Synthesis of Polyenes. VI. Isoprenoid Polyenes Containing Sterically Hindered *cis* Configurations[1]

BY WILLIAM OROSHNIK AND ALEXANDER D. MEBANE

To establish as a general principle that sterically hindered *cis* configurations of type 1, first discovered in 4,5-*cis-retro*-vitamin A methyl ether (I) can be achieved in practically any kind of isoprenoid polyene, a series of examples among dienes, trienes, tetraenes and pentaenes were synthesized. Pauling's "rule" relating to these stereoisomers has been clarified, and shown not to be inconsistent with the recently acquired evidence in this field. The structures of these new *cis* compounds and those previously reported have been correlated with their ultraviolet and infrared spectra.

From a study of molecular dimensions in the carotenoids, Pauling, some time ago, postulated that type I *cis* configurations (Fig. 1) would show pronounced steric hindrance and that *cis* configurations, therefore, " . . . will be assumed only by those double bonds which are of type II."[2] In thus limiting the number of "stereochemically effective double bonds" to a select few, this principle greatly simplified the configurational problems involved in the carotenoids.[3] Unfortunately, however, it was interpreted as a hard and fast rule precluding the existence of type I *cis* configurations. With the recent synthesis of 4,5-*cis*-I and 4,5-*cis*-II it became clear that such an interpretation was not valid.[4] Additional examples of such compounds reported since, namely, 5,6-*cis*-III, 5,6;13,14-di-*cis*-III and the corresponding di- *cis*-lycopene (IV),[5] have substantiated this conclusion.[6]

Fig. 1.

I

II

III
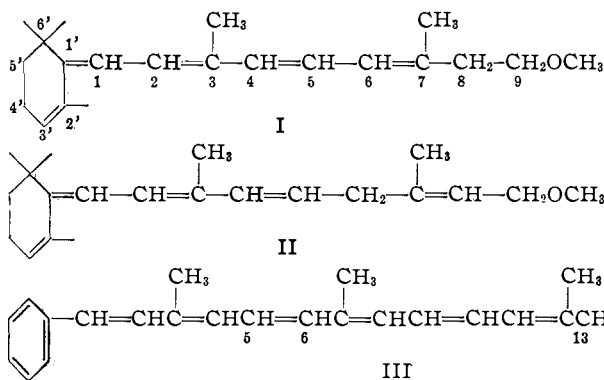
The possibility of synthesizing such compounds was in fact recognized by Pauling himself,[7] but the great instability he predicted for them was apparently misconstrued to apply to the question of their existence. Actually this instability refers only to

cases of catalyzed equilibrium mixtures, and it must be emphasized therefore that Pauling's rule can be applied only to such conditions. As is now known, type I *cis* isomers isomerize very readily and completely in the presence of iodine, and their absence in such catalyzed equilibrium mixtures as studied by Zechmeister and his collaborators[3] is therefore understandable and in agreement with Pauling's predictions. Application of the rule, however, to such quasi-equilibrium mixtures as produced by heat or light is questionable, for recent evidence indicates that, at least in certain compounds, type I *cis* configurations can be achieved photochemically.[6]

The present work was undertaken to extend the number of examples of compounds having type I and Ia[8] *cis* configurations in order to attain some generalizations concerning their nature. In addition to several new pentaenes and tetraenes similar to I and II, a sterically hindered *cis*-triene and several type Ia dienes were studied. All were prepared by the semihydrogenation of the corresponding acetylenic compounds. Once obtained, these sterically hindered *cis* compounds are quite stable and do not spontaneously stereoisomerize at ordinary temperatures and laboratory light conditions.

On treatment with catalytic quantities of iodine, the pentaenes, tetraenes and triene completely iso-

(1) Presented before the 123rd Meeting of the American Chemical Society, Los Angeles, Calif., March 15–19, 1953.

(2) L. Pauling. *Fortschr. Chem. organ. Naturstoffe*, **3**, 203 (1939).

(3) L. Zechmeister, *Chem. Revs.*, **34**, 267 (1944).

(4) W. Oroshnik, G. Karmas and A. D. Mebane, THIS JOURNAL, **74**, 295 (1952). A previous report attesting to the synthesis of *cis-cis-β*-methylmuconic acid [P. Karrer, R. Schwyzer and A. Neuwirth, *Helv. Chim. Acta*, **31**, 1210 (1948)], which has a type I *cis* configuration, was later shown to be in error [J. A. Elvidge, R. P. Linstead and P. Sims, *J. Chem. Soc.*, 3398 (1951)].

(5) C. F. Garbers, C. H. Eugster and P. Karrer, *Helv. Chim. Acta*, **35**, 1850 (1952); **36**, 562 (1953); C. F. Garbers and P. Karrer, *ibid.*, **36**, 828 (1953).

(6) A fifth stereoisomer of retinene reported recently [R. Hubbard, R. I. Gregerman and G. Wald, *J. Gen. Physiol.*, **36**, 415 (1953)] as an irradiation product of all-*trans*- or neoretinene, undoubtedly also has a type I *cis* configuration.

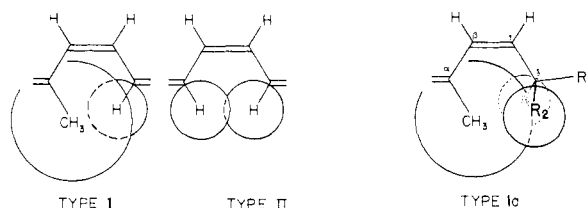(7) L. Pauling, *Helv. Chim. Acta*, **32**, 2241 (1949).

(8) The designation "type Ia" is used herein to represent a variation of a type I *cis* configuration as it occurs around the last double bond of a chromophore (Fig. 1). Since in such cases the δ-carbon is not attached to a double bond it is freer to rotate around the γ,δ-single bond here than it would be in a true type I configuration. Therefore interference is theoretically possible here between the methyl group and any one of the three substituents on the δ-carbon, as compared to interference with only a hydrogen on the δ-carbon in the type I configuration. Actually, however, the spectral evidence shows that the largest group, R_1, is always out of the radius of interference with the methyl group and the degree of break in coplanarity depends on the size of the two remaining smaller substituents, R_1 and R_2. In the examples presented, such as 4,5-*cis*-II, R_1 is always hydrogen and R_2 is hydrogen, hydroxyl or acetoxyl.

merized to the *trans* forms, the speed of reaction decreasing in the order named. It is of interest that these relative reactivities corresponded to the relative instabilities calculated by Pauling for type I *cis* polyenes of differing chromophoric length.[7]

Surprisingly, the hindered *cis*-dienes exhibited remarkable stability toward iodine, yielding no trace of the *trans* isomer even after long treatment in the presence of sunlight. Although the stereoisomerization of conjugated dienes is normally less facile than that of higher polyenes, it does seem odd that hindered *cis*-dienes should be unaffected by conditions to which unhindered dienes are known to respond.[9]

When subjected to temperatures of 100–150°, the sterically hindered *cis*-polyenes suffered little or no change, and in many cases could be distilled. In this respect their behavior is comparable to that of most *cis*-polyenes. *cis-cis*-1,4-Diphenylbutadiene, for example, undergoes only very moderate stereoisomerization even at 205°.[10] Similar heat stability has been reported also for di-*cis*-III. The thermal stability of these sterically hindered *cis* compounds need not be too surprising when viewed in light of the fact that *cis*-polyenes in general show a considerably smaller tendency to stereoisomerize on heating than do the *trans* compounds. Thus pro-γ-carotene and prolycopene, both of which are poly-*cis* compounds, are virtually unchanged in refluxing hexane, while the corresponding all-*trans* forms undergo substantial steric modification under these conditions.[11] These facts are in accord with a theoretical observation of Schomaker[11] that any influence which tends to decrease the amount of conjugation in a polyene and thereby increase the

Fig. 2.

(9) P. L. Nichols, S. F. Herb and R. W. Riemenschneider, This Journal, **73**, 247 (1951).

(10) J. H. Pinckard, B. Wille and L. Zechmeister, *ibid.*, **70**, 1938 (1948).

(11) L. Zechmeister, A. L. LeRosen, W. A. Schroeder, A. Polgar and L. Pauling, *ibid.*, **65**, 1940 (1943).

amount of double bond character in the unsaturated linkages would raise the activation energy for thermal stereoisomerization. Such an influence would be a *cis* double bond. In the case of the type I *cis*-polyenes, where conjugation across the polyene chain is partially destroyed not only by the *cis* configuration but by the break in coplanarity as well, it would be expected, on the basis of the above argument, that a thermal *cis* → *trans* shift would not easily be effected.

Dienes

Attention was first directed to the diene[12] V because of its abnormal ultraviolet absorption
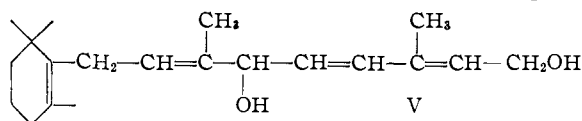
spectrum. This was described originally by Isler, *et al.*, as simply "end absorption."[13] Measurements in this Laboratory have confirmed this in showing only decreasing absorption from 210 to 270 mμ with no trace at all of a diene peak in this range (Fig. 2). Such absence of absorption maxima ordinarily would lead one to suspect that none of the double bonds were conjugated. However, since the over-all structure of V was already unequivocally established,[13] this premise was untenable, and the anomalous spectrum was therefore considered here to be due to some hitherto unrecognized structural feature of V. Examination of molecular models of 5,6-*cis*- and *trans*-V revealed severe steric hindrance between the 4-hydroxyl and 7-methyl groups in the *cis* isomer. Since the form of V being dealt with was obtained by the catalytic semi-hydrogenation of the 5,6-acetylenic analog, and was, therefore, undoubtedly *cis*, it was clear that here was a case of spectral degradation arising from a sterically hindered *cis* configuration of type Ia. Further confirmation of the *cis* configuration was obtained from the infrared spectrum, which showed no absorption band around 10.35 μ.

For comparison, the corresponding 5,6-*trans* isomer was prepared. This proved readily obtainable by reduction of the acetylenic precursor with lithium aluminum hydride. It was characterized by a normal diene peak in the ultraviolet (Fig. 2) and an intense absorption band in the infrared at 10.35 μ (Fig. 15). All attempts to crystallize the *trans* isomer, however, were unsuccessful, which was surprising in view of the crystalline nature of the *cis* isomer. This may be due to steric inhomogeneity in this product at the 7,8-double bond, since evidence obtained with compound XVIc indicates that the reduction of an acetylenic bond in a conjugated enynol with lithium aluminum hydride can be accompanied by steric inversion of the adjacent ethylenic bond.

The 9-methyl ethers of 5,6-*cis*- and *trans*-V were also prepared by reduction of the acetylenic analogs catalytically and with lithium aluminum hydride,
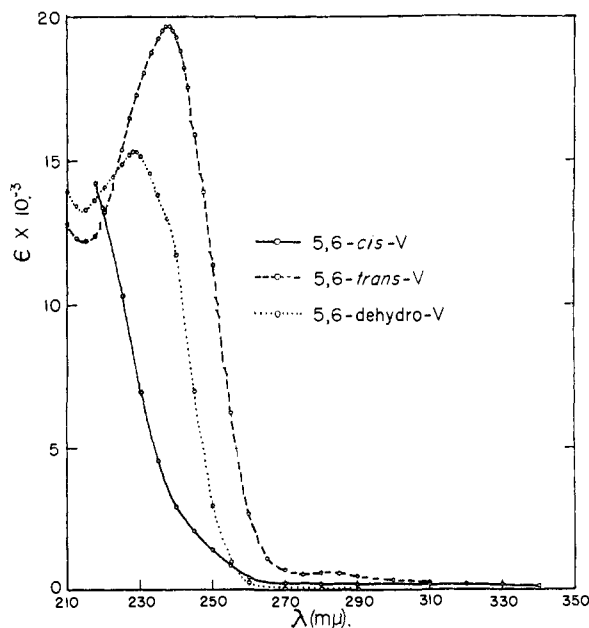
(12) The terms "diene," "triene," "tetraene," etc., as used herein, refer only to the conjugated chromophore, ignoring any isolated double bonds.

(13) O. Isler, W. Huber, A. Ronco and M. Kofler, *Helv. Chim. Acta*, **30**, 1911 (1947); O. Isler, *et al.*, *ibid.*, **32**, 489 (1949).
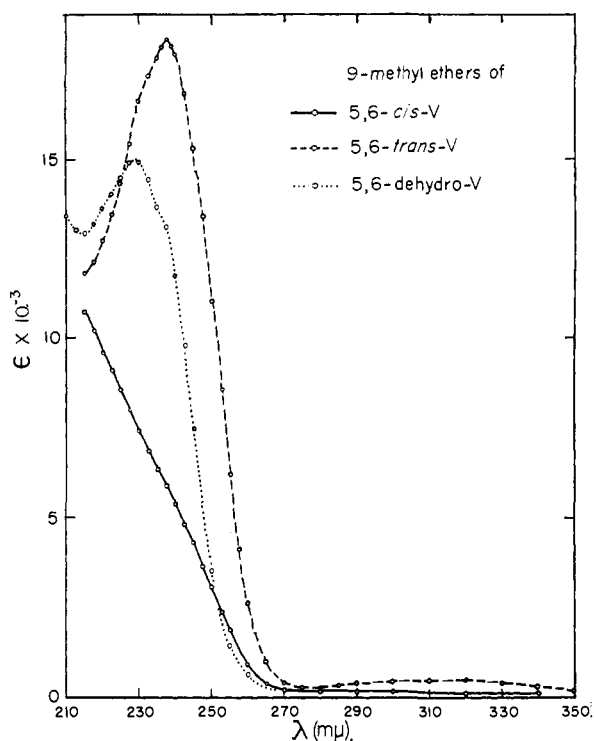
Fig. 3.

respectively. Their spectral characteristics agreed closely with those of the parent glycols (Fig. 3).
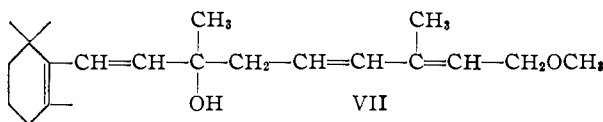
Both *cis* isomers could be distilled at temperatures as high as 150° without steric inversion. Intense illumination (500-watt bulb) was likewise ineffectual, as was iodine catalysis both in the dark and in the presence of sunlight.

It is interesting to note that both 5,6-*cis*- and *trans*-V yield only the 5,6-*trans*-triene VI upon allylic rearrangement. The corresponding 9-methyl
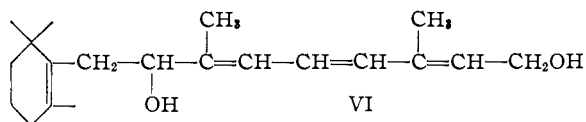
ethers behaved similarly. This represents another case of steric inversion of an ethylenic bond adjacent to, but not part of, an allylically rearranging system.[14]

A *cis* configuration of type Ia, but this time involving hindrance between a methyl group and hydrogen (R_2 = H) rather than hydroxyl (R_2 = OH), is found in 5,6-*cis*-VII.[14] Its spectral deg-

radation is clearly manifested on comparison (Fig. 4) with the unhindered *trans* isomer, which was obtained by the chromous hydroxide reduction of the corresponding acetylenic compound. However, the

(14) For previous examples, see Part II [W. Oroshnik, G. Karmas and A. D. Mebane, THIS JOURNAL, **74**, 3807 (1952)].

exact spectral effects of the methyl–hydrogen hindrance are obscured here because of the contribution existing from the β-ionol chromophore.
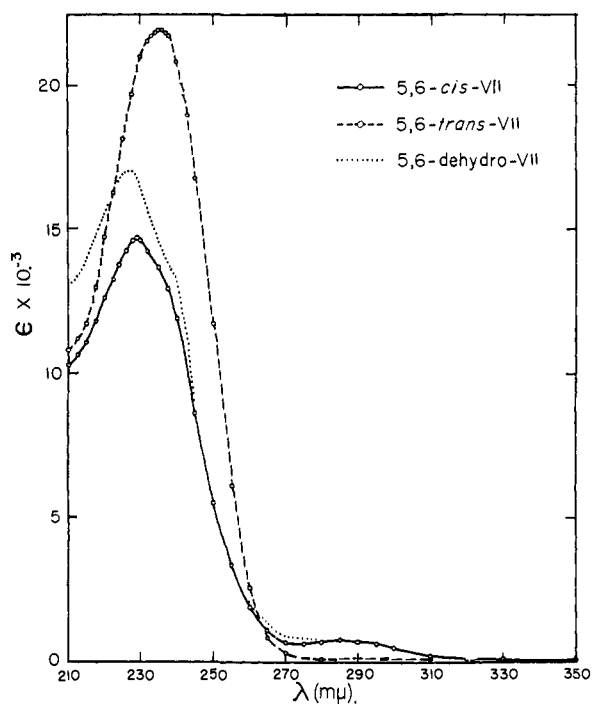

Fig. 4.

An example free from this ambiguity, 4,5-*cis*-3,7-dimethyl-9-methoxynona-2,4,7-triene (IX), was therefore synthesized (Chart I).
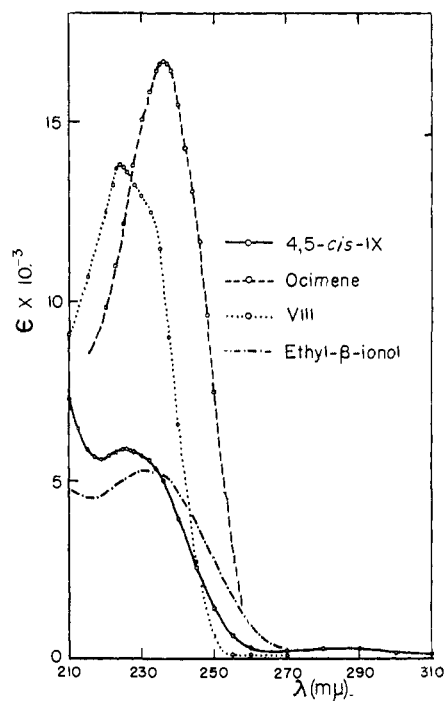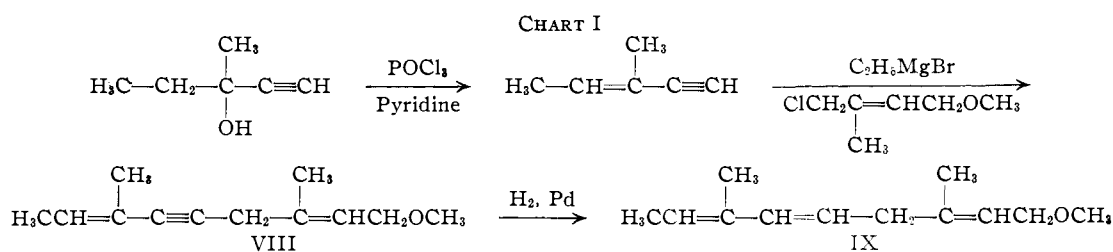
Comparison of its spectrum with that of the

Fig. 5.

CHART I

$$H_3C-CH_2-\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-C\equiv CH \xrightarrow[\text{Pyridine}]{POCl_3} H_3C-CH=\underset{}{\overset{\overset{CH_3}{|}}{C}}-C\equiv CH \xrightarrow[\underset{\underset{CH_3}{|}}{ClCH_2C=CHCH_2OCH_3}]{C_2H_5MgBr}$$

$$\underset{VIII}{H_3CCH=\overset{\overset{CH_2}{|}}{C}-C\equiv C-CH_2-\overset{\overset{CH_3}{|}}{C}=CHCH_2OCH_3} \xrightarrow{H_2,\ Pd} \underset{IX}{H_3CCH=\overset{\overset{CH_3}{|}}{C}-CH=CH-CH_2-\overset{\overset{CH_3}{|}}{C}=CHCH_2OCH_3}$$

closely related *trans*-diene, ocimene[15] (Fig. 5), reveals severe hypsochromic and hypochromic degradation. The retention of a well-defined although small absorption peak contrasts to the absence of any in the case of methyl–hydroxyl hindrance as in 5,6-*cis*-V.

4,5-*cis*-IX showed the same steric stability to heat, light and iodine catalysis as 5,6-*cis*-V. On heating *cis*-IX with alkali, the isolated double bond moved into conjugation to give the triene IXa, but not without some inversion of the 4,5-*cis* configuration. This was evident from its ultraviolet spectrum, which was that of an unhindered

triene (*cf.* Fig. 6). A similar case of steric inversion of a double bond adjacent to, but not part of, a prototropically rearranging system has been described in connection with the action of alkali on II.[4] This inversion, like that of a configuration

$$H_3C-CH=\overset{\overset{CH_3}{|}}{C}-CH=CH-CH=\overset{\overset{CH_3}{|}}{C}-CH_2-CH_2OCH_3 \quad IXa$$
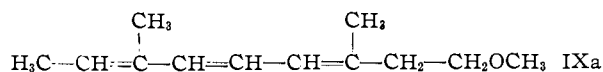
adjacent to an allylically rearranging system, undoubtedly proceeds through the formation of an intermediate mesomeric ion involving the entire conjugated system (see Chart II).
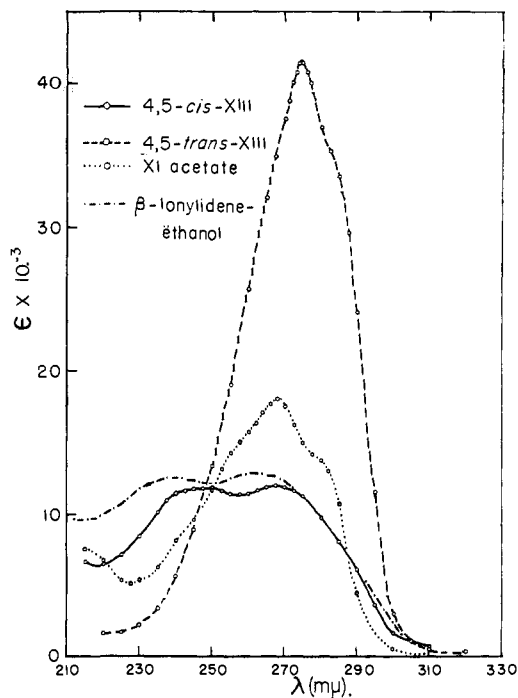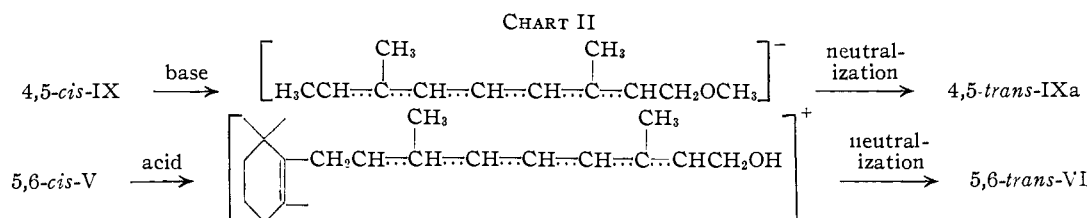
CHART II

$$4,5\text{-}cis\text{-}IX \xrightarrow{\text{base}} \left[H_3CCH\text{---}\overset{\overset{CH_3}{|}}{C}\text{---}CH\text{---}CH\text{---}CH\text{---}\overset{\overset{CH_2}{|}}{C}\text{---}CHCH_2OCH_3 \right]^{-} \xrightarrow{\substack{\text{neutral-}\\ \text{ization}}} 4,5\text{-}trans\text{-}IXa$$

$$5,6\text{-}cis\text{-}V \xrightarrow{\text{acid}} \left[\overset{\overset{CH_3}{|}}{}\text{---}CH_2CH\text{---}CH\text{---}CH\text{---}CH\text{---}CH\text{---}\overset{\overset{CH_3}{|}}{C}\text{---}CHCH_2OH \right]^{+} \xrightarrow{\substack{\text{neutral-}\\ \text{ization}}} 5,6\text{-}trans\text{-}VI$$

Fig. 6.

(15) Part III: W. Oroshnik, A. D. Mebane and G. Karmas, THIS JOURNAL, 75, 1050 (1953). It was pointed out here that the absorption spectrum of ocimene indicates that it is 3,7-dimethylocta-2,4,7-(or 1,4,6)-triene, and not 3,7-dimethylocta-1,3,6-triene as previously accepted.

We are indebted to Dr. L. A. Goldblatt of the U. S. Dept. of Agriculture (Naval Stores Research Division), New Orleans, La., for the absorption curve of ocimene; λmax. 236 mμ, ε 16,700.

However, it should be emphasized that this mesomeric ion mechanism must not be assumed to be the *only* one operating, since, as in the case of II,[4] an appreciable proportion of the final conjugated product still retained the original *cis* bond. Likewise, in the analogous allylic rearrangements, examples also exist wherein a portion of the rearranged product retains the original *cis* bond.[4,14]

Trienes

A type-I *cis* configuration in a triene was investigated in the compound 3,7-dimethylnona-2,4,6-trien-7-ol (XIII). The 4,5-*cis* and *trans* isomers

$$H_3C-CH=\overset{\overset{CH_3}{|}}{C}-CH=CH-CH=\overset{\overset{CH_3}{|}}{C}-\underset{\underset{OH}{|}}{CH}-CH_3$$
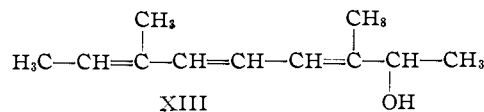
$$XIII$$

were synthesized as shown in Chart III.

The semi-hydrogenation of XI proceeded with pronounced lack of specificity with either Lindlar catalyst or Raney nickel, and a sterically pure specimen of 4,5-*cis*-XIII could not be obtained even after several chromatographic treatments. The final product still showed a moderately strong *trans* band in the infrared at 10.35 μ (Fig. 16). Catalysis with iodine gave a clean *trans* curve (Fig. 6) indicating that the product was free from acetylenic precursor as well as over-hydrogenated product. The appearance of its absorption curve (Fig. 6) suggests the presence of partials, as would be expected from a break in coplanarity [*cf.* β-ionylidene-

CHART III

$$H_3CCH=C(CH_3)-C\equiv CMgBr + HC(=O)-C(CH_3)=CCH_3 \longrightarrow H_3CCH=C(CH_3)-C\equiv C-CH(X)-C(CH_3)=CHCH_3$$

$$\underset{XI}{H_3CCH=C(CH_3)-C\equiv C-CH=C(CH_3)-CH(OH)CH_3} \xleftarrow{H^+}$$

$$\xrightarrow{LiAlH_4} H_3CCH=C(CH_3)-CH=CH-CH(OH)-C(CH_3)=CHCH_3$$

$$H_2 \mid (Pd) \qquad \xrightarrow{\quad} 4,5\text{-}cis\text{-XIII} \xrightarrow{I_2} 4,5\text{-}trans\text{-XIII} \xleftarrow{\qquad H^+ \qquad} 4,5\text{-}trans\text{-XII}$$
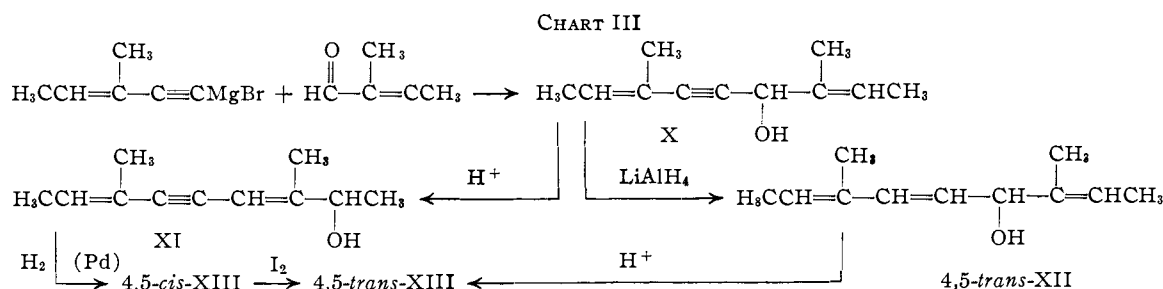
ethanol (Fig. 6)[16]], but any discussion along this line must be deferred until a sterically pure specimen of 4,5-cis-XIII is available.

Tetraenes

The cis-tetraenes studied had their cis configuration at the terminus of the polyene chromophore (type Ia). All were derived from differently alkylated ethynyl-β-ionols by allylic rearrangement and dehydration as shown in Chart IV. The examples chosen illustrate interference of a methyl group with hydrogen, hydroxyl and acetoxyl groups.

The establishment of these small, but significant, spectral differences as real required assurance that they were not due to the presence of impurities arising from non-specific reduction, i.e., over-reduced product or unreduced acetylene. The latter was always readily removed chromatographically. However, when the over-reduced product was retroionylidene triene (as in formula XXII), it could not be separated completely and was present to the extent of about 3% in the best specimen of 4,5-cis-XVIa obtained. In spite of this impurity, λ_{max} 284 mμ, which would have a hypsochromic

CHART IV

$$R-C\equiv CH \xrightarrow[\beta\text{-ionone}]{EtMgBr} \underset{XIV}{[\text{ring}]-CH=CH-C(CH_3)(OH)-C\equiv C-R} \xrightarrow[(-H_2O)]{H^+}$$

$$\underset{XV}{[\text{ring}]=CH-CH=C(CH_3)-C\equiv C-R} \xrightarrow{H_2(Ni\ or\ Pd)} \underset{XVI}{[\text{ring}]=CH-CH=C(CH_3)-CH=CH-R}$$

a: R = n-C₄H₉   b: R = —CH₂—C(CH₃)(OH)—CH=CH₂   c: R = —CH(OH)—C₃H₇

The spectra of the cis-tetraenes (Figs. 7–10) were very similar, and the differences to be expected from the variation in the size of the interfering groups were confined to the shape of the curve around the maximum. Instead of the usual peak, all showed a plateau-like top with the maximum depending on the direction of tilt of this plateau. In those compounds with methyl–hydrogen hindrance (II, XVIa and XVIb) the plateaus tilted toward the higher wave lengths, setting the maximum in the region 295–297 mμ. In XVIc, with methyl–hydroxyl hindrance, the plateau was horizontal with the maximum at 292 mμ, while in the corresponding acetate the plateau tilted toward the lower wave lengths, coming to a maximum at 288 mμ.

effect on the spectrum, the cis-hydrocarbon still showed a higher λ_{max} than its hydroxyl analog.

An unambiguously pure specimen of 4,5-cis-XVIc was obtained by acetylating the semi-hydrogenation mixture prior to chromatography. This changed the adsorption properties of the mixture so that the cis-tetraene was first to emerge from the column. By taking only the first two-thirds of this fraction, the pure cis-acetate, λ_{max} 288 mμ, was obtained. On mild alkaline hydrolysis it yielded the pure cis-carbinol, λ_{max} 292 mμ. Reacetylation shifted the λ_{max} back to 288 mμ, showing that no steric changes occurred in the acetylation and hydrolysis steps.

The isolation of pure 4,5-cis-XVIb incurred no difficulties.

All of the cis-tetraenes were relatively stable to heat and light. In the presence of iodine they quickly stereoisomerized, thus affording easy access to the all-trans isomers.

By reducing XVc with lithium aluminum hydride, a 4,5-trans-XVIc was obtained (strong infrared band at 10.4 μ) which differed from the all-trans isomer in showing considerably less extinction and a hypsochromic displacement of 3 mμ in the ultraviolet (Fig. 10). This indicated the presence of a

(16) It was pointed out in Part I[4] that the absorption spectra of β-ionylidene compounds, in which there is a break in coplanarity at the ring-side chain junction, are best interpreted as consisting of the band of the side-chain partial chromophore overlapping that of the degraded total chromophore. The absorption spectrum of β-ionylidene-ethanol (Fig. 6) is in agreement with this hypothesis in clearly showing a diene band, λ_{max} 240 mμ, and a degraded triene band, λ_{max} 263 mμ (see also ref. 20). The type of hindrance involved here is that shown in Fig. 14.

The β-ionylideneethanol was prepared by the lithium aluminum hydride reduction of ethyl β-ionylideneacetate. It showed $n^{20}D$ 1.5400; $\lambda\lambda_{max}$. 240 mμ (ε 12,500), 263 mμ (ε 12,800).
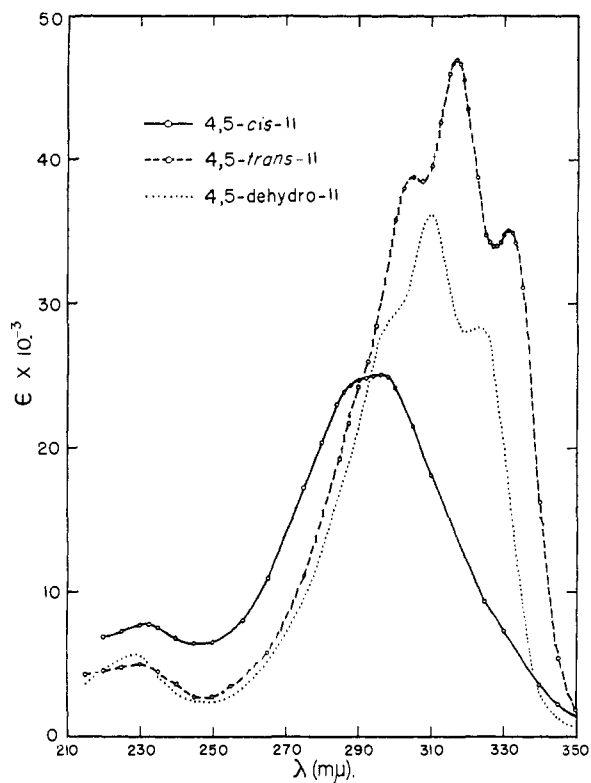
Fig. 7.

Fig. 9.

Fig. 8.

Fig. 10.

type II *cis* configuration,[17] which was confirmed by isomerization to all-*trans*-XVIc on treatment with

(17) A 1,1'-*cis* configuration (type I) was ruled out since it would have caused severe spectral degradation.

iodine. The lithium aluminum hydride product must therefore be assigned the 2,3-*cis*-4,5-*trans* configuration. Further support for this conclusion is seen in the presence of a higher *cis*-peak in this iso-
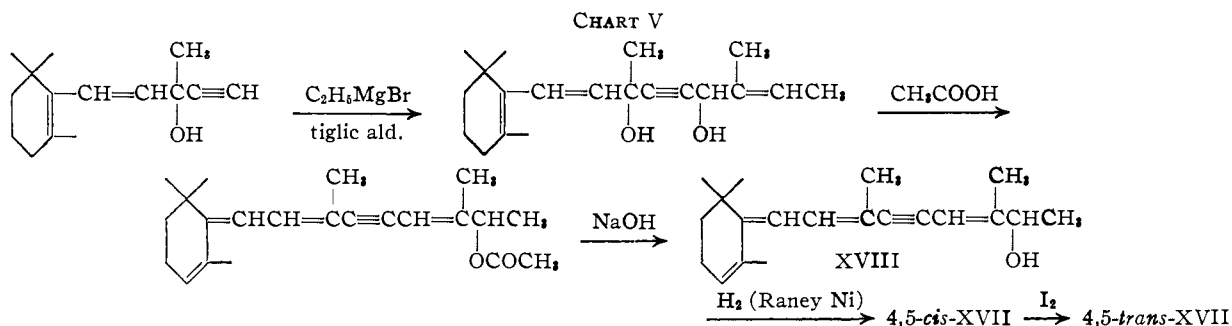
mer than in the all-*trans* product (Fig. 10). Considerable caution is thus indicated in the assignment of steric configurations to dienes or polyenes obtained through lithium aluminum hydride reductions.

Pentaenes

The pentaene XVII, having the same chromophoric system as *retro*vitamin A methyl ether (I),

XVII
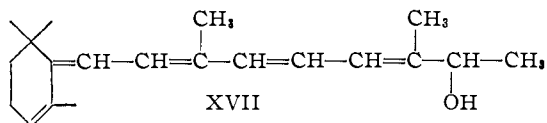
was synthesized as shown in Chart V. As expected,

The *cis* isomer was obtained in this case as a crystalline solid. The corresponding carbinol, on the other hand, could not be induced to crystallize, even after repeated chromatographic treatments. The lower extinction of its 255-mμ band suggests this may be due to steric impurities.

In order to ascertain that the unusual spectral characteristics of 4,5-*cis*-I and 4,5-*cis*-XVII were not a consequence of any unforeseen peculiarities of the cyclohexenylidene system present in *retro*ionylidene compounds, it was deemed advisable to compare them with an acyclic example of a sterically hindered *cis*-pentaene. For this purpose 4,5-*cis*-XIX,[19] the open-chain analog of 4,5-*cis*-I, was synthesized, utilizing the scheme set forth in Chart VI

CHART V

the 4,5-*cis* and *trans* isomers[18] thus obtained showed ultraviolet absorption characteristics agreeing closely with those of the corresponding stereoisomers of I (Figs. 11, 12).

Again the type of spectral phenomena observed for I were repeated (Fig. 13). The hypsochromic displacement of the maxima by a few mμ with respect to I, observed in both the *cis* and *trans* iso-

Fig. 11.

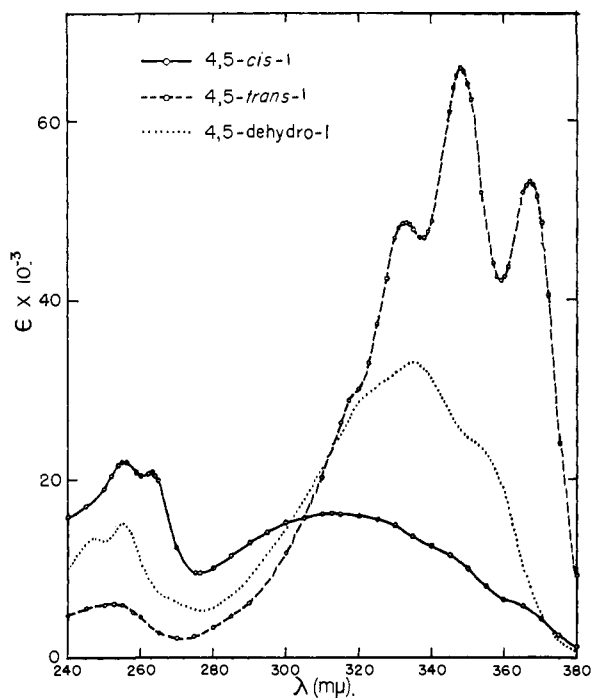Substituting ethanol and boron trifluoride for the acetic acid in the rearrangement–dehydration step in Chart V yielded the corresponding ethyl ethers.

Fig. 12.

(18) In spite of the close structural relationship of this carbinol to vitamin A it showed no biological activity.
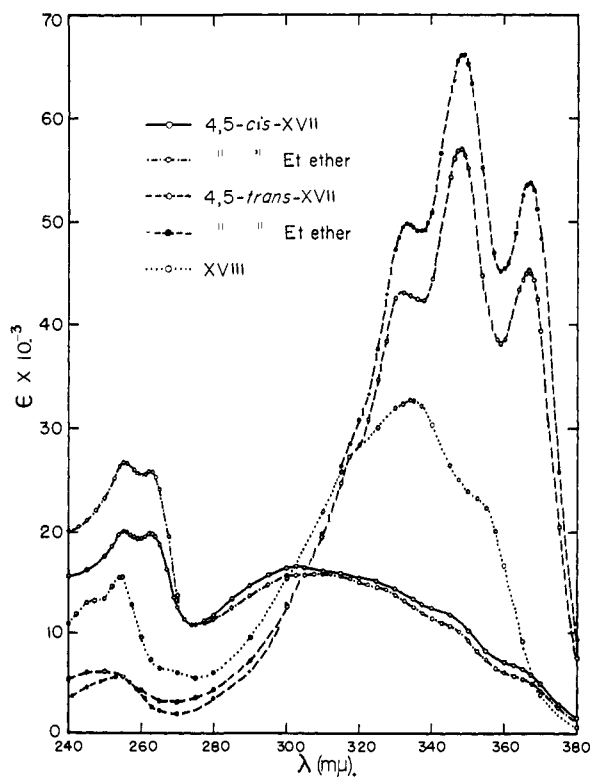
(19) For convenience of comparison the numbering system used for **XIX** was arbitrarily chosen to correspond to that in the cyclic analog **I**.

mers, is to be expected since, as a result of ring opening, there is one less alkyl substituent in the chromophore of XIX.
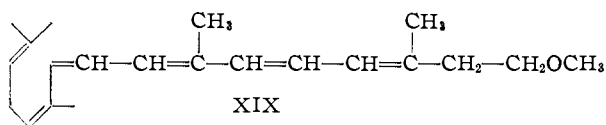
$$CH_3 \quad\quad CH_3$$
$$=CH-CH=C-CH=CH-CH=C-CH_2-CH_2OCH_3$$
$$XIX$$

CHART VI

$$CH_3$$
$$HC\equiv CCH=CCH_2CH_2OCH_3 \xrightarrow[\psi\text{-ionone}]{C_2H_5MgBr}$$

$$CH_3 \quad\quad CH_3$$
$$-CH=CHCC\equiv CCH=CCH_2CH_2OCH_3 \xrightarrow{H^+}$$
$$\overset{|}{OH} \quad XX$$

$$CH_3 \quad\quad CH_3$$
$$=CH-CH=C-C\equiv C-CH=C-CH_2-CH_2OCH_3$$
$$XXI$$

$$\xrightarrow{H_2 \text{ (Raney Ni)}} 4,5\text{-}cis\text{-XIX} \xrightarrow{I_2} 4,5\text{-}trans\text{-XIX}$$
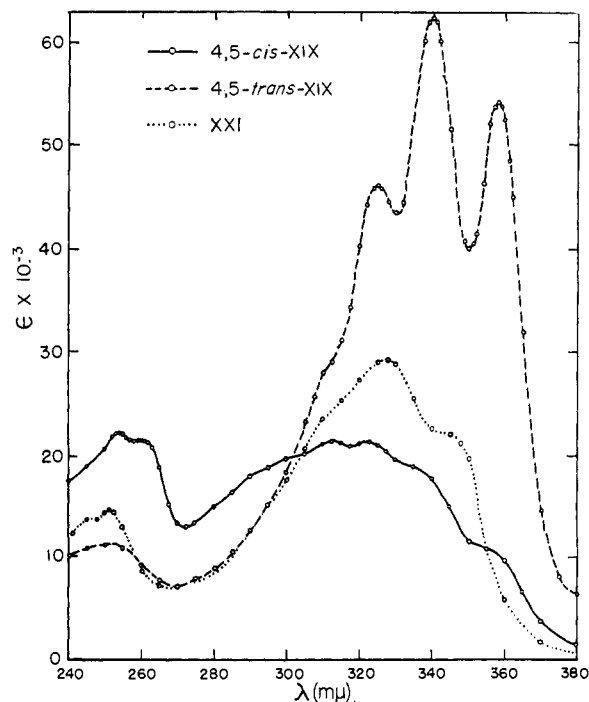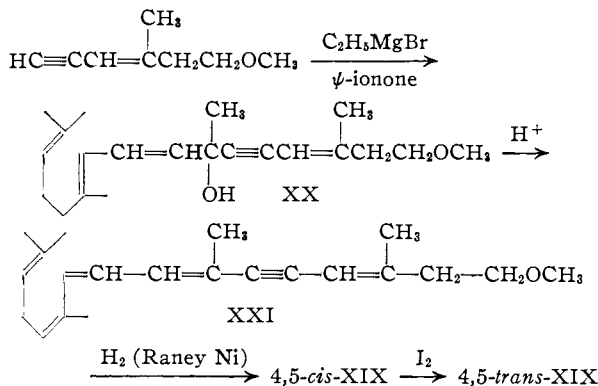

Fig. 13.

All attempts to crystallize the 4,5-*trans*-pentaenes described herein were disappointing. In all likelihood, this is due to the fact that these products, while sterically pure in their 4,5- configuration, contained varying amounts of type-II *cis* isomers. This was evidenced by the varying ratio of the extinctions of the three main bands during chromatographic elution. The concomitant slight variation shown in the *cis*-peak region would indicate that this steric inhomogeneity was confined, at least for the most part, to the terminal 6,7-double bond rather than to the 2,3-bond, which would bend the molecule sharply,

The Ultraviolet Spectra

A. The Sterically Hindered *cis*-Polyenes.— It is of interest to compare the observed spectral degradation arising from hindered terminal *cis* configurations (type Ia) with that arising from hindered interior *cis* configurations (type I).

The dienes and tetraenes studied herein furnish examples of the first class. Examination of the spectral data reveals that in general the type Ia configuration has the effect of "shortening" the polyene chain by one double bond or a part thereof. This is exactly what one would expect from a break in coplanarity which removes the last double bond from the plane of the rest of the chromophore. The degree of out-of-plane distortion of this double bond, which determines the extent of its loss of conjugation, should be proportional to the bulk of the interfering groups (R_1 and R_2 in Fig. 1). This is illustrated clearly in the dienes. Methyl–hydroxyl hindrance (5,6-*cis*-V and its methyl ether) results in a complete loss of a double bond as shown by the absence of absorption peaks in the ultraviolet, while methyl–hydrogen hindrance (4,5-*cis*-IX) causes only partial loss of a double bond, the diene band being very weak and hypsochromically displaced by almost 10 mμ.

These effects also are seen, although not so prominently, in the tetraenes. Here the difference between methyl–hydroxyl (4,5-*cis*-XVIc) and methyl–hydrogen (4,5-*cis*-XVIa) hindrance is only about 3 mμ in λ_{max}. With methyl–acetoxyl hindrance (4,5-*cis*-XVIc acetate) the λ_{max} is still further displaced hypsochromically and its spectral constants (λ_{max} 288 mμ, ϵ 25,400) actually conform more closely to those of the homologous and equally substituted *retro*ionylidene triene (*cf.* XXII, λ_{max} 284 mμ, ϵ 29,300),[4] than to those expected for a tetraene.

$$CH_3$$
$$=CH-CH=C-CH_2-CH_3$$
$$XXII$$
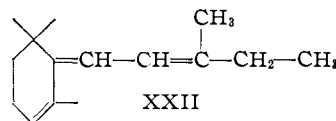
Interestingly enough, on models, the steric interference in 4,5-*cis*-XVIc and its acetate occurs between the methyl group and the oxygen atom on carbon-6, and the consequent deviation from coplanarity is the same in both. It would be expected therefore that the two compounds should show almost identical spectra. The difference observed may be due to the different polarization effects of the acetoxy and hydroxyl groups.

As far as extinction is concerned, there appears to be little difference between methyl–hydroxyl and methyl–hydrogen hindrance. All show a large drop relative to the *trans* isomer, ranging from about 60% in the dienes to about 45% in the tetraenes. The smaller drop in the tetraenes is to be expected, since the longer the polyene, the smaller will be the percentage effect on losing one double bond or part thereof.

It is interesting to note the great similarity of the absorption curves of 4,5-*cis*-IX and ethyl-β-ionol, a *trans*-diene (Fig. 5). Each exhibits only a very small diene peak superimposed on end-absorption. Their extinction coefficients are virtually the same,

as are their λ_{max}'s when corrected for differences in substitution. Figure 14 shows the reason for this. In spite of the fact that ethyl-β-ionol is a *trans*-diene, interference between one of the ring *gem*-methyl groups and a side-chain hydrogen brings about a steric configuration resembling that of type Ia.[20]

Other examples of non-*cis*-dienes having a break in coplanarity due to methyl–hydrogen hindrance, and consequently exhibiting spectral degradation, are to be found in 1,1,3-trimethylbutadiene (λ_{max} 232 mμ, ϵ 8,500),[21] and 2,4,7-trimethylocta-2,4-dien-7-ol (λ_{max} 229 mμ, ϵ 8,000).[22]

In contrast to the above-mentioned spectral effects are those of *unhindered* terminal *cis* configurations. It is now well established that such *cis*-monoölefins and mono-*cis*-dienes have their absorption maxima at somewhat *higher* wave lengths than the corresponding *trans* isomers.[14] Although this appears contrary to the usually assumed relationship between *cis* and *trans* isomers, gradually accumulating evidence appears to indicate that this may turn out to be the general rule for polyenes with unhindered terminal *cis* configurations. Thus neovitamin A shows λ_{max} 328 mμ as compared to 325 mμ for all-*trans*-vitamin A, and 4,5-*cis*-XXIII shows λ_{max} 274 as compared to λ_{max} 271 mμ for

$$\text{CH}=\text{CH}-\overset{\overset{\displaystyle \text{CH}_3}{|}}{\underset{\underset{\displaystyle \text{OH}}{|}}{\text{C}}}-\text{CH}=\text{CH}-\text{CH}=\overset{\overset{\displaystyle \text{CH}_3}{|}}{\text{C}}-\text{CH}=\text{CH}_2$$
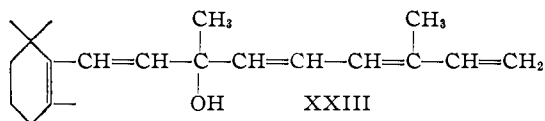
XXIII

4,5-*trans*-XXIII.[23] This seemingly anomalous situation need not be too surprising if it is borne in mind that the effective length[24] of a polyene chromophore is not decreased by an unhindered terminal *cis* configuration as it is with internal *cis* configuration.

Examples of spectral degradation arising from hindered *interior cis* configurations (type I) are to be found in the pentaenes I, XVII and XIX described herein and in mono- and di-*cis*-III[25] recently reported by the Karrer school. Instead of the usual hypsochromic shift of 3–7 mμ, minor drop in extinction, and retention of fine structure encountered with unhindered internal *cis* configurations, the above compounds exhibit radically altered spectra. The main band suffers an unusually large drop in extinction, loses its fine structure, and appears simply as a long broad curve of very low slope. Its ill-defined maximum is hypsochromically displaced from that of the *trans* isomer by about

(20) W. Oroshnik, G. Karmas and R. A. Mallory, THIS JOURNAL, **76**, 2325 (1954). This type of hindrance was first noted in β-ionone by E. A. Braude, *et al.*, *J. Chem. Soc.*, 1890 (1949).

(21) J. C. Lunt and F. Sondheimer, *ibid.*, 2957 (1950). While this compound shows the hypsochromic degradation to be expected from methyl-hydrogen hindrance, there is surprisingly none of the expected hypsochromic effect.

(22) E. A. Braude and J. A. Coles, *J. Chem. Soc.*, 1425 (1952).

(23) Unpublished observation in this Laboratory.

(24) The straight-line distance between the terminal carbons of the chromophore.

(25) The triene, 4,5-*cis*-XIII, and di-*cis*-lycopene are, of course, also such examples. However, since the former was not obtained in sufficient steric purity to establish its true spectral characteristics, and since the spectral data for di-*cis*-lycopene in the region below 330 mμ were not published, these compounds are not further discussed here.

40 mμ in the pentaenes, 50 mμ in mono-*cis*-III[26] and 60 mμ in di-*cis*-III.[26]

In each of the above compounds, three small inflections (sometimes very minor peaks) appear in the main band at positions corresponding roughly to those of the three main absorption

Fig. 14.

peaks of the all-*trans*-isomer. Although this resembles *trans* contamination, the steric purity of mono- and di-*cis*-III and of 4,5-*cis*-XVII ethyl ether, all of which were obtained crystalline, leaves no doubt that these inflections represent a specific mode of vibration inherent in these hindered *cis* compounds.

Perhaps the most striking feature of the absorption curves of the type I *cis* compounds is the very strong subsidiary peak at the lower wave lengths, which in the pentaenes is considerably higher than the main peak and in di-*cis*-III is about the same height as the main peak. This strong peak in the case of 4,5-*cis*-I was referred to in Part I as a *cis* peak. However, it is felt at present that these bands are of different origin from the *cis* peaks first recognized by Zechmeister and his collaborators in the spectra of the carotenoids. True *cis* peaks are considered, according to present theory, to be the first overtone of the main band, and are correlated with coplanar *cis* bending of the molecule. Their location is independent of the position of the *cis* bond and so is the same for all members of a set of stereoisomers. Their extinction coefficients, however, are dependent on the amount of bending of the molecule, being highest with a centrally located *cis* bond and decreasing as the *cis* bond is shifted toward the terminus of the chromophore.[3]

In the present compounds, any rationalization of the strong subsidiary bands must take into account the partial chromophores that would be expected to arise from the break in coplanarity. That this break is very large follows from the very low extinction and hypsochromic displacement of the main bands, which indicate that electronic vibrations across the entire polyene chain are attained to only a minor degree. In the pentaenes, for example, electronic vibrations would consequently tend to be confined to the triene and diene partials produced by the break in coplanarity, and a prominent absorption band in the lower wave lengths should therefore be expected.

It so happens that the normal *cis*-peak for these pentaenes appears in the region 250–260 mμ[27] which coincides with the location of the observed

(26) In estimating the position of the λ_{max} of the main band the triplet system of inflexions or small peaks, referred to subsequently in the text, was ignored, as being another mode of vibration of the molecule superimposed on the main band. Corrected in this way, the curves of mono-*cis*-III and di-*cis*-III show λ_{max} *ca.* 420 mμ and λ_{max} 410 mμ, respectively, for their main bands.

(27) This assumption is based on the data obtained for phytofluene [J. F. Petracek and L. Zechmeister, THIS JOURNAL, **74**, 184 (1952)] whose absorption spectrum, $\lambda\lambda$ 331, *348* and 367 mμ, indicates it has either the same chromophore present in I or one closely related to it.
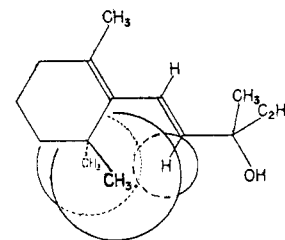
subsidiary bands, 254–255.5 mμ. It is therefore not possible here to estimate the extent of the contribution of the *cis* peak to these bands.

In mono-*cis*-III,[5] the break in coplanarity would be expected to set up a phenyltriene and a tetrasubstituted phenylhexaene chromophore. The strong subsidiary band at 298 mμ corresponds in location with that expected for the former, but the expected λ_{max} of the latter chromophore (*ca.* 400 mμ) falls within the area of the main band and hence cannot be distinguished here. In this compound the *cis* peak is well outside the range of either partial, appearing at 366 mμ. The distance between this peak and the longest-wave-length band of the all-*trans* isomer, 137.5 mμ, corresponds closely to that found in the carotenoids (142 mμ ± 2 mμ[3]).

The stronger 298-mμ band in di-*cis*-III[5] is adequately accounted for by the two phenyltriene chromophores arising from the two hindered *cis* bonds. The remaining tetrasubstituted triene chromophore, with an expected λ_{max} of *ca.* 280 mμ, is indistinguishable in the spectrum, and is probably merged into the large general absorption in this area. As would be expected from the straight over-all form of the molecule, this compound does not show the *cis*-peak observed in the spectrum of mono-*cis*-III.

B. The Acetylenic Polyenes.—The spectra of the acetylenic precursors of I, XVII, XIX, III, and of lycopene, show the normally expected hypsochromic and hypochromic displacement of their main bands from those of the *trans* isomers. However, each exhibits, in addition, a subsidiary band of high extinction at practically the same wave length as that of the derived sterically hindered *cis*-polyene, indicating the presence of similar partial chromophores in both. These, however, cannot be due alone to the inhibition of resonance caused by the acetylenic group, for some acetylenic polyenes are known, such as 9,9'-dehydro-β-carotene[28] and 8,9-dehydrocrocetin,[29] which show no subsidiary bands either in the *cis*-peak region or where their presumed partials would be expected to absorb.

An inspection of the structural differences between these two groups of acetylenic polyenes indicates that methyl substitution alpha to the triple bond may be the factor that enables the acetylenic bond to cause an appreciable break in conjugation. For example, the 3-methyl group in the 4,5-dehydropentaenes, coming at the end of a triene chromophore, may through its hyperconjugation with this triene divert electronic vibrations to an appreciable extent from across the acetylenic group. The resulting triene and enyne partials would correspond to the triene and diene partials of the related hindered *cis*-pentaene.

In 5-monodehydro-III[5] the 7-methyl group defines two partials, a phenyldienyne and a phenylhexaene. The very strong subsidiary band at 301 mμ is consistent with the former. The phenylhexa-

ene partial, however, being tetrasubstituted, would be expected to have its band around 400 mμ, and would therefore be masked by the main band of the total chromophore.

In 5,13-bisdehydro-III,[5] the methyl groups at carbons 7 and 12 demark two phenyldienyne partials and the resulting subsidiary band (λ_{max} 299 mμ) should therefore show considerably greater extinction than that of monodehydro-III. This is indeed observed (ϵ *ca.* 72,000 as compared to ϵ *ca.* 55,000). As in the analogous di-*cis*-III, the triene partial is not obvious in the spectrum. Bisdehydrolycopene[5] shows an almost identical spectrum.

The absorption spectrum of the recently reported 1,2-dehydrovitamin A (XXIV), (ϵ_{252} mμ 19,400,

$$\text{C}{\equiv}\text{C}-\overset{\overset{\displaystyle CH_3}{|}}{\text{C}}{=}\text{CH}-\text{CH}{=}\text{CH}-\overset{\overset{\displaystyle CH_3}{|}}{\text{C}}{=}\text{CH}-\text{CH}_2\text{OH}$$

XXIV

ϵ_{328} mμ 35,000)[30] also falls into line with the α-methyl hypothesis, the methyl group at carbon 3 defining a triene and an enyne partial.

The situation in 5,6-dehydrovitamin A (XXV)[31] is somewhat different.

$$-\text{CH}{=}\text{CH}-\overset{\overset{\displaystyle CH_3}{|}}{\text{C}}{=}\text{CH}-\text{C}{\equiv}\text{C}-\overset{\overset{\displaystyle CH_3}{|}}{\text{C}}{=}\text{CH}-\text{CH}_2\text{OH}$$

XXV

In this compound the 7-methyl group alpha to the triple bond should define, according to the above hypothesis, a trienyne and a single olefinic chromophore, but no evidence of any partials is seen in its spectrum. If the "α-methyl" hypothesis is true this would imply that the 7-methyl group here is not effectively hyperconjugated with so short a partial chromophore as a single bond. There is strong evidence in support of such an assumption. From the spectral data of the simple vinylacetylenes[32] it can be seen by the lack of bathochromic effects that a methyl group in the middle of an enyne system is not hyperconjugated with the chromophore.

In the non-isoprenoid acetylenic polyenes, these correlations do not hold. The multiplicity of subsidiary bands in such compounds as XXVI[33] has yet to be rationalized with their structure.

$$\underset{\overset{|}{\text{OH}}}{\text{H}_3\text{CCH}}-(\text{CH}{=}\text{CH})_3-\text{C}{\equiv}\text{C}-(\text{CH}{=}\text{CH})_3-\underset{\overset{|}{\text{OH}}}{\text{CHCH}_3}$$
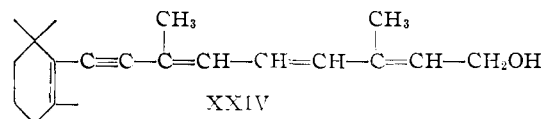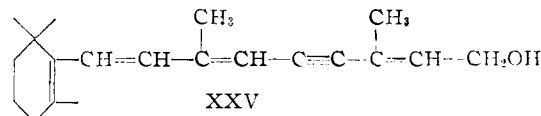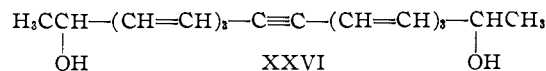
XXVI

(28) H. H. Inhoffen, F. Bohlmann, K. Bartram, G. Rummert and H. Pommer, *Ann.*, **570**, 54 (1950).

(29) H. H. Inhoffen, O. Isler, G. von der Bey, G. Raspe, P. Zeller and R. Ahrens, *ibid.*, **580**, 7 (1953).

(30) 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).

(31) Only the methyl ether of this compound has been described (Part II).[14] The published absorption curve shows a subsidiary band around 225 mμ but this has now been found to be due to an impurity. The free alcohol, synthesized in this Laboratory, likewise shows no subsidiary peaks. This will be reported in a later publication.

(32) 3-Methylpent-2-en-4-yne shows λ_{max} 219.5 mμ [1. M. Heilbron, A. W. Johnson, E. R. H. Jones and R. A. Raphael, *J. Chem. Soc.*, 265 (1943)] as compared to 219.5 mμ for its unmethylated analog [G. Eglinton and M. C. Whiting, *ibid.*, 3650 (1950)]. Methylation of vinylacetylene (λ_{max} 219 mμ) to 2-methylbut-1-en-3-yne actually produces a hypsochromic effect of 1.5 mμ. Measurements on the latter compound, which was kindly furnished us by Air Reduction Co., Inc., Murray Hill, N. J., were made in this Laboratory.

(33) 1. M. Heilbron, E. R. H. Jones and R. A. Raphael, *J. Chem. Soc.*, 137 (1944).

The Infrared Spectra

To corroborate the steric configurations assigned in the present work, the infrared spectra of all the *cis–trans* pairs were examined with particular reference to bands around 10.35 μ, the *trans* —CH=CH— region, and to those around 13–15 μ, the *cis* —CH=CH— region.[34]

In all cases, the *trans* configurations were confirmed readily by a very strong band at or near 10.35 μ.

However, the identification of *cis* —CH=CH— configurations by specific absorption bands in the 13–15 μ region is not easy. In the first place the exact location of *cis* bands seems to be subject to considerable variation depending on the type of compound involved. For example, most *cis*-mono-olefins will exhibit a *cis* band somewhere between 13.7 and 14.8 μ,[35] but very recent data show that conjugation on each side of the *cis* double bond can cause a pronounced hypsochromic shift in this band (to 12.88 μ in 8,8'-*cis*-crocetin dimethyl ester,[36] and 12.84 μ in 9,9'-*cis*-β-carotene[37]). Furthermore, in addition to being relatively weak, *cis* bands are often found overlapping with other bands normally occurring in this region, such as that due to the methylene wagging mode of vibration.[38] For these reasons a reliable identification of *cis* bands can be made only by comparison with the *trans* isomer, which has been the criterion followed in the present work.

All of the type I *cis*-polyenes studied herein exhibited a well-defined *cis* band at 13.0–13.15 μ, in accord with the hypsochromic shift to be expected from conjugation (Fig. 18). The larger shift observed with *cis*-crocetin and cis-β-carotene is undoubtedly due to the longer conjugated chromophores on each side of the *cis* double bond.

The type Ia compounds, where conjugation exists only on one side of the *cis* double bond, appear to fall into two groups: (a) those with no functional groups allylic to the *cis* bond, and showing a *cis* band at 13.43–13.8 (VIII, IX, XVIa and XVIb) (Figs. 15–17), and (b) those having allylic hydroxyl or acetoxy groups, showing this band shifted to 13.05–13.15 (V and its 9-methyl ether, and XVIc and its acetate) (Figs. 15, 17). It would appear from these data that a hyperconjugated hydroxyl or acetoxy group can cause a hypsochromic shift of the *cis* band comparable to that observed above with conjugation. A similar shift has been reported in the allylic chlorides, *cis*-crotyl chloride (13.1 μ)[39] and 1,4-dichloro-*cis*-2-butene (13.1 μ).[40]

No effects in the infrared spectra that can be at-

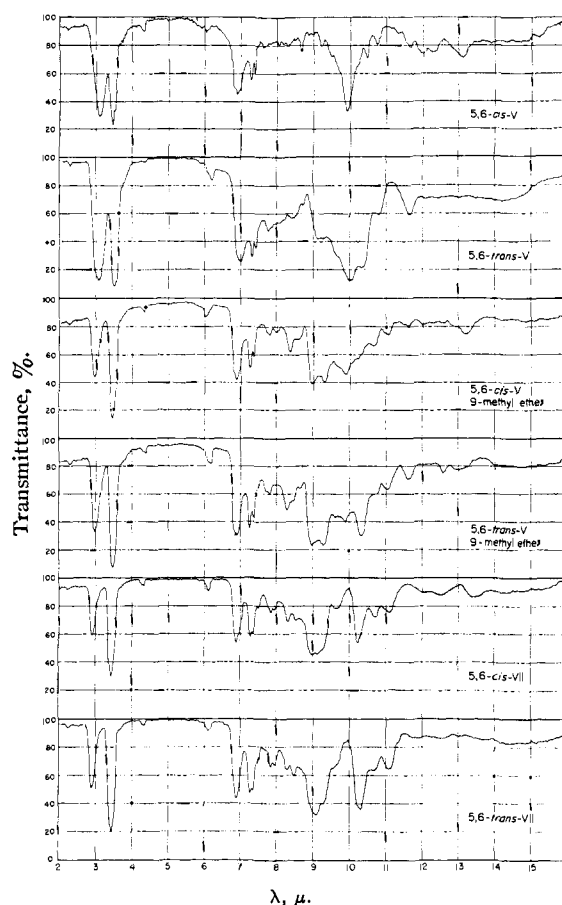tributed to the steric hindrance present are immediately apparent.

λ, μ.

Fig. 15.

It is of interest to note the small amount of "*trans*-like" vibration (band around 10.4 μ) in the infrared spectra of 4,5-*cis*-I, 4,5-*cis*-XVII and 4,5-*cis*-XVII ethyl ether (Fig. 18)[41] which possibly bears some connection to the "*trans*-like" vibration observed in the ultraviolet spectra of these compounds (see preceding section).

Experimental[42]

General Procedures.—The following procedures were used unless otherwise stated. Work-up of reaction mixtures consisted of quenching with water (or other solutions as indicated), partitioning with petroleum ether (b.p. 30–60°), washing as indicated, and drying by filtering through anhydrous potassium carbonate. Concentration was always carried out at water-pump vacuum. Ether was avoided whenever possible because of its tendency to acquire peroxides.

All distillations at 0.01 mm. or less were performed from a simple Claisen flask (with sealed-on condenser) immersed in an oil-bath up to its take-off side-arm. The large distillation ranges frequently noted are indicative of super-

(34) (a) R. S. Rasmussen and R. R. Brattain, *J. Chem. Phys.*, **15**, 120, 131 (1947); (b) N. Sheppard and G. B. B. M. Sutherland, *Proc. Roy. Soc. (London)*, **A196**, 195 (1949); (c) J. A. Anderson, Jr., and W. D. Seyfried, *Anal. Chem.*, **20**, 998 (1948); (d) O. D. Shreve, M. R. Heether, H. B. Knight and D. Swern, *ibid.*, **22**, 1498 (1950).

(35) H. L. McMurry and V. Thornton, *ibid.*, **24**, 318 (1952).

(36) R. Kuhn, H. H. Inhoffen, H. A. Staab and W. Otting, *Chem. Ber.*, **86**, 965 (1953).

(37) L. Zechmeister, *Experientia*, **10**, 9 (1954).

(38) N. Sheppard and G. B. B. M. Sutherland, *Nature*, **159**, 739 (1947). A good example is the *cis–trans* pair, oleic and elaidic acids, both of which exhibit a band at 13.7 μ. In the *cis*-olefin this band is much stronger.[34d]

(39) L. F. Hatch and S. S. Nesbitt, THIS JOURNAL, **72**, 727 (1950).

(40) K. Mislow and H. M. Hellman, *ibid.*, **73**, 243 (1951).

(41) The 10.4 μ band in 4,5-*cis*-XIX is much stronger and, while undoubtedly containing some contribution from this effect, is due essentially to the other —CH=CH— double bond in the molecule, which is *trans*. That in 5,6-*cis*-VIII is due to the *trans*-1,2-double bond (cf. other β-ionols discussed in Part IV[10]).

(42) (a) The products denoted in this section with an asterisk are those whose absorption curves appear in the figures. (b) The spectra given for *cis*- and *trans*-XVII ethyl ether were taken in 10% solution, using CCl₄ from 2 to 7.5 μ and CS₂ from 7.5 to 16 μ; cell length 0.2 mm.
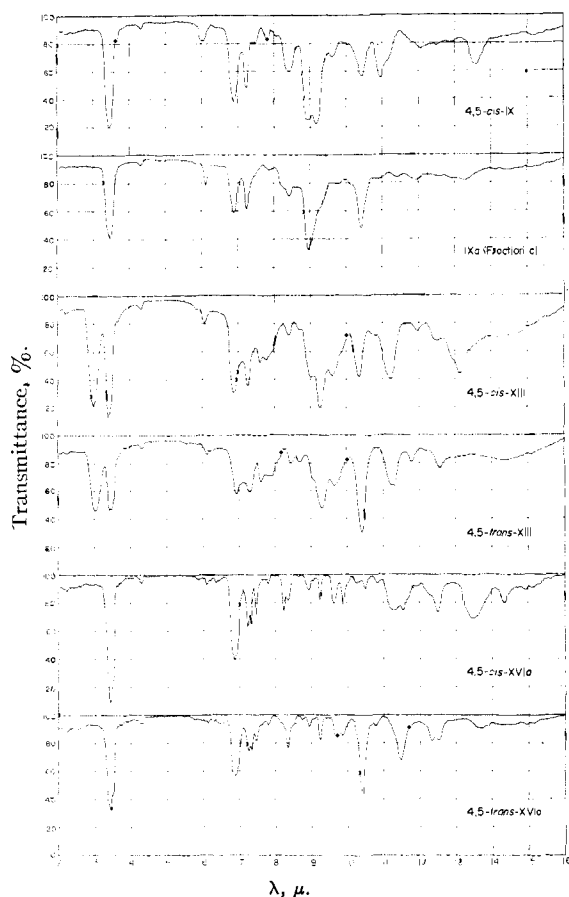
Fig. 16.

heating rather than a mixture of fractions. A 20-cm. vacuum-jacketed Vigreux column was used for distillations at pressures greater than 0.01 mm.

Alcoa F-20 alumina was used for all the chromatographic separations. It was deactivated or neutralized, when indicated, by adding the specified amount of water or 1.5 N acetic acid and mixing on a ball-mill for an hour. The chromatograms were in most cases developed with petroleum ether and eluted with increasing proportion of ether and in some cases a little methanol. Elution was followed spectrally (ultraviolet).

Catalytic semi-hydrogenation was carried out at room temperature and atmospheric pressure in a Parr apparatus. Only the theoretical amount of hydrogen was admitted.

For stereoisomerization, 10 mg. of iodine in 250 ml. of petroleum ether was used for each gram of compound. The solution was stirred under nitrogen at room temperature and in ordinary artificial light for the specified time and then immediately washed with sodium thiosulfate solution.

Ultraviolet absorption spectra were determined in 95% ethanol with a Beckman DU spectrophotometer. The infrared spectra were determined on neat samples of the same specimens with a Baird double-beam spectrophotometer, by Samuel P. Sadtler and Son, Inc., of Philadelphia, Pa.

Dienes

5,6-cis-V.—The product herein designated as having this configuration is the crystalline isomer described by Isler, et al.,[13,43a]* who obtained it by catalytically semi-hydrogenating the corresponding 5,6-dehydro compound[43a] (λ_{max}. 228.5 mμ, ϵ 15,300*).

The 9-methyl ether of 5,6-cis-V[43b] was obtained by semi-hydrogenation of 11.0 g. of 5,6-dehydro-V-9-methyl ether[43b] (λ_{max}. 228.5 mμ, ϵ 15,000*) in 25 ml. of isoöctane with 1 g.

(43) (a) We are indebted to Dr. J. A. Aeschlimann, Hoffmann–La Roche, Inc., Nutley, N. J., for samples of the 5,6-dehydro compound and its pure crystalline semi-hydrogenation product. (b) O. Isler, A. Ronco and M. Kofler, Festschrift E. C. Barell, 31 (1946).
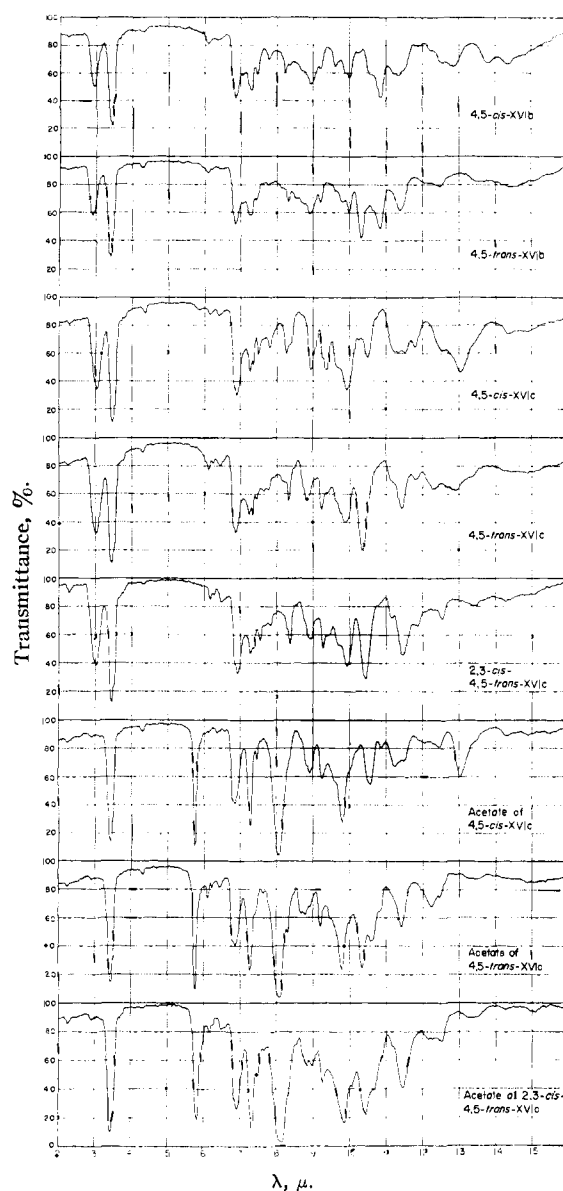
Fig. 17.

of Lindlar poisoned-palladium catalyst[44] and 0.36 ml. of quinoline[45]; yield on distillation: 9.4 g. at 112–118° (0.001 mm.), $n^{22}D$ 1.5150.*

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; methoxyl, 9.74. Found: C, 79.17; H, 10.96; methoxyl, 9.65.

5,6-trans-V.—A solution of 12.0 g. of 5,6-dehydro-V[43a] in 50 ml. of dry ether was added, at 0°, to a suspension of 1.4 g. of commercial LiAlH$_4$ in 450 ml. of dry ether. A bulky precipitate formed which went into solution on warming. After refluxing for two hours, the solution was cooled and hydrolyzed at −20° with 100 ml. of 70% methanol. The precipitated alumina was filtered off, and the filtrate worked up with water and added petroleum ether. Distillation yielded 7.0 g. of product as a very thick viscous liquid, col-

(44) H. Lindlar, Helv. Chim. Acta, 35, 446 (1952).

(45) The semi-hydrogenation of this acetylene with Lindlar catalyst produced no sharp cut-off at the theoretical end-point as has been reported in the case of 5,6-dehydro-V.[44] There was instead a general decrease in the rate of absorption and unless hydrogenation was interrupted at the theoretical end-point, considerable overhydrogenation would occur. In some experiments, a large drop in the rate of absorption occurred long before the theoretical end-point, necessitating further addition of catalyst.

lected at 145–155° (0.001 mm.), n^{23}D 1.5375, λ_{max}. 239 mμ, ϵ 17,800.

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.88; H, 10.59. Found: C, 79.10; H, 10.69.

An undistilled reaction product obtained as described above from 6.0 g. of the enyne was dissolved in petroleum ether and chromatographed on a 3 × 60 cm. column of alumina deactivated with 10% of water. Elution was carried out at first with 25% ether. This removed a small fraction consisting of a conjugated tetraene, $\lambda\lambda_{max}$. 292.5, *304* and 318.5 mμ. (This fraction was also visible in the spectrum of the crude undistilled product.) Following this (50% ether) came a very small quantity of product showing only "end absorption." Elution into this fraction was continued until a diene peak at 237 mμ appeared.

The fraction showing a constant spectrum, λ_{max}. 237–238 mμ, was collected as the desired product (75–100% ether) and yielded 3.6 g. after concentration. On distillation it came over at 145–148° (0.003 mm.), n^{20}D 1.5406; λ_{max}. 237.5 mμ, ϵ 19,700.*

Anal. Found: C, 79.14; H, 10.46.

The 9-methyl ether was obtained similarly but at 0°,[46] from 10.7 g. of the corresponding dehydro methyl ether,[43] 0.85 g. of commercial lithium aluminum hydride and 200 ml. of dry ether. Chromatography was omitted. Distillation yielded 6.6 g. of product at 120–125° (0.001 mm.), n^{22}D 1.5266; λ_{max}. 237.5 mμ, ϵ 18,300.*

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; methoxyl, 9.74. Found: C, 79.41; H, 10.65; methoxyl, 9.40.

Allylic Rearrangement of V and its 9-Methyl Ether.—Rearrangements of the free glycol usually were accompanied by dehydration. It was therefore completely acetylated, and the diacetate rearranged.

A solution of 1.25 g. of *cis*- or *trans*-V in a mixture of 5 ml. of pyridine and 2.5 ml. of acetic anhydride was allowed to stand under nitrogen for 15 hr. The mixture was worked up with water and petroleum ether, washing twice with 5% sulfuric acid to remove the pyridine and finally with water and sodium bicarbonate solution. After drying and concentration the diacetate was dissolved in 20 ml. of glacial acetic acid, and allowed to stand under nitrogen for 18 hr. After work-up and removal of volatiles (0.001 mm.), the product from *cis*-V showed λ_{max}. 280 mμ, $E^{1\%}_{1\,cm}$ 780; from *trans*-V, λ_{max}. 280 mμ, $E^{1\%}_{1\,cm}$ 710.

The *cis*- and *trans*-9-methyl ethers rearranged smoothly under the above conditions without prior acetylation. The product from the *cis*-ether showed λ_{max}. 280 mμ, $E^{1\%}_{1\,cm}$ 985; from the *trans*-ether λ_{max}. 280 mμ, $E^{1\%}_{1\,cm}$ 995.

5,6-*cis*-VII.—This compound, λ_{max}. 229 mμ, ϵ 14,600,* was prepared by the semi-hydrogenation of 5,6-dehydro-VII, λ_{max}. 228 mμ, ϵ 17,000,* as described in Part II.[14]

5,6-*trans*-VII.—A wet pressed-out filter cake of chromous acetate[47] containing approximately 42 g. of the salt, was added to a stirred solution of 23 g. of sodium hydroxide (95%) in 100 ml. of water. Methanol was used to wash in the last portions of the salt. After stirring the purple suspension under nitrogen for one-half hour, a solution of 9.7 g. of 5,6-dehydro-VII in 50 ml. of methanol was added. The reaction mixture was brought to a volume of 400 ml. by the addition of more methanol, and allowed to stir under nitrogen at room temperature for four days. It was then poured into an equal volume of ether, filtered and the filtrate worked up with water and additional ether. Distillation yielded 8.5 g. of product at 115–125° (0.001 mm.). A small amount of dehydration product present (small band in the ultraviolet at 300–315 mμ) was removed by chromatography. The pure product distilled at 115° (0.003 mm.), n^{21}D 1.5210; λ_{max}. 235.5 mμ, ϵ 22,100.*

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; methoxyl, 9.74. Found: C, 79.42; H, 10.80; methoxyl, 9.43.

3-Methylpent-2-en-4-yne.—This enyne has been reported to be obtainable in 30–40% yields by dehydrating methylethylethynylcarbinol in acetic anhydride catalyzed with sulfuric acid.[48] The procedure described below was found

(46) Refluxing the reaction mixture causes extensive demethoxylation.

(47) 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.

(48) A. F. Thompson, Jr., J. G. Burr and E. N. Shaw, THIS JOURNAL, **63**, 186 (1941).

λ, μ.
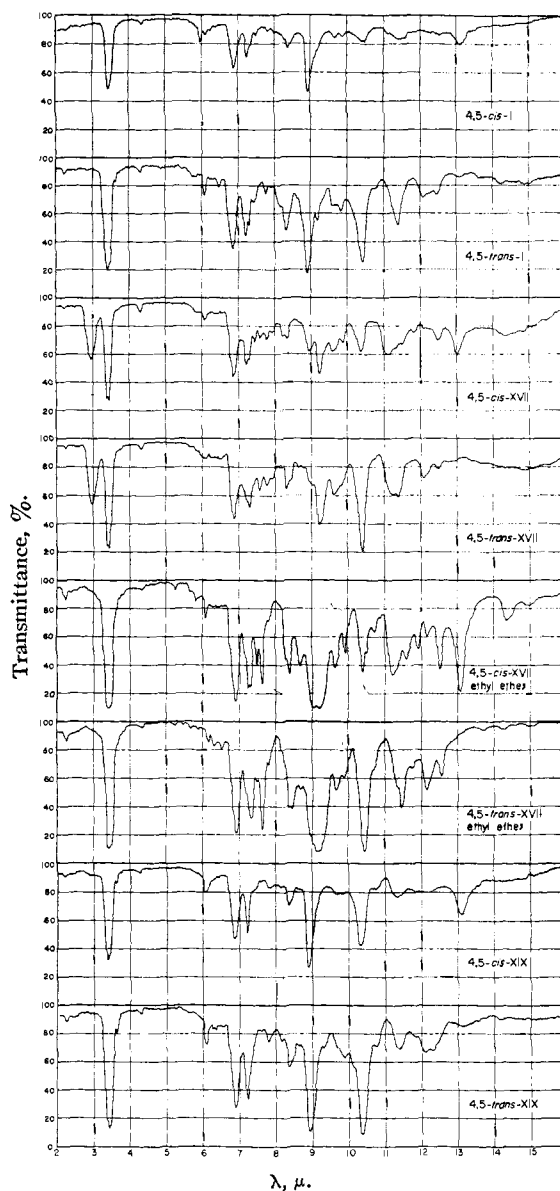
Fig. 18.[42]

to be considerably simpler and to give much better yields.

A solution of 154 g. of phosphorus oxychloride in 600 ml. of pyridine was added slowly to a stirred solution of 100 g. of methylethylethynylcarbinol in 600 ml. of pyridine. The temperature was maintained at 30–35° during the addition. The flask was then fitted with a 45-cm. Vigreux column, and the mixture slowly distilled during several hours until the distillate temperature reached 100°. Without further treatment, the distillate was redistilled through a 20-cm. vacuum jacketed Vigreux column; yield 52.0 g. (63%), b.p. 68–69°, n^{23}D 1.4370; λ_{max} 220.5 mμ, ϵ 10,700. (Thompson, *et al.*,[48] reported b.p. 68–71°.)

VIII (4,5-Dehydro-IX).—A solution of 64.4 g. of 3-methylpent-2-en-4-yne in 1500 ml. of dry ether was treated at 10° with 387 ml. of 2.2 M ethylmagnesium bromide. The solution was allowed to stand at room temperature overnight and then refluxed for seven hours. On cooling to 10°, 131 g. of 1-chloro-2-methyl-4-methoxybut-2-ene[49] was added followed by 5.0 g. of anhydrous cupric chloride. The mixture soon turned a deep maroon color which remained for about an hour. It was allowed to stir at room temperature overnight.

The light brown mixture, which now contained consid-

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

erable precipitated salt, was cooled to $-30°$ and hydrolyzed with 30% ammonium acetate solution. The ether layer was separated and, without drying, concentrated under vacuum in the presence of 75 ml. of diethylamine and the whole allowed to stand under nitrogen for 24 hours. The mixture was then poured into water and the product taken up in petroleum ether. After two water washes to remove the bulk of the excess diethylamine and several washes with 20% acetic acid to remove the 1-diethylamino-2-methyl-4-methoxybut-2-ene, the organic layer was washed with sodium bicarbonate solution, dried and concentrated. Distillation yielded 80.6 g., b.p. 90–94° (3.2 mm.), $n^{20}D$ 1.4920; λ_{max}. 224 mμ, ϵ 13,800.*

Anal. Calcd. for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.95; H, 10.02.

4,5-*cis*-IX.—A solution of 16.2 g. of 4,5-dehydro-IX in 50 ml. of isoöctane was hydrogenated with 1.0 g. of Lindlar catalyst.[45] Distillation gave 14.5 g. of product at 48–52° (0.25 mm.) ($n^{20}D$ 1.4765) and 1.8 g. ($n^{20}D$ 1.4822) of a higher boiling product. The main fraction was redistilled; yield 9.1 g., b.p. 56–59° (0.6 mm.), $n^{20.5}D$ 1.4753; λ_{max}. 225.5 mμ, ϵ 5,900.*

Anal. Calcd. for $C_{21}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.88; H, 11.21.

Alkali Isomerization of 4,5-*cis*-IX to the Conjugated Triene IXa.—A solution of 9.1 g. of 4,5-*cis*-IX in 200 ml. of 2 M absolute ethanolic potassium hydroxide was refluxed under nitrogen until the λ_{max}. had shifted from 226 to 275 mμ, and no longer showed a tendency to change. This required about four hours. After work-up the product was distilled, cutting three fractions: (a) 0.9 g. at 50–56° (0.5 mm.), $n^{22.5}D$ 1.5012, λ_{max}. 280 mμ. This was discarded.

(b) 4.2 g. at 56–62° (0.5 mm.), $n^{22.5}D$ 1.4959, λ_{max}. 270 mμ, $E_{1cm}^{1\%}$ 537, λ_{infl} 250 mμ. *Anal.* Calcd. for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 80.04; H, 11.30. The infrared spectrum showed bands at 10.4 and 13.1 μ of about equal intensity, indicating a *cis–trans* mixture. The presence of *cis* isomer in this specimen of triene was confirmed by the shift of the ultraviolet spectrum to that of 4,5-*trans*-XIII, λ_{max}. 274.5 mμ (Fig. 6), upon treatment with iodine.

(c) 1.3 g. at 64–69° (0.5 mm.), $n^{22}D$ 1.5179; λ_{max}. 275 mμ, $E_{1cm}^{1\%}$ 1190. *Anal.* Calcd. for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.97; H, 10.95. The infrared spectrum (Fig. 16) showed a strong *trans* band at 10.4 μ, with the *cis* band at 13.1 μ barely perceptible. On this basis the product was identified as a *cis–trans* mixture like fraction b, but considerably richer in *trans* isomer.

Attempts to isolate the pure *cis*- or *trans*-triene by alumina chromatography failed.

Trienes

Preparation of X (4,5-Dehydro-XII).—A Grignard reagent from 49.5 g. of 3-methylpent-2-en-4-yne was prepared as described above under 4,5-dehydro-IX. A solution of 66 g. of tiglic aldehyde in an equal volume of ether was then added at 0°, and the mixture was refluxed for 30 min. Hydrolysis was effected at $-20°$ with 30% ammonium acetate. After work-up of the ether layer distillation gave 79.6 g., b.p. 87–88° (1.2 mm.), $n^{20}D$ 1.5050; λ_{max}. 227 mμ, ϵ 13,600.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.14; H, 9.78.

Allylic Rearrangement of X to XI.—A solution of 10.0 g. of X in 150 ml. of glacial acetic acid containing 150 mg. of tosic acid monohydrate was allowed to stand under nitrogen for one hour. A spectroscopic probe showed rearrangement was then complete; *i.e.*, λ_{max}. 227 mμ → λ_{max}. 267 mμ (without tosic acid the reaction was very slow). After work-up, distillation yielded 10.5 g. of the acetate, b.p. 83–86° (0.8 mm.), $n^{20.5}D$ 1.5078; λ_{max}. 268 mμ, ϵ 18,100.*

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.89; H, 8.72.

A 38-g. sample of the acetate was hydrolyzed by refluxing for 15 minutes in 200 ml. of 5% methanolic sodium hydroxide, and then worked up and distilled; yield 29.3 g., b.p. 79.5–81.5° (0.6 mm.), $n^{21}D$ 1.5301; λ_{max}. 267.5 mμ. ϵ 16,800.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.10; H, 9.74.

4,5-*cis*-XIII.—A solution of 30.1 g. of XI and 0.8 ml. of quinoline in 250 ml. of isoöctane was semi-hydrogenated with 4 g. of Lindlar catalyst.[45] The absorption curve of the

crude product showed a single broad irregular band with a maximum at 267 mμ.

The filtered solution was poured onto a 3 × 100-cm. column of alumina deactivated with 5% of water, and the chromatogram was developed with 10% ether–petroleum ether until the emergence of a narrow yellow band immediately preceding the main zone. Thereafter, 20% ether was used. The first half of the main zone contained a diene, λ_{max}. 240 mμ (overhydrogenation product); in the last portion of the main zone the spectrum of unchanged XI began to appear. Only eluate producing a clean *trans*-triene curve free of these contaminants, when a drop was stereoisomerized with iodine and light, was accepted. The relative extinctions at 250 and 267 mμ varied considerably during elution. Yield was 3.8 g., b.p. 61–63° (0.2 mm.), $n^{20}D$ 1.5320; $\lambda\lambda_{max}$. 249.5 mμ (ϵ 11,700), 267.5 mμ (ϵ 11,900).*

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.28; H, 10.89.

Similar results were obtained with Raney nickel. Semihydrogenation of the acetate was equally unspecific.

Stereoisomerization of 4,5-*cis*-XIII to the *trans*-Isomer.—A solution of 13 mg. of 4,5-*cis*-XIII and 0.5 mg. of iodine in 100 ml. of 95% ethanol (or isoöctane) was irradiated for one minute with a 500-watt lamp. The absorption curve then was that shown for the *trans* isomer in Fig. 6; λ_{max}. 274 mμ, $E_{1cm}^{1\%}$ 1520.

Reduction of X to 4,5-*trans*-XII.—A 25.5-g. sample of X was reduced with 4.1 g. of commercial LiAlH$_4$ in 550 ml. of dry ether in the same manner as described above under 5,6-*trans*-V. Distillation yielded 15.7 g. of product, b.p. 63–66° (0.25 mm.), $n^{20}D$ 1.5045; λ_{max}. 236 mμ, ϵ 17,000.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.56; H, 10.70.

Allylic Rearrangement of 4,5-*trans*-XII to 4,5-*trans*-XIII.—A solution of 10.2 g. of 4,5-*trans*-XII in 100 ml. of glacial acetic acid was allowed to stand under nitrogen for two hours and then for an additional hour with 50 ml. of added acetic anhydride, to assure complete acetylation. After working up, distillation yielded 5.0 g. of acetate, b.p. 85–88° (0.6 mm.), $n^{20}D$ 1.5303; λ_{max}. 275 mμ, ϵ 37,600.

Anal. Calcd. for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.95; H, 9.66.

A 5.0-g. sample of the above acetate was hydrolyzed by refluxing for 10 min. in 60 ml. of 5% methanolic sodium hydroxide. Work-up and distillation yielded 3.1 g. of carbinol, b.p. 80–81° (0.3 mm.). The first two-thirds of this fraction showed $n^{20}D$ 1.5567, λ_{max}. 274.5 mμ, ϵ 39,800 and the last third $n^{20}D$ 1.5601, λ_{max}. 274.5 mμ, ϵ 41,400.* The latter is judged on this basis to be more nearly pure all-*trans* isomer. Analytically both were identical.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.25; H, 10.84.

Tetraenes

Preparation of XIVa.—A stirred solution of 21.8 g. of 1-hexyne in 300 ml. of dry ether was treated at 0° with 130 ml. of 2.1 M ethylmagnesium bromide and refluxed for 90 minutes, by which time evolution of ethane had ceased. It was then cooled to 0°, and a solution of 45 g. of β-ionone ($\epsilon_{296\ m\mu}$ 10,300) in 50 ml. of dry ether was added. The mixture was refluxed for 30 minutes, cooled to $-30°$ and hydrolyzed with 30% ammonium acetate. Work-up and distillation yielded 56.1 g. of product at 100–104° (0.001 mm.), $n^{22}D$ 1.4987. The ultraviolet absorption curve showed no unreacted β-ionone; λ_{max}. 236 mμ, ϵ 6,100.

Anal. Calcd. for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.05; H, 11.19.

Allylic Rearrangement–Dehydration of XIVa to XVa.—A solution of 30.0 g. of XIVa in 500 ml. of glacial acetic acid containing 100 mg. of tosic acid monohydrate was allowed to stand overnight under nitrogen and then worked up with water and petroleum ether. Distillation yielded 20.5 g. of product at 98–102° (0.007 mm.), $n^{20}D$ 1.5707; $\lambda\lambda_{max}$. 299 mμ (infl.), 309 mμ (ϵ 36,200), 322.5 mμ (ϵ 28,200).*

Anal. Calcd. for $C_{19}H_{28}$: C, 89.03; H, 10.97. Found: C, 88.85; H, 11.01.

4,5-*cis*-XVIa.—A solution of 9.5 g. of XVa in 120 ml. of absolute ethanol was hydrogenated with 1.0 g. of Lindlar catalyst. Hydrogenation appeared to be much more specific in this case than in those described above, as indi-

cated by a sharp drop in the rate of absorption on approaching the end-point. Similar behavior also was observed with isoöctane as solvent as well as with poisoned (zinc acetate and piperidine) Raney nickel[4] catalyst. Work-up and distillation yielded 6.1 g. at 88–92° (0.01 mm.), $n^{20}D$ 1.5496, λ_{max}. 297 mμ. A post-run of 2.2 g. at 92–95° (0.01 mm.), $n^{20}D$ 1.5534, contained appreciable unreduced XVa (spectrum) and a forerun, 1.0 g., at 75–88° (0.01 mm.), $n^{20}D$ 1.5468, therefore was assumed to be contaminated with over-hydrogenated material.

Anal. Calcd. for $C_{19}H_{30}$: C, 88.30; H, 11.70. Found: C, 88.02; H, 11.55.

A 27.8-g. sample of undistilled semi-hydrogenation product in petroleum ether was chromatographed on a 4 × 75 cm. column of alumina, developing and eluting with petroleum ether only. The first eluates showed the typical spectrum of a *retro*ionylidene triene with a sharp peak at 284 mμ. This was followed by a mixture of triene and *cis*-tetraene as evidenced by a flat-topped curve with bumps at 288 and 296 mμ. The next fraction was that showing the absorption curve of the *cis*-tetraene, λ_{max}. 296 mμ (Fig. 8) and was collected separately until the λ_{max}. began to shift bathochromically. Concentration of this fraction and final removal of volatiles at 0.003 mm. gave 14.2 g. of product as a colorless oil, $n^{20}D$ 1.5519; λ_{max}. 295 mμ, ϵ 26,800.*

Anal. Found: C, 88.32; H, 11.49.

Stereoisomerization of 4,5-*cis*-XVIa to 4,5-*trans*-XVIa.— A solution of 2 g. of chromatographed 4,5-*cis*-XVIa was stereoisomerized by contact with iodine in the standard fashion for one hour. Without working up, the solution was concentrated to about 100 ml. and chromatographed on alumina, using petroleum ether for development and elution. The first eluates showed the spectrum of *retro*ionylidene triene, λ_{max}. 284 mμ. Elution was continued into this fraction until the *trans*-tetraene was evident spectrally. After a small intermediate fraction, the *trans*-tetraene appeared and was collected separately and distilled; yield 1.2 g. at 98–105°, $n^{24}D$ 1.5877; $\lambda\lambda_{max}$. 304 mμ (ϵ 37,700), 315.5 mμ (ϵ 47,400), 330.5 mμ (ϵ 36,100).*

Anal. Calcd. for $C_{19}H_{30}$: C, 88.30; H, 11.70. Found: C, 88.03; H, 11.90.

It is estimated from the spectra of the chromatographic foreruns that about 3% of *retro*ionylidene triene was present in the original sample of *cis*-tetraene.

Preparation of XIVb.— A stirred solution of 22.0 g. of methylvinylpropargylcarbinol[50] in 500 ml. of methylene dichloride[51] was treated at 0° with 196 ml. of 2.1 M ethylmagnesium bromide. Evolution of ethane ceased after three hours of refluxing. The solution was then cooled to 0°, 44.5 g. of β-ionone ($\epsilon_{296\ m\mu}$ 10,300) added, and the mixture refluxed for 30 minutes. Hydrolysis was effected at −30° with 30% ammonium acetate. Work-up of the organic layer and distillation yielded 38.0 g. of product at 110–120° (0.001 mm.), $n^{26}D$ 1.5169; λ_{max}. 234 mμ, ϵ 5,580.

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.17; H, 9.82.

Allylic Rearrangement-Dehydration of XIVb to XVb.— The concentrate of a reaction mixture identical with that just described above was dissolved in 500 ml. of 5% potassium acetate–glacial acetic acid, and allowed to stand under nitrogen for 15 hours. Work-up and distillation yielded 43.0 g. of product at 100–110° (0.001 mm.), $n^{20}D$ 1.5822; $\lambda\lambda_{max}$. 300 mμ (infl.), 310 mμ (ϵ 36,000), 323.5 mμ (ϵ 28,400).*

Anal. Calcd. for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.20; H, 10.14.

4,5-*cis*-XVIb.— A solution of 8.3 g. of XVb in 50 ml. of absolute ethanol was semi-hydrogenated with 1.0 g. of Lindlar catalyst. The rate of hydrogen absorption was similar to that encountered with XVa but the drop at the end-point was not so sharp. The same was true with poisoned (zinc acetate–piperidine) Raney nickel[4]; yield after distillation 6.5 g. at 97–103° (0.005 mm.), $n^{20}D$ 1.5681. The absorption curve showed λ_{max}. 298 mμ, ϵ 25,600, with inflections at 300–305 and 320–325 mμ.

(50) O. Isler, U. S. Patent 2,529,498 (November 14, 1950).

(51) Methylene dichloride appears to be unreactive toward Grignard reagents under ordinary conditions. It has been found extremely useful in this Laboratory as a solvent for ether-insoluble acetylenic Grignard reagents.

The combined distilled products of several hydrogenations, 33.5 g., were chromatographed as described above for 4,5-*cis*-XVIa. This product was much more strongly absorbed than the corresponding *cis*-XVIa and elution was consequently carried out with 50% ether and 2% methanol in petroleum ether. Here no *retro*ionylidene triene or smaller chromophores were observed and the first eluates of carbinol consisted substantially of 292-mμ material. Collection was continued until the λ_{max}. shifted to 296 mμ. On concentration this fraction amounted to 2.0 g. The eluates following were spectrally constant, showing λ_{max}. 296 mμ, and these were collected as the main fraction until the spectrum showed signs of alteration. It gradually changed on further elution to that of XVb. This last fraction gave 7.0 g. on concentration.

Concentration of the main fraction and final removal of volatiles at 0.001 mm. yielded 13.5 g. of product, $n^{20}D$ 1.5628; λ_{max} 295 mμ, ϵ 24,600.*

Anal. Calcd. for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.49; H, 10.62.

Stereoisomerization of 4,5-*cis*-XVIb to All-*trans*-XVIb.— A 5.0-g. sample of the pure *cis* isomer was stereoisomerized by contact with iodine in the standard fashion for one hour. After work-up and concentration to about 100 ml., the petroleum ether solution was chromatographed on a 3 × 30 cm. column of alumina deactivated with 5% of water. Development and elution were carried out with 10% ether–petroleum ether. The absence of *retro*ionylidene triene was corroborated. The *trans*-tetraene fraction was concentrated and distilled; yield 2.2 g. at 100–105° (0.001 mm.), $n^{20}D$ 1.601; $\lambda\lambda_{max}$. 306.5 mμ (infl.), 317 mμ (ϵ 48,500), 331.5 mμ (ϵ 36,000).*

Anal. Calcd. for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.70; H, 10.67.

Preparation of XVc and its Acetate.— Although this compound was synthesized readily by condensing β-ionone with propylethynylcarbinol, according to the method outlined in Chart IV, it was found simpler to prepare it by condensing ethynyl-β-ionol[52] with butyraldehyde as described below.

A stirred solution of 33.7 g. of ethynyl-β-ionol in 400 ml. of dry ether was treated at 10° with 157 ml. of 2.1 M ethylmagnesium bromide and then refluxed for 30–45 minutes, to complete formation of the acetylenic Grignard reagent. A solution of 12.3 g. of freshly distilled butyraldehyde in 50 ml. of dry ether was then added at 0° and the mixture refluxed for 30–40 minutes, hydrolyzed at −30° with 30% ammonium acetate, and worked up.

All attempts to distil the resulting acetylenic glycol XIVc resulted in partial dehydration. The undistilled concentrate therefore was dissolved in one liter of 5% potassium acetate–glacial acetic acid and allowed to stand under nitrogen for 15 hours. Under these conditions the β-ionol group rearranges and dehydrates (see Parts I[4] and II[14]) while the remaining propargylic hydroxyl group is unaffected. The mixture was then worked up with water and petroleum ether and concentrated. Because of the possibility of some acetylation of the propargylic hydroxyl group having occurred, the concentrate was dissolved in 200 ml. of 4% methanolic sodium hydroxide and allowed to stand overnight under nitrogen. This was then again worked up with water and petroleum ether and the product isolated by chromatographing on a 4 × 65 cm. alumina column. Development and elution were carried out with increasing proportions of ether in petroleum ether and, finally, for the desired fraction, with 30% ether and 2% methanol in petroleum ether. Concentration and final removal of volatiles at 0.001 mm. gave 35 g. of golden-yellow material, $n^{20}D$ 1.5788; $\lambda\lambda$ 301 mμ (infl.), 310.5 mμ (ϵ 34,400), 324 mμ (ϵ 27,600).*

Anal. Calcd. for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.54; H, 10.46.

Distillation did not improve the quality of the above product and was, in fact, accompanied by considerable losses due to polymerization.

The acetate was prepared by dissolving the concentrate from a reaction mixture similar to that above, derived from 44 g. of ethynyl-β-ionol, in a mixture of 80 ml. of pyridine and 40 ml. of acetic anhydride. The reaction was moderately exothermic and the mixture was intermittently cooled during the next hour to maintain 25°. It then was allowed

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

to stand under nitrogen overnight and worked up. Distillation yielded 22.0 g. at 104–115° (0.003 mm.), n^{21}D 1.5540.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 79.98; H, 9.63.

A specimen chromatographed on neutralized alumina (10% of 1.5 N acetic acid) showed n^{20}D 1.5582; $\lambda\lambda_{max}$. 301 mμ (infl.), 311.5 mμ (ϵ 33,900), 324 mμ (infl.).

Anal. Found: C, 80.28; H, 9.66.

4,5-cis-XVIc.—A solution of 18.0 g. of XVc in 150 ml. of methanol was hydrogenated with 0.5 g. of Lindlar catalyst. The rate of absorption was similar to that encountered with XVa. In isoöctane the drop in rate at the end-point was considerably sharper. The absorption curve of the crude product showed a plateau-like top tilted toward the higher wave lengths with λ_{max}. 297.5 mμ.

Alumina chromatography showed considerable triene to be present, and the best specimen of cis-tetraene that could be obtained by this method still contained an appreciable quantity of this over-hydrogenation product.

The pure cis-carbinol was obtained eventually by way of the acetate. A 12.4-g. sample of chromatographically purified 4,5-cis-XVIc acetate, described in the following section, was hydrolyzed by standing in 300 ml. of 2% methanolic sodium hydroxide and nitrogen at 5° for 15 hours. The spectrum at this point was qualitatively identical with that shown for 4,5-cis-XVIc in Fig. 10. After work-up the crude product was chromatographed on a 3 × 40 cm. column of alumina, developing with petroleum ether and eluting with increasing proportions of ether in petroleum ether. About 1.0 g. of extraneous material (probably hydrocarbon) came out first, showing bands in the diene, tetraene and pentaene regions. These were absent in the crude carbinol and are therefore assumed to be chromatographic artifacts.

The following eluates showed the curve of 4,5-cis-XVIc (Fig. 10) and were collected in a single fraction, until the absorption curve showed signs of change. After concentrating and finally removing volatiles at 0.001 mm., this fraction yielded 2.7 g. of product, n^{25}D 1.5625; λ_{max}. 292 mμ. ϵ 25,200.* The infrared spectrum showed no bands around 10.4 μ.

Anal. Calcd. for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 82.97; H, 11.03.

The following fraction (2.1 g. after removal of volatiles) showed the presence of trans isomer, undoubtedly arising as a chromatographic artifact.

About 0.5 g. of pure cis-carbinol was acetylated and worked up into petroleum ether as described in the following section. After concentration and removal of volatiles at 0.001 mm., the product, λ_{max}. 288 mμ, ϵ 24,600, showed the same absorption curve as the original acetate, λ_{max}. 288 mμ, ϵ 25,400 (including the loss of the subsidiary band at 230 mμ; see Fig. 10).

4,5-cis-XVIc Acetate.—The crude semi-hydrogenation product from 24.0 g. of XVc was acetylated with a mixture of 16.6 ml. of acetic anhydride and 33 ml. of pyridine, as described above for XVc acetate. The crude product was chromatographed on a 4 × 70 cm. column of neutral alumina (10% of 1.5 N acetic acid). Development and elution were carried out with petroleum ether, changing later to increasing proportions of ether up to 15%. The first eluates showed the absorption curve of the 4,5-cis-XVIc acetate. This was collected as the major fraction until the relative extinction in the diene region (220–250 mμ) showed indication of rising. Concentration and final removal of volatiles at 0.001 mm. yielded 18.5 g. of product, n^{20}D 1.5413; λ_{max}. 288 mμ, ϵ 25,400.*

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19. Found: C, 79.78; H, 10.38.

Further elution (15% ether) brought out a diene–triene mixture (λ_{max}. 240 and 280 mμ) and then (30% ether) the retroionylidene triene, λ_{max}. 284 mμ. Unreduced trienyne came as the last fraction.

Stereoisomerization of 4,5-cis-XVIc to All-trans-XVIc.— A 2.0-g. sample of the pure cis-carbinol was stereoisomerized by contact with iodine in the usual fashion for 30 minutes, worked up and chromatographed on a 2 × 15 cm. column of alumina. The initial eluates (15% ether–petroleum ether) contained only higher polyenic hydrocarbons. No triene was observed. The eluates immediately follow-

ing showed a constant spectrum of the trans-carbinol, λ_{max}. 316.5, and were collected as the main fraction. Concentration and distillation yielded 1.2 g. at 110–115° (0.001 mm.), n^{20}D 1.5941; λ_{max}. 316.5 mμ, ϵ 41,700.

Anal. Calcd. for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.23; H, 11.00.

Stereoisomerization of a 4.0-g. sample of 4,5-cis-XVIc acetate with iodine in the usual fashion (30 minutes) gave after concentration and final removal of volatiles at 0.001 mm., 3.9 g. of the 4,5-trans-acetate; λ_{max}. 318 mμ, ϵ 43,000.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19. Found: C, 79.64; H, 10.19.

2,3-cis-4,5-trans-XVIc.—A solution of 10.4 g. of XVc in 185 ml. of dry ether was reduced with 1.1 g. of commercial LiAlH$_4$ and worked up as described for 5,6-trans-V. Distillation yielded 9.4 g. at 114–123° (0.004 mm.), n^{20}D 1.5818; λ_{max}. 313.5, ϵ 34,400.

Anal. Calcd. for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 82.95; H, 10.93.

Chromatography on deactivated alumina (5% water) gave a spectrally homogeneous product, n^{20}D 1.5838 (after concentration and final removal of volatiles at 0.001 mm). No indications of the all-trans compound, λ_{max}. 316.5, were observed during the elution (5% ether–petroleum ether); $\lambda\lambda_{max}$. 305 mμ (infl.), 314 mμ (ϵ 35,700), 326.5 mμ (ϵ 27,-500).*

Anal. Found: C, 82.94; H, 11.02.

A 3.4-g. sample of the chromatographed carbinol was acetylated with 14 ml. of pyridine and 7 ml. of acetic anhydride as described for XVc acetate. After work-up the product was chromatographed on a 3 × 36 cm. column of neutralized alumina (10% 1.5 M acetic acid). Elution with 5% ether–petroleum ether removed the main band which was spectrally homogeneous. Concentration and final removal of volatiles at 0.001 mm. yielded 2.0 g. of product; n^{20}D 1.5665. No trace of the all-trans acetate, λ_{max}. 318 mμ, was observed; $\lambda\lambda_{max}$. 305 mμ (infl.), 314.5 mμ (ϵ 35,500), 326 mμ (infl.).

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19. Found: C, 79.68; H, 10.30.

Stereoisomerization of 2,3-cis-4,5-trans-XVIc to All-trans-XVIc.—A 13.5-g. sample of the cis–trans-carbinol (a distilled but unchromatographed product as obtained above) was stereoisomerized by contact with iodine in the standard fashion (30 minutes) and the product after work-up chromatographed on a 3 × 40 cm. column of alumina. Elution of the main band was effected with 1% methanol–10% ether in petroleum ether. Concentration and distillation yielded 5.0 g. of product at 113–115° (0.001 mm.), n^{27}D 1.5964. The ultraviolet absorption curve was identical with that of the trans-carbinol obtained above from the stereoisomerization of 4,5-cis-XVIc, except for the higher extinction here which indicated a product richer in all-trans isomer; $\lambda\lambda_{max}$. 306 mμ (infl.), 316.5 mμ (ϵ 45,700), 330.5 mμ (ϵ 34,600).*

Anal. Calcd. for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 82.98; H, 11.04.

The above carbinol (4.5 g.) was acetylated with 25 ml. of pyridine and 12 ml. of acetic anhydride as described for XVc acetate. Distillation yielded 5.0 g. of acetate at 110–120° (0.001 mm.), n^{20}D 1.5763; $\lambda\lambda_{max}$. 307 mμ (infl.), 318 mμ (ϵ 43,900), 330 mμ (ϵ 33,400). The absorption curve was identical with that of the product obtained above by stereoisomerization of 4,5-cis-XVIc acetate.

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

Pentaenes

Preparation of XVIII.—A solution of 10.0 g. of tiglic aldehyde in 50 ml. of ether was added at 0° to the Grignard reagent prepared from 21.5 g. of ethynyl-β-ionol (see above under XVc). The mixture was refluxed for 30 minutes then hydrolyzed at -20° with 30% ammonium acetate, and the ether layer worked up in the usual fashion.

The acetylenic glycol (Chart V) could not be distilled without extensive decomposition. The allylic rearrangement-dehydration (Chart V) was therefore carried out on the above crude concentrate by dissolving it in 900 ml. of glacial acetic acid and allowing to stand under nitrogen 24 hours. Work-up and distillation yielded 26.3 g. of acetate

at 120–130° (0.002 mm.), n^{20}D 1.5967; $\lambda\lambda_{max.}$ 254.5 mμ (ϵ 16,300), 334.5 mμ (ϵ 32,600).

Anal. Calcd. for $C_{22}H_{30}O_2$: C, 80.93; H, 9.26. Found: C, 80.91; H, 9.36.

A 29.6-g. sample of the above acetate was hydrolyzed by warming in 200 ml. of 10% ethanolic potassium hydroxide under nitrogen for one hour at 60–70°. Work-up and distillation yielded 23.9 g. of carbinol at 130–140° (0.002 mm.), n^{20}D 1.62; $\lambda\lambda_{max.}$ 254.5 mμ (ϵ 15,300), 334.5 mμ (ϵ 32,600).[*]

Anal. Calcd. for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.30; H, 9.87.

XVIII Ethyl Ether.—This was prepared by carrying out the allylic rearrangement–dehydration of the acetylenic glycol (Chart V) in ethanol. The concentrate of a reaction mixture from 21.8 g. of ethynyl-β-ionol and 9.3 g. of tiglic aldehyde was dissolved in 500 ml. of absolute ethanol containing 10 ml. of boron trifluoride. The reaction was followed spectrally by observing the rise in extinction at 333 mμ. This reached a maximum within an hour, and the mixture was then neutralized with ammonium hydroxide and worked up with water and petroleum ether. Distillation yielded 25.3 g. of product at 120–125° (0.005 mm.), n^{20}D 1.5925; $\lambda\lambda_{max.}$ 254.5 mμ (ϵ 16,100), 334.5 mμ (ϵ 31,400).

Anal. Calcd. for $C_{22}H_{32}O$: C, 84.56; H, 10.32. Found: C, 84.18; H, 10.14.

4,5-cis-XVII.—A solution of 26.6 g. of XVIII in 150 ml. of methanol containing 1.0 g. of zinc acetate dihydrate and 10 ml. of piperidine was hydrogenated at room temperature and atmospheric pressure with 3.5 g. of Raney nickel.[53] The rate of absorption was fairly constant with a rather sharp drop at the theoretical end-point. (The Lindlar catalyst, very surprisingly, proved to be completely inert toward this acetylene in both alcohol and isoöctane.) The mixture was worked up with 10% ammonium hydroxide (to dissolve the basic zinc salts) and petroleum ether, washing twice with 10% acetic acid to remove the piperidine. The absorption curve of the crude mixture at this point was similar in general shape to that of the pure cis-pentaene except for its higher extinction in the 325–375 mμ region.

A chromatogram of the crude product, developed with 20% ether–petroleum ether on alumina, consisted of one homogeneous orange-yellow fluorescent zone (under ultraviolet light) with a bottom red-fluorescent yellow ring. The latter was eluted with the same solvent.

Elution was then continued with 1% methanol–20% ether in petroleum ether. Collection of the main fraction was commenced with the appearance of the curve of 4,5-cis-XVII (Fig. 12) and continued until the ratio $E_{255 \text{ m}\mu}/E_{302 \text{ m}\mu}$ dropped from 1.3 to 1.1. No evidence of the trans isomer was observed. The spectra of the subsequent eluates gradually merged into that of the acetylenic starting material.

Concentration of the main fraction yielded 15.0 g. of product. This was rechromatographed on a 3 × 40 cm. column collecting that portion of the cis-pentaene fraction whose values for $E_{255 \text{ m}\mu}/E_{302 \text{ m}\mu}$ fell between 1.30 and 1.28.

Concentration and final removal of volatiles at 0.001 mm. yielded 12.0 g. of product, n^{20}D 1.5960; $\lambda\lambda_{max.}$ 255.5 mμ (ϵ 19,200), 262.5 mμ (ϵ 19,600), 302 mμ (ϵ 16,400).[*]

Anal. Calcd. for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found C, 83.55; H, 10.78.

On distillation of a 10-g. portion of the pure cis isomer, about two-thirds of it came over spectrally unchanged at 105–115° (0.001 mm.). The trans isomer was evident spectrally only in the last third of the distillate.

4,5-cis-XVII Ethyl Ether.—A 25.0-g. sample of XVIII ethyl ether was semi-hydrogenated with poisoned Raney nickel and worked up as described above for the corresponding carbinol. The rate of absorption here was also fairly constant with a sharp drop at the theoretical end-point. The crude product was chromatographed as described for the carbinol using the same criterion, $E_{255 \text{ m}\mu}/E_{302 \text{ m}\mu}$, for selecting the cis fraction. On vacuum concentration, 12.0 g. of pure cis isomer and 10.5 g. of a cis–trans mixture were obtained.

On standing in an equal volume of petroleum ether at

−70° for several days, the cis isomer crystallized. A small portion, m.p. 46–47°, was recrystallized by solution in petroleum ether and cooling to −15°, filtering and washing at the same temperature. Two such recrystallizations gave lemon-yellow crystals of constant melting point, 48.5–49° (Fisher–Johns block); $\lambda\lambda_{max.}$ 255 mμ (ϵ 26,700), 262.5 mμ (ϵ 25,700), 310 mμ (ϵ 15,800).[*]

Anal. Calcd. for $C_{22}H_{34}O$: C, 84.01; H, 10.90. Found: C, 83.95; H, 10.94.

Stereoisomerization of 4,5-cis-XVII to 4,5-trans-XVII.—A 9.8-g. sample of the pure cis-carbinol was stereoisomerized by contact with iodine in the usual fashion for 10 minutes. The crude product, after work-up, was chromatographed on a 3 × 35 cm. column of alumina.

The trans fraction (elution with 30% ether–1% methanol in petroleum ether) was chosen by the criterion $E_{332 \text{ m}\mu}/E_{366 \text{ m}\mu} \leq 1$. Concentration and final removal of volatiles at 0.001 mm. gave 5.2 g., n^{20}D 1.653; $\lambda\lambda_{max.}$ 332 mμ (ϵ 43,000), 347.5 mμ (ϵ 57,100), 366.5 mμ (ϵ 45,000).[*]

Anal. Calcd. for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.87; H, 10.87.

Stereoisomerization of 4,5-cis-XVII Ethyl Ether to 4,5-trans-XVII Ethyl Ether.—A 9.0-g. portion of the pure cis isomer was stereoisomerized with iodine and chromatographed as described above for the carbinol. Concentration of the trans fraction and final removal of volatiles at 0.001 mm. gave 6.3 g. of product, n^{20}D 1.64; $\lambda\lambda_{max.}$ 333 mμ (ϵ 49,700), 348.5 mμ (66,400), 367 mμ (ϵ 53,900).[*]

Anal. Calcd. for $C_{22}H_{34}O$: C, 84.01; H, 10.90. Found: C, 83.81; H, 10.89.

Preparation of XX.—A stirred solution of 18.4 g. of 4-methyl-6-methoxy-3-hexen-1-yne[14] in 250 ml. of methylene dichloride[51] was treated at 0° with 80 ml. of 2.1 M ethylmagnesium bromide and then allowed to stir at room temperature overnight. A solution of 31.2 g. of ψ-ionone in 50 ml. of methylene dichloride then was added at 0° and the mixture stirred at room temperature for six hours. Hydrolysis was effected at −20° with 30% ammonium acetate solution and the organic layer worked up in the usual manner and concentrated. The last traces of methylene dichloride were removed by adding 100 ml. of isoöctane and reconcentrating. Chromatography on a 3 × 100 cm. column of alumina yielded 22.2 g. of carbinol (undistilled; freed of volatiles at 0.001 mm.), n^{20}D 1.5274.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19. Found: C, 79.87; H, 10.08.

The absorption curve consists of one band with a double peak, $\lambda\lambda_{max.}$ 234 (ϵ 28,700), 243 mμ (ϵ 29,000) attributable to the overlapping enyne and diene chromophores, respectively.[54]

Allylic Rearrangement–Dehydration of XX to XXI.—A solution of 2.0 g. of XX in 50 ml. of glacial acetic acid containing a few mg. of hydroquinone was allowed to stand under nitrogen for 15 hours. Work-up and distillation yielded 1.1 g. at 119–125° (0.005 mm.), n^{20}D 1.5806; $\lambda\lambda_{max.}$ 251 mμ (ϵ 14,300), 327.5 mμ (ϵ 29,300).[*]

Anal. Calcd. for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.51; H, 10.17.

This compound is much more sensitive to air than its cyclized analog, 4,5-dehydro-I, and polymerizes very readily.

4,5-cis-XIX.—A solution of 9.2 g. of XXI in 100 ml. of methanol was semi-hydrogenated with poisoned Raney nickel and worked up as described for 4,5-cis-XVII. The rate of absorption was rather constant with a sharp drop at the theoretical end-point. (As in the case of XVII, no absorption occurred with Lindlar catalyst in either alcohol or isoöctane.) The crude product was chromatographed on a 3 × 35 cm. column of alumina. Initial eluates (3–5% ether–petroleum ether) contained considerable diene and triene material ($\lambda\lambda_{max.}$ 240 and 280 mμ). Collection of the desired fraction was begun when the curve of 4,5-cis-XIX, free of these extraneous products, appeared, and was continued until $E_{325 \text{ m}\mu}$ rose to equality with $E_{254 \text{ m}\mu}$. Con-

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(53) This weight actually refers to a wet cake of Raney nickel, obtained by pressing an aqueous paste between two layers of filter paper. The aqueous paste was purchased from the Raney Catalyst Co., Chattanooga 2, Tennessee.

(54) The corresponding cyclized compound, containing the β-ionol chromophore, shows only one peak, $\lambda_{max.}$ 235 mμ,[14] in spite of the presence of the enyne and diene chromophores. This is another example of the effect of steric hindrance in the β-ionol chromophore: the hypsochromically degraded diene peak, occurring at 236 mμ, becomes completely masked by the much stronger enyne band at ca. 235 mμ.

tinued elution then showed increasing amounts of acetylenic material.

The *cis* fraction was concentrated and freed of volatiles at 0.001 mm.; yield 2.1 g., $n^{20}D$ 1.5830; $\lambda\lambda_{max}$. 254 mμ (ϵ 27,000), 260 mμ (21,200), 312.5 mμ (ϵ 21,200).*

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74. Found: C, 83.80; H, 10.74.

Stereoisomerization of 4,5-*cis*-XIX to 4,5-*trans*-XIX.— A 2.0-g. sample of the chromatographed *cis* isomer was stereoisomerized by contact with iodine for 10 minutes, worked up and chromatographed on a 3 × 35 cm. column of alumina deactivated with 10% of water. Collection of the main fraction was begun when E_{358} mμ/E_{325} mμ = 1. By this time a contaminant (λ_{max}. 295 mμ) observed in the

foregoing eluates had been removed. Progressive elution (3% ether–petroleum ether) was accompanied by an increase in E_{358} mμ/E_{325} mμ, and was continued until the Carr–Price test showed negligible solute.

Concentration under vacuum and final removal of solvent at 0.001 mm. gave 0.8 g. of product, $n^{20}D$ 1.634; $\lambda\lambda_{max}$. 325 mμ (ϵ 46,000), 340 mμ (ϵ 62,500), 358 mμ (ϵ 54,400).*

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74. Found: C, 84.02; H, 10.70.

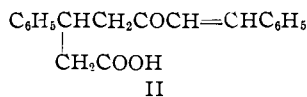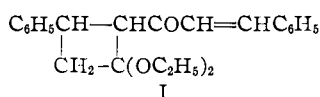[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Ketene Acetals. XXXII. The Condensation of Ketene Dimethylacetal with Various Aldehydes and Ketones

BY S. M. McELVAIN, EDWARD R. DEGGINGER AND JOHN D. BEHUN

Ketene dimethylacetal reacts with acrolein, cinnamaldehyde and benzalacetone to yield the dihydropyrans III, IV and V. These unsaturated cyclic *ortho* esters are hydrolyzed to the corresponding aldehydo and keto esters. Caproaldehyde condenses with the ketene acetal to give methyl 2-octenoate; acetaldehyde similarly gives methyl crotonate. Benzaldehyde and acetone do not react; formaldehyde causes some reduction of the ketene acetal to dimethylacetal with the concurrent oxidation of the formaldehyde to glyoxal.

The reactions of ketene diethylacetal with a variety of α,β-unsaturated carbonyl compounds were reported in the eighth[1a] and fourteenth[1b] papers of this series. Dibenzalacetone was found to react with one equivalent of the ketene acetal at 125° to yield a product, to which the structure I was assigned because of its hydrolysis in dilute acid solution to β-phenyl-γ-cinnamoylbutyric acid (II).[1a] Benzalacetone gave only a non-distillable product, which was thought to be a mixture of the ketene acetal polymer and self-condensed benzalacetone; benzalacetophenone yielded a product analogous to I that could be hydrolyzed to β-phenyl-γ-benzoylbutyric acid; phorone did not react with the ketene acetal.[1a]

$$C_6H_5CH\!-\!CHCOCH\!=\!CHC_6H_5$$
$$\underset{\displaystyle CH_2\!-\!C(OC_2H_5)_2}{|\qquad\qquad|}$$
$$I$$

$$C_6H_5CHCH_2COCH\!=\!CHC_6H_5$$
$$\underset{\displaystyle CH_2COOH}{|}$$
$$II$$

The present paper describes the reaction of ketene dimethylacetal, used in preference to the diethylacetal because of its greater stability at higher temperatures, with certain α,β-unsaturated aldehydes and ketones as well as with simple aldehydes. Acrolein reacted with this ketene acetal at 100° in a period of 24–40 hours to give 2,2-dimethoxy-2,3-dihydropyran (III) in 65–70% yields; the reaction time could be reduced to 8 hours if a temperature of 150° were used. Also the condensation could be effected in 0.5 hour at the reflux temperature of the reactants in the presence of 5 mole per cent. of aluminum *t*-butoxide; however, in this

(1) (a) S. M. McElvain and H. Cohen, THIS JOURNAL, **64**, 260 (1942); (b) S. M. McElvain and E. Engelhardt, *ibid.*, **66**, 1077 (1944).

case the yield of III dropped to about 40%. The structure of III was shown by (a) the presence of an enol ether band and the absence of the carbonyl band in its infrared spectrum and (b) its hydrolysis to methyl γ-formylbutyrate.

III, R = R' = H
IV, R = C_6H_5; R' = H
V, R = C_6H_5; R' = CH_3
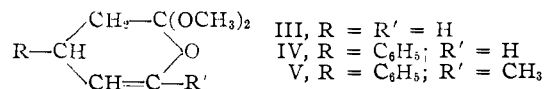
Cinnamaldehyde reacted with the ketene acetal in 24 hours at 150° to give 59% of the dihydropyran IV; after this time 30–35% of the aldehyde and 20–35% of the ketene acetal were recovered from the reaction mixture. When the reaction time at 150° was reduced to four hours the yield of IV dropped to 28%; a reaction temperature of 200° did not improve the yield and at 100° the yield of IV was only 23%. Hydrolysis of IV yielded methyl β-phenyl-γ-formylbutyrate, which was converted by oxidation and saponification to β-phenylglutaric acid.

Although benzalacetone and ketene diethylacetal at 125° gave mainly polymeric material,[1a] it was found in the present work that this ketone and ketene dimethylacetal react at 150–200° to give low yields (27–30%) of the dihydropyran V, which may be hydrolyzed to methyl β-phenyl-γ-acetylbutyrate. A considerable amount of a non-volatile, polymeric material was formed simultaneously with V. It appears that the reaction temperature used in the earlier work[1a] was not sufficiently high to permit the simple condensation of these reactants to compete successfully with their polymerization reactions.

The conclusive evidence supporting the structure III strongly indicates that the cyclobutane structure I should be discarded in favor of a dihydropyran structure corresponding to III, IV and V. All of the reactions reported for these original ad-