B. Alkaline Hydrolysis in Methanol.—Tetrahydroelatericin B diacetate (III, 500 mg.) was dissolved in methanol (100 ml.) and treated with aqueous sodium hydroxide as above: after 0.5 hr.—ν_{max} 1705, 1692, 1660, and 1410 cm.$^{-1}$; λ_{max} 268 mμ (ϵ 4900); positive ferric chloride.

C. Hydrolysis in Methanol at pH 9.—Tetrahydroelatericin B diacetate (III, 60 mg.) was dissolved in methanol (30 ml.) and 4% aqueous sodium hydroxide solution was added to pH 9. The alkaline methanolic solution of III was allowed to stand for 5 hr., then treated as above. The residue (50 mg.) produced one major spot on a chromatoplate: ν_{max} 1704 (broad), 1672 (very weak), and 1264 cm.$^{-1}$; slightly positive ferric chloride test.

Acknowledgment.—We thank Dr. Y. Shvo for the n.m.r. measurements and for contributing to their interpretation. We also thank Mrs. R. Lazar for technical assistance.

Helichrysum Seed Oil. II. Structure and Chemistry of a New Enynolic Acid[1]

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Helenynolic acid, a new hydroxy acid isolated from *Helichrysum bracteatum* seed oil, is shown to have the structure 9-hydroxy-*trans*-10-octadecen-12-ynoic acid (Ia) by oxidative degradation, spectral properties, and lithium aluminum hydride reduction. This acid is resistant to acid-catalyzed dehydration, but undergoes etherification in acidic methanol with considerable facility.

The isolation of a new hydroxy acid having a conjugated enyne grouping was described in part I of this series.[3] This acid was found as one of several unusual triglyceride substituents in *Helichrysum bracteatum* seed oil. This present paper deals with the proof of structure of this new acid and some of its chemistry.

The pure methyl ester of helenynolic acid (Ib) had absorption maxima at 4.54 and 10.46 μ in its infrared spectrum (see Figure 1), and at 228 mμ in its ultraviolet spectrum, that indicated a conjugated *trans*-enyne chromophore.[4,5] Ib was also indicated to be a monohydroxy ester by an infrared maximum of moderate intensity in the OH region (2.77 μ). It was found to be slightly levorotatory.

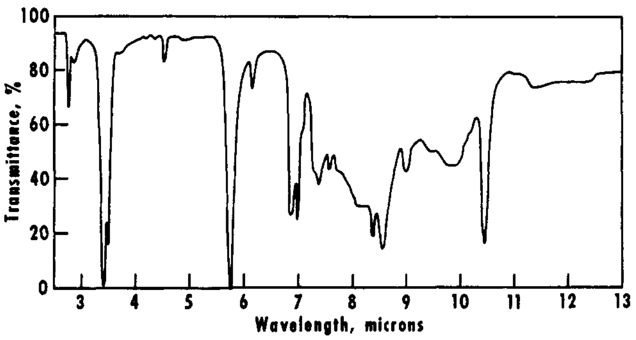
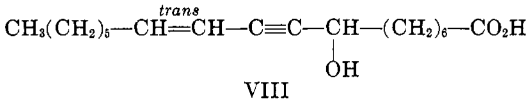


Figure 1.—Infrared spectrum of methyl helenynolate (Ib).

Hydrogenation of Ib with Adams catalyst in ethanol did not give satisfactory results. The desired product II, the saturated hydroxy ester corresponding to Ib, was formed in poor yield (50%). It was accompanied by a considerable amount (45%) of hydrogenolysis product (methyl stearate) and small amounts of keto ester as well as other minor components. II was obtained in much better yield (80%) by hydrogenating Ib in acetic acid solution with palladium–charcoal catalyst. Formation of keto esters by double-bond migration during hydrogenation had been observed previously.[6] Equally contrasting results in the use of platinum and palladium catalysts for hydrogenating compounds with activated hydroxyl groups was observed in work on oenanthotoxin and cicutoxin.[7] Similar hydrogenolyses of activated hydroxyls in acetylenic acids in isano oil[8] and in methyl dimorphecolate[9a] also have been reported. Results obtained on hydrogenating Ib with a rhodium–alumina catalyst in acetic acid[9b] were comparable with those obtained with palladium–charcoal. Ib consumed 3.25 moles of hydrogen in the presence of the rhodium–alumina catalyst.

The structure of saturated hydroxy ester II was established by oxidative cleavage with chromium trioxide in acetic acid. The cleavage products obtained, nonanoic and decanoic acids in nearly equal amounts together with half esters of octanedioic and nonanedioic acids in nearly equal amounts, placed the hydroxyl at C-9 on a normal C_{18} skeleton. (See Chart I.)

Permanganate–periodate cleavage of methyl helenynolate (Ib) yielded hexanoic acid and nonanedioic acid half ester. This result indicated that the enyne grouping and the hydroxyl group were located between C-9 and C-13, and suggested that helenynolic acid was closely analogous to 8-hydroxyimenynic (8-hydroxy-*trans*-11-octadecen-9-ynoic) acid (VIII). The latter acid, a constituent of *Ximenia caffra* kernel oil, was characterized by Ligthelm[10] and later synthesized by Crombie and Griffin.[11] However, lithium aluminum hydride reduction of Ib demonstrated that it was not an analog of VIII. Ligthelm[10] obtained *trans*-9,*trans*-



$$CH_3(CH_2)_5\text{—}\overset{trans}{CH\text{=}CH}\text{—}C\equiv C\text{—}\underset{\displaystyle OH}{\underset{|}{CH}}\text{—}(CH_2)_6\text{—}CO_2H$$

VIII

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[1] Presented at the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964.

[2] This is a laboratory of the Northern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article is not copyrighted.

[3] R. G. Powell, C. R. Smith, Jr., and I. A. Wolff, *J. Am. Oil Chemists' Soc.*, submitted for publication.

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

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

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

[7] E. F. L. J. Anet, B. Lythgoe, M. H. Silk, and S. Trippett, *J. Chem. Soc.*, 309 (1953).

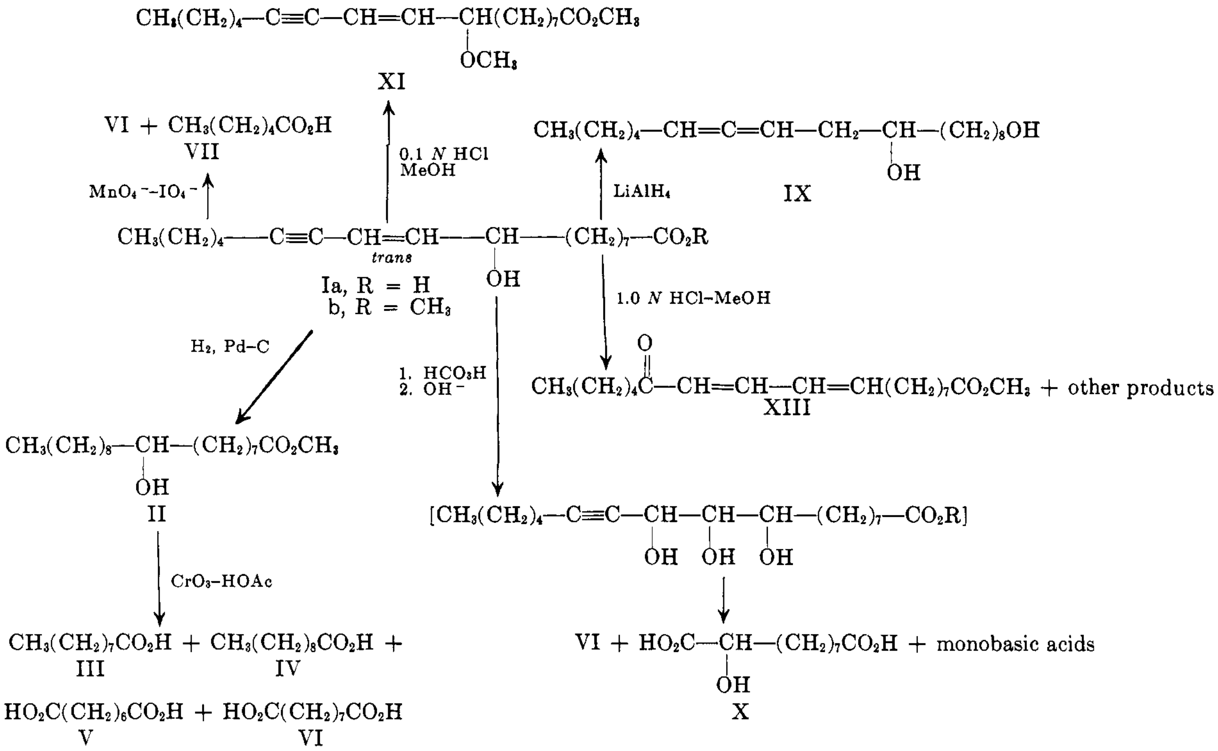
[8] F. D. Gunstone and A. J. Sealy, *ibid.*, 5772 (1963).

[9] (a) C. R. Smith, Jr., T. L. Wilson, E. H. Melvin, and I. A. Wolff, *J. Am. Chem. Soc.*, **76**, 1417 (1960); (b) T. H. Applewhite, personal communication.

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

[11] L. Crombie and B. P. Griffin, *J. Chem. Soc.*, 4435 (1958).

CHART I



11-octadecadiene-1,8-diol when he reduced VIII with lithium aluminum hydride, in accord with known precedents involving α-hydroxyacetylenes with or without conjugation to double bonds.[12] In contrast, the diol obtained by reducing Ib with the same reagent was not a conjugated diene, as evidenced by the absence of maxima near 233 mμ in its ultraviolet spectrum and near 10.1 μ in its infrared spectrum. A sharp maximum at 5.13 μ in the infrared indicated it to be an allene.[13] The only maximum in its ultraviolet spectrum was at 181 mμ, indicating that the allene was unconjugated as in structure IX.[14,15] This unexpected spectrum suggested that helenynolic acid did not have a structure analogous to VIII, but instead has the hydroxyl α to the double bond rather than the triple bond. In contrast to the better known reduction of the grouping, —CH=CH—C≡C—CHOH—, compounds having the grouping, —C≡C—CH=CH—CHOH—, are reduced to allenes on treatment with lithium aluminum hydride.[16] Thus it was indicated that helenynolic acid was not a positional isomer of VIII, but instead had structure Ia.

Confirmation for structure Ia was obtained by oxidative cleavage. Ib was subjected to performic acid oxidation followed by alkaline hydrolysis essentially as described by Raphael[17] for 2-penten-4-yn-1-ol. The expected triol was not obtained, but instead a mixture of acids whose infrared spectrum indicated relatively little OH absorption; acetylenic absorption (4.54 μ) was present in the spectrum of this reaction product, however. This mixture proved to be cleavage products of the sort expected if the C-9–C-10 or the C-10–C-11 bond in Ib were cleaved. Gas–liquid chromatographic (g.l.c.) analyses of these products indicated the presence of nonanedioic (55%) and α-hydroxydecanedioic (7%) acids. These cleavage products are consistent with structure Ib but not the isomeric structure analogous to VIII. Further degradative evidence supporting structure Ib was the absence of hexanoic acid from the cleavage products. If Ib had the double and triple bonds reversed, as in VIII, it would be expected to form a triol that would yield hexanoic acid if cleaved to acidic fragments.

The n.m.r. spectrum of methyl helenynolate (Figure 2) is in full accord with the structure assigned on chemical grounds. Table I summarizes the assignments based on this spectrum. The signals of the protons on C-10 and C-11 would be expected to split each other into doublets as in an AB system. The signal due to the C-10 proton is further split into a pair of relatively widely spaced doublets (τ 3.7–4.1, J = 6.0 c.p.s.) by coupling with the proton on C-9. Apparently there is

TABLE I

N.M.R. SPECTRUM OF METHYL HELENYNOLATE (Ib)

Assignment	τ-value	No. of protons
CH_3, terminal	9.08	3
CH_2, in chain	8.65	18
CH_2, α to carbonyl and triple bond; OH	7.68	5
OCH_3	6.32	3
CH, proton on C-9	5.87	1
Olefinic H, α to acetylene	4.20–4.47	1
Olefinic H, β to acetylene	3.77–4.02	1

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[12] R. A. Raphael, "Acetylenic Compounds in Organic Syntheses," Academic Press Inc., New York, N. Y., 1955, p. 29.

[13] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 61.

[14] S. F. Mason, *Quart. Rev.* (London), **15**, 287 (1961).

[15] Unpublished results from this laboratory indicate that a long-chain allene conjugated with a double bond absorbs at 222 mμ (K. L. Mikolajczak, M. O. Bagby, and I. A. Wolff, *J. Org. Chem.*, submitted for publication).

[16] (a) K. R. Bharucha and B. C. L. Weedon, *J. Chem. Soc.*, 1584 (1953); (b) E. B. Bates, E. R. H. Jones, and M. C. Whiting, *ibid.*, 1854 (1954); (c) W. Oroshnik, *J. Am. Chem. Soc.*, **77**, 4048 (1955); (d) F. Bohlmann, R. Enkelmann, and W. Plettner, *Chem. Ber.*, **97**, 2118 (1964).

[17] R. A. Raphael, *J. Chem. Soc.*, S44 (1949).

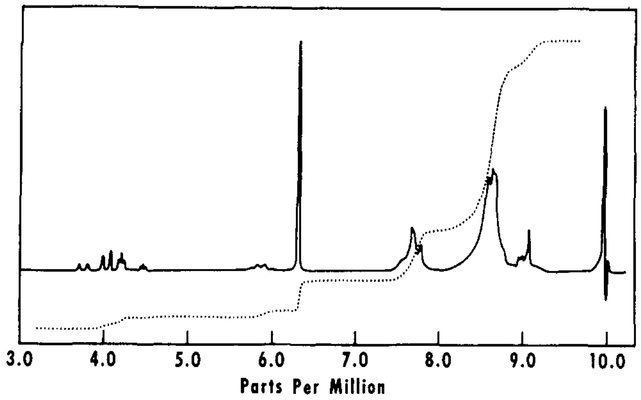


Figure 2.—N.m.r. spectrum of methyl helenynolate (Ib).

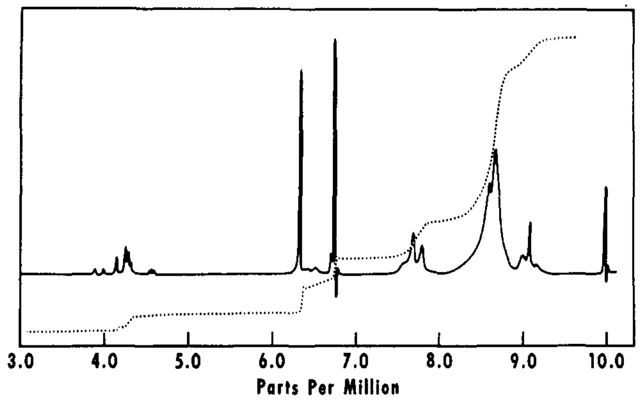
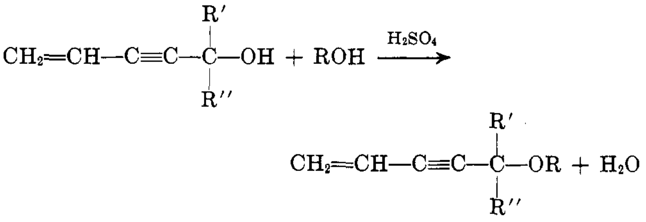


Figure 3.—N.m.r. spectrum of methyl helenynolate methyl ether (XI).

long-range coupling between the proton on C-11 and the two on C-14 as evidenced by the pair of closely spaced triplets at τ 4.1–4.5 (J = 1.8 c.p.s.). The coupling constant between the two olefinic protons, J = 14.1 c.p.s., is roughly comparable to the chemical shift, δ_{AB}. If the double and triple bonds of Ib were reversed in order, as in VIII, the olefinic protons would be expected to appear in its n.m.r. spectrum as two *widely spaced* triplets and two *closely spaced* doublets.

Methyl helenynolate (Ib) proved to be resistant to dehydration in methanolic hydrochloric acid. Apparently no attempts to dehydrate 8-hydroxyximenynic acid have been recorded, but resistance of α-hydroxyacetylenes to dehydration has been noted in a number of other cases.[18–20] Gunstone[8] recently reported that α-hydroxydiynoid acids were similarly resistant to dehydration. In contrast, conjugated dienols are readily dehydrated under acidic conditions, including dilute methanolic hydrochloric acid.[9,21] However, Ib was not recovered unchanged when heated 1.5 hr. with boiling 0.1 N methanolic hydrochloric acid, but was converted to a new substance in 70% yield. Similar results were obtained when Ib was heated under reflux 1.5 hr. with 0.1 N methanolic sulfuric acid. The new substance was readily purified chromatographically, and was shown to have two methoxyl groups by a modified Zeisel determination. The absorption maxima associated with the conjugated enyne chromophore (228 mμ and 10.45 μ) were essentially unchanged by the reaction, but the hydroxyl peak at 2.77 μ was eliminated and replaced by new maxima at 9.05 and 9.18 μ attributable to an ether linkage. The new compound proved to be stable under conditions of g.l.c. analysis at temperatures that decomposed Ib extensively, and to have retention times much lower than Ib on both polar and nonpolar columns. The lower retention times indicated a substance of lesser polarity than Ib. The n.m.r. spectrum of the new compound (Figure 3) differed from that of Ib principally in having a new, very sharp signal at τ 6.75 due to protons in a new methoxyl group. One less proton is observed at τ 7.68 and the proton on C-9 is shifted upfield to 6.40. Thus the reaction product must be methyl ether XI.

Acid-catalyzed etherifications have, in general, been less widely studied than those that occur under more rigorous conditions. Nazarov[22] found that dimethylvinylethynyl carbinol was converted to the corresponding methyl ether in 60–80% yield when warmed in *ca.* 1 N methanolic sulfuric acid. Homologs of this ether were similarly prepared by reaction of various conjugated enynols with appropriate primary alcohols. These etherifications were said to be accompanied by some dehydration.[23] Pansevich-Kolyada and co-workers investigated the acid-catalyzed etherification of allyl alcohols.[24] They found that a variety of substituted allyl alcohols readily undergo etherification with primary alcohols in the presence of aqueous sulfuric acid at ambient temperature. Nes and Kim[25] have reported that both 3β- and 3α-hydroxy-Δ^4-androsten-17-one ethylene ketal afforded the corresponding methyl ethers when refluxed with a mixture of methanol, acetic acid, and water. In contrast to these various results, Heilbron, Jones, and Weedon[26] detected no methyl ether formation after treating 3-hexen-5-yn-2-ol with 2 N methanolic sulfuric acid for 1 week at 20°.[27]



$$CH_2{=}CH{-}C{\equiv}C{-}\overset{R'}{\underset{R''}{C}}{-}OH + ROH \xrightarrow{H_2SO_4} CH_2{=}CH{-}C{\equiv}C{-}\overset{R'}{\underset{R''}{C}}{-}OR + H_2O$$

When Ib was heated with 1 N methanolic hydrochloric acid, the reaction took a different course than it did with 0.1 N acid. The main product formed under the influence of the more concentrated acid appeared to be neither methyl ether XI nor the compound that would have been formed by straightforward elimination of the elements of water (XII). XII would be expected to have an ultraviolet absorption maximum at 266 mμ with a shoulder at 277 mμ.[28,29] In contrast, the

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[18] H. Sobotka and J. D. Chanley, *J. Am. Chem. Soc.*, **70**, 3914 (1948).

[19] J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J. Chem. Soc.*, 1094 (1952).

[20] See ref. 12, p. 107.

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

[22] I. N. Nazarov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 706 (1938).

[23] I. N. Nazarov, *ibid.*, 719 (1938).

[24] V. I. Pansevich-Kolyada and B. K. Bogush, *Zh. Obshch. Khim.*, **33**, 2137 (1963), and several preceding papers cited therein.

[25] W. R. Nes and U. H. Kim, *Steroids*, **1**, 594 (1963).

[26] I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 81 (1945).

[27] These authors found, however, that, under these same conditions, propenylethynyl carbinol readily underwent aniontropic rearrangement with concurrent methyl ether formation. 2-Methoxy-3-hexen-5-yne was the product obtained.[26]

[28] H. H. Hatt, A. C. K. Triffett, and D. C. Wailes, *Australian J. Chem.*, **13**, 488 (1960).

[29] L. Crombie and A. G. Jacklin, *J. Chem. Soc.*, 1632 (1957).

reaction product had its main absorption maximum at 270 mμ. When methyl ether XI was similarly treated with 1 *N* methanolic hydrochloric acid, it afforded a comparable reaction product. Column chromatography of this product afforded two major fractions, one of which appeared to be ketodiene XIII. The other was indicated by thin layer chromatography (t.l.c.) to be a nonpolar substance, evidently a deoxygenated product (see Experimental).

The ultraviolet and infrared spectra of XIII closely resemble those of methyl 9-oxo-*trans*-10,*trans*-12-octadecadienoate. The infrared spectra of both compounds are distinguished by a similar series of peaks in the 5.9–6.5-μ region.[30] Upon hydrogenation, XIII yielded an impure saturated keto ester XIV which was, in turn, oxidatively cleaved with chromium trioxide–acetic acid. The result was inconclusive, but suggested that XIII was methyl 13-oxo-9,11-octadecadienoate. This transformation is analogous to a known rearrangement of α-hydroxyacetylenes. Some aryl-substituted α-hydroxyacetylenes have been similarly rearranged to α,β-unsaturated ketones under acidic conditions.[31,32] Melent'eva and co-workers[33] recently reported on certain highly substituted α-hydroxyacetylenes in the hydroxyphthalan series that are either etherified or rearranged to α,β-unsaturated ketones in the presence of methanol–acetic acid. Ethers were formed preferentially under very mild acidic reaction conditions, but ketones were formed under more vigorous conditions.

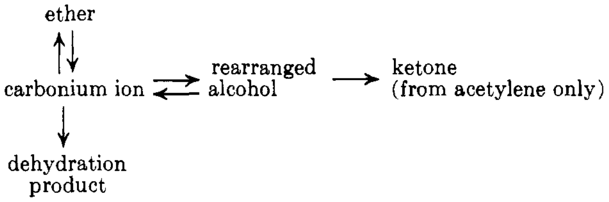
Dehydration of aethusanol A (*trans,trans*-5,11-tridecadien-7,9-diyn-4-ol) with *p*-toluenesulfonic acid in benzene solution was effected by Bohlmann and coworkers.[34] These workers thus obtained the hydrocarbon resulting from straightforward dehydration. However, when their toluenesulfonic acid method was applied to methyl helenynolate, a product was obtained showing an absorption maximum at 271 mμ—again different from that reported for an authentic conjugated dienyne chromophore. The transformation products from these attempted dehydrations appeared to be quite unstable and were not characterized except for determination of their spectral properties. We hope to elucidate the nature of these products later.

The chemistry of the enynol ($-C{\equiv}C-CH{=}CH-CHOH-$) grouping evidently differs from that of the analogous dienol grouping in certain respects. The reactivity of α-hydroxyacetylenes is influenced by the strong electron-withdrawing character of the triple bond.[35,36] This electron-withdrawing property deters carbonium ion formation on the α-carbon thus inhibiting acid-catalyzed dehydration *via* an E1 mechanism. The system $-C{\equiv}C-CH{=}CH-CHOH-$ evidently behaves chemically as a vinylog of an α-hydroxyacetylene rather than as an ordinary allylic alcohol or as a conjugated dienol. The dienoid analog of Ib, methyl dimorphecolate, is readily dehydrated by 0.1 *N* methanolic hydrochloric acid under reaction conditions identical with those affording XI as the primary product from Ib.[3] In connection with a related system, Henbest, *et al.*,[37] found that propargylic bromides undergo the Reformatskii reaction typical of α-bromo esters. They also found that the vinylogous bromides, $-C{\equiv}C-CH{=}CH-CHBr-$, react similarly.[38] A carbonium ion derived from a conjugated enynol system XV appears to be less readily formed than one from a corresponding dienol XVI. The differences in reactivity

$$\underbrace{-C{\equiv}C{=}CH{=}CH{=}CH-}_{+} \qquad \underbrace{-HC{=}CH{=}CH{=}CH{=}CH-}_{+}$$

XV XVI

of the two systems can be rationalized by assuming that the energy barrier for reactions proceeding through XV is appreciably greater than the corresponding energy barrier for reactions proceeding through XVI. Thus reactions requiring XV as an intermediate (etherification, rearrangement, or dehydration) will be much slower than the corresponding reactions requiring XVI.



With each system, the etherification would be the fastest of the three competing reactions and the dehydration the slowest.

Helenynolic acid is an addition to the growing list of naturally occurring fatty acids having varying numbers of both double and triple bonds in conjugation.[39] A few of these conjugated enynes have a hydroxyl α to a triple bond. To our knowledge, helenynolic acid is the first natural product having the grouping $-C{\equiv}C-CH{=}CH-CHOH-$ without further conjugation. Certain long-chain alcohols—cicutoxin,[7] oenanthotoxin,[7] and aethusanol A[34]—have an analogous grouping, but as part of a more extended system of conjugation.

Experimental

Infrared spectra were determined with an Infracord Model 137[40] 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. G.l.c. analyses were carried out as described by Miwa and co-workers[41]; free acids or half esters were analyzed in certain cases under similar operating conditions. The optical rotation was determined by means of Cary Model 60 recording spectropolarimeter. The n.m.r. spectra were determined with a Varian A-60 spectrometer on deuteriochloroform solutions containing 1% tetramethylsilane. T.l.c. was carried out on silica gel G plates (according to Stahl) using the solvent system hexane–ethyl ether–acetic acid (80:20:1).

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[30] R. G. Binder, T. H. Applewhite, M. J. Diamond, and L. A. Goldblatt, *J. Am. Oil Chemists' Soc.*, **41**, 108 (1964).

[31] K. H. Meyer and K. Schuster, *Ber.*, **55**, 819 (1922).

[32] See ref. 12, p. 78, and references cited there.

[33] T. G. Melent'eva, L. A. Pavlova, and E. D. Venus-Danilova, *Zh. Obshch. Khim.*, **33**, 2126 (1963).

[34] F. Bohlmann, C. Arndt, H. Bornowski, and P. Herbst, *Chem. Ber.*, **93**, 981 (1960).

[35] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 70.

[36] E. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 122, 128 (1946).

[37] H. B. Henbest, E. R. H. Jones, and I. M. S. Walls, *ibid.*, 2696 (1949).

[38] H. B. Henbest, E. R. H. Jones, and I. M. S. Walls, *ibid.*, 3646 (1950).

[39] For summaries of the structures and natural sources of these acids, see ref. 8 and N. A. Sørensen in "Chemical Plant Taxonomy," T. Swain, Ed., Academic Press Inc., New York, N. Y., 1963, p. 219.

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

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

Preliminary Characterization of Methyl Helenynolate (Ib).—Details of the isolation of helenynolic acid and its purification were described in part I.[3] Methyl helenynolate, prepared by treating the acid with diazomethane,[3] had infrared maxima at 2.77 (OH), 4.54 (C≡C), 5.78 (ester), 6.17 (conjugated C=C),[13] and 10.46 μ (*trans*-enyne)[5]; its ultraviolet spectrum showed $\lambda_{max}^{isooctane}$ 228 mμ (ε 17,400) and 238 mμ (ε 14,300); Ib had $[\alpha]^{26}_{600}$ −7° (*c* 3.6, ethanol); and it absorbed 3.25 moles of hydrogen (Rh–Al_2O_3 catalyst). N.m.r. spectral data are summarized in Figure 2 and Table I.

Anal. Calcd. for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. Found: C, 73.60; H, 10.42.

Hydrogenation of Methyl Helenynolate (Ib). A. With Platinum Oxide Catalyst.—Ib (11.4 mg.) was hydrogenated at atmospheric pressure and room temperature in ethanol solution with platinum oxide catalyst. G.l.c. analysis of the product revealed 51.3% methyl hydroxyoctadecanoate, 45.2% methyl stearate, 0.6% methyl oxooctadecanoate, and small amounts of other components.

B. With Palladium–Charcoal Catalyst.—Ib (0.086 g.) was hydrogenated with 5% palladium–charcoal in acetic acid solution at atmospheric pressure and room temperature. G.l.c. analysis of the product revealed 80% methyl hydroxyoctadecanoate, 12% methyl oxooctadecanoate, and 7% methyl stearate. This product was purified by chromatography on silica gel. The major fraction, 0.046 g. of methyl 9-hydroxyoctadecanoate eluted with hexane–ethyl ether (9:1), had m.p. 43–44.5°; two recrystallizations from hexane raised the melting point of this substance to 44–45°.

C. With Rhodium–Alumina Catalyst.—Ib was hydrogenated at atmospheric pressure and room temperature in acetic acid solution with 10% rhodium–alumina catalyst. An uptake of 3.25 moles of hydrogen was observed. The product contained 81% methyl hydroxyoctadecanoate, 13% methyl oxooctadecanoate, and 4% methyl stearate.

Chromium Trioxide Oxidation of II.—An 0.046-g. portion of II was oxidized with chromium trioxide in acetic acid by methods described previously for long-chain hydroxy acids.[42,43] The oxidation product was shown by g.l.c. analyses of the corresponding methyl esters to contain nonanoic (16.7%), decanoic (11.7%), octanedioic (26.6%), and nonanedioic (30.1%) acids together with smaller amounts of homologous degradation products of these acids.

Permanganate–Periodate Oxidation of Ib.[44]—An 0.066-g. portion of Ib was stirred 4 hr. with 0.547 g. of sodium periodate, 0.013 g. of potassium permanganate, and 0.252 g. of potassium carbonate in 45 ml. of water. The reaction was terminated by addition of excess sodium bisulfite. The mixture was acidified with dilute sulfuric acid and extracted repeatedly with ethyl ether. Combined ether extracts were dried over sodium sulfate and evaporated *in vacuo*. G.l.c. analyses were carried out on the cleavage products both as free acids and as methyl esters. The main short-chain ($<C_9$) component found among the free acids was hexanoic acid. The ester preparation contained nonanedioate (66.7%) along with hexanoate and some unidentified minor components.

Reaction of Ib with Methanolic Hydrochloric Acid.—Ib (0.065 g.) was refluxed 1.5 hr. with 15 ml. of 0.1 *N* methanolic hydrochloric acid. The mixture was diluted with 30 ml. of water and extracted five times with ethyl ether. The combined ether extracts were dried over sodium sulfate and evaporated *in vacuo*. The residue (0.045 g.) was shown by g.l.c. analyses to contain an unfamiliar component—70.9% having equivalent chain lengths[41] of 20.2 on an Apiezon L column, and 24.1 on a Resoflex column. T.l.c. of the product gave four spots having R_f values 0.20 (Ib, strong intensity), 0.66 (unknown substance, light), 0.70 (XI, strong), and 0.91 (probably deoxygenated product, light intensity), respectively. The crude reaction product was chromatographed on a silica gel column. The major fraction, 0.032 g. of XI eluted with hexane–ethyl ether (9:1), was a liquid having infrared maxima at 4.54 (C≡C), 5.78 (ester), 6.17 (conjugated C=C), 9.05, 9.18 (ether),[13,45] and 10.46 μ (*trans*-C=C); there was no OH absorption (2.5–3.0 μ). The ultraviolet spectrum of VIII showed $\lambda_{max}^{cyclohexane}$ 229 mμ (ε 17,500) and 239 mμ (ε 14,800); the n.m.r. spectrum is in Figure 3.

Anal. Calcd. for $C_{20}H_{34}O_3$: C, 74.7; H, 11.0; 2OCH_3, 19.3. Found: C, 74.5; H, 10.6; OCH_3, 19.7.

Ib (0.017 g.) was refluxed 25 hr. in 15 ml. of 1.0 *N* methanolic hydrochloric acid. The mixture was worked up as described in the preceding section. The infrared spectrum of the product showed very little OH absorption (2.75 μ), and very little of the original maximum at 10.46 μ. New maxima appeared 6.0–6.8, 9.0–9.2, and 10.0–10.3 μ. The ultraviolet spectrum of this product showed $\lambda_{max}^{cyclohexane}$ 270 mμ ($E^{1\%}_{1\,cm}$ 491), with minor peaks at 228 and 239 mμ. T.l.c. of the mixture gave three major spots: the R_f's were 0.68 (probably XIII), 0.71 (XI), and 0.91 (probably deoxygenated material). This mixture was not further characterized.

Reaction of Ib with Methanolic Sulfuric Acid.—Ib (20.6 mg.) was refluxed 1.5 hr. with 15 ml. of 0.1 *N* methanolic sulfuric acid. The reaction mixture was worked up as in the preceding section. G.l.c. analysis of the recovered product (15.6 mg.) revealed 39.6% of XI. An infrared spectrum, as well as the g.l.c. analysis, showed the products to be similar to those obtained when the reaction was carried out in 0.1 *N* hydrochloric acid in methanol.

Reaction of XI with Methanolic Hydrochloric Acid.—XI (0.070 g.) was refluxed 18 hr. with 30 ml. of 1.0 *N* methanolic hydrochloric acid under a nitrogen atmosphere. The mixture was diluted with 15 ml. of water and extracted five times with 1:1 ethyl ether–hexane. The combined extracts were dried over sodium sulfate and evaporated *in vacuo*. Column chromatography of the residue on silica gel, with hexane as the eluting solvent, afforded two fractions, A and B: 19 mg. of A, the less polar of the two, was obtained, and 13 mg. of B, the mole polar.

The ultraviolet spectrum of A showed maxima at 228.6, 239.0, 271.0, and 278.8 mμ in ethanol; its infrared spectrum had maxima at 4.51 (C≡C), 9.0–9.2, 10.18, and 10.43 μ. It was not characterized further.

The ultraviolet spectrum of B showed a single maximum at 275 mμ in ethanol, $E^{1\%}_{1\,cm}$ 364 (conjugated ketodiene[30]). Its infrared spectrum had peaks at 5.72 (strong), 5.90 (medium), 5.98 (medium), 6.10 (medium), 6.28 (medium), and 10.04 μ (strong), but no OH absorption (2.5–3.0 μ). Thus a conjugated ketodiene grouping was indicated[30] as in XIII.

Hydrogenation of fraction B in ethanol with Adams catalyst afforded 8 mg. of a saturated keto ester (XIV). This compound had infrared maxima at 5.73 and 5.82 μ; it was judged to be rather impure from the relative intensities of these two carbonyl peaks and from its melting point (31–36°).

XIV (8 mg.) was dissolved in 0.5 ml. of glacial acetic acid. To this solution was added another containing 63 mg. of chromium trioxide, 0.4 ml. of acetic acid, and 1 drop of water. The mixture was stirred at room temperature for 5.5 hr., then diluted with water. The products after recovery by ether extraction, were esterified with diazomethane and subjected to g.l.c. analysis. The following amounts of dicarboxylic acids were found (expressed as area per cents): C_6, 6.5; C_7, 8.3; C_8, 6.9; C_9, 4.0; C_{10}, 2.0; C_{11}, 17.4; C_{12}, 12.7; and C_{13}, 2.3%. Monobasic cleavage products and unchanged XIV also were present. It was surmised that considerable degradation of the primary cleavage products occurred because of an excessively long reaction time, and that XIV was C-13-oxygenated although contaminated with a C-9-oxygenated compound. A C-9-oxygenated compound might have been formed by hydrogenation of XI.

Lithium Aluminum Hydride Reduction of Ib.—An 0.093-g. portion of Ib dissolved in 2.5 ml. of anhydrous ethyl ether was added dropwise to a suspension of 0.50 g. of lithium aluminum hydride in 7.5 ml. of ether. The mixture was refluxed 2.5 hr. Excess reagent was destroyed by adding moist ether, then 10 ml. of 5% sulfuric acid. The solid residue was extracted several times with ether. The combined ether extracts were dried over sodium sulfate and evaporated *in vacuo*. The product (0.051 g.) was shown by t.l.c. to be primarily one component IX. Its infrared spectrum had maxima at 2.77 (very strong OH), 5.12 (allene), and 11.37 μ (allene)[46]; peaks at 4.54, 5.78, and 10.45 μ were negligible or absent. The ultraviolet spectrum showed $\lambda_{max}^{cyclohexane}$ 181 mμ ($E^{1\%}_{1\,cm}$ 518), a value corresponding to 75% allene.[14] Attempted purification of this allene-containing product was unsuccessful, apparently owing to rapid polymerization or oxidation.

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

[43] C. R. Smith, Jr., T. L. Wilson, R. B. Bates, and C. R. Scholfield, *J. Org. Chem.*, **27**, 3112 (1962).

[44] (a) R. U. Lemieux and E. von Rudolff, *Can. J. Chem.*, **33**, 1710 (1955); (b) E. von Rudloff, *J. Am. Oil Chemists' Soc.*, **33**, 126 (1956).

[45] A. K. Lough, *Biochem. J.*, **90**, 4C (1964).

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

Reaction of Ib with Performic Acid.[17]—A 25.5-mg. portion of Ib (8.3 × 10^{-5} mole) was mixed with 0.2 ml. (4 × 10^{-3} mole) of 90% formic acid and 0.05 ml. (4.4 × 10^{-4} mole) of 30% hydrogen peroxide. The mixture was warmed 3 hr. at 40–50°, then refluxed with 5 ml. of 3 *N* potassium hydroxide for 1.5 hr. The alkaline hydrolysate was neutralized with hydrochloric acid, then extracted repeatedly with ether. The combined ether extracts were dried over sodium sulfate and evaporated *in vacuo.* The recovered product consisted of 15.0 mg. of liquid; its infrared spectrum had only a small OH peak (2.75 μ), but had absorption 2.8–3.3, 3.6–3.8, and 10.6 μ indicating free carboxylic acid, and a small C≡C peak at 4.54 μ; there was no maximum at 10.46 μ. These cleavage products were converted to methyl esters by treatment with diazomethane and were subjected to g.l.c. analyses. Nonanedioic acid (55%) was identified among the products. β-Hydroxydecanedioic acid (*ca.* 7%) was tentatively identified on the basis of equivalent chain length.[41] Short-chain acids were present that were not readily identified by equivalent chain length, but no hexanoic acid was found.

Attempted Dehydration of Ib with Toluenesulfonic Acid.[34]—Ib (12.3 mg.) and *p*-toluenesulfonic acid (5 mg.) were refluxed 15 min. in 1 ml. of benzene under a nitrogen atmosphere. The mixture was shaken with sodium bicarbonate solution, dried over sodium sulfate, and evaporated *in vacuo.* The recovered product (8.4 mg.) showed ultraviolet maxima at 194, 226, 271 ($E^{1\%}_{1\,\mathrm{cm}}$ 845), and 280 mμ (inflection.) It had an infrared maximum at 10.2, but had none at 2.75 (OH) or 10.46 μ (conjugated enyne). The product did not form a maleic anhydride adduct and appeared to be quite unstable. It was not further characterized.

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A Free-Electron Model for Kinetic Substituent Effects[1]

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A qualitative treatment of the distribution of electron density in a three-nucleus, four-electron system is developed using the free-electron method. The method is shown to be inappropriate to stable systems, but appropriate to systems with highly polarizable electron groups, such as transition states.

The free-electron (electron-gas) method is a conceptually simple approximation which has been applied with signal success to the spectroscopic problems of polyenes[2] but not, to our knowledge, to problems in chemical reactivity. The analytic simplicity of the free-electron wave functions encouraged us to develop the qualitative model for kinetic substituent effects presented here, with a view toward quantitative extensions in the future.

A linear system composed of three nuclei, A, B and C, can be regarded as a one-dimensional potential box (Figure 1). If the three nuclei are of equal electronegativity and are assumed to lie at such a separation that the overlap of their positive fields results in a nearly constant electrical field out to, say, half a bond length beyond A on the one end and C on the other,[2] then the potential box will be flat over this distance and rise to infinity at either end. If four electrons are added to the system, as in a hydrogen bond or in the transition states for proton-transfer or nucleophilic-displacement reactions, they can be regarded as particles enclosed in this potential box and will occupy the first two particles-in-the-box[3] energy levels for a box of this size. Since we are interested in the electron-density distribution for this system, we require the squares of the first two wave functions of the system; these are shown in Figure 1. The lowest wave function is a simple sine function and the next is its first harmonic.[4] To find the electron-density function for the system we have only to superimpose these functions for the individual energy levels (Figure 2).

In order to apply this model to the prediction of substituent effects, we consider the perturbation on this electron distribution induced by a change in the electrical character of one of the nuclei. Organic chemists usually discuss substituent effects in terms of "electron withdrawal from X" and "electron release to X." For our purposes we will consider the former to represent an increase in the effective electronegativity of X and the latter a decrease in the effective electronegativity of X; in the absence of strong conjugation effects this will be a good approximation.

Center-Atom Substituent Effects.—Figure 3 shows the potential box corresponding to a system in which the effective electronegativity of B has been increased ("electron withdrawal from B"), represented in the model by a dip in the potential in the neighborhood of B. The qualitative nature of the perturbed electron-density distribution can be deduced by considering that the more favorable potential in the vicinity of B will cause a drift of electrons toward B from both sides of the box; since the total number of electrons remains four, the increase in density about B must occur with a corresponding decrease in density about A and C.

The opposite situation, a higher potential near B than near A or C, thus a decrease in the effective electronegativity of B ("electron release to B"), by

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[2] H. Kuhn, *Progr. Chem. Org. Nat. Prod.*, **16**, 169 (1958); **17**, 404 (1959). See earlier and more exact treatments of σ-electrons: J. R. Arnold, *J. Chem. Phys.*, **22**, 757 (1954); **24**, 181 (1956); A. A. Frost, *ibid.*, **25**, 1150 (1956); G. M. Barrow, *ibid.*, **26**, 558 (1957); **28**, 485 (1958).

[3] L. Pauling and E. B. Wilson, Jr., "Introduction to Quantum Mechanics," McGraw-Hill Book Co., Inc., New York, N. Y., 1935, p. 95 ff.

[4] Wave functions of the same general form are obtained by an MO method [*e.g.*, C. G. Swain, R. A. Wiles, and R. F. W. Bader, *J. Am. Chem. Soc.*, **83**, 1945 (1961)]; hence, the free-electron approximation in no way affects the generality of our results.