The Structure, Chemistry, and Synthesis of Solanone. A New Anomalous Terpenoid Ketone from Tobacco[1]

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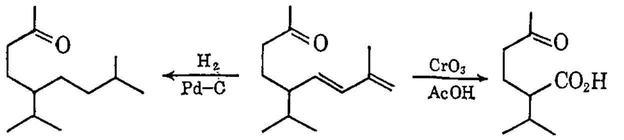
A new 13-carbon ketone, solanone, has been isolated in 0.0036% yield from tobacco and identified as L-(+)-2-methyl-5-isopropyl-1,3-nonadien-8-one. Solanone is stable under basic conditions, but rearranges in acid to the geometrical isomers of 2-methyl-5-isopropyl-2,4-nonadien-8-one, isosolanone-A and isosolanone-B. Air oxidation of solanone proceeds through a nonvolatile intermediate to form 5-isopropyl-3-nonene-2,8-dione which has been named norsolanadione. Separate syntheses of solanone and norsolanadione from readily available starting materials are described.

The isoprene rule which predicts head-to-tail arrangement of isoprene units in terpenoids has been put on a firm theoretical basis by the establishment of the mevalonate biosynthesis of these compounds.[2] A small number of terpenoids are known which violate this rule and these are generally considered to be degradation or rearrangement products from precursors which abide by the rule. We wish to report the isolation of a new tobacco terpenoid and its identification as L-(+)-2-methyl-5-isopropyl-1,3-nonadien-8-one (I), an obvious exception to the isoprene rule, which we have named solanone.[3]

A small amount of free I occurs in aged tobacco and can be isolated by subjecting the tobacco to high vacuum at room temperature for several days. Preparative gas chromatographic separation of the pentane-soluble portion of the collected volatiles gives a small amount of (+)-I with larger quantities of the much higher boiling neophytadiene.[4] These two compounds are, by far, the major constituents of this fraction. Far larger yields of I are realized when tobacco is heated under vacuum, presumably by pyrolytic formation, and this procedure was adopted to prepare the samples required for identification. The maximum isolated yield of I was 0.0036% based on the dry weight of the burley tobacco used. However, analytical runs showed that the amount released was 0.009%. Turkish tobacco was found to release about the same amount of I as burley, while flue-cured tobacco gave a lower yield.

Solanone, $C_{13}H_{22}O$, is a clear, colorless, mobile oil with a faint aroma reminiscent of carrots. Hydrogenation of (+)-I gives (−)-tetrahydrosolanone (II). Both I and II give positive iodoform tests and both show isolated carbonyl adsorption in the infrared at 1716 cm.$^{-1}$. Thus, the single oxygen in I must be in a methyl ketone function.



(−)-II (+)-I III

The presence of a conjugated diene function in I was indicated by intense ultraviolet absorption at 230 mμ in both ethanol and hexane. Infrared absorption at 1607 cm.$^{-1}$ confirmed this assignment. The nature of these two double bonds is indicated by infrared absorption at 882 $(\substack{C\\C}{>}C{=}CH_2)$ and 970 cm.$^{-1}$ $(\substack{H\\C}{>}C{=}C{<}\substack{C\\H})$. With the empirical formula $C_{13}H_{22}O$, a ketone function, and two double bonds I must be an open-chain compound and can contain no additional functional groups.

Oxidation of I with chromic oxide in acetic acid gave 2-isopropyl-5-ketohexanoic acid (III) which was isolated as the methyl ester after treating the acidic products with diazomethane. This was the only major high-boiling methyl ester found.

The n.m.r. spectrum of I provided enough additional information to allow assignment of a unique structure. A two-proton AB quartet (J = 16 c.p.s.) is present, centered at τ 4.32, in which each component of the high-field branch has been further split into doublets (J = 8 c.p.s.). This resonance pattern must be due to a *trans* double bond which is adjacent to a carbon bearing a single proton and leaves I as the only possible structure for solanone. Further confirmatory evidence is available from the n.m.r. spectrum such as the integral which shows 22 protons, a single two-proton resonance at τ 5.15 for the vinylidine function, a sharp three-proton resonance at τ 8.00 for the methyl ketone, and a three-proton resonance at τ 8.20 with fine second-order splitting which is assigned to the isopropenyl methyl group. The two methyls in the isopropyl function are not equivalent and give two superimposed doublets centered at τ 9.10.

Synthesis of D-(+)-II from D-3-isopropyl-6-ketoheptanal[5] (IV) confirmed the carbon skeleton of I and established the absolute L configuration of the tobacco-derived substance. IV was treated with a slight excess of isopropylmagnesium bromide and the resulting mixture of carbinols was dehydrated to form D-(−)-2-methyl-5-isopropyl-2-nonen-8-one (V). Hydrogenation of V gave (+)-II. When isopropenylmagnesium bromide[6] was substituted in the synthesis

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(1) Presented at the 18th Tobacco Chemists' Research Conference, Raleigh, N. C., Oct. 20–22, 1964.

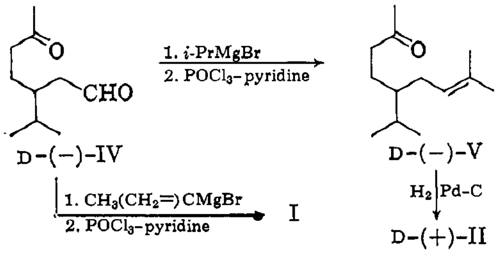
(2) L. D. Wright, *Ann. Rev. Biochem.*, **30**, 525 (1961).

(3) The trivial name solanone which has been applied to I is derived from the botanical family *Solanaceae* of which tobacco is genus *Nicotiana*. Virtually all of the available solanone in tobacco is in the form of nonvolatile precursors and the small amount of free solanone found is attributed to previous processing of the tobacco. Alternate procedures for the purification of solanone and carboxylic acid precursors of solanone are reported by R. B. Griffith, R. R. Johnson, and A. D. Quinn, U. S. Patent 3,174,485 (1965).

(4) R. L. Rowland, *J. Am. Chem. Soc.*, **79**, 5007 (1957).

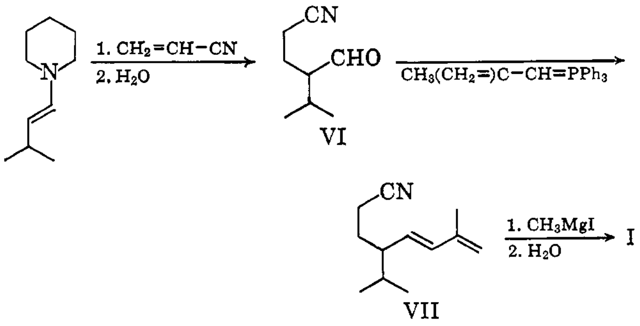
(5) Y. Kishida [*Chem. Ind.*, (London), 465 (1960)] reported $[\alpha]^{25}D$ −5.93° for IV. A sample with $[\alpha]^{25}D$ −3.26 was used to prepare D-(+)-II.

(6) H. Normant [*Compt. rend.*, **239**, 1510 (1964); *Bull. soc. chim. France*, 728 (1957)] described methods for preparing vinyl Grignard reagents.



a minute yield of I was obtained and was isolated only with difficulty.

A convenient synthesis of *dl*-I was developed to make larger quantities readily available and provide a final proof of structure. The piperidine enamine of isovaleraldehyde was cyanoethylated[7] to form, after hydrolysis, 2-isopropyl-4-cyanobutyraldehyde (VI). A Wittig reaction[8] between VI and methallylidenetriphenylphosphorane in anhydrous tetrahydrofuran gave predominantly 3,4-*trans*-2-methyl-5-isopropyl-7-cyano-1,3-heptadiene (VII). The higher boiling *trans* isomer was treated with excess methylmagnesium iodide to form the intermediate ketimine[9] which was hydrolyzed under slightly basic conditions to form I. Synthetic I, which was formed in 19% over-all yield, was identical with natural I from tobacco in all respects but optical activity.

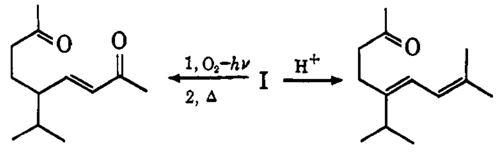


During the structure determination it became apparent that I was sensitive to acid and easily oxidized by air. The air oxidation first gives a viscous glass which decomposes on mild heating to form a mobile liquid which was named norsolanadione (VIII). Treatment of I with mineral acid first gives two new dienones and eventually leads to nonvolatile products. These two new dienones (IX) were named isosolanone-A and isosolanone-B in their order of elution from a polar (PDEAS) g.l.c. column. The isosolanones were also formed when a high injection-block temperature (360°) was used in the g.l.c. purification of I, but I was still the major substance isolated. Treatment of I with boiling ethanolic potassium hydroxide for 2 hr. gave only unchanged I.

Hydrogenation of both IX-A and IX-B gave II which demonstrates that both have the same carbon skeleton as I. IX-A has $\lambda_{\max}$ 246 mμ (ethanol) and IX-B has $\lambda_{\max}$ 244 mμ (ethanol). Both give similar infrared spectra showing isolated carbonyl absorption at 1718 cm.$^{-1}$, diene absorption at 1615 cm.$^{-1}$, and trisubstituted double-bond absorption at 850 cm.$^{-1}$ for IX-A and 843 cm.$^{-1}$ for IX-B.

N.m.r. spectra of IX-A and IX-B showed 22 protons in each compound. Both spectra show five methyl groups, two around τ 8.9, two around τ 8.25, and the methyl ketone at τ 7.95. IX-A showed two olefinic protons in a sharp band at τ 4.1, while IX-B showed two protons in what appears to be an AB quartet (J = 10 c.p.s.) centered at τ 4.1. Both spectra show five methylene and methine allylic protons, these appearing in one strong resonance at τ 7.65 in the IX-A spectrum, and between τ 6.9 and 7.7 in the IX-B spectrum. These data show that IX-A and IX-B are the two geometrical isomers of 2-methyl-5-isopropyl-2,4-nonadien-8-one.

The assigned structure for IX-A and IX-B is supported by observations that they are slowly equilibrated with iodine in refluxing ethanol, but not by acid under their conditions of formation. Also, their rates of formation are identical through at least 75% reaction.



VIII IX

Samples of I which had been exposed to air for several months were found to be extremely viscous. These were subjected to high vacuum at room temperature to remove any unreacted I and volatile oxidation products. A pentane-soluble distillate was obtained which gave I and another more polar substance which was named norsolanadione (VIII). The residue from the distillation was insoluble in pentane, but gave VIII and carbon monoxide with slight heating. The efficiency of this conversion was studied by irradiating pure *dl*-I for 8 days at room temperature under a mercury ultraviolet lamp and then analyzing a toluene solution of the resulting tacky mixture by g.l.c. The analysis showed that 11.5% of the original I was unreacted while 52% had been converted to VIII. Instantaneous conversion of the intermediate oxidation product to VIII on the gas chromatograph injection block at 240° was assumed and no allowance was made for evaporation of materials during irradiation.

Norsolanadione, $C_{12}H_{20}O_2$, is a colorless, odorless mobile oil which shows $\lambda_{\max}$ 217 mμ in hexane and $\lambda_{\max}$ 224 mμ in ethanol, this shift indicating the presence of an α,β-unsaturated ketone function. The infrared spectrum shows two carbonyl bands at 1675 and 1715 cm.$^{-1}$, a conjugated double-bond band at 1624 cm.$^{-1}$, and *trans* disubstituted double-bond absorption at 990 cm.$^{-1}$. These data indicate the presence of two carbonyl functions, one α,β-unsaturated and one isolated.

The n.m.r. spectrum of VIII gives an integral for 20 protons, two of which are olefinic and appear in an AB quartet (J = 16 c.p.s.) centered at τ 3.75 with each component of the low-field branch being further split into doublets (J = 8 c.p.s.). This resonance pattern must again be due to a *trans* double bond adjacent to a carbon bearing a methine hydrogen. A two-proton triplet centered at τ 7.65 is attributed to a methylene group flanked by carbonyl and methylene groups. A pair of sharp three-proton resonances at τ 7.85 and

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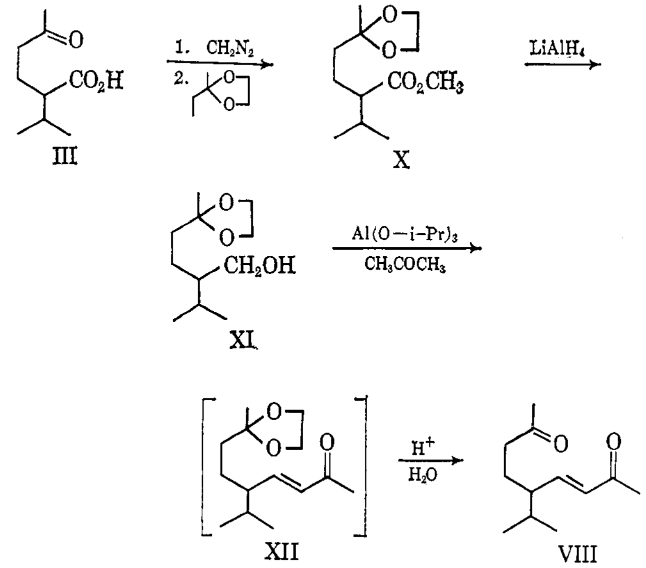
(7) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

(8) S. Triplett, *Advan. Org. Chem.*, **1**, 83 (1960).

(9) M. Julia, S. Julia, and B. Stalla-Bourdillon [*Compt. rend.*, **253**, 951 (1961)] described an analogous Grignard reaction with a cyanodiene to form a ketodiene.

7.96 are assigned as two methyl ketone functions while two superimposed doublets with six protons centered at τ 9.08 must be due to two nonequivalent methyl groups in an isopropyl group.

On the basis of the data outlined above, VIII was identified as 5-isopropyl-3-nonene-2,8-dione. This structure was confirmed by synthesis starting with III.[10] Treatment of III with ethereal diazomethane and transketalization[11] of the resulting methyl ester gave methyl 2-isopropyl-5,5-ethylenedioxyhexanoate (X). This ketal ester X was reduced to form 2-isopropyl-5,5-ethylenedioxyhexan-1-ol (XI). Condensation of XI with acetone and aluminum isopropoxide for 144 hr. at reflux[12] gave 5-isopropyl-8,8-ethylenedioxy-3-nonen-2-one (XII) which was not isolated, but directly hydrolyzed with dilute acid to give *dl*-VIII.



Although the efficient air oxidation of I to form VIII was unexpected, an analogy does exist in the air oxidation of β-phellandrene which has been reported[13] to produce cryptone and formaldehyde. At present the details of the oxidation mechanisms involved are not understood.

Experimental

General.—All n.m.r. spectra were obtained on a Varian Associates A-60 spectrometer (60 Mc., 37 ± 1°) in carbon tetrachloride solutions with tetramethylsilane as an internal reference. Infrared spectra were obtained on a Perkin-Elmer 421 spectrometer employing a grating monochrometer. Ultraviolet spectra were obtained on a Beckman DK-2 spectrometer. Elemental analyses were performed by the Micro-Tech Laboratories, Inc., Skokie, Ill. Densities were measured with micro specific gravity pipets. Semicarbazones were recrystallized to constant melting point using solvents listed in parentheses. Melting points are corrected, but boiling points are not. Gas liquid chromatography (g.l.c.) was accomplished with methyl silicone gum (SE-30), diethylene glycol succinate (DEGS), and phenyldiethanolamine succinate (PDEAS) substrates on Chromosorb-P. Hydrogenations were accomplished at atmospheric pressure employing methanolic solutions and 10% Pd–C catalyst.

Isolation of (+)-Solanone (I) from Tobacco.[3]—Scrap burley tobacco (100 kg. dry weight) was heated in several batches at 150° and 1 mm. for 48 hr. with the released volatiles being condensed in a trap at −50°. The neutral pentane-soluble portion of the distillate was steam distilled until g.l.c. analyses showed the distillation of I to be essentially complete. G.l.c. analysis of the neutral pentane-soluble portion of the steam distillate showed the presence of 3.6 g. of I (0.0036% yield). This fraction was distilled through a spinning-band column to give I, b.p. 60° (1 mm.), and pure I was then obtained by g.l.c. (PDEAS at 160°). (+)-I had n^{20}_{D} 1.4755, d^{20}_{4} 0.870, $[\alpha]^{23}_{\text{D}}$ +13.6° (neat), and λ_{max} at 230 mμ in both ethanol (log ϵ 4.07) and hexane.

Anal. Calcd. for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.45; H, 11.07.

The semicarbazone had (from ethanol–water, toluene) m.p. 160.5–161.5°.

Anal. Calcd. for $C_{14}H_{25}N_3O$: C, 66.89; H, 10.03; N, 16.72. Found: C, 67.13; H, 10.08; N, 16.76.

Hydrogenation of (+)-I gave (−)-tetrahydrosolanone (II) which was purified by g.l.c. (SE-30). (−)-II had n^{20}_{D} 1.4390, d^{20}_{4} 0.842, and $[\alpha]^{22}_{\text{D}}$ −0.45° (neat).

Anal. Calcd. for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.74; H, 13.15.

The semicarbazone had (from water–ethanol, hexane) m.p. 116.5–117°.

Anal. Calcd. for $C_{14}H_{29}N_3O$: C, 65.83; H, 11.45. Found: C, 65.70; H, 11.33.

Analyses of tobacco samples for available I were performed by heating 5-g. tobacco samples at 150° at 20 μ for 48 hr. and analyzing the neutral pentane-soluble portion of the distillate by g.l.c. using a PDEAS column and a flame ionization detector. The average yield of I from burley tobacco was 0.0091% while flue-cured grades gave an average yield of 0.0049%. The yields from Turkish and burley tobacco were about the same.

Chromic Oxide Oxidation of (+)-I.—A mixture of 8.0 g. of chromic oxide, 6.5 g. of water, and 43 ml. of acetic acid was slowly added to a solution of 1.1 g. of I in 10 ml. of acetic acid at 35–40°. The reaction temperature was then raised to 60° for 10 min. and, after cooling, 7 ml. of methanol was slowly added with cooling. Solvents were removed at 20° and 1 mm. and the residue was partitioned between 4 *N* hydrochloric acid and chloroform. After removing the chloroform under vacuum, the residual organic acids were treated with excess ethereal diazomethane and concentrated to give 0.34 g. of residue. Purification by g.l.c. (PDEAS) gave methyl 2-isopropyl-5-ketohexanoate which was identical with an authentic sample.

D-2-Methyl-5-isopropyl-2-nonen-8-one (V).—Isopropylmagnesium bromide (0.28 mole) in ether was slowly added to an ethereal solution of D-3-isopropyl-6-ketoheptanal[5] (32.2 g., 0.230 mole, $[\alpha]^{25}_{\text{D}}$ −3.26°) with stirring and the resulting white complex was decomposed with dilute sulfuric acid. The neutral ether-soluble products were concentrated and then added in 150 ml. of dry pyridine to phosphorus oxychloride (60 g., 0.39 mole) in 150 ml. of dry pyridine at 10–15° with stirring. After remaining at 20° for 45 hr., the mixture was poured over crushed ice and extracted with hexane. The neutral hexane-soluble materials were distilled through a spinning-band column to give V (6.17 g., 13.7%) with b.p. 60–62° (0.3 mm.). A g.l.c. (DEGS) purified sample had n^{20}_{D} 1.4557, d^{24}_{4} 0.868, and $[\alpha]^{24}_{\text{D}}$ −4.95° (neat).

Anal. Calcd. for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.45; H, 12.30.

The semicarbazone had (from water–ethanol, hexane) m.p. 96–97°.

Anal. Calcd. for $C_{14}H_{27}N_3O$: C, 66.36; H, 10.74. Found: C, 66.26; H, 10.74.

Treatment of D-3-isopropyl-6-ketoheptanal with isopropenylmagnesium bromide[6] gave a 0.21% yield of D-(−)-I.[3]

D-(+)-(II).—Hydrogenation of D-V gave D-(+)-II which was purified by g.l.c. (SE-30). The pure sample had n^{20}_{D} 1.4391 and $[\alpha]^{20}_{\text{D}}$ +0.31° (neat). The infrared spectrum and g.l.c. retention times on two columns were identical with those from (−)-II and the semicarbazone (m.p. 116–116.5°) had m.m.p. 116–116.5° with (−)-II semicarbazone, although a racemic mixture is approximated.

***dl*-2-Isopropyl-4-cyanobutyraldehyde** (VI).—The piperidine enamine of isovaleraldehyde[7] was cyanoethylated with acrylonitrile using the procedures described by Stork[7] to give VI, b.p. 72–74° (0.7 mm.), in 51.3% yield. G.l.c. (DEGS) gave pure VI with n^{20}_{D} 1.4430 and d^{22}_{4} 0.946.

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[10] J. C. Bardhan, N. C. De, and B. B. Datta, *J. Chem. Soc.*, 3195 (1951).

[11] H. J. Dauben, Jr., B. Löken, and H. J. Ringold, *J. Am. Chem. Soc.*, **76**, 1359 (1954).

[12] M. Yamashita and M. Shimano, *J. Chem. Soc. Japan*, **63**, 1338 (1942).

[13] O. Wallach, *Ann.*, **343**, 29 (1905).

Anal. Calcd. for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 69.10; H, 9.46; N, 10.01.

The semicarbazone had (from water–ethanol, toluene) m.p. 141–142°.

dl-**2-Methyl-5-isopropyl-7-cyano-1,3-heptadiene (VII).**—Triphenylphosphine with excess 3-chloro-2-methylpropene in refluxing dry benzene gave a 98% yield of methallyltriphenylphosphonium chloride in 2 weeks. The product crystallized as it was formed and was removed at intervals by filtration and utilized without further purification.

A solution of *n*-butyllithium (215 ml., 1.62 *N*, 0.348 mole) in hexane was slowly added to a stirring suspension of methallyltriphenylphosphonium chloride (129 g., 0.366 mole) in 500 ml. of tetrahydrofuran (freshly distilled from $LiAlH_4$) under a nitrogen atmosphere. The resulting intensely red solution of methallylidenetriphenylphosphorane was stirred for 16 hr. at 20° and then VI (30.6 g., 0.220 mole) in 35 ml. of dry tetrahydrofuran was slowly added. The mixture was stirred at room temperature for 1 hr., refluxed for 3 hr., and then concentrated under vacuum. Water was added to the residue and the mixture was extracted several times with hexane after which the combined hexane extracts were cooled to 0° and filtered to remove triphenylphosphine oxide. Fractional distillation of the hexane-soluble materials gave VII (32.64 g., 83.9%), b.p. 67–73° (0.9 mm.). The higher boiling fractions were almost entirely the 3,4-*trans* product while some of the 3,4-*cis*-cyanodiene was found in the lower boiling fractions. A pure sample of 3,4-*trans*-VII was obtained by g.l.c. (PDEAS) and had n^{20}_D 1.4795 and d^{20}_4 0.872.

Anal. Calcd. for $C_{12}H_{19}N$: C, 81.30; H, 10.80; N, 7.90. Found: C, 81.36; H, 10.97; N, 8.21.

dl-**Solanone (I).**—A mixture of 3,4-*trans*-VII (10.0 g., 0.056 mole) and 30 ml. of anhydrous ether was slowly added to a stirring solution of methylmagnesium iodide (0.175 mole) in 175 ml. of ether. When the addition was complete, 200 ml. of dry benzene was added and ether was removed by distillation until a reflux temperature of 73° was attained. Refluxing was continued for 24 hr. after which the mixture was cooled and poured over crushed ice to hydrolyze the intermediate ketimine. This mixture was stirred for 4 hr. at 20° after which the benzene layer was removed and the residual aqueous mixture was extracted with ether. The combined organic layers were fractionally distilled to give *dl*-I (5.96 g., 54.2%). A sample was purified by g.l.c. (DEGS) and had n^{20}_D 1.4746 and d^{21}_4 0.863. This sample gave infrared and n.m.r. spectra which were identical with those from (+)-I. G.l.c. retention times on DEGS and SE-30 columns were identical for the (+)- and *dl*-I.

Anal. Calcd. for $C_{13}H_{20}O$: C, 80.35; H, 11.41. Found: C, 80.23; H, 11.51.

The semicarbazone had (from water–ethanol, toluene) m.p. 156–157.5°.

Hydrogenation of *dl*-I gave *dl*-II, which was purified by g.l.c. (SE-30). This sample had n^{20}_D 1.4390 and d^{20}_4 0.840 and formed a semicarbazone with m.p. 117–118°. A mixture with (−)-II semicarbazone gave m.p. 117–117.5°.

In one preparation the *dl*-I ketimine salt in ether was decomposed by the addition of 6 *N* hydrochloric acid followed by 3 hr. stirring at room temperature. The usual work-up of products gave a mixture of *dl*-I, IX-A, and IX-B. These products were isolated by g.l.c. and identified by their infrared and n.m.r. spectra.

Air Oxidation of I.—A 0.77-g. sample of *dl*-I in a 50-ml. beaker was irradiated for 8 days with a mercury ultraviolet lamp. No significant weight gain or loss, or discoloration, were noted although the originally mobile liquid became viscous. G.l.c. (SE-30) analysis of a toluene solution of the oxidized mixture showed that 11.5% of the original I remained and 52% had been converted to norsolanadione (VIII). Pure VIII was isolated by distilling the product mixture at 1 mm. with strong heating and then subjecting the distillate to g.l.c. (SE-30/205°). VIII is a colorless, mobile liquid with n^{20}_D 1.4727.

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.49; H, 10.37.

When the viscous intermediate oxidation product was heated in a sealed system, carbon monoxide was, by far, the major one-carbon fragment found. The intermediate shows considerable hydroxyl stretching absorption in the infrared, but gives only a weak peroxide test.

Acid-Catalyzed Isomerization of I.—A mixture of 0.42 g. of I and 25 ml. of 1 *N* ethanolic *p*-toluenesulfonic acid was refluxed for 2 hr., cooled, poured into 125 ml. of water, and extracted with pentane. G.l.c. (DEGS at 160°) of the neutral pentane-soluble fraction allowed collection of three peaks with elution times of 14.7, 19.7, and 24.8 min. with approximate relative areas of 1, 4, and 3, respectively. The 14.7-min. peak was identified as I and the 19.7- and 24.8-min. peaks were named isosolanone-A (IX-A) and isosolanone-B (IX-B), respectively. Both IX-A and IX-B gave II on hydrogenation, with the identification being based on g.l.c. retention times, infrared spectra, and mixture melting points of the semicarbazones with *dl*-II semicarbazone.

IX-A had n^{20}_D 1.4912 and d^{22}_4 0.831. The semicarbazone (from water–ethanol, toluene–hexane) had m.p. 120.5–122°.

IX-B had n^{20}_D 1.4942 and d^{22}_4 0.879. The semicarbazone (from water–ethanol, toluene) had m.p. 166.5–167.5°.

Several isomerization runs were made in ethanolic 1 *N* acid at reflux in which aliquots were removed at various times and analyzed by g.l.c. The IX-A : IX-B product ratio remained unchanged through 75% reaction, and both products were slowly transformed to nonvolatile materials. When IX-A was used as the starting material, the analyses showed that none of the other isomer was formed. The isosolanones were, however, partially equilibrated in refluxing dilute ethanolic iodine solution.

dl-**Methyl 2-Isopropyl-5,5-ethylenedioxyhexanoate (X).**—Excess ethereal diazomethane was slowly added to *dl*-III[10] (32.1 g., 0.186 mole) in 100 ml. of ether. The ether and excess diazomethane were removed at 45° and 20 mm. and the residual methyl ester was dissolved in 2-ethyl-2-methyl-1,3-dioxolane[11] (43.0 g., 0.372 mole) containing 0.5 g. of *p*-toluenesulfonic acid. This mixture was refluxed into a spinning-band column for 24 hr. with 2-butanone being removed as it was formed. Distillation of the products gave X (40.82 g., 95.5%), b.p. 67° (0.25 mm.). A pure sample was prepared by g.l.c. (PDEAS) and had n^{20}_D 1.4444 and d^{20}_4 0.832.

Anal. Calcd. for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.44; H, 9.62.

dl-**Norsolanadione (VIII).**—A solution of X (40.7 g., 0.177 mole) in ether was slowly added to a stirring solution of lithium aluminum hydride (3.8 g., 0.10 mole) in 100 ml. of ether. After decomposing the excess hydride with 6 *N* sodium hydroxide solution, the aqueous layer was extracted with four 200-ml. portions of fresh ether. The combined ether extracts were washed with 200 ml. of water and then were distilled to give 2-isopropyl-5,5-ethylenedioxyhexan-1-ol (XI, 30.7 g., 85.5%), b.p. 96° (0.54 mm.).

A mixture of crude XI (10.0 g., 0.0495 mole), 250 ml. of acetone, and freshly distilled aluminum isopropoxide (24.2 g. in 75 ml. of toluene, 0.118 mole) was refluxed for 144 hr. and then concentrated under vacuum. The residual material was treated with ether and dilute acid until g.l.c. analysis showed hydrolysis of the ketal to be complete. After washing the ether layer with water and dilute sodium bicarbonate solution, the ether was removed under vacuum. G.l.c. analysis of the residue showed the presence of VIII (1.03 g., 10.6%) and a larger quantity of 2-isopropyl-5-ketohexan-1-ol. Pure VIII was prepared by g.l.c. (PDEAS) and had n^{20}_D 1.4729. This sample gave infrared, ultraviolet, and n.m.r. spectra which were identical with the spectra of VIII from (+)-I. The two samples had identical g.l.c. retention times on SE-30 and PDEAS columns.

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