n = 6$; R = CH_3

esters without terminal double bonds[6] (IIIb and IVb). By removing the faster moving peak and continuing the distribution (solid-line portion of Figure 1) for another 4000 transfers, we were able to obtain good separation of Ib and IIb, as shown in Figure 2. IIIb and IVb were not separated but were treated as a mixture.

Methyl esters Ib, IIb, and the mixture of IIIb and IVb all had maxima at 4.52 and 10.48 μ in their infrared spectra and at 228 mμ in their ultraviolet spectra, indicating the presence of a *trans*-enyne chromophore.[7,8] A maximum at 2.76 μ in the spectrum of each denoted hydroxyl. In addition, both Ib and IIb had a strong band at 10.95 μ associated with the terminal double bond.[6] Ib was found to be slightly levorotatory.

Hydrogenation of Ib with 10% palladium-on-charcoal catalyst in glacial acetic acid produced a hydroxy ester (V) in 84% yield (*cf.* Chart I), as well as small amounts of a keto ester (VII) and methyl heptadecanoate (IX). The formation of both a keto ester and a hydrogenolysis product under these conditions was expected since similar results have been obtained in hydrogenating allylic or propargylic alcohols.[9-11] IIb was hydrogenated similarly and yielded a hydroxy ester (VI), 84%, as well as small amounts of a keto ester (VIII) and methyl octadecanoate (X). When the mixture of IIIb and IVb was hydrogenated, six products were found (V–X).

It was conclusively shown that Ib has a normal C_{17} skeleton by reducing V with hydrogen iodide–phosphorus.[12] .The resulting product was identified unequivocally as heptadecanoic acid by melting point and mixture melting point determinations.

The structures of the saturated hydroxy esters V and VI were established by oxidative cleavage with chromium trioxide in acetic acid. Cleavage of V gave decanoic and undecanoic acids in nearly equal amounts, together with half-esters of hexanedioic and heptanedioic acids, also in nearly equal amounts. Thus, both Ia and IIIa have normal C_{17} skeletons with a hydroxyl at C-7. When VI was cleaved, the products were decanoic and undecanoic acids in nearly equal amounts, together with half-esters of heptanedioic and octanedioic acids, again, in nearly equal amounts. Thus, both IIa and IVa have normal C_{18} skeletons with a hydroxyl at C-8.

Permanganate–periodate cleavage of Ib gave hexanedioic acid along with half-esters of heptanedioic

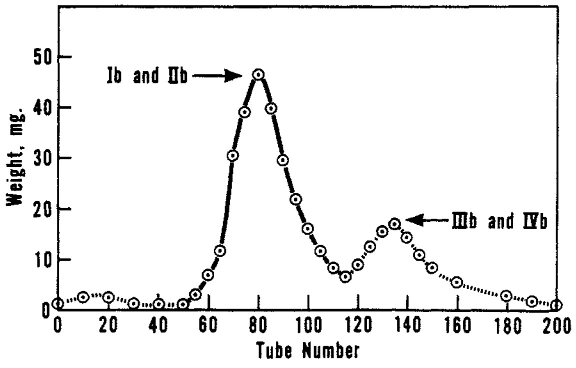


Figure 1.—Countercurrent distribution of *Acanthosyris* hydroxy esters I–IVb (1500 transfers).

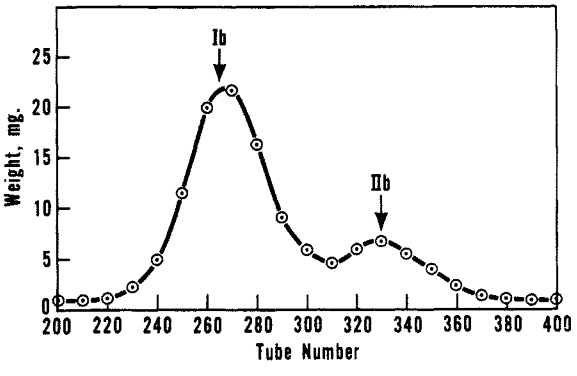


Figure 2.—Countercurrent distribution of the solid-line portion of Figure 1 (4000 additional transfers).

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[6] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, p 49.

[7] S. P. Ligthelm, H. M. Schwartz, and M. M. von Holdt, *J. Chem. Soc.*, 1088 (1952).

[8] L. Crombie and A. G. Jacklin, *ibid.*, 1622 (1957).

[9] T. H. Applewhite, M. J. Diamond, and L. A. Goldblatt, *J. Am. Oil Chemists' Soc.*, **38**, 609 (1961).

[10] F. D. Gunstone and A. J. Sealy, *J. Chem. Soc.*, 5772 (1963).

[11] R. G. Powell, C. R. Smith, Jr., C. A. Glass, and I. A. Wolff, *J. Org. Chem.*, **30**, 610 (1965).

[12] G. D. Meakins and R. Swindells, *J. Chem. Soc.*, 1044 (1959).

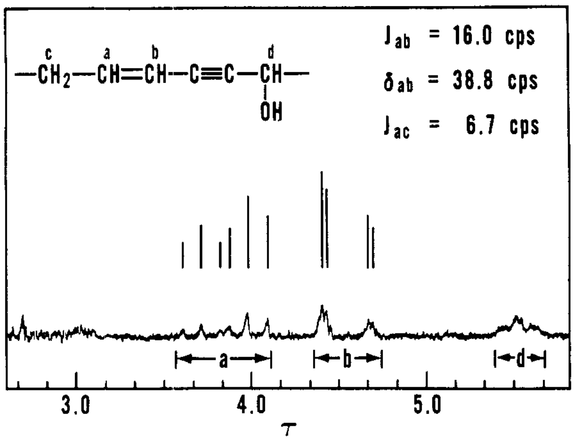
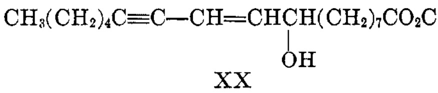


Figure 3.—Vinyl proton region of the nmr spectrum of IIIb.

and 2-hydroxyoctanedioic (XVI) acids. This result placed the enyne group in Ia between C-8 and C-11. The cleavage products from IIb, hexanedioic acid along with half-esters of octanedioic and 2-hydroxynonanedioic (XVII) acids, placed the enyne grouping in IIa between C-9 and C-12. Cleavage of the mixture of IIIb and IVb gave heptanoic acid (XVIII) and half-esters of heptanedioic, octanedioic, and 2-hydroxyoctanedioic acids. This result placed the enyne grouping between C-8 and C-11 in IIIa and between C-9 and C-12 in IVa.

The remaining problem concerning Ia, IIa, and IIIa was to determine whether the hydroxyl was α to the double or to the triple bond in each case. Lithium aluminum hydride reduction of Ib gave a diol (XIX) (see Chart II), mp 56–57°, containing a *trans,trans*-conjugated diene chromophore: $\lambda_{\max}^{\mathrm{EtOH}}$ 231 mμ (ϵ 28,600), 10.13 μ. Thus, Ib must contain the grouping -CH=CHC≡CCHOH-, since the alternative grouping -C≡CCH=CHCHOH-[13] would have given an allene rather than a conjugated diene when reduced with lithium aluminum hydride.[11,14,15] From this observation, it follows that Ia is 7-hydroxy-*trans*-10,16-heptadecadien-8-ynoic acid, and that the lithium aluminum hydride reduced product XIX is *trans*-8-*trans*-10,16-heptadecatriene-1,7-diol.

The nmr spectrum of Ib confirmed the structural assignment based on lithium aluminum hydride reduction. Nmr spectra of IIb and of the mixture of IIIb and IVb clearly showed that these also had hydroxyl α to a triple rather than to a double bond. The vinyl proton region of the spectrum of IIIb is reproduced in Figure 3 along with a simplified line spectrum. The pair of widely spaced triplets (τ 3.60–4.10) and the pair of rough doublets (τ 4.35–4.75) are in sharp contrast to the spectrum observed in the τ 3.60–4.75 region of methyl helenynolate (XX);



$$\mathrm{CH_3(CH_2)_4C{\equiv}C{-}CH{=}CH\underset{OH}{C}H(CH_2)_7CO_2CH_3}$$

XX

XX has a pair of widely spaced doublets (τ 3.77–4.02) and a pair of rough triplets (τ 4.20–4.47).[11] The nmr spectra of Ib and IIb resembled that in Figure 3, but there were additional signals due to terminal vinyl protons superimposed in the τ 3.80–5.20 region. These additional signals were the same as those found in the τ 3.80–5.20 region of the spectrum of 10-undecenoic acid.[16] Table I and Figure 3 summarize all the nmr data for Ib, IIb, and IIIb. The hydroxyl proton of Ib (τ 7.42) was assigned on the basis of a D_2O-exchange experiment.

CHART II

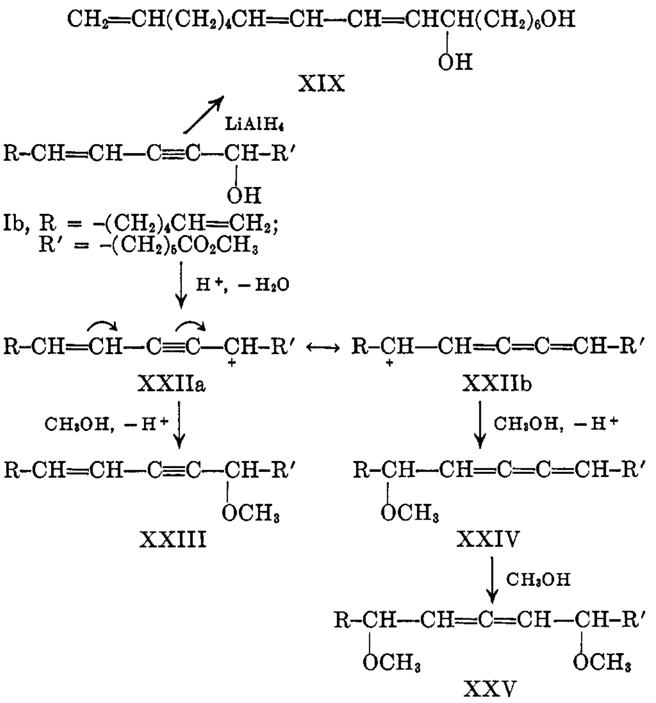


TABLE I

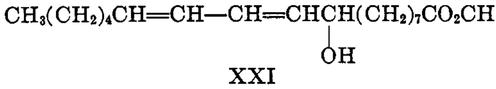
NMR SPECTRA OF *Acanthosyris* HYDROXY ESTERS

Assignment	τ value	No. of protons: Ib	IIb	IIIb[a]
CH_3, terminal	9.12	..	..	3
CH_2, in chain	8.63	12	14	16
CH_2, α to unsaturation	7.83	6	6	4
OH	7.42	1	1	1
OCH_3	6.33	3	3	3
CH	5.55	1	1	1
Olefinic H, α to C≡C	4.35–4.75	1	1	1
Olefinic H, β to C≡C	3.60–4.10	1	1	1
CH_2=CH-	3.80–5.20	3	3	..

[a] This sample contained 4% of IVb.

Thus, IIa is 8-hydroxy-*trans*-11,17-octadecadien-9-ynoic acid and IIIa is 7-hydroxy-*trans*-10-heptadecen-8-ynoic acid. IVb was present to the extent of only 4% in the mixture of IIIb and IVb, and was not fully characterized. However, our results suggest that it is the previously known 8-hydroxy-*trans*-11-octadecen-9-ynoic (hydroxyximenynic) acid.[13]

Ib proved to be much less reactive in acidic methanol than either methyl helenynolate (XX) or methyl dimorphecolate (XXI). Previous investigations have



$$\mathrm{CH_3(CH_2)_4CH{=}CH{-}CH{=}CH\underset{OH}{C}H(CH_2)_7CO_2CH_3}$$

XXI

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[13] S. P. Ligthelm, *Chem. Ind.* (London), 249 (1954).

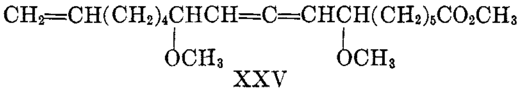
[14] W. Oroshnik, *J. Am. Chem. Soc.*, **77**, 4048 (1955).

[15] F. Bohlmann, R. Enkelmann, and W. Plettner, *Chem. Ber.*, **97**, 2118 (1964).

[16] C. Y. Hopkins, *J. Am. Oil Chemists' Soc.*, **38**, 664 (1961).

shown that dimorphecolate is easily dehydrated to a conjugated triene in acidic methanol, whereas helenynolate gives a 9-methoxy derivative under identical reaction conditions.[11,17,18] In contrast, when Ib was refluxed with 0.1 *N* methanolic hydrochloric acid for 1.5 hr, essentially only unreacted Ib was recovered. However, extended periods of reflux (up to 18 hr) did effect a partial conversion of Ib to a mixture of unidentified products (see Experimental Section). Under more rigorous conditions (1.2 *N* sulfuric acid in methanol, 50°, 22 hr) two products were detected by thin layer chromatography (tlc). These two products (XXIII and XXV, Chart II) were easily separated on a silica gel column in yields of 25 and 11%, respectively. The remaining material was mostly unreacted Ib. No dehydration products were found in the reaction mixture. The less polar of the two reaction products (XXIII) was shown to have two methoxyl groups by a modified Zeisel determination. The absorption maxima associated with the conjugated enyne chromophore (228 mμ and 10.48 μ) and with the terminal methylene chromophore (10.95 μ) were essentially unchanged by the reaction. However, the hydroxyl peak at 2.76 μ had been eliminated and replaced by a new maximum at 9.03 μ attributable to an ether linkage. The nmr spectrum of XXIII differed from that of Ib principally in having a new, very sharp singlet at τ 6.62 due to protons in a new methoxyl group. The hydroxyl signal at τ 7.42 was absent and the signal due to the proton on C-7 was shifted upfield to τ 5.96. Consequently, XXIII has the structure indicated in Chart II.

The more polar product of the acid-catalyzed methanolysis (XXV) was shown to contain three methoxyl groups by a modified Zeisel determination. In the infrared spectrum, the conjugated enyne peak (10.48 μ) was absent and had been replaced by a strong allene band at 5.11 μ. The original hydroxyl peak was also absent and had been replaced by a strong methoxyl peak at 9.05 μ. The only maximum in the ultraviolet was at 178 mμ, indicating that conjugated chromophores —diene, enyne, or enallene—were not present. We could not fully characterize XXV because of the small amount in hand. However, we suggest that the following structure is in accord with the observed properties of the substance, and that it can be derived in a manner that is mechanistically reasonable. Elimination of the OH from Ib would produce a carbonium ion (XXIIa, Chart II) which would be in resonance with a "rearranged" carbonium ion (XXIIb). Reaction of XXIIb with methanol presumably would yield a methoxycumulene (XXIV). However, Kosower and Sorenson[19] observed that the 4,5 double bond of 5-methyl-2,3,4-hexatrienal is highly labile and rapidly adds methanol to give 5-methyl-5-methoxy-2,3-hexadienal. In view of this precedent, it would be expected that, if a cumulene such as XXIV were formed during our etherification, it would be rapidly converted to XXV. The nmr spectrum of XXV, which was obtained on a 10-mg sample, was not easily interpreted because of a high level of background noise. The allenic proton signals were intermingled with terminal olefin signals and could not be sorted out. A new singlet, due to ether methoxyl protons, appeared at τ 6.69, a position significantly upfield from the signal due to the ether methoxyl of XXIII. The methine protons associated with the ether groupings apparently overlap the ester methoxyl signal at τ 6.33. Because of this overlap, the ester peak is integrated as though it had roughly the same number of protons as the ether methoxyl (τ 6.69). The two methoxyl groups indicated in structure XXV might be expected to give essentially equivalent nmr signals as in the observed spectrum.



$$CH_2{=}CH(CH_2)_4\underset{OCH_3}{CH}CH{=}C{=}CH\underset{OCH_3}{CH}(CH_2)_5CO_2CH_3$$

XXV

In a recent paper from this laboratory,[11] it was pointed out that helenynolic acid, which contains the grouping –C≡CCH=CHCHOH–, is much more resistant to dehydration than is a compound having the analogous grouping –CH=CHCH=CHCHOH–. This difference may be explained in terms of the electron-withdrawing property of a triple bond, and its low conjugating power compared with that of a double bond.[20,21] Our experimental results with *Acanthosyris* constituents indicate that the hydroxyl in the grouping –CH=CHC≡CCHOH– is distinctly less reactive in reactions requiring a carbonium ion intermediate than that in the isomeric grouping found in helenynolic acid. Thus the acetylenic linkage inhibits the development of a positive charge more powerfully at the α-position than at the vinylogous position.

Acanthosyris spinescens seed oil thus contains four hydroxylated acetylenic fatty acids in addition to the five nonoxygenated acetylenic fatty acids reported in our earlier paper.[3] The structures of all these unusual acids are summarized in Table II. All of the acids having conjugated unsaturation exist in both nonoxygenated and in hydroxylated form. In accordance with previous observations concerning acetylenic fatty acids found in *Santalaceae* and *Olacaceae* species,[10] the C_{18} hydroxy acids of *Acanthosyris* have hydroxyl at C-8. The C_{17} acids differ from the C_{18} acids only in having one less methylene group between the triple bond and the carboxyl end of the chain. *A. spinescens*

TABLE II

ACETYLENIC ACIDS OF *Acanthosyris* SEED OIL

Carbon skeleton	Position of triple bond	Positions of double bonds	Position of hydroxyl	Wt % of oil	Ref[a]
C_{17}	8[b]	10[b]	..	9	3
C_{17}	8	10	7	9	(IIIa)
C_{17}	8	10, 16	..	10	3
C_{17}	8	10, 16	7	6	(Ia)
C_{18}	9	17	..	18	3
C_{18}	9[b]	11[b]	..	1	3, 7
C_{18}	9[b]	11[b]	8	1	13 (IVa)
C_{18}	9	11, 17	..	4	3
C_{18}	9	11, 17	8	4	(IIa)

[a] Roman numerals correspond to compounds cited in the text and charts. [b] The conjugated enyne group is present and presumed to be in the positions indicated.

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(17) C. R. Smith, Jr., C. A. Glass, and I. A. Wolff, U. S. Patent 3,027,388 (March 27, 1962).

(18) R. G. Powell, C. R. Smith, Jr., and I. A. Wolff, *J. Am. Oil Chemists' Soc.*, **42**, 165 (1965).

(19) E. M. Kosower and T. S. Sorenson, *J. Org. Chem.*, **28**, 687 (1963).

(20) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p 70.

(21) E. E. Royals, "Advanced Organic Chemistry," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1954, p 514.

may be of further importance in studies of fatty acid biosynthesis. It is apparent, from our reactions in acidic methanol, that the grouping -CH=CHC≡CCHOH- has unusual reactivity. Compounds having this grouping may warrant further study as routes to substituted allenes and possibly to aliphatic cumulenes.

Experimental Section

Infrared spectra were determined with an Infracord Model 137 spectrophotometer, on 1% carbon tetrachloride solutions unless otherwise specified. Ultraviolet spectra were determined with a Beckman DK-2A far-ultraviolet spectrophotometer. Melting points were determined with a Fisher-Johns block and are uncorrected. Glpc analyses were carried out as described by Miwa and co-workers.[22] The optical rotation was determined by means of a Cary Model 60 recording spectropolarimeter. Nmr spectra were determined with a Varian A-60 spectrometer on deuteriochloroform solutions containing 1% tetramethylsilane. Tlc was carried out on silica gel G plates (according to Stahl) with the solvent system hexane–ethyl ether–acetic acid (70:30:1).

Isolation, Esterification, and Preliminary Examination of *Acanthosyris* Hydroxy Acids.—The separation of *Acanthosyris* free fatty acids into hydroxy and nonhydroxy acid fractions was described earlier.[3] The hydroxy acid fraction was 20% of the total acids obtained by saponifying the oil. This fraction, 2.1 g, was esterified in small portions with diazomethane; 2.3 g of methyl esters, $\lambda_{\max}^{\mathrm{EtOH}}$ 228 mμ ($E_{1\,\mathrm{cm}}^{1\%}$ 525), was obtained. The infrared spectrum showed hydroxyl (2.76 μ), acetylene (4.52 μ), conjugated *trans*-enyne (10.48 μ), and terminal methylene (10.95 μ).

A small portion of the hydroxy ester mixture was hydrogenated with 10% palladium-on-charcoal catalyst in glacial acetic acid. Glpc analyses of the saturated product indicated the following composition: $C_{17:0}$, 10%; $C_{18:0}$, 5%; C_{17} oxo, 20%; C_{17} hydroxy, 44%; C_{18} oxo, 7%; and C_{18} hydroxy, 14%.[23] Equivalent chain lengths[22] on Apiezon L were 17.0, 18.0, 18.4, 18.8, 19.4, and 19.7, respectively.

Countercurrent Distribution of *Acanthosyris* Hydroxy Esters.—The mixed hydroxy esters (2.1 g) were divided evenly among the first two tubes of a 200-tube countercurrent distribution apparatus with 40 ml of lower phase (acetonitrile) and 40 ml of upper phase (hexane). The remaining tubes each contained 40 ml of acetonitrile. The instrument was set to deliver 40 ml of upper phase into the first tube after each transfer. After 198 transfers, introduction of upper phase was halted and the instrument was set for recycle operation. The weight distribution after 1500 transfers is indicated in Figure 1. Infrared spectra showed that terminal methylene-containing esters were concentrated in tubes 50–120 and that nonterminal methylene esters were concentrated in tubes 110–170. At this point the contents of tubes 125–150 (containing a mixture of IIIb and IVb) were withdrawn and combined to give, after removal of solvent, 0.38 g of a pale yellow oil. All later experimental work involving IIIb and IVb was carried out on this fraction.

Tubes 0–50, 110–124, and 151–200 were emptied and their contents were replaced with fresh solvent. The apparatus was set for recycle operation and the distribution was then continued, on the material remaining in tubes 51–115, for 4000 additional transfers. The weight distribution at this point (Figure 2) showed that the original peak at tubes 50–110 had been resolved into two components (Ib and IIb). All experimental work involving Ib was carried out on the combined material recovered from tubes 25–80 (tubes 225–280 of Figure 2 as one complete cycle had occurred).[24] All experimental work involving IIb was carried out on the combined material recovered from tubes 120–170 (tubes 320–370 of Figure 2). These combinations gave 0.65 g of Ib and 0.23 g of IIb, both as pale yellow liquids.

Preliminary Characterization of the Hydroxy Esters. Ib.—Ester Ib had infrared maxima at 2.76 (OH), 4.52 (-C≡C-), 6.13 (C=C), 10.48 (*trans*-enyne), and 10.95 μ (CH$_2$=CH-). Its ultraviolet spectrum showed $\lambda_{\max}^{\mathrm{cyclohexane}}$ 229 mμ ($E_{1\,\mathrm{cm}}^{1\%}$ 536). It had $[\alpha]^{27}\mathrm{D}$ −3° (*c* 3.7, cyclohexane). Analysis of the nmr spectrum (summarized in Table I and in Figure 3) indicates the hydroxyl is α to a triple bond.

Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.95; H, 9.65. Found: C, 73.5; H, 9.6.

IIb.—Methyl ester IIb had an infrared spectrum that was almost identical with that of Ib. Its ultraviolet spectrum showed $\lambda_{\max}^{\mathrm{cyclohexane}}$ 229 mμ ($E_{1\,\mathrm{cm}}^{1\%}$ 461). The nmr spectrum of IIb was identical with that of Ib except that IIb had two more methylene protons (see Table I).

IIIb and IVb.—The mixture of IIIb and IVb had infrared maxima at 2.76 (OH), 4.52 (C≡C), and 10.50 μ (*trans*-enyne). The ultraviolet spectrum showed $\lambda_{\max}^{\mathrm{cyclohexane}}$ 229 mμ ($E_{1\,\mathrm{cm}}^{1\%}$ 488). The vinyl proton region of the nmr spectrum is presented in Figure 3 and the entire nmr spectrum is summarized in Table I.

Hydrogenation of Ib.—A 128-mg portion of Ib was hydrogenated using 10% Pd-C in glacial acetic acid. Glpc of the saturated product gave $C_{17:0}$, 7%; C_{17} oxo, 9%; and C_{17} hydroxy, 84%. Column chromatography of the product (130 mg) on Adsorbosil (Applied Science Laboratories, State College, Pa.) gave methyl heptadecanoate (IX), 9 mg; methyl 7-oxoheptadecanoate (VII), 16 mg (mp 44.0–44.5°); and methyl 7-hydroxyheptadecanoate (V), 103 mg (mp 47.5–48.5°).

Anal. Calcd for $C_{18}H_{36}O_3$: C, 71.95; H, 12.08. Found: C, 71.9; H, 12.0.

Hydrogenation of IIb.—A 90-mg portion of IIb was hydrogenated as before for Ib. Glpc of the saturated product gave $C_{18:0}$, 6%; C_{18} oxo, 9%; and C_{18} hydroxy, 84%. Column chromatography on Adsorbosil gave methyl octadecanoate (X), 6 mg; methyl 8-oxooctadecanoate (VIII), 7 mg (mp 44.5–45.5°);[25] and methyl 8-hydroxyoctadecanoate (VI), 53 mg (mp 54.5–55.5°).[25]

Hydrogenation of IIIb and IVb.—A 48-mg portion of the mixture of IIIb and IVb was hydrogenated as before. Glpc of the saturated product gave $C_{17:0}$, 5%; $C_{18:0}$, 1%; C_{17} oxo, 1%; C_{18} oxo, trace; C_{17} hydroxy, 90%; and C_{18} hydroxy, 3%. This result shows the mixture of IIIb and IVb to be approximately 96% IIIb and only 4% IVb.

Chromium Trioxide Oxidation Studies.—A 35-mg portion of V was dissolved in 3 ml of glacial acetic acid. To this mixture was added, dropwise and with continuous stirring, a solution of 350 mg of chromium trioxide, 2.5 ml of acetic acid, and 0.3 ml of water. The mixture was stirred at room temperature for 2.5 hr and diluted with 5 ml of water; the products were recovered by extraction with ethyl ether. The recovered acids were esterified with diazomethane and glpc analyses gave the following results: decanoic (16.6%), undecanoic (18.5%), hexanedioic (23.8%), and heptanedioic (22.4%) acids, together with smaller amounts of homologous degradation products of these acids.

A 20-mg portion of VI was oxidized exactly as was V. The recovered acids were esterified with diazomethane, and glpc analyses gave the following results: decanoic (16.7%), undecanoic (13.3%), heptanedioic (24.2%), and octanedioic (29.2%) acids, together with smaller amounts of homologous degradation products of these acids.

A 43-mg portion of the mixture obtained on hydrogenation of IIIb and IVb was oxidized exactly as was V. The recovered acids were esterified with diazomethane, and glpc analyses gave the following results: decanoic (21.9%), undecanoic (18.8%), hexanedioic (18.8%), heptanedioic (27.1%), and octanedioic (3.2%) acids, together with smaller amounts of homologous degradation products.

Permanganate-Periodate Oxidation Studies.—A 53-mg portion of Ib was stirred at room temperature with 15 ml of *t*-butyl alcohol, 0.4 g of potassium carbonate, and 25 ml of standard oxidant solution prepared according to von Rudloff.[26] The reaction was continued for 17 hr and then terminated by the addition of excess sodium metabisulfite. An excess of solid potassium hydroxide was then added, and solvent was removed under reduced pressure. The solid obtained was acidified with concentrated hydrochloric acid, and free acids were recovered by ether extraction. Methyl esters were prepared with diazomethane, and glpc analyses gave the following results: hexanedioic (42%), heptanedioic (18%), and 2-hydroxyoctanedioic

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[22] T. K. Miwa, K. L. Mikolajczak, F. R. Earle, and I. A. Wolff, *Anal. Chem.*, **32**, 1739 (1960).

[23] In notations such as $C_{17:0}$ the subscripts refer to the number of carbon atoms and the number of double bonds in the fatty acids.

[24] Tube number, as given in Figures 1 and 2, is the total number of tubes through which the material had progressed.

[25] Gunstone and Sealy[10] reported mp 45.5–46.0° for 8-oxooctadecanoate and mp 55–55.5° for 8-hydroxyoctadecanoate.

[26] E. von Rudloff, *Can. J. Chem.*, **34**, 1413 (1956).

(27%) acids, together with smaller amounts of homologous degradation products of these acids. The equivalent chain length of the fragment tentatively identified as 2-hydroxyoctanedioate was 19.3 on an R-446 column.

A 40-mg portion of IIb was oxidized exactly as was Ib. The recovered acids were esterified with diazomethane, and glpc analyses gave the following results: hexanedioic (30%), octanedioic (17%), and 2-hydroxynonanedioic (24%) acids, together with smaller amounts of homologous degradation products. The equivalent chain length of the fragment tentatively identified as 2-hydroxynonanedioate was 20.1 on an R-446 column.

A 59-mg portion of III (containing 4% IV) was oxidized exactly as was Ib. The recovered acids were esterified with diazomethane, and glpc analyses gave the following results: heptanoic (43%), heptanedioic (28%), octanedioic (3%), and 2-hydroxyoctanedioic (11%) acids, together with smaller amounts of homologous degradation products of these acids.

Lithium Aluminum Hydride Reduction of Ib.—A 69-mg portion of Ib in 3 ml of dry ether was added to a suspension of 400 mg of lithium aluminum hydride in 8 ml of ether, and the mixture was refluxed for 3 hr. After cooling, excess hydride was destroyed by the addition of moist ether followed by 10 ml of 5% sulfuric acid. The mixture was extracted with ethyl ether, and the combined ether extracts were dried over anhydrous sodium sulfate. The crude material (43 mg) was recrystallized from hexane to give 21 mg of a diol, mp 56–57°. Infrared showed maxima at 2.72 (OH), 6.12 (C=C), 10.13 (*trans,trans*-diene), and 10.93 μ (CH$_2$=CH–). The ultraviolet spectrum gave $\lambda_{\max}^{\text{EtOH}}$ 231 mμ (ϵ 28,600).

Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.0; H, 11.5.

Conversion of V to Heptadecanoic Acid.—A 65-mg portion of V was refluxed 17 hr with 37 mg of red phosphorus and 3 ml of hydriodic acid (sp gr 1.7).[12] The reaction mixture was then diluted with 10 ml of water and extracted repeatedly with ethyl ether. Combined ether extracts were washed with 5% sodium metabisulfite, then dried over sodium sulfate. Upon evaporation, 61 mg of a clear oil remained. This was reduced by heating at reflux 4 hr with 200 mg of granular zinc, 5 ml of methanol, and 1 ml of concentrated hydrochloric acid. The mixture was then diluted with water and extracted repeatedly with ether. After drying over sodium sulfate and removing solvent, 42 mg of methyl heptadecanoate remained (mp 27–28°). A 40-mg portion was then refluxed 1 hr with 5 ml of 1 *N* potassium hydroxide in ethanol. Heptadecanoic acid was recovered by acidifying with hydrochloric acid and extracting with ether; 34 mg of product was obtained, mp 59.5–60.5°, undepressed upon admixture with authentic heptadecanoic acid.

Reaction of Ib with Methanolic Hydrochloric Acid.—A 113-mg portion of Ib was dissolved in 15 ml of 0.1 *N* methanolic hydrochloric acid and refluxed for 1.5 hr. Infrared and ultraviolet spectra of the product, after recovery by ether extraction, showed essentially no reaction. By extending the reaction period to 18 hr, Ib (80 mg) was converted to a mixture of products as shown by tlc. Allene was present in the product (infrared maximum at 5.1 μ), as well as ether (9.0–9.1 μ), and the carbonyl peak (5.72 μ) had a pronounced shoulder, suggesting the presence of a ketone. Maxima appeared at 228.3, 267.2, 277.6, and 289.0 mμ in the ultraviolet spectrum of the product mixture. No further characterization of these materials was attempted, as they were apparently present only in minor amounts.

Reaction of Ib with Methanolic Sulfuric Acid.—A 103-mg portion of Ib was added to 10 ml of 1.2 *N* sulfuric acid in methanol. The flask was flushed with nitrogen, then stoppered, and held at 50° for 22 hr. The mixture was then diluted with 20 ml of water and extracted repeatedly with ethyl ether. The combined ether extracts yielded 97 mg of product. Examination of the product by tlc gave three spots (R_f 0.83, 0.52, and 0.25). These components were separated by column chromatography on silica gel. The first fraction, 26 mg, had the following absorption maxima: infrared, 4.52 (C≡C), 6.13 (C=C), 9.03 (OCH$_3$), 10.95 (CH$_2$=CH–), and 10.48 μ (*trans*-enyne); ultraviolet, $\lambda_{\max}^{\text{cyclohexane}}$ 229 mμ ($E_{1\,\text{cm}}^{1\%}$ 510).

Anal. Calcd for $C_{19}H_{30}O_3$: 2OCH$_3$, 20.2. Found: OCH$_3$, 18.8.

The second fraction (11 mg) had the following spectral characteristics: infrared, 5.11 (allene), 6.13 (C=C), 9.05 (OCH$_3$), 10.95 (CH$_2$=CH–), and 11.40 μ (allene);[27] ultraviolet, $\lambda_{\max}^{\text{cyclohexane}}$ 178 mμ ($E_{1\,\text{cm}}^{1\%}$ 935).

Anal. Calcd for $C_{20}H_{34}O_4$: 3OCH$_3$, 27.5. Found: OCH$_3$, 24.8.

Nmr spectra of these first two fractions are discussed in the text. The third fraction (most polar), 42 mg, was primarily unreacted Ib.

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[27] This peak is tentatively assigned to the allene grouping on the basis of the spectra of other known allenes examined in this laboratory.

The Interpretation of Enthalpy and Entropy Data

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Practical criteria are described for using enthalpies and entropies of reaction or activation and for assessing the possible relations among them.

Some Definitions.—The close analogy between standard enthalpies or entropies of reaction and enthalpies or entropies of activation makes it possible to discuss them in a unified way, and in this paper the symbol ΔH (ΔS) will be used to represent either $\Delta \bar{H}°$ ($\Delta \bar{S}°$) or ΔH^* (ΔS^*). Some substituents and some solvents probably exert their influence on reactions by very similar mechanisms, but even when this is not the case the formal treatment of substituent and medium effects can always be the same. In this paper the operator, δ, will serve for both δ_{M} (now almost a standard symbol for the effect of a change in reaction medium) and δ_{R} (effect of a change in structure or substituent).[1] The operator, δ, is convenient not only because it eliminates unwanted quantities analogous to constants of integration, but also because it avoids confusion with the reaction operator, Δ, which might otherwise be used.

$$\delta \Delta H = \Delta H - \Delta H_{\text{ref structure or solvent}}$$
$$\delta \Delta S = \Delta S - \Delta S_{\text{ref structure or solvent}}$$

Isokinetic Temperature.—It is often enlightening to display enthalpy–entropy data as points on a graph of enthalpy as ordinate *vs.* entropy as abscissa. The slope of a line in such a graph has the dimensions calories per mole over calories per mole degree, hence absolute temperature. At a temperature correspond-

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[1] J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963.