

[CONTRIBUTION FROM THE DIVISION OF ORGANIC CHEMISTRY OF THE ORTHO RESEARCH FOUNDATION]

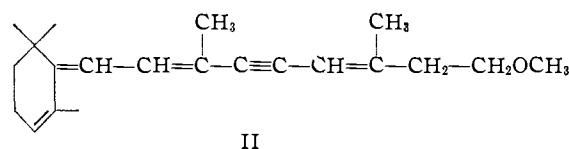
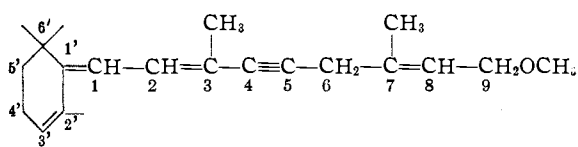
Synthesis of Polyenes. III. Prototropic Rearrangements in β -Ionols and Related Compounds

BY WILLIAM OROSHNIK, ALEXANDER D. MEBANE AND GEORGE KARMAS

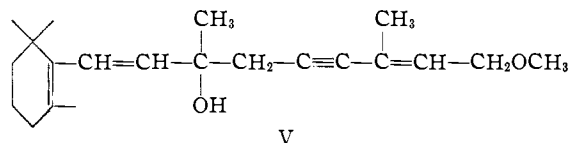
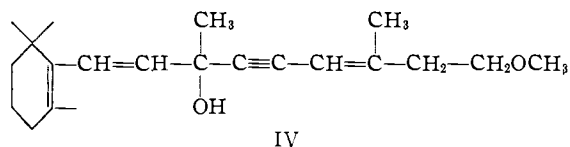
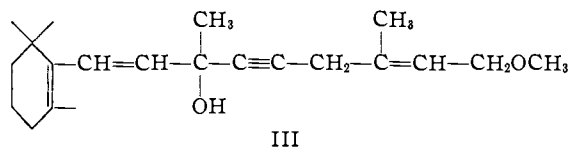
RECEIVED AUGUST 1, 1952

The prototropic rearrangement of compounds having two unsaturated systems separated by a methylenic group has been studied. As a result a new prototropically stable allene system has been discovered, the conjugated vinylalleneol. Its dehydration and semihydrogenation were investigated and the structure of the products obtained therefrom elucidated. A conjugated polyene system containing an internal allene bond has been demonstrated for the first time, as have diene and triene shifts without benefit of an influencing carbonyl group.

In Part I of this series¹ it was shown that, in the presence of alkali, the isolated 7,8-double bond in I readily moves into conjugation with the trienyne system to yield 4,5-dehydroretrovitamin A methyl ether, II. This suggested that a similar shift in III

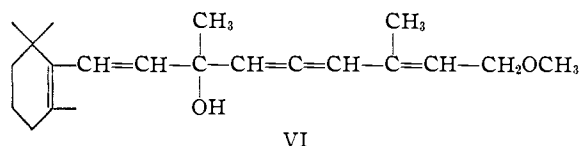


might be possible, thus affording a simple synthesis of IV. The carbinol, III, was indeed found to undergo a facile alkali-catalyzed isomerization. Stand-



ing in alcoholic alkali, or on an alumina column, or heating with organic bases such as diethylamine, resulted in its complete conversion to an isomeric carbinol. However, this carbinol proved to be neither the expected IV nor its isomer, V, differing materially from both in its ultraviolet absorption spectrum (Fig. 1), and other physical and chemical properties. Its infrared spectrum (Fig. 4) revealed the structural dissimilarity to be the presence of an allene group (5.19μ) in place of the acetylenic group (4.52μ). The other structural features of III, the β -ionol and the allylic methoxyl groups, remained intact, as de-

termined by ozonolysis to 44% geronic acid and 20% formaldehyde,² respectively. (III gives 35% geronic acid and 20% formaldehyde² on ozonolysis.) Thus the data clearly establish the structure of the isomerized carbinol as the conjugated vinylalleneol, VI.



Only two examples of conjugated vinylallenes appear in the literature,³ and, unfortunately, no absorption spectral data are available for either. As shown in Fig. 1, the spectrum of the vinylallene chromophore is qualitatively very similar to that of the corresponding conjugated enyne, V, but shows much higher extinction.⁴ The unusual broadness of the band is also distinctive.

The prototropic shift occurring in the formation of VI is undoubtedly of the type involved in the 1-alkyne \rightarrow 2-alkyne isomerization. While it is generally accepted that this reaction goes through an allene intermediate,⁵ only a few examples are available wherein the allene is isolable. Benzylacetylene, which has a triad system similar to that of III, readily isomerizes in the presence of alkali and Bourguel⁶ has shown that the intermediate 1-phenylallene can be isolated. However, alkali easily rearranges it to phenylmethylacetylene.^{6,7} Jones⁸ has recently reported the rearrangement of β,γ -butynoic acid to the corresponding allenic acid by warming with slightly alkaline reagents like sodium

(2) It has been shown in Part I of this series¹ that allylic methoxyl groups give about 20-25% yields of formaldehyde upon ozonolysis.

(3) These are 1,4-dichloro-2,3,5-hexatriene and 1,3,4-trichloro-2,4,5-hexatriene: D. D. Coffman and W. H. Carothers, *THIS JOURNAL*, **55**, 2040 (1933). A. F. Thompson, Jr. and E. N. Shaw, *ibid.*, **64**, 363 (1942), tentatively assigned conjugated vinylallene structures to the semi-hydrogenation products of 2,5-dimethyl-1,5-hexadiene-3-yne and di-(cyclohexen-1-yl)-2-acetylene, but their contentions are as yet unproven. 1,3,4-Hexatriene has been listed in G. Egloff's "Phys. Const. of Hydrocarbons," Vol. I, Reinhold Publishing Corp., New York, N. Y., 1939, p. 348. However, this is an error due to a misprint in *C. A.*, **17**, 2866 (1923). The compound described actually is 1,3,5-heptatriene.

(4) 5,6-*cis*-XIII, the diene derived from V, also shows λ_{max} 229 $m\mu$, but because of its steric hindrance and consequent spectral degradation, comparison with the vinylallene VI is hardly significant.

(5) T. L. Jacobs, R. Akawie and R. G. Cooper, *THIS JOURNAL*, **73**, 1273 (1951).

(6) M. Bourguel, *Compt. rend.*, **192**, 686 (1931); E. F. Zeburk, *J. Gen. Chem. (U.S.S.R.)*, **5**, 1016 (1935).

(7) Ya. I. Ginzburg, *ibid.*, **8**, 1029 (1938).

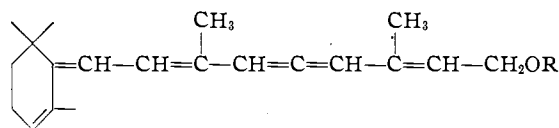
(8) E. R. H. Jones, 120th Meeting, American Chemical Society, New York, N. Y., September 3-7, 1951.

(1) W. Oroshnik, G. Karmas and A. D. Mebane, *THIS JOURNAL*, **74**, 295 (1952).

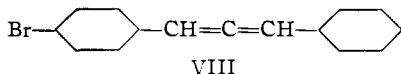
bicarbonate. No details are as yet available concerning the alkali stability of this allenic acid but it would appear from the fact that in alcoholic alkali β,γ -butynoic acid readily yields β -ethoxycrotonic acid,⁸ that the most stable isomer in this system is the 2-alkyne or tetrolic acid. Only when 2-alkyne formation was structurally impossible have allenes been the only isomerization products formed. This is well illustrated by isopropylacetylene which gives a high yield of 1,1-dimethylallene on treatment with alcoholic alkali.⁵

Thus, the stability of the vinylallenol, VI, toward further isomerization to either IV or V is indeed unique.

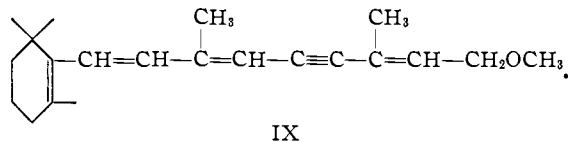
The question naturally arises as to the reasons for the difference in behavior between I and III on prototropic rearrangement. In both cases the prototropic changes are undoubtedly initiated by the separation of a proton from the highly activated 6-methylene group. The subsequent electronic shift could involve an electron pair from either the 7,8-ethylenic bond, to yield an enyne, or the 4,5-acetylenic bond, to yield an allene. Although only II was obtained from I, the possibility did



exist that VII may have been first formed and then isomerized to II by the alkali present. (Compound VII, as will be shown below, readily isomerizes to II in the presence of alkali.) However, on following the reaction spectroscopically no evidence for any intermediate allene stage could be found. It must therefore be concluded that the acetylenic group is not prone to isomerization when it is part of a conjugated system. Further support for this contention is found in the isomeric pair 1-*p*-bromophenyl-3-phenylpropyne and 1-phenyl-3-*p*-bromophenylpropyne, where the acetylenic group is conjugated with either a phenyl or *p*-bromophenyl group. Neither is convertible to the allenic isomer, VIII, nor are the two isomers interconvertible on alkali treatment.⁹



Comparison of the dehydration products of IV, V, and VI, served further to differentiate VI from its two acetylenic isomers. Compound IV underwent, as expected, a facile allylic rearrangement and dehydration. The product, II, proved identical with that obtained by the alkali isomerization of I (Fig. 3). The dehydration of V to 5,6-dehydrovitamin A methyl ether, IX, has been described



(9) J. R. Johnson, T. L. Jacobs and A. M. Schwartz, *THIS JOURNAL*, **60**, 1885 (1938).

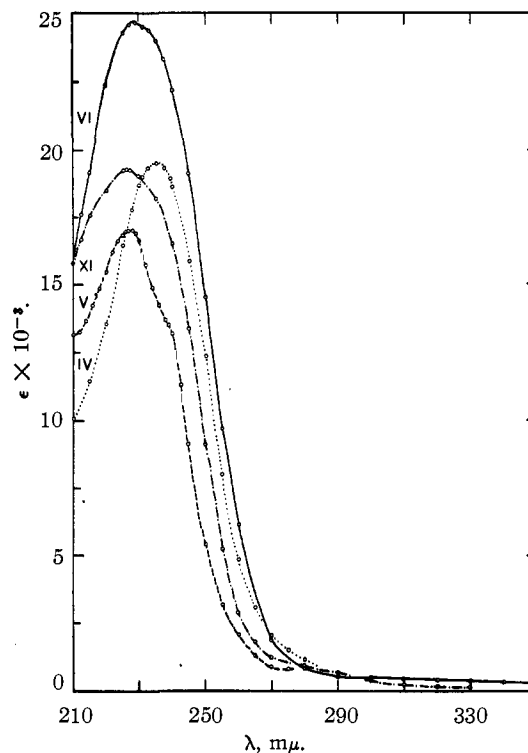


Fig. 1.—Ultraviolet absorption spectra in ethanol of vinylallenols, VI and XI, compared to those of the enynes, IV and V.

in a previous publication.¹⁰ Compound VI showed the same facility of dehydration exhibited by IV. The product, however, proved quite unstable and isomerized readily upon heating, or during chromatography on Florisil, Floridin or alumina columns. However, a pure sample of the unisomerized compound could be separated from the alumina column.

TABLE I
ULTRAVIOLET ABSORPTION DATA^a

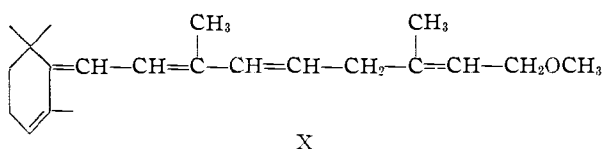
Compound	λ_{\max} (m μ)	ϵ_{\max}	Compound	λ_{\max} (m μ)	ϵ_{\max}
I ¹	310	36,100	5,6- <i>cis</i> -XIII ¹⁰	229	14,600
II ¹	255	15,000	5,6- <i>trans</i> -Desmethoxy-XIII	234	22,700
	335	33,000	XIV ¹	236	6,500
III ¹	236	6,200	4,5- <i>cis</i> -XV ¹⁰	243.5	25,100
IV ¹⁰	235	19,500	4,5- <i>trans</i> -XV ¹⁰	241.5	27,800
V ¹⁰	228 ^b	17,000	XVI ¹⁰	332.5	48,800
VI	229	24,700		348	65,900
VII	229	19,200		367	53,100
	317.5	49,400			
IX ¹⁰	317	24,800	Desmethoxy-XVI ^c	332.5	
4,5- <i>trans</i> -X ¹	317	47,000		348.5
XI	227	19,400		367	
			XVII ^d	286	29,300
			Desmethoxy-XVII ^c	287
			XVIII	326 ^e	52,000 ^f
			Desmethoxy-XVIII	320 ^g	34,000

^a Solvent: 95% ethanol. ^b Previously given as 229 m μ .¹⁰ ^c Not a pure specimen. ^d Identified in Part II,¹⁰ but not previously obtained in a state of purity. ^e A. R. Hanze, T. W. Conger, E. C. Wise and D. I. Weisblat, *THIS JOURNAL*, **70**, 1253 (1948). ^f O. Isler, *et al.*, *Helv. Chim. Acta*, **32**, 501 (1949). ^g On catalytic iodine treatment the max. shifted to 321.5 m μ .

(10) W. Croshnik, G. Karmas and A. D. Mebane, *ibid.*, **74**, 3807 (1952).

Its infrared spectrum (Fig. 4) showed the allene group to have remained intact during the dehydration. Ozonolysis gave no geronic acid and 22% formaldehyde, attesting to *retroionylidene* formation rather than β -ionylidene formation and to the retention of the allylic methoxyl group.² Thus the data demonstrate the structure of the dehydration product to be VII.

Further confirmation of structure VII comes from its ultraviolet absorption spectrum. As a consequence of the break in coplanarity caused by the allene group, two chromophores should arise, the conjugated 3',1',2,4-tetraene, corresponding to that in *trans*-X, λ_{\max} 317 $m\mu$, and the conjugated 5,7-diene corresponding to that in VI, λ_{\max} 229 $m\mu$. The observed absorption curve is completely in accordance with these postulations, its similarity to that of X both in λ_{\max} and extinction being



indeed striking (Fig. 2). The extinction at 229 $m\mu$ can be seen to agree closely with that of the vinylallene chromophore in VI if one subtracts the contribution of the β -ionol chromophore from the latter (*i.e.*, 19,200 as compared to 24,700 minus 6,000). However, truer comparison is had with XI, the α -ionol analog of VI. This has no other contributing chromophore and shows ϵ 19,400 at its maximum, 227 $m\mu$.

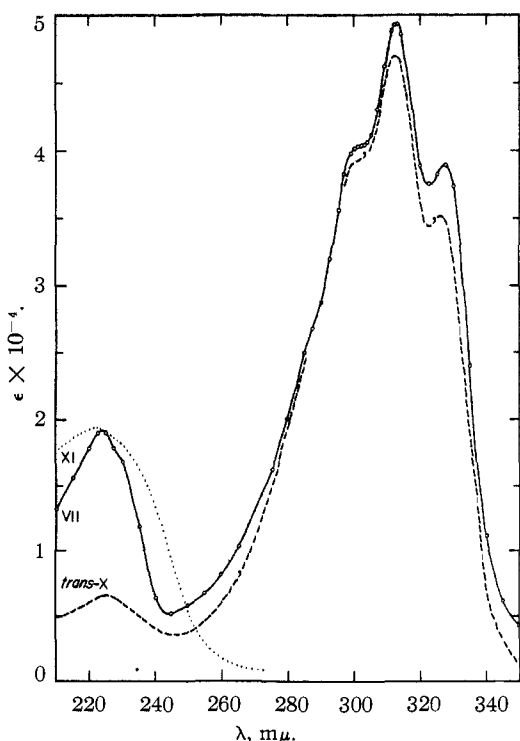
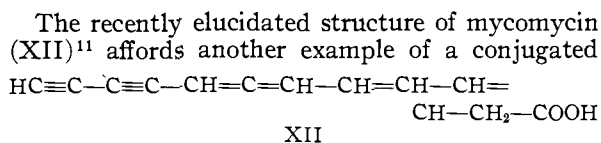
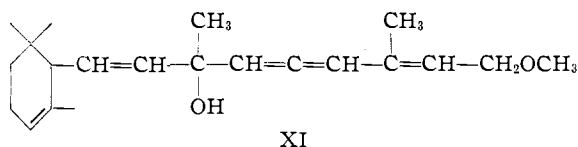


Fig. 2.—Ultraviolet absorption spectrum in ethanol of the dehydrated vinylallenol, VII, compared to XI which shows only the vinylallene chromophore and to *trans*-X which shows only the *retroionylidene* tetraene chromophore.



system containing an internal allene group. Its spectrum likewise shows the presence of two chromophores as a result of the position of the allene group; the maxima at 267 and 281 $m\mu$ corresponding to one or the other of the triene and endiayne systems.

Treatment of VII with alkali resulted in a prototropic rearrangement of the allene to an acetylene group. This was confirmed by the infrared spectrum (Fig. 4). The ultraviolet absorption spectrum (Fig. 3) revealed that the product consisted for the most part of II, but a slight hypsochromic displacement of the main band and a lower extinction at 255 $m\mu$ indicated the presence of an isomeric impurity. Although this impurity could not be separated by alumina chromatography, evidence that it was an allylic methoxyl compound was obtained by ozonolysis to 15% formaldehyde (pure II, with no allylic methoxyl group, gives 8% formaldehyde). This suggested that the impurity

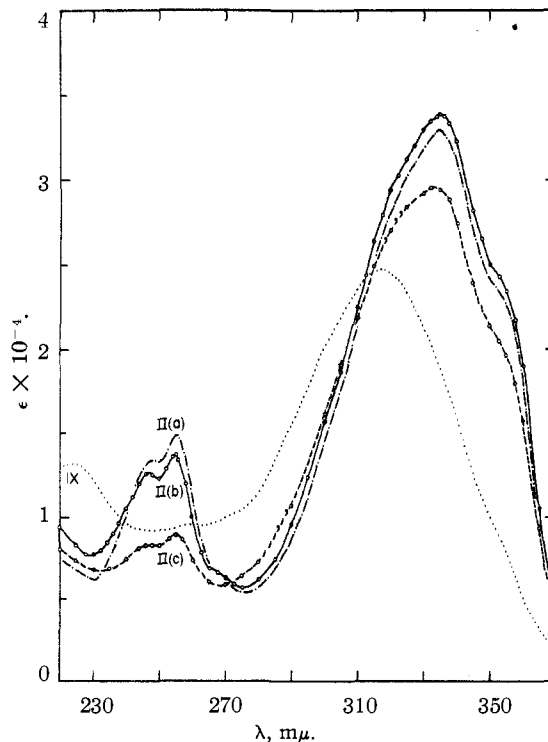
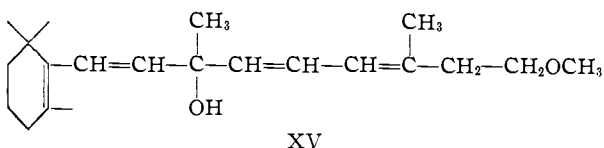
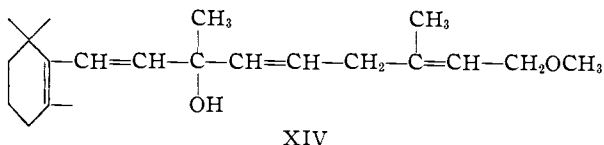
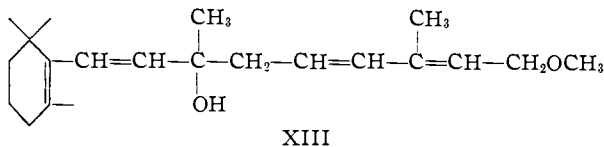


Fig. 3.—Ultraviolet absorption spectrum in ethanol of 4,5-dehydroretrovitamin A methyl ether, II, as prepared (a) by alkali conjugation of I¹; (b) by dehydration of IV; (c) by alkali isomerization of VII. These are compared to that of 5,6-dehydrovitamin A methyl ether, IX.¹⁰

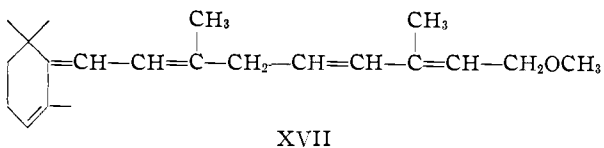
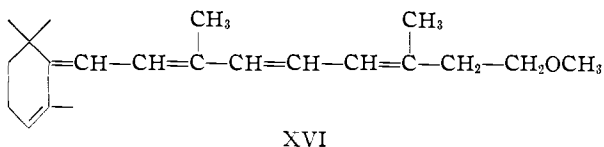
(11) W. D. Celmer and I. A. Solomons, *THIS JOURNAL*, **74**, 1870 (1952).

was perhaps identifiable with IX, which would imply a prototropic shift in the reverse direction.

The semi-hydrogenation of the vinylallenol, VI, presented several possibilities: 4,5-addition to give XIII; 5,6-addition giving XIV; 5,8-addition giving XV; and finally, but not likely, 7,8-addition to give 7,8-dihydro-VI. Catalytic semi-hydrogenation



with poisoned Raney nickel gave a product contaminated with considerable over-hydrogenated and unhydrogenated material. These were removed for the most part by fractional distillation as fore-runs and post-runs. The major fraction, λ_{max} 237 μ , distributed itself into three main zones on an alumina column: λ_{max} 235 μ , λ_{max} 240 μ and λ_{max} 237 μ , the last being by far the largest. The properties of the major fraction corresponded to no single one of the above-mentioned reduction possibilities and dehydration was relied upon for its identification. The absorption curve of the dehydration product was that of a mixture but the presence and predominance of 4,5-*cis*- and *trans*-X and a considerable amount of 4,5-*trans*-retrovitamin A methyl ether, XVI, were clearly evident. Chromatography of this mixture also revealed some evidence of XVII, λ_{max} 286 μ , and about 3% vitamin A methyl ether, XVIII. The latter was con-



firmed by biological assay. The bulk of the product obtained on alumina chromatography was XVI, as was to be expected since X is known to conjugate to XVI on an alumina column.¹ The same result was achieved by heating the crude dehydration product in alkali.

Dehydration of the two minor fractions gave similar results. The semi-hydrogenated carbinol was thus identified as a mixture consisting predominantly of XIV, some XV, and possibly a little XIII.

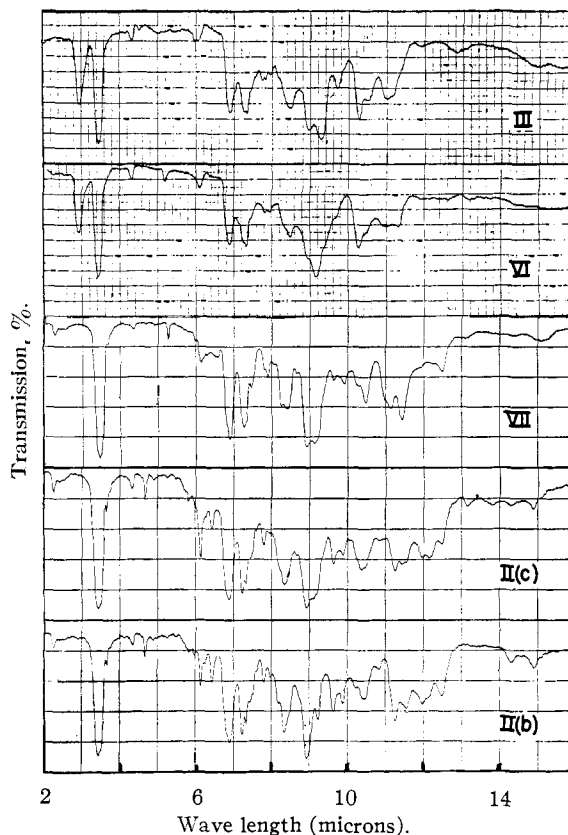


Fig. 4.—Infrared spectra of acetylenic carbinol, III; vinylallenol, VI; dehydrated vinylallenol, VII; and 4,5-dehydroretrovitamin A methyl ether: II(c), prepared by alkali isomerization of VII; II(b), prepared by dehydration of IV.

Chromous hydroxide reduction was next tried. This reagent proved remarkably specific in attacking no ethylenic bonds other than those of the vinylallene group. However, it did affect, though only to a slight extent, the allylic methoxyl group, as indicated by the somewhat low methoxyl values for the unchromatographed product. A typical product showed, after chromatography, λ_{max} 241.5 μ , ϵ 24,300. This corresponded to 4,5-*trans*-XV, but the extinction indicated about 10% of an isomeric impurity. The dehydration product exhibited the typical absorption maxima of XVI. However, the 332 μ band was higher than usual and this suggested the presence of some X. Al-

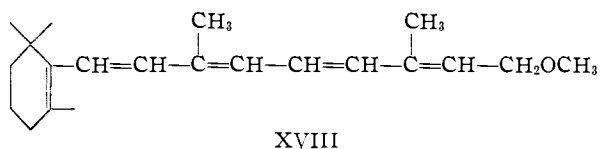
TABLE II
INFRARED ABSORPTION DATA

Compound	$\lambda_{\text{max}}, \mu$		Compound	$\lambda_{\text{max}}, \mu$	
	Of allene band	Of acetylene band		Of allene band	Of acetylene band
III	..	4.52 ^a	II ^c	..	4.67
VI	5.19	..	1,2-Pentadiene ^b	5.13	..
VII	5.26	..	1-Pentyne ^b	..	4.72
II ^b	..	4.69	Mycomycin ^d	5.18	4.53

^a The weakness of this band (Fig. 4) is in accord with the finding of J. H. Wotiz and F. A. Miller [THIS JOURNAL, 71, 3441 (1949)] that "as the triple bond is moved toward the center of the chain, the corresponding absorption band weakens and virtually disappears." ^b By dehydration of IV. ^c By alkali isomerization of VII. ^d W. D. Celmer and I. A. Solomons, THIS JOURNAL, 74, 2245 (1952).

though X could not be isolated chromatographically for the reason cited above, evidence for its presence was obtained by treating the mixture before chromatography with alcoholic alkali, which conjugates X to XVI. The product then obtained showed the normal curve for XVI. Only 3-4% of vitamin A methyl ether could be isolated from the dehydration product on chromatography, but biological assays showed 290,000 units of vitamin A activity per gram. No evidence of XVII was observed. The chromous hydroxide product was thus established as consisting of about 90% of XV and 10% of XIV.

Semi-hydrogenation with lithium aluminum hydride proved rather surprising. The reduction product separated into three major components on an alumina column. The first, amounting to more than 10% of the whole, turned out to be vitamin A methyl ether, XVIII. This was identified by analysis, absorption spectrum and ozo-



XVIII

nolysis to geronic acid. An accompanying 22% yield of formaldehyde attested to its allylic methoxyl group.² The reaction leading to its formation is at present obscure. The hypothesis that it arose from the splitting out of lithium or aluminum hydroxide from the alkoxides of XIII, XIV, or XV, was discarded on finding that none of these three carbinols gave any discernible trace of vitamin A methyl ether on refluxing with ethereal lithium aluminum hydride.

The bulk of the reduction product showed only a trace of methoxyl on analysis. Its behavior on dehydration was similar to that of XIII¹⁰ in giving mainly *retroionylidene* triene, λ_{\max} 287 $m\mu$, accompanied by some β -ionylidene pentaene, λ_{\max} 323 $m\mu$. It was therefore identified as desmethoxy-XIII. This was confirmed by analysis as well as by the behavior of its dehydration product on alkali isomerization described below. Inasmuch as its λ_{\max} falls at 234 $m\mu$ as compared to 229 $m\mu$ for 5,6-*cis*-XIII, its 5,6-configuration must be *trans*. A higher λ_{\max} of the *trans*-isomer in this particular case is to be expected since the *cis*-isomer suffers from steric hindrance.¹⁰

The remainder of the reduction product was only 14% demethoxylated. Its λ_{\max} , 240 $m\mu$, corresponded most closely to XV, and its identification as such was confirmed by dehydration to 4,5-*trans-retrovitamin* A methyl ether, XVI.

It is evident that in none of the three methods does the semi-hydrogenation of the vinylallene follow one exclusive course. Nevertheless, judging from the major products obtained in each case, it may be seen that the general tendency is for it to undergo 5,6-addition on catalytic semi-hydrogenation, 5,8-addition on chromous hydroxide reduction and 4,5-addition with lithium aluminum hydride.

The isolated ethylenic groups in XIV were also found to conjugate on heating in alcoholic alkali, although less readily than in the case of I or X.

The longer conjugated systems in the latter two undoubtedly account for the difference. The product, as revealed by dehydration studies, was a mixture of XV with unisomerized starting material XIV. Biological assays of the dehydration product showed 275,000-300,000 units of vitamin A activity per gram.

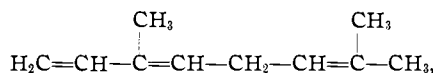
Although the prototropic rearrangement of XIV could theoretically also have resulted in a shift of the 4,5-double bond to give XIII, only suggestive evidence for the presence of this isomer was found. This was a very small fraction observed on an alumina chromatogram of the dehydration product, showing λ_{\max} 286 $m\mu$ and perhaps to be identified with XVII.

The alkali-induced conjugations dealt with so far have involved only the shift of an isolated ethylenic group. Prototropic shifts of conjugated diene groups appear to be rare and the only authentic examples¹² found in the literature were confined to the isomerization of $\Delta^{\beta,\delta}$ -dienoic acids to their $\Delta^{\alpha,\gamma}$ -analogs.¹³ In the present work the shift of a diene group into conjugation with a triene was accomplished, as was the shift of a triene into conjugation with a diene. The first type of change was observed in the case of XVII. On heating in alcoholic alkali it was converted into *retrovitamin* A methyl ether, the change being easily followed spectrophotometrically (Fig. 5) by the gradual disappearance of the 286 $m\mu$ peak and the simultaneous appearance of the typical three-banded spectrum of XVI.

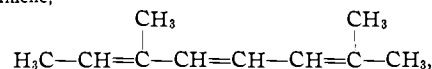
The shift of a triene was, surprisingly enough, observed with desmethoxy-XVII. On heating in alkali, the 287- $m\mu$ band completely disappeared, as in the case of XVII above. The new absorption curve showed only one maximum, 323 $m\mu$. Small plateaus at 345 and 365 $m\mu$ indicated some *retroionylidene* pentaene also was formed.

Upon chromatographic separation, the major fraction analyzed properly for $C_{20}H_{30}$. The shape of its absorption curve was typical of that exhibited by vitamin A although hypsochromically displaced to 320 $m\mu$ (Fig. 6). The molecular extinction was also lower. Ozonolysis to geronic acid and no significant formaldehyde confirmed its structure as

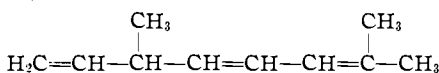
(12) The isomerization of ocimene,



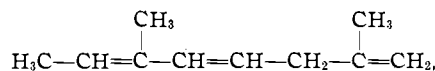
to alloocimene,



would be an example of a diene shift were it not for the fact that the above structure assigned to ocimene appears to be incorrect. Its λ_{\max} , 235 $m\mu$, agrees with the trisubstituted diene isomers,



and



rather than with the disubstituted diene formula above [J. E. Hawkins and H. G. Hunt, *THIS JOURNAL*, **73**, 5379 (1951)].

(13) R. Kuhn and M. Hoffer, *Ber.*, **66B**, 170 (1932); R. Paul and S. Tchelitcheff, *Bull. soc. chim.*, [5] **15**, 108 (1948).

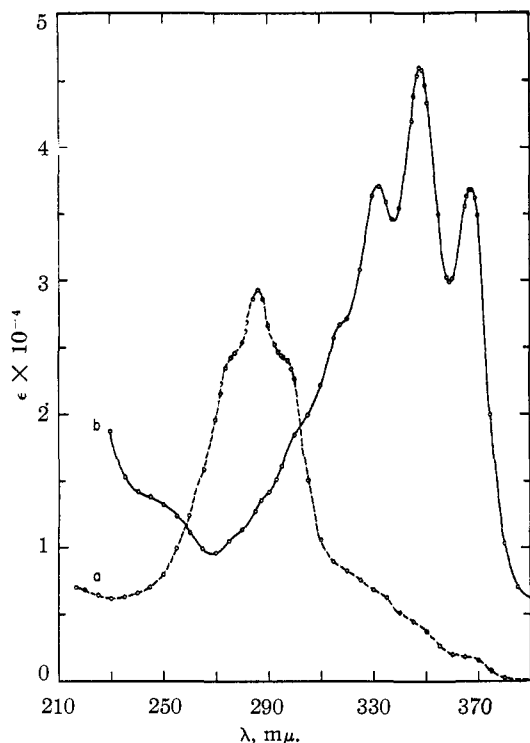


Fig. 5.—a, Ultraviolet absorption spectrum of XVII; b, that of crude reaction mixture after alkali treatment of XVII (qualitative curve, ϵ units to be ignored).

vitamin A hydrocarbon, desmethoxy-XVIII.¹⁴ On contact with catalytic quantities of iodine in iso-

TABLE III

EFFECT OF PRIMARY ALLYLIC HYDROXYL ON ULTRAVIOLET ABSORPTION SPECTRA^a

Compound	λ_{\max} , $m\mu^b$	ϵ_{\max}
2,4-Hexadiene ^c	227	22,500
Sorbyl alcohol ^d	227.5	28,200
1-Phenylpropene ^e	249	14,700
Cinnamyl alcohol ^e	250	17,000
2,4,6-Octatriene ^f	263
2,4,6-Octatrienol	264.5 ^g ; 267 ^h	53,000 ^{g,h}
2,4,6,8-Decatetraene	295 ⁱ ; 296 ⁱ	52,000 ⁱ
2,4,6,8-Decatetraenol ^j	298.5	64,000

^a This principle has also been recognized by J. B. Armitage and M. C. Whiting (*J. Chem. Soc.*, 2005 (1952)), who have discussed the matter at some length, and have pointed out that "in every case, bathochromic and hyperchromic displacements increase in the order $H < OH < OAc < Cl < Br$." ^b Solvent: alcohol, except for decatetraene, which was measured in hexane. ^c H. Booker, L. K. Evans and A. E. Gillam, *J. Chem. Soc.*, 1453 (1940). ^d Prepared in this Laboratory by the lithium aluminum hydride reduction of ethyl sorbate; m.p. of specimen measured, 25–28°. ^e T. W. Campbell, S. Linden, S. Godshalk and W. G. Young, *THIS JOURNAL*, 69, 880 (1947). ^f E. R. Blout and M. Fields, *ibid.*, 70, 189 (1948). ^g I. M. Heilbron, A. W. Johnson, E. R. H. Jones and R. A. Raphael, *J. Chem. Soc.*, 265 (1943). ^h H. v. Euler, P. Karrer, E. Klusman and R. Morf, *Helv. Chim. Acta*, 15, 502 (1932). ⁱ R. Kuhn, *Angew. Chem.*, 50, 703 (1937). ^j T. Reichstein and G. Trivelli, *Helv. Chim. Acta*, 15, 1074 (1932).

(14) P. Karrer and J. Benz [*Helv. Chim. Acta*, 31, 1048 (1948)] have reported the synthesis of a product which they designated as vitamin A hydrocarbon. Their published absorption data, however, λ_{\max} 331, 346, 364 $m\mu$, leave no doubt that their product consisted largely, if not entirely, of the *retroionylidene* isomer, desmethoxy-XVI.

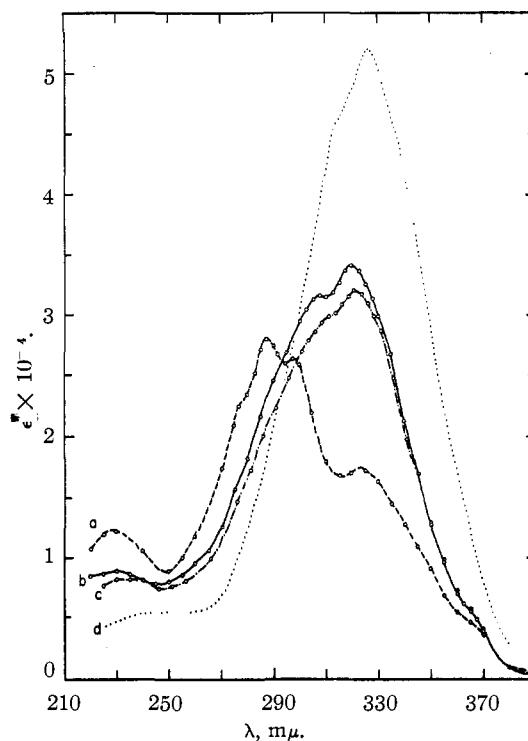


Fig. 6.—Ultraviolet absorption spectra of: a, crude desmethoxy-XVII (qualitative curve, ϵ units to be ignored); b, vitamin A hydrocarbon, desmethoxy-XVIII; c, desmethoxy-XVIII after treatment in isoöctane with 1% its weight of iodine for 15 minutes; d, vitamin A acetate.

octane the λ_{\max} rose to 321.5 $m\mu$, suggestive of the stereoisomerization of vitamin A to neovitamin A under similar conditions.

The minor component of the isomerization mixture was present in too small a quantity to render an analytically pure material. On the basis of its absorption spectrum it was identified as desmethoxy-XVI.

The hypsochromic and hypochromic displacement of the curve of vitamin A hydrocarbon as compared to vitamin A is typical of the spectral relationship between polyene hydrocarbons and their corresponding primary allylic alcohols. This is illustrated by Table III. While a lower extinction for vitamin A hydrocarbon is therefore to be expected, that exhibited by this specimen is perhaps excessively so, and suggests the product may not have been completely purified with respect to other isomeric pentaenes.

Experimental

Absorption Spectral Data.—The ultraviolet absorption data of all new compounds described in this section are in Table I. All measurements were made on solutions in 95% ethanol with a Beckman spectrophotometer.

The infrared absorption measurements were made on the neat compounds by Samuel P. Sadtler & Son, Inc., Philadelphia, Pa. A Baird double beam infrared spectrophotometer was used. The data appear in Table II and Fig. 4.

Ozonolysis.—The procedure used was that described in detail in Part I of this series.¹

Preparation of the Vinylallenol, VI.—A solution of 10.0 g. of acetylenic carbinol, III,¹ n_D^{20} 1.5110, in 250 ml. of 5% methanolic sodium hydroxide was refluxed for three hours. On cooling the solution was worked up with water and petroleum ether and dried with anhydrous potassium carbonate. It was then concentrated under vacuum and distilled

at 0.001 mm. from a simple claisen flask immersed up to its side-arm in an oil-bath.¹⁵ The product, a viscous golden-yellow liquid, was collected at 110–125°. The yield was 7.5 g., n_D^{20} 1.5353. The same results were obtained by allowing a solution of III in 10% methanolic alkali to stand at room temperature for two to three days.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19; methoxyl, 9.81. Found: C, 79.56; H, 10.13; methoxyl, 9.51.

A distillation residue of 2.0 g. of clear transparent resin accounted for the remainder of the starting material. The vinylallenol polymerizes readily on heating above 100°, and unless distillation is fairly rapid, the residues tend to be larger. This can be overcome by the use of a conventional falling-film molecular still, with peanut oil as a carrier. However, a more practical and less time-consuming procedure consists in merely subjecting the undistilled product to a vacuum of 0.001 mm. for 24 hours at room temperature. An analytically and spectrally pure product was easily obtained in this way. The yield, based on III, was quantitative, n_D^{20} 1.5354.

Chromatography on alumina produced no change in the properties of either the distilled or undistilled products.

Ozonolysis gave 44% geronic acid and 20% formaldehyde. Under the same conditions III gave 35% geronic acid and 20% formaldehyde.

Preparation of the Vinylallenol, XI.—Ethylnyl- α -ionol¹⁶ was condensed with 1-chloro-2-methyl-4-methoxy-2-butene¹⁷ in the same manner as described for the corresponding ethynyl- β -ionol in Part I¹ of this series. The yields were the same, 75–85%. The product, the α -ionol analog of III, was distilled and collected at 105–120° (0.001 mm.). It is a very viscous and almost colorless liquid, n_D^{20} 1.5048. As expected, because of the absence of conjugation, the ultraviolet absorption spectrum showed no maxima in the region 210–350 $m\mu$.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19; methoxyl, 9.81. Found: C, 79.83; H, 10.29; methoxyl, 9.60.

A solution of 52 g. of the above acetylenic carbinol in 600 ml. of 10% methanolic sodium hydroxide was allowed to stand under nitrogen at room temperature for three days. It was then worked up with water and petroleum ether and dried with anhydrous potassium carbonate. Distillation yielded 32 g. of a very viscous, light-yellow liquid collected at 105–120° (0.001 mm.), n_D^{20} 1.5223.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19; methoxyl, 9.81. Found: C, 79.79; H, 10.17; methoxyl, 9.74.

The product, like the β -ionol analog, VI, polymerizes readily when heated above 100°. If the reaction product is not distilled, but freed of volatiles at 0.001 mm. as described above for VI, a quantitative yield of analytically pure material can be obtained.

Preparation of the Allenic Polyene, VII.—A solution of 11.2 g. of VI in 140 ml. of glacial acetic acid containing 0.1 g. of hydroquinone was allowed to stand under nitrogen at room temperature for two hours. It was then worked up with water and petroleum ether. After drying with anhydrous potassium carbonate the petroleum ether solution was concentrated under vacuum to a sirup. This was then completely freed of volatiles by subjecting to a vacuum of 0.001 mm. for 24 hours. The deep orange-red product weighed 10 g. A Zerewitinoff analysis showed no active hydrogen. The typical ultraviolet absorption curve of the crude product was as shown in Fig. 2, but $E_{1\text{cm}}^{1\%}$ at 317.5 $m\mu$ was only 1025 as compared to 1660 for the pure compound described below. On the basis of these figures the yield was calculated to be about 62%.

The same product was obtained when a solution of 25 g. of VI in 600 ml. of benzene was refluxed with 0.75 g. of *p*-toluenesulfonic acid. The theoretical amount of water was given off in 90 minutes. However, in this case the yield, calculated as above, was only 45%.

Since VII could not be distilled, even at 0.001 mm., without extensive decomposition and isomerization, chromatography was relied upon for an analytically pure sample.

(15) All distillations at 0.005 mm. or less described herein were performed in this manner. The large distillation ranges noted are usually a consequence of superheating rather than an impure product.

(16) W. Oroshnik and A. D. Mebane, *THIS JOURNAL*, **71**, 2062 (1949).

(17) W. Oroshnik and R. A. Mallory, *ibid.*, **72**, 4608 (1950).

Even by this method, only a small portion of VII was obtainable because of the isomerizing effect of the alumina. The crude dehydration product from an 11.0-g. sample of VI was dissolved in 50 ml. of petroleum ether and poured onto a 3 × 95-cm. column of Alcoa F-20 alumina. When developed with 20% ether-petroleum ether, the chromatogram consisted, when viewed under ultraviolet light, of one main pink-fluorescing zone with a small red leading edge and a somewhat larger red following edge. The first eluates of the main zone showed the absorption curve of impure II and gave a red Carr-Price test. The end of this fraction could not be seen on the column, but was detected by a change in the Carr-Price color to prussian blue. The yield of this fraction amounted to 3.6 g.

The spectrum of the next fraction was that of VII. Elution was continued with 3% methanol and 25% ether in petroleum ether. After washing the eluate with water, drying with anhydrous potassium carbonate and concentrating under vacuum, the product was freed of volatiles under a vacuum of 0.001 mm.; yield 1.8 g., n_D^{20} 1.628.

Anal. Calcd. for $C_{21}H_{30}O$: C, 84.51; H, 10.13; methoxyl, 10.40; active H, none. Found: C, 84.43; H, 10.04; methoxyl, 10.49; active H, none.

Ozonolysis produced 22.5% formaldehyde and no geronic acid.

Isomerization of the Allenic Polyene, VII.—A 16.0-g. sample of crude VII, $E_{1\text{cm}}^{1\%}$ 760 at 317.5 $m\mu$, obtained by the *p*-toluenesulfonic acid dehydration of VI as described above, was dissolved in 400 ml. of 1 *M* absolute ethanolic sodium hydroxide. After refluxing for four hours, the solution was cooled and worked up with water and petroleum ether. The product was distilled at 0.001 mm., collecting at 110–130°; yield 8.5 g., n_D^{20} 1.5901. The absorption curve showed a maximum at 332 $m\mu$ and an extinction only two-thirds of that of pure II.

The entire distillate was then dissolved in 100 ml. of petroleum ether and poured into a 3 × 31-cm. column of Alcoa F-20 alumina. On development with increasing proportions of ether in petroleum ether there appeared two large bands fluorescing red under ultraviolet light. The eluate of the first zone gave a dull-red Carr-Price color and showed λ_{max} 324 $m\mu$; yield 1.0 g. The eluates of the second zone gave a violet Carr-Price color and had λ_{max} 332 $m\mu$. This was concentrated and distilled. The yield was 3.0 g. of product, collected at 101–121° (0.002 mm.); n_D^{20} 1.601; λ_{max} 334 $m\mu$, ϵ 29,500; λ_{min} 255 $m\mu$, ϵ 9,600. For comparison of this absorption curve with those of pure II and IX, see Fig. 3.

Anal. Calcd. for $C_{21}H_{30}O$: C, 84.51; H, 10.13; methoxyl, 10.40. Found: C, 84.26; H, 10.05; methoxyl, 10.62.

Ozonolysis gave 15% formaldehyde and no geronic acid.

Preparation of II by Dehydration of Enyne IV.—A solution of 3.2 g. of IV in 75 ml. of glacial acetic acid containing a few mg. of hydroquinone was allowed to stand under nitrogen at room temperature for 24 hours. It was then worked up with water and petroleum ether. Distillation at 0.001 mm. yielded 2.9 g. of a lemon-yellow product, collected at 122–124°; n_D^{20} 1.607, λ_{max} 335 $m\mu$, ϵ 33,900; λ_{min} 255 $m\mu$, ϵ 13,700 (Fig. 3).

Anal. Calcd. for $C_{21}H_{30}O$: C, 84.51; H, 10.13; methoxyl, 10.40. Found: C, 84.29; H, 10.10; methoxyl, 10.60.

Ozonolysis gave 8% formaldehyde¹⁸ and no geronic acid.

Semi-hydrogenation of the Vinylallenol, VI. A. By Catalytic Hydrogenation.—A solution of 31.6 g. of VI, 150 ml. of methanol, 10 ml. of piperidine and 0.5 g. of zinc acetate was shaken under hydrogen at atmospheric pressure in the presence of 5.0 g. of Raney nickel. Absorption proceeded at an average rate of 50 cc./min., but dropped to 5 cc./min. for the last 100 cc. When the theoretical quantity of hydrogen had been absorbed, the solution was removed, filtered and worked up with water and petroleum ether.

(18) In Part I of this series a blank determination of 5% formaldehyde on ozonolysis was found acceptable. In the present work compounds IV and XV, whose structures are now unequivocally established,¹⁰ and which have no terminal vinyl groups or allylic methoxyl groups, gave, respectively, 7 and 8% yields of formaldehyde on ozonolysis. A blank of 8% formaldehyde was therefore accepted in this work. Positive controls for the terminal vinyl group and allylic methoxyl group were again experimentally confirmed as 43–48% and 20–25%, respectively.

The product was distilled at 0.001 mm. The fore-runs and post-runs were discarded since they were shown by analysis to be largely over-hydrogenated and unhydrogenated, respectively. The major fraction, 22.0 g., collected at 110–120°, was chosen within the refractive index range of n_D^{20} 1.5160–1.5190. The bulk had n_D^{20} 1.5170, λ_{\max} 237 μ , ϵ 16,400.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; methoxyl, 9.74. Found: C, 79.31; H, 10.72; methoxyl, 9.50.

The distilled product was then dissolved in heptane and chromatographed on a column of F-20 Alcoa alumina. On development with increasing proportions of ether in heptane, the compound distributed itself into three main zones as viewed under ultraviolet light: the first, an orange-fluorescing zone, bordered on both sides by red-fluorescing edges, yielded 2.2 g. of product which showed λ_{\max} 235 μ and had an absorption curve almost identical with that of XIV. The next, a lighter reddish zone, gave 3.3 g. of product, λ_{\max} 240 μ . Following this was the major fraction, a large white-fluorescing zone. This yielded 14.3 g. On distillation at 0.001 mm. it came over completely at 107–110°, leaving no residue; n_D^{20} 1.5175; λ_{\max} 237 μ , ϵ 18,100.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; methoxyl, 9.74. Found: C, 79.05; H, 10.82; methoxyl, 9.66.

B. With Chromous Hydroxide.—A solution of 55 g. of sodium hydroxide (95%) in 55 ml. of water was added with cooling to 400 ml. of ethanol in a one-liter three-necked flask. To this solution was added 20.8 g. (0.066 mole) of VI. The resulting mixture was then stirred at 15°, with nitrogen gently flowing in through one side-neck, and flushing the flask. Then a wet pressed-out fresh filter cake of chromous acetate,¹⁹ containing about 90 g. (0.53 mole) of the salt, was quickly cut up with a spatula and added through the other side-arm. The brown-black to brown-purple suspension was then allowed to stir at room temperature with nitrogen constantly passing over it, until the color changed to the bright green of Cr_2O_3 . The time for this change varied from one to three days. The reason for the time differences is at present obscure but appears to be related to the physical state of the chromous hydroxide formed. This seems to vary in different experiments as evidenced by the differences in initial color of the precipitated chromous hydroxide.

The mixture was then diluted with half of its volume of ether and filtered, washing the filter cake thoroughly with ether. The filtrate was worked up with water, and the ether extracts removed, dried with anhydrous potassium carbonate and distilled. The product, 18.8 g., was collected at 110–125° (0.001 mm.); n_D^{20} 1.5254; λ_{\max} 240 μ , ϵ 20,200.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; methoxyl, 9.74. Found: C, 79.24; H, 10.68; methoxyl, 8.96.

The product was chromatographed on alumina as described above, and yielded 78% of a fraction which distilled completely at 112–114° (0.001 mm.); n_D^{20} 1.5224; λ_{\max} 241.5 μ , ϵ 24,300.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; methoxyl, 9.74. Found: C, 79.59; H, 10.63; methoxyl, 9.45.

C. With Lithium Aluminum Hydride.—A solution of 31.6 g. (0.1 mole) of VI in 200 ml. of dry ether was added gradually to a stirred suspension of 2.5 g. of commercial lithium aluminum hydride in 300 ml. of dry ether. The addition product dissolved completely. After six hours of refluxing, the solution was cooled to –20° and hydrolyzed with 200 ml. of 70% aqueous methanol.²⁰ After the addition of a few grams of Super-Cel, the mixture was filtered and the filtrate worked up with water and ether. The ether solution was dried and concentrated under vacuum. The residual oil was redissolved in 100 ml. of petroleum ether and poured onto a 3 × 75-cm. column of Alcoa F-20 alumina. Under ultraviolet light, the column showed two white-fluorescent zones. The first and smaller of these,

giving a prussian blue Carr–Price test, was vitamin A methyl ether and was eluted with increasing proportions of ether in petroleum ether (20–30%). This was concentrated under vacuum and eventually freed of volatiles by warming at 40° under 0.001 mm. pressure for two hours. The residual yellow-orange oil weighed 4.0 g.; n_D^{20} 1.611; λ_{\max} 324.5 μ , ϵ 50,300. The spectral constants of authentic vitamin A methyl ether are in Table I. Attempts were not made to crystallize the product.

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74; methoxyl, 10.33. Found: C, 84.00; H, 10.70; methoxyl, 10.23.

Ozonolysis yielded 26% geronic acid and 22% formaldehyde.

The larger zone, giving a red-violet Carr–Price test, was also eluted with increasing proportions of ether (30–50%) in petroleum ether, and the process followed spectrophotometrically. Four fractions were obtained from this zone: (a) λ_{\max} 233–236 μ , 9.8 g.; (b) λ_{\max} 236–239 μ , 1.9 g.; (c) λ_{\max} 239–236 μ , 5.9 g.; (d) λ_{\max} 236–231 μ , 6.7 g.

Fraction (d) judged from its dehydration product was largely unreacted starting material, VI. Fraction (b) was a mixture of (a) and (c).

Fraction (a), identified below by its dehydration product as desmethoxy-XIII, was distilled. The fore-runs and tails were discarded and the main fraction, 8.0 g., was collected at 102–105° (0.001 mm.), n_D^{20} 1.5231.

Anal. Calcd. for $C_{20}H_{32}O$: C, 83.27; H, 11.18; methoxyl, 0.00. Found: C, 83.13; H, 11.18; methoxyl, 0.65.

Fraction (c), identified below by its dehydration product as consisting essentially of XV, was also distilled at 0.001 mm., collecting 4.7 g. at 110–120°; n_D^{20} 1.5290; λ_{\max} 240 μ , ϵ 24,600.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.74; methoxyl, 9.74. Found: C, 79.16; H, 10.56; methoxyl, 8.39.

Dehydration Studies of the Semi-hydrogenation Products.

A. The Catalytic Hydrogenation Product.—A solution of 10.0 g. of chromatographed product in 25 ml. of glacial acetic acid containing a few mg. of hydroquinone was allowed to stand under nitrogen at room temperature for two days. It was then worked up with water and petroleum ether, dried and distilled, collecting 8.4 g. of product at 110–125° (0.001 mm.); n_D^{20} 1.5806; λ_{\max} 301, 318, 332, 348, 367 μ . The peaks at 301 and 318 μ were considered as indicative of *cis*- and *trans*-X, respectively, and 332, 348 and 367 μ those of *trans*-XVI. Biological assay showed 120,000 units of vitamin A activity per gram.

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74; methoxyl, 10.33. Found: C, 83.54; H, 10.85; methoxyl, 10.20.

The product was then chromatographed on an alumina column and the following fractions identified: (a) 12% showing the typical curve of anhydrovitamin A, λ_{\max} 352, 370, 391 μ ; (b) 37% showing the typical curve of *trans-retrovitamin A* methyl ether, XVI, λ_{\max} 333, 348, 367 μ ; (c) 4.5% vitamin A methyl ether, also identified by its spectrum, λ_{\max} 328 μ .

The appearance of fraction (a) is a chromatographic artifact, since it is completely absent in the distilled product. It has also been shown to appear as a by-product when X is isomerized to XVI by alkali or on an alumina column as well as when vitamin A is chromatographed on an alumina column.

When the dehydration product described above, before chromatography, was treated with alkali, the 301 and 318 μ peaks completely disappeared and the absorption spectrum was wholly that of *trans-retrovitamin A* methyl ether, XVI. A solution of 5.4 g. of dehydration product in 100 ml. of 2 *M* absolute ethanolic sodium hydroxide was refluxed for six hours. It was then worked up with water and petroleum ether, dried and distilled, yielding 4.9 g. of product at 110–130° (0.001 mm.); n_D^{20} 1.62; λ_{\max} 332, 348, 367 μ ; ϵ_{348} 40,000.

The analytical data were essentially the same as those noted above, before alkali treatment.

B. The Chromous Hydroxide Product.—A solution of 5.4 g. of chromatographed product in 50 ml. of glacial acetic acid containing a few mg. of hydroquinone was allowed to stand for two days under nitrogen at room temperature. On working up with water and petroleum ether and distilling at 0.001 mm., there were obtained 3.2 g. of product at 115–120°, n_D^{20} 1.62; λ_{\max} 332, 347, 367 μ ; ϵ_{347} 40,000.

(19) J. H. Balthis, Jr., and J. C. Bailar, Jr., "Inorganic Syntheses," Vol. I, McGraw-Hill Book Co., Inc., New York, N. Y., 1939, p. 122.

(20) The non-acidic hydrolysis of lithium aluminum hydride reaction mixtures always precipitates alumina in an almost non-filterable form, which makes separation of the ether layer a most tedious task. The use of caustic solutions was found to be of little advantage. Methanol-water, however, precipitates the alumina in a more crystalline state and filtration is relatively easy.

Bioassays showed 290,000 units of vitamin A activity per gram.

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74; methoxyl, 10.33. Found: C, 83.74; H, 10.66; methoxyl, 10.01.

Upon alumina chromatography, the following fractions were obtained: (a) 5.5% anhydrovitamin A, λ_{\max} 352, 369, 390 $m\mu$; (b) 46% *retrovitamin* A methyl ether, XVI; (c) 4.5% crude vitamin A methyl ether, λ_{\max} 325 $m\mu$.

Fraction (b) was distilled. The product, collected at 110–115° (0.0005 mm.), had n_D^{20} 1.63–1.64; λ_{\max} 333, 348, 367 $m\mu$; ϵ_{348} $m\mu$ 54,100.

The analytical data were essentially the same as those noted above before chromatography.

C. The Lithium Aluminum Hydride Product. 1. **Dehydration of Desmethoxy-XVII.**—Eight grams of the carbinol was dissolved in 160 ml. of absolute alcohol containing 0.8 ml. of concd. hydrochloric acid and the mixture allowed to stand for three hours. It was then worked up with water and petroleum ether. The yield of crude product was 6.4 g. Its absorption spectrum (Fig. 6) showed a preponderance of *retroionylidene* triene (λ_{\max} 287 $m\mu$) accompanied by β -ionylidene pentaene (λ_{\max} 323 $m\mu$). Neither alumina nor Florisil chromatography succeeded in separating the two isomers. The product was used as such in the alkali isomerization described below.

2. **Dehydration of the 240- $m\mu$ Diene.**—A solution of 4.7 g. of the carbinol in 100 ml. of 2.5% potassium acetate-glacial acetic acid was allowed to stand for 20 hours at room temperature. (Solution of the carbinol was accompanied by the formation of a strong rose-red color which faded to orange-yellow within a minute. This is characteristic of 4,5-*trans*-XV.¹⁰) On working up with water and petroleum ether and distilling at 0.001 mm. there were obtained 3.2 g. of *retrovitamin* A methyl ether, X; n_D^{20} 1.630; λ_{\max} 333, 348.5, 367 $m\mu$; $\epsilon_{348.5}$ $m\mu$ 45,100.

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74; methoxyl, 10.33. Found: C, 83.00; H, 10.71; methoxyl, 9.13.

The low carbon and methoxyl values were expected because of the presence in the starting carbinol of some demethoxylated material.

Isomerization of XIV.—A solution of 25.0 g. of XIV, n_D^{20} 1.5100,¹ in 250 ml. of 1 *M* alcoholic sodium hydroxide was refluxed for three hours. It was then cooled and worked up in the usual fashion with water and petroleum ether. Distillation at 0.001 mm. gave 20.8 g. of product collected at 110–125°; n_D^{20} 1.5235; λ_{\max} 238 $m\mu$, ϵ 19,300.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; methoxyl, 9.74. Found: C, 79.02; H, 10.69; methoxyl, 9.56.

A 10.4-g. sample of the above distillate was dissolved in 50 ml. of petroleum ether and poured onto a column of Alcoa F-20 alumina. After development with 20% ether in isoheptane, the column appeared very similar to that described above for the catalytic semihydrogenation product of VI. The two lower bands in this case, however, represented much greater proportions of the total and had different spectral constants. The column was extruded and the three major bands cut out and eluted. The first yielded 2.0 g. (19%) of material, λ_{\max} 243 $m\mu$. The second gave 2.8 g. (27%), λ_{\max} 240 $m\mu$. These two products corresponded spectrally to 4,5-*cis*-XV and 4,5-*trans*-XV, respectively, and this was confirmed by dehydration of both to 4,5-*trans*-XVI.

The major fraction, 5.0 g. (48%), λ_{\max} 238.5 $m\mu$, was distilled at 0.001 mm. The product came over completely at 110–125°; n_D^{20} 1.5190; λ_{\max} 238 $m\mu$, ϵ 23,200.

The analytical data were substantially the same as those of the unchromatographed product. As shown below this product was a mixture of XV and some isomerized XIV.

Dehydration of Isomerized XIV.—A distilled but unchromatographed sample of isomerized XIV, 10.0 g., was dissolved in 100 ml. of 10% potassium acetate-glacial acetic acid. The characteristic rose-red color formed on dissolving 4,5-*trans*-XV in glacial acetic acid¹⁰ was also observed here. After standing overnight at room temperature under nitrogen, the solution was worked up in the usual fashion with

water and petroleum ether. On distillation at 0.001 mm., 9.0 g. of product was collected at 110–130°; n_D^{20} 1.601; λ_{\max} 333, 348, and 367 $m\mu$, ϵ_{348} $m\mu$ 28,600. A plateau at 300–310 $m\mu$ was considered as the contribution of 4,5-*cis*- and *trans*-X, the dehydration product of XIV.

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74; methoxyl, 10.33. Found: C, 83.76; H, 10.75; methoxyl, 10.21.

After refluxing in 1 *M* absolute ethanolic sodium hydroxide for six hours, the plateau at 300–310 $m\mu$ completely disappeared and ϵ_{348} $m\mu$ increased to 36,000. The analytical data were unchanged.

Preparation of XVII.²¹—A solution of 10.6 g. of XIII in 180 ml. of methanol was treated with 0.9 ml. of concd. hydrochloric acid. After standing under nitrogen at room temperature for three hours, the solution was worked up with water and petroleum ether. The crude product in 70 ml. of petroleum ether was then poured onto a 4 × 28-cm. column of F-20 alumina. After development with 2% ether in petroleum ether, the column consisted of a homogeneous white fluorescent bottom border. On elution with increasing proportions of ether in petroleum ether (5–20%), and by following spectrophotometrically, the fraction showing only λ_{\max} 286 $m\mu$, was separated. On distillation this yielded 5.8 g. of a yellow mobile oil collected at 105–115° (0.002 mm.), n_D^{20} 1.5578.

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74. Found: C, 84.11; H, 11.04.

Isomerization of XVII.—A solution of 5.0 g. of XVII in 200 ml. of 10% ethanolic sodium hydroxide was refluxed for three hours. By this time the spectrum had completely changed to that of XVI (see Fig. 5). The solution was worked up with water and petroleum ether, and the product isolated from the latter solvent by alumina chromatography in the usual manner described herein. The major fraction, 3.0 g., after freeing of volatiles at 0.001 mm., showed the characteristic spectrum of *retrovitamin* A methyl ether, X; λ_{\max} 333, 348, 367 $m\mu$, ϵ_{348} $m\mu$ 45,800.

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74; methoxyl, 10.33. Found: C, 83.90; H, 11.05; methoxyl, 10.02.

Isomerization of Desmethoxy-XVII.—The crude product, 5.6 g., obtained from desmethoxy-XIII as described above, was dissolved in 250 ml. of 10% sodium hydroxide—absolute ethanol and refluxed for 3.5 hours. After working up in the usual fashion with water and petroleum ether, the product was distilled at 0.005 mm. It came over completely at 115–120°; yield 5.2 g.; n_D^{20} 1.6095; λ_{\max} 323 $m\mu$, ϵ_{\max} 31,900.

The entire product was dissolved in petroleum ether and chromatographed on a 3 × 40-cm. column of Alcoa F-20 alumina. Development with 2% ether—petroleum ether gave, when viewed under ultraviolet light, two white-fluorescent zones separated by a non-fluorescing space.

On elution, the first of these gave 3.2 g. of a nearly colorless mobile oil which was identified as vitamin A hydrocarbon, desmethoxy-XVII. The product was analyzed after freeing of volatiles at 0.001 mm., n_D^{20} 1.6035.

Anal. Calcd. for $C_{20}H_{30}$: C, 88.82; H, 11.18. Found: C, 88.63; H, 11.12.

Ozonolysis gave 15% geronic acid and 8.8%¹⁸ formaldehyde.

Elution of the second zone yielded 0.9 g. of product after removal of volatiles at 0.001 mm. This showed λ_{\max} 332, 348.5, 367 $m\mu$ and an apparent $\epsilon_{348.5}$ $m\mu$ 38,700. However, the product was not pure as indicated by the analysis below as well as by a small residue of polymeric material remaining after dissolving the compound in absolute ethanol.

Anal. Calcd. for $C_{20}H_{30}$: C, 88.82; H, 11.18; methoxyl, none. Found: C, 87.14; H, 11.40; methoxyl, 0.56.

Acknowledgment.—The authors are indebted to Mr. Joseph Grodsky for the microanalyses.

RARITAN, NEW JERSEY

(21) This procedure is superior to the one described previously in Part II¹⁰ where glacial acetic acid was used as the dehydrating agent.