were washed out of the bomb with water and ether. The ether layer was washed several times with water and dried over anhydrous calcium chloride. The solution was reduced to 50.0 ml and analyzed employing glpc. The reaction products included 1.83 g (35.8%; CWA, 110°) of 1-chlorocycloheptene-2,7,7-d_3 and 0.97 g (14.6%; CWA, 170°) of deuterated 1-phenylcycloheptene. Both compounds were isolated utilizing preparative glpc (CWP, 140; CWA, 170°). The nmr and infrared spectra of the recovered chloride were virtually identical with those of the starting material. Proton nmr analysis of the deuterated 1-phenylcycloheptene indicated the presence of 0.17 ± 0.02 deuteron and 1.96 ± 0.12 deuterons in the olefinic and saturated ring positions, respectively. The results of dmr measurements are reported in Table I and Figure 1.

Salt-Free Phenyllithium. About 220 ml (0.44 mole) of 2 *M* *n*-butyllithium in *n*-hexane (Alfa Inorganics) was maintained at 0° under an argon atmosphere. Iodobenzene (41.6 g, 0.204 mole) was added dropwise to the solution over a 20-min period. Stirring was continued at 0° for an additional 20 min. The phenyllithium precipitated out as a fine white solid. The solvent was filtered off and the precipitate washed successively with 200 ml of pentane, 150 ml of benzene, and two 150-ml portions of pentane. All manipulations were carried out under argon. The solvents had been distilled and stored over 4A Molecular Sieves. About 60 ml of anhydrous ether was added dropwise with stirring to the phenyllithium (0°). Double titration[20b] indicated that the solution was 1.43 *M* in phenyllithium.

Catalyzed Coupling of 1-Chlorocyclohexene and Phenyllithium. A solution of 6.01 g (51.7 mmoles) of 1-chlorocyclohexene, 0.747 g (8.79 mmoles) of piperidine, and 50 ml (85.0 mmoles) of 1.70 *M* salt-free phenyllithium solution in ether was heated in a sealed ampoule at 35° for 66.5 hr. *t*-Butyl alcohol was added to the products. The solution was made up to 100 ml with ether. The products were analyzed employing glpc. The reaction products included 2.10 g (34.9%; XEA, 90°) of 1-chlorocyclohexene and 2.39 g (29.3%; XEA, 160°) of 1-phenylcyclohexene.

Catalyzed Coupling of 1-Chlorocyclohexene-2,6,6-d_3 and Phenyllithium. A solution of 8.87 g (74.4 mmoles) of 1-chlorocyclohexene-2,6,6-d_3, 0.758 g (8.92 mmoles) of piperidine, and 50 ml (71.5 mmoles) of 1.42 *M* salt-free phenyllithium solution in ether was heated in a sealed ampoule at 35° for 155.5 hr. Water was used for quenching. Analysis of the reaction products by glpc indicated that 4.14 g (46.8%; XEA 60°) of 1-chlorocyclohexene-2,6,6-d_3 and 1.17 g (9.8%; XEA, 160°) of 1-phenylcyclohexene-*x*-d_n were present. These compounds were isolated by glpc. The proton nmr and infrared spectra of the recovered 1-chlorocyclohexene-2,6,6-d_3 (XEP, 100°) were very similar to those of the starting material. The ratio of saturated to olefinic deuterons (dmr) was 1.93 ± 0.03. Both the proton and deuteron nmr spectra of the 1-phenylcyclohexene-*x*-d_n (XEP, 160°) showed that 0.1 deuteron and 2.0 deuterons were present in the olefinic and saturated ring positions, respectively. The saturated deuteron absorption is shown in Figure 2B.

1-Phenylcyclohexene-2,6,6-d_3 was synthesized by way of a two-step sequence. Cyclohexanone-2,2,6,6-d_4 was converted to 1-phenylcyclohexanol-2,2,6,6-d_4 employing phenylmagnesium bromide. The recrystallized (pentane) carbinol, mp 61–65.5°, was dehydrated using formic acid.[7c] Chromatographed (XEP, 160°) 1-phenylcyclohexene-2,6,6-d_3 was deuterated to an extent greater than 99% (nmr). The ratio of saturated to olefinic deuterons as determined by dmr was 2.1 ± 0.1. Additional dmr data are provided in Table I and Figure 2.

The Stereospecific Synthesis and Electronic Absorption Properties of *cis*- and *trans*-4-Acetoxyisopulegone

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Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02138. *Received June 16, 1966*

Abstract: *trans*- (**1a**) and *cis*-4-acetoxyisopulegone (**1e**) have been synthesized stereospecifically from α- and β-epoxypulegone, respectively. This chemical correlation supports the epoxide stereochemistry predicted by the "reverse octant rule." An unusual equilibrium between **1a** and **1e** is reported together with the thermal isomerization of these isomers to *cis*- and *trans*-2-acetoxypulegone. The optical rotatory dispersion and the absorption properties of **1a** and **1e** have been examined in detail and applied to the interpretation of the utraviolet spectrum of 3-acetoxy-4-methyl-4-penten-2-one (**3**), a freely rotating system possessing the same chromophoric array.

The thermal elimination of acetic acid from both 4-acetoxyisopulegone (**1**)[1a] and 2-acetoxypulegone (**2**)[1b] to form menthofuran has been of special interest to us since we had observed an apparently analogous, although photochemical, cyclization in various desyl systems (Figure 1).[1c] Even though this comparison is somewhat tenuous in view of the fact that benzoin acetate is cleaved thermally to benzaldehyde and α-ketopropiophenone,[2] the 4-acetoxyisopulegone molecule does offer the opportunity to restrict the orientation of the acetoxy and isopropenyl groups with respect to the ketone carbonyl. Since it has been shown in a number of instances that carbonyl $n \rightarrow \pi^*$ transitions are influenced by the nature and relative orientation of α substituents,[3] it was of interest to assess the effect of these interactions upon the reactivity of the carbonyl $n \rightarrow \pi^*$ state. In this accounting we relate the synthetic approach to and electronic absorption properties of the 4-acetoxyisopulegones as a foundation for future publications dealing with the photochemical behavior of these molecules.

The system selected for this investigation (**1**) may exist in two isomeric modifications which will be designated **1a** for the isomer with an *axial* isopropenyl group and **1e** for the isomer with an *equatorial* isopropenyl group. To date these isomers have not been separately characterized, and so the first objective was to remedy this deficiency by means of an independent stereospecific synthesis for each isomer.

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(1) (a) L. H. Zalkow and J. W. Ellis, *J. Org. Chem.*, **29**, 2626 (1964); (b) L. H. Zalkow, J. W. Ellis, and M. R. Brennan, *ibid.*, **28**, 1705 (1963); (c) J. C. Sheehan and R. M. Wilson, *J. Am. Chem. Soc.*, **86**, 5277 (1964).

(2) E. Jones and P. D. Ritchie, *J. Chem. Soc.*, 4141 (1960).

(3) C. Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, pp 111–122; R. C. Cookson, *J. Chem. Soc.*, 282 (1954); H. Labhart and G. Wagniere, *Helv. Chim. Acta*, **42**, 2219 (1959); to mention only a few of the notable efforts in this area.

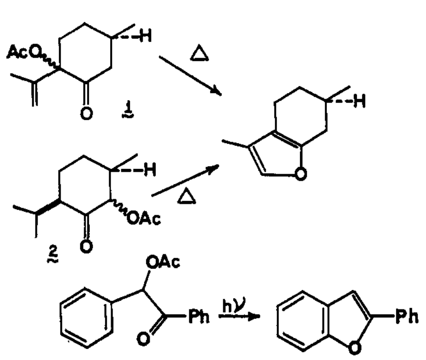


Figure 1. Furan formation from α-acetoxy-β,γ-unsaturated ketones.

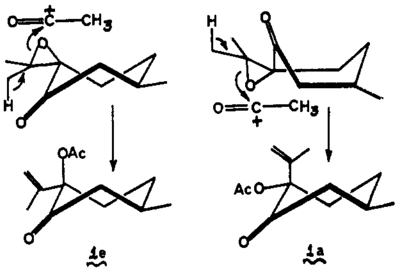
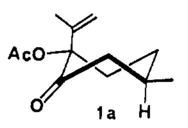
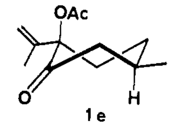


Figure 2. Stereospecific conversion of the epoxypulegones to the 4-acetoxyisopulegones.

Previously **1** had been synthesized directly from pulegone by oxidation with lead tetraacetate, but since the resultant isomeric mixture (**1a** and **e**) was separated only by vpc,[4] this method was not suitable for our purposes. However, the epoxidation of pulegone produces two compounds which are readily separated by distillation.[5] The stereochemistry of these isomers was assigned originally on the assumption that the sign of the Cotton effect of α,β-epoxy ketones could be predicted by the octant rule. Subsequently it has been shown that a "reverse octant rule" must be applied in order to arrive at the correct stereochemistry of α,β-epoxy and cyclopropyl ketones.[6] It seemed likely that the assigned stereochemistry of the pulegone oxides must be reversed to conform with this finding.



1a



1e

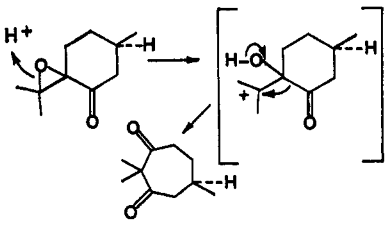


Figure 3. Acid-catalyzed rearrangement of pulegone epoxide.

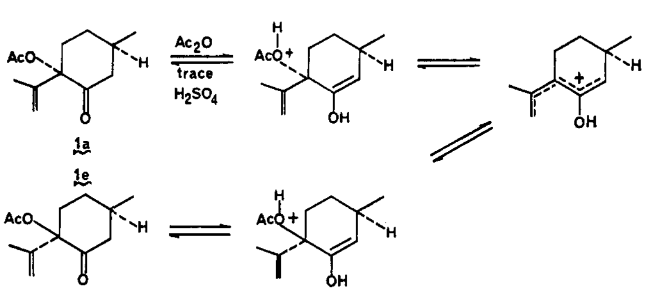


Figure 4. The interconversion of **1a** and **1e** in acetic anhydride-sulfuric acid solution.

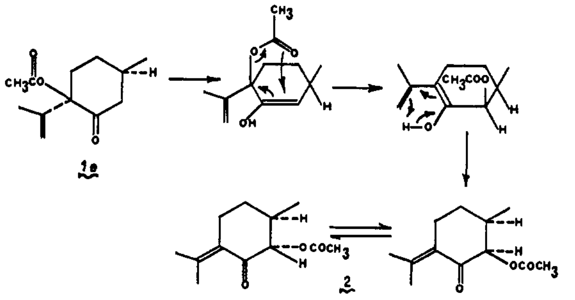


Figure 5. The conversion of 4-acetoxyisopulegone to 2-acetoxypulegone *via* collapse of a tight ion pair to the thermodynamically more stable dienoid enol.

With these considerations in mind the α- and β-epoxypulegones were prepared and treated with acetic anhydride–sulfuric acid in the hope that they would be transformed to **1a** and **1e**, respectively, each free from contamination by the other (Figure 2).[7] Bothersome acid-catalyzed rearrangements, one of which is shown in Figure 3, could be suppressed by adjusting carefully the acid concentration to a low level which favored the formation of **1**. Curiously, however, both the epoxide isomers were converted to mixtures of **1a** and **1e**.[8] That this lack of stereospecificity was not caused by the epimerization of the starting epoxide was clear since examination of incomplete reaction mixtures revealed only the one epoxide. However, when **1a** was treated under the reaction conditions for an extended period (60° for 4 hr) a mixture of **1a** and **1e** resulted.

Of the possible mechanisms that would account for this interesting transformation the most reasonable would seem to require a prior enolization of the ketone. From this form the epimerization might well proceed with ionization of the tertiary acetate assisted by protonation of the acetate, as depicted in Figure 4. Such a protonation scheme is indicated since a tight ion pair would be expected to collapse to the thermodynamically more stable product, according to the scheme shown in Figure 5, instead of undergoing the observed solvent attack.[9]

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(4) It was observed in the course of this work that **1a** and **1e** are cleanly separated when passed through a Xe-60 column.

(5) W. Reusch and C. K. Johnson, *J. Org. Chem.*, 28, 2557 (1963).

(6) Indeed, Djerassi and co-workers have noted this inconsistency in the pulegone oxide assignments: C. Djerassi, W. Klyne, T. Norin, G. Ohloff, and E. Klein, *Tetrahedron*, 21, 173 (1965), Table 1B, footnote C.

(7) E. Vogel and H. Schinz, *Helv. Chim. Acta*, 33, 116 (1950); D. N. Kirk, V. Petrow, and D. M. Williamson, *J. Chem. Soc.*, 2821 (1961).

(8) The ratio of **1a**:**1e** was dependent on the configuration of the starting epoxide, as well as the reaction temperature and time.

(9) This argument is based on the observation that the rates of racemization of the *p*-nitrobenzoates of *cis*- and *trans*-5-methylcyclohexen-3-ol are more rapid than those of solvolysis in the uncatalyzed system, whereas with acid catalysis they are the same, the indication being that

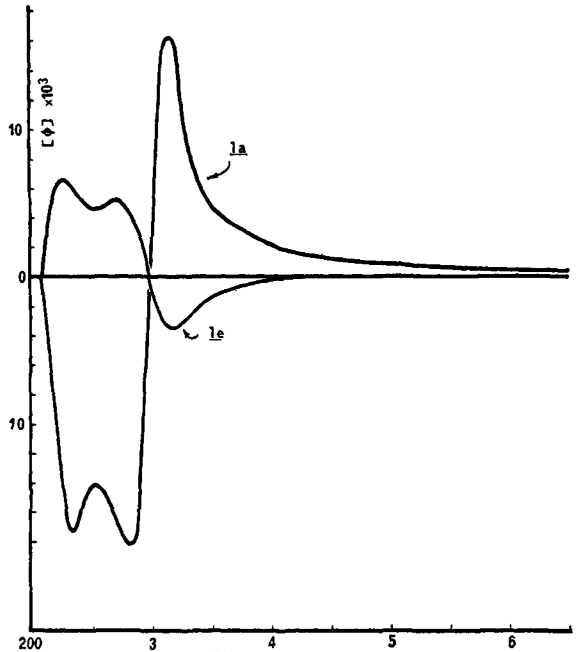

Figure 6. Cotton effects of the 4-acetoxyisopulegones.

This undesirable epimerization can be eliminated completely if the reaction is conducted at ambient temperatures over an extended period (3 days). However, by monitoring carefully the 60° reaction of the α-epoxide, **1a** can be obtained essentially free from contamination by **1e**. This is not the case with the β-epoxide, which yields the apparently more labile axial acetate **1e**. The source of this enhanced lability of **1e** is unclear. However, it may be associated with the 1–4 interaction between the acetoxy and *cis* ring methyl group in the enolic form of **1e**.

A further interesting aspect of the chemistry of **1a** and **1e** was observed when purification by an extended fractional distillation was attempted. In several of the later fractions significant amounts of the α,β-unsaturated isomer **2** were found. The possibility that **1** was converted thermally to **2** was confirmed by heating both **1e** and **1a** in sealed tubes to 200°, whereupon a rapid conversion took place to a mixture of *cis*- and *trans*-**2**.

A six-centered 1–3 shift of the acetoxy group through the enol form of **1**, as shown in Figure 5, would seem to account for this transformation.[9,10] The alternative S$_N$2′ process is regarded as unlikely since the attacking nucleophile (acetic acid) would have to be generated initially through the decomposition of **1**, and in the case of the enol of **1e** would have to undergo a sterically unfavorable *cis* approach.[11] Nevertheless, both of these possible mechanisms would require that the product **2** be the *cis* analog of the starting isomer, and in fact both isomers of **2** are formed from either isomer of **1**. Since **1e** and **1a** were not observed to equilibrate under the conditions of this rearrangement, but *cis*- and *trans*-**2** do equilibrate, an acceptable explanation for this lack of stereospecificity would be that once formed the isomers of **2** equilibrate at a faster rate than that of the isomerization.

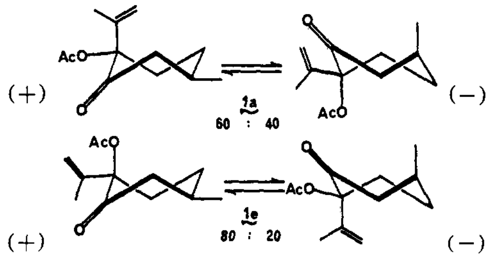

Figure 7. Rotational polarizations for the conformations of **1a** and **1e**.

With the observation of this rearrangement it should be noted that previous syntheses of **2** may proceed along a similar path. Thus, the observation that lead tetraacetate in refluxing benzene after about 2 hr oxidizes pulegone to a mixture of acetates **1** and **2** where **1** predominates,[1a] and mercuric acetate in refluxing acetic acid after 3 hr produces only **2**,[12] may be a function of the reaction conditions rather than the specificity of the oxidizing agent. In support of this contention, if **1a** is refluxed in acetic acid for 3 hr, it is isomerized to a mixture of *cis*- and *trans*-**2** to the extent of about 85%. In this work it has been possible to eliminate effectively this isomerization by a rapid, short-path distillation from the crude, resinous mixture, and thus to affect a reasonably facile, stereospecific synthesis of **1a** and **1e**.

Rather than rely completely on the contested stereochemistry of the starting epoxide, it was thought advisable to obtain direct evidence for the stereochemistry of **1a** and **1e**. This should be most readily acquired from optical rotary dispersion and ultraviolet absorption data.

Measurement of the Cotton effects of the isomers derived from α- and β-epoxypulegone produced values of $[\Phi]_{316}$ +16,200° and $[\Phi]_{318}$ −3460°, respectively (see Figure 6). In accounting for the Cotton effect signs of cyclohexanone systems such as **1a** or **1e**, one must take into consideration the extent of chair–chair interconversion and the rotational strength of each of these chair forms. A crude analysis of this equilibrium for **1a** and **1e** gives a diequatorial:diaxial ratio of 60:40 for **1a** and 80:20 for **1e**.[13] Reference to Figure 7 shows the sign that would be associated with each of these forms. Those conformations with an axial isopropenyl group will have a much higher rotational strength than those with an axial acetoxy group.[14] On this basis it would seem that **1a** must display a strong positive Cotton effect, whereas **1e** is a borderline case, which could display either a small positive or a negative effect.

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internal return from a tight ion pair does not play a significant role in the acid-catalyzed system: H. L. Goering and E. F. Silversmith, *J. Am. Chem. Soc.*, 77, 6249 (1955). However, a detailed analysis of the isopulegone case is in order before any authoritative mechanistic conclusions can be offered.

(10) H. L. Goering and E. F. Silversmith, *ibid.*, 77, 1129 (1955); H. L. Goering, T. D. Nevitt, and E. F. Silversmith, *ibid.*, 77, 5026 (1955).

(11) R. H. deWolfe and W. G. Young, *Chem. Rev.*, **56**, 769 (1956).

(12) R. H. Reitsema, *J. Am. Chem. Soc.*, **79**, 4465 (1957).

(13) This ratio was calculated considering the isopropenyl group to be slightly smaller than an isopropyl group, a 2-alkyl ketone effect to be applicable to the isopropenyl group but not to the acetoxy group, a 3-alkyl ketone effect to apply to the ring methyl group, and according to the techniques and data found in the following references: E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 8; N. L. Allinger and H. M. Blatter, *J. Am. Chem. Soc.*, **83**, 994 (1961); N. L. Allinger and L. A. Freiberg, *ibid.*, **84**, 2201 (1962); B. Rickborn, *ibid.*, **84**, 2414 (1962).

(14) A. Moscowitz, K. Mislow, M. A. W. Glass, and C. Djerassi, *ibid.*, **84**, 1945 (1962), and C. Djerassi in ref 3.

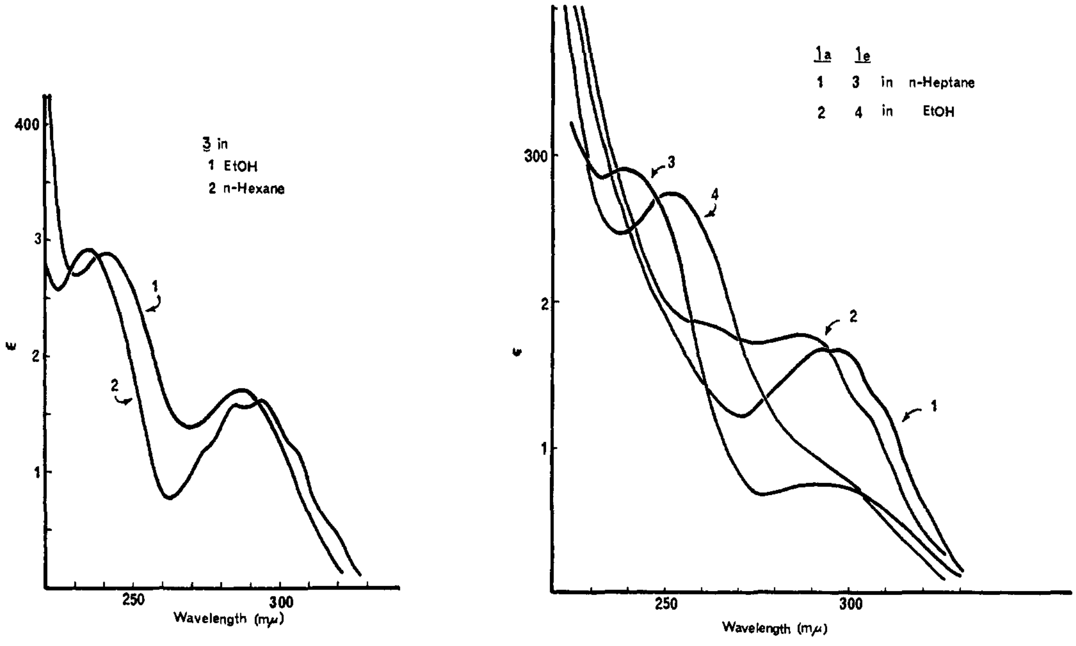
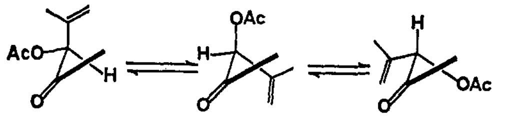


Figure 8. β,γ-Unsaturated ketone solvent effects.



3a (n → π*) 3b (n → π*; CT) 3c (CT)

Figure 9. The dependence of electronic transitions upon rotational conformers.

In agreement with this projection the +16,200° isomer must be **1a** and the −3460° isomer must be **1e**.[15] Extension of these assignments to the epoxypulegones supports the stereochemistry predicted by the "reverse octant rule."

The ultraviolet spectra of **1a** and **1e** confirm the above assignments, but they also supply additional information of interest (see Figure 8). The spectrum of **1a** in *n*-heptane most clearly displays the intense 295 mμ n → π* transition associated with a carbonyl interacting with an axially oriented β,γ double bond. This envelope undergoes the expected hypsochromic shift when the spectrum is observed in the more polar solvent, ethanol. Also a new peak is just visible in the 260-mμ region. As shall be seen this peak probably arises from the diaxial conformation of **1a** and thus corresponds to the short-wavelength transition observed for **1e**. This interesting feature is shown most clearly in curve 4 at 254 mμ. A reasonable argument can be advanced to show that this transition may well be of a charge-transfer type not to be associated with any one of the three possible isolated chromophores. The charge-transfer aspect of the transition is indicated by the 12-mμ bathochromic shift displayed on going from *n*-heptane to ethanol. Because of the low energy it is most certainly not a "pure" π → π* transition of the carbon–carbon double bond, and both the energy and intensity speak against its being either a n_1 → π* or a n_2 → π* acetoxy transition.[16] While it may contain some elements of a carbonyl π → π* transition it must not be a "pure" transition of this type since it is so dependent on the stereochemistry at the α-carbon atom. By analogy with the axial β,γ-unsaturated ketone system where a change-transfer transition is observed from the carbon–carbon to the carbon–oxygen double bond (not shown for **1a** but expected to fall in the 200-mμ region), the transition under consideration here may arise from a charge transfer between the acetoxy and the ketone, although the donor and acceptor orbitals must remain unspecified for the present. Furthermore, as with an axial β,γ-unsaturated ketone, the intensified n → π* carbonyl transition of **1e** must derive its additional intensity from just such a charge-transfer excitation if an "intensity borrowing" scheme is to be used as a basis for this effect.[17] Alternatively it must be mentioned that there is a possibility that this transition could arise from a charge-transfer interaction between the carbonyl and the equatorially oriented carbon–carbon double bond.[18]

In conjunction with the work which has just been described a model system, 3-acetoxy-4-methyl-4-penten-2-one (**3**), was prepared by the same procedure used in the pulegone series. The ultraviolet characteristic of this material (Figure 8) displays the expected intense n → π* transition and a 240-mμ charge-transfer transition. Through the medium of the previously discussed spectra one can say that the greater part of the n → π* intensity must arise from molecules with a "pseudo-axial" carbon–carbon double bond as approximated by

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(15) A similar effect has been noted in the case of *trans*-2-chloro-5-methylcyclohexanone where the more powerfully rotating axial chloride in the less stable diaxial conformation determines the sign of the Cotton effect: A. Moscowitz, K. Wellman, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 3515 (1963).

(16) The acetoxy system generally displays a long wavelength transition in the 209–217-mμ region which is associated with one of the two sets of nonbonding electrons. The least energetic of the series examined was *t*-butyl acetate [λ_{max} 216.1 mμ (ε 53)]: W. D. Closson and P. Haug, *ibid.*, **86**, 2384 (1964).

(17) J. N. Murrell, "The Theory of the Electronic Spectra of Organic Molecules," John Wiley and Sons, Inc., New York, N. Y., 1963, pp 158–168.

(18) For the present an acetate CT interaction is favored since 1-phenyl-1-acetoxypropan-2-one, but not 1-phenyl-1-dimethylaminopropan-2-one hydrochloride, displays a similar transition: unpublished data, J. C. Sheehan and R. M. Wilson.

3a or **3b** in Figure 9, whereas the 240-mμ CT excitation would have to be associated with molecules possessing a "pseudo-axial" acetoxy group as approximated by **3b** or **3c**.

Preliminary photochemical studies have been conducted with each of these three systems. The acetoxyisopulegones (**1a** and **1e**) do indeed yield menthofuran, however, only as a minor product. The major products appear to be the four possible methylenecyclobutanols which would be expected to arise from a Yang-type cyclization between the ketone carbonyl and the isopropenyl groups. The freely rotating system **3** also yields, as the only product isolated thus far, a methylenecyclobutanol, but until the stereochemistry of these products can be defined clearly a detailed accounting of the excited-state behavior of these ketones must be deferred.

Experimental Section[19]

Synthesis of *trans*-4-Acetoxyisopulegone (1a). A solution of 18.5 g (0.0881 mole) of α-epoxypulegone[5] (mp 57–59°) and 0.600 g (about 27 drops) of concentrated sulfuric acid in 90 ml of acetic anhydride was warmed gently on a steam bath for 1 hr. The acetic anhydride solution was poured onto ice chips. After most of the anhydride had been destroyed the oily residue was taken up in ether and extracted with portions of a sodium carbonate solution until no more carbon dioxide was evolved, then dried, concentrated, and the volatiles separated from high boiling substances by a short-path distillation at 0.07 mm. The distillate (16.1 g) was analyzed by vpc on a SE-30 column programmed at 10°/min and using indene as the internal standard (calculated yield of **1a**, 25%). The above distillate was redistilled (0.01 mm) using a 10-cm Vigreux column, and three fractions were collected: (1) 30–65°, 4.9 g, 80% **1a**; and (2) 65–68°, 6.8 g and (3) 68–69°, 2.8 g, both pure **1a**, for a total isolated yield of 9.6 g (41%). This yield discrepancy is attributed to the decomposition of the acetate on the vpc column. Analysis of these fractions by vpc under the same conditions used for **1e** showed only a trace (<1%) of what might have been the axial acetate **1e**. An analytical sample of **1a** had $n^{25}\mathrm{D}$ 1.4712; $\nu_{\max}^{\mathrm{CCl_4}}$ 3080, 1745, 1725, 1640, 1380, 1245, 1090, 1040, and 930 cm^{-1}; $\lambda_{\max}^{\mathrm{EtOH}}$ 287 mμ (log ϵ 2.24); $\lambda_{\max}^{n\text{-hep}}$ 297 mμ (log ϵ 2.22) and 292 mμ (log ϵ 2.22); in absolute EtOH $[\Phi]_{589}$ +543°, $[\Phi]_{500}$ +908°, $[\Phi]_{400}$ +2190°, $[\Phi]_{316}$ +16200°, $[\Phi]_{297}$ 0°, $[\Phi]_{274}$ −18200°, $[\Phi]_{245}$ −14100°, $[\Phi]_{226}$ −17300°; nmr (CDCl$_3$): doublet J = 6 cps, 0.99 (3 H), triplet J = 1 cps, 1.76 (3 H), singlet 2.01 (3 H), broad singlet 5.07 (1 H), and doublet J = 1.5 cps, 5.13 ppm (1 H).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.72; H, 8.67.

Synthesis of *cis*-4-Acetoxyisopulegone (1e). A solution of 19.7 g (0.117 mole) of β-epoxypulegone[5] (mp 53–55°) and 0.220 g (about nine drops) of concentrated sulfuric acid in 110 ml of acetic anhydride was warmed on a steam bath for 2 hr. The acetic anhydride was then destroyed by pouring onto ice chips. The dark residue was taken up in ether and the ethereal solution washed with a sodium carbonate solution until no more gas was evolved, then with water, and dried. After removal of the ether the residue was processed with a rapid, short-path distillation. All volatile material [bp 30–100° (0.01 mm), 18.5 g] was collected. Analysis of this mixture by vpc on a Xe-60 column (helium flow rate 60 cc/min at 40 psi) at 190° isothermal separated three major components: 2,2,5-trimethyl-1,3-cycloheptanedione, retention time 6.0 min; *trans*-4-acetoxyisopulegone, 11.0 min; *cis*-4-acetoxyisopulegone, 12.9 min (*cis*:*trans*, 80:20). This volatile material was distilled (0.01 mm) again using a 10-cm Vigreux column to give four fractions: (1) bp 30–69°, diketone:acetates, 50:50 (4.7 g); (2) 69–69.5°, 10:90 (4.8 g); and (3) 69.5–70° (5.3 g) and (4) 70–71° (1.6 g), both pure acetates.

The isomerization to the *trans*-acetate **1a** could be prevented if a reaction mixture of the same composition as that formulated above was protected from light, allowed to stand at room temperature for 3 days, and processed in the same fashion. However, in this procedure the yield of **1e** is lower as a result of the higher yield of the diketone and the incomplete consumption of starting material.

A. *cis*-4-Acetoxyisopulegone. An analytical sample had $n^{25}\mathrm{D}$ 1.4722; $\nu_{\max}^{\mathrm{CCl_4}}$ 3080, 1745, 1730, 1640, 1375, 1240, and 910 cm^{-1}; $\lambda_{\max}^{\mathrm{EtOH}}$ 252 mμ (log ϵ 2.44) and shoulder 290 mμ (log ϵ 1.98); $\lambda_{\max}^{n\text{-hep}}$ 294 mμ (log ϵ 1.87) and 240 mμ (log ϵ 2.46); in absolute EtOH $[\Phi]_{589}$ −29°, $[\Phi]_{500}$ −63°, $[\Phi]_{400}$ −264°, $[\Phi]_{318}$ −3460°, $[\Phi]_{300}$ 0°, $[\Phi]_{273}$ +5160°, $[\Phi]_{254}$ +4680°, $[\Phi]_{228}$ +6650°; nmr (CDCl$_3$): doublet J = 6 cps, 1.05 (3 H), broad singlet 1.77 (3 H), singlet 2.09 (3 H), singlet 4.90 (1 H), and broad singlet 5.02 ppm (1 H).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.83; H, 8.62.

B. 2,2,5-Trimethyl-1,3-cycloheptanedione (recrystallized from *n*-pentane) had mp 53–55°; $\nu_{\max}^{\mathrm{CCl_4}}$ 3400 (harmonic of the 1700-cm^{-1} band), 1700, 1490, 1470, 1375, 1355, 1300, 1125, 1095, 1080, and 1040 cm^{-1}; $\lambda_{\max}^{\mathrm{EtOH}}$ 290 mμ (log ϵ 1.62) and shoulder 207 mμ (log ϵ 2.87); $\lambda_{\max}^{n\text{-hex}}$ 294 mμ (log ϵ 1.55); nmr (CDCl$_3$): doublet J = 6 cps, 1.06 (3 H) and singlet 1.22 ppm (6 H).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.29; H, 9.67.

Isomerization of 4-Acetoxyisopulegone (1a and e). Two samples of **1a** were sealed under nitrogen in a Pyrex tube and heated in an air bath at 190–210°. The first sample (0.227 g, 0.00107 mole) was heated for 0.5 hr, and the second (0.389 g, 0.00178 mole) for 1 hr. Both samples were then distilled (0.02 mm) in a Hickman still, and all material boiling below 150° was collected (sample 1, 0.206 g; sample 2, 0.342 g). Analysis of these samples by vpc on an SE-30 column, programmed at 10°/min, and an Xe-60 column, at 190° isothermal, showed that sample 1 still contained some unreacted **1a** (**2**:**1a** = 1.5), but did not contain any **1e**. Sample 2 contained only *cis*- and *trans*-**2**, which were collected by vpc and found to have infrared and nmr spectra comparable to those of authentic samples. The integrated areas of the >C*H*OAc-CO- protons for the *cis* and *trans* isomers indicate that the mixture contains about 25% *cis*- and 75% *trans*-**2**.

The same isomerization also took place, albeit more slowly, in refluxing acetic acid. Refluxing **1a** (0.385 g, 0.00177 mole) in 15 ml of glacial acetic acid resulted in the following ratio of **1a**:**2** as determined by vpc on a Xe-60 column; after 1 hr 63:37; after 2 hr 33:66; after 3 hr 15:85.

The axial acetate **1e** was converted completely to the same mixture of *cis*- and *trans*-**2** after being pyrolyzed by the same method for 0.5 hr at 200°.

Synthesis of 3-Acetoxy-4-methyl-4-penten-2-one (3). A solution of 72 g (0.631 mole) of epoxymesityl oxide in 150 ml of acetic anhydride was cooled to ice-bath temperature and 1 ml of concentrated sulfuric acid was added with stirring. The solution was warmed to room temperature and allowed to stand 30 hr, then poured onto ice chips and allowed to stand for several more hours. The residual acetic acid was removed by extraction with a sodium carbonate solution, the resulting dark oil dissolved in ether, and the ethereal solution dried over sodium sulfate. After removal of the ether, the residue was distilled through a 12-in. platinum spinning-band column under high vacuum. The distillation was conducted as rapidly as possible to prevent isomerization of **3** to the conjugated acetoxy ketone, which occurs quite easily in this first distillation where higher pot temperatures are necessary to remove the volatiles from the polymer. Fractions were collected as follows: fraction 1, room temperature–70° (1 mm), 21.6 g, cut when the distillate was no longer yellow; fraction 2, 70–60° (1–0.3 mm), 24.6 g, cut as soon as the reflux dropped drastically; fraction 3, 60–100° (0.3 mm), 21.3 g, collected until no more material could be forced from the highly viscous residue.

Fraction 1 was not examined further. Fraction 2 was redistilled through the same column at 0.4 mm. The first compound was collected in several fractions, and had bp 30–55° (8.0 g), purest fraction bp 35–41° (5.7 g). This material was mostly 2,2-dimethylacetoacetaldehyde (constants reported below). The second compound (**3**) was cleanly separated from the first, bp 61–70° (12.4 g), purest fractions bp 65–70° (11.5 g).

Fraction 3 from the initial distillation was redistilled using the

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(19) All melting points are uncorrected and were taken on a Reichert hot-stage microscope. The infrared spectra were determined with a Perkin-Elmer Model 237 grating spectrophotometer. The ultraviolet spectra were determined with a Cary Model 14 recording spectrophotometer. The nmr spectra were determined at 60 Mc with a Varian Model A-60 spectrometer. The ORD spectra were determined on a Cary Model 60 spectropolarimeter. The vpc analyses and separations were conducted with an F & M Model 720 gas chromatograph. All columns were 12 ft × 1/4 in. 10% substrate on 60–80 mesh Diatoport W, unless otherwise noted. The drying agent was magnesium sulfate, and solvents were removed under reduced pressure unless stated otherwise. The microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Ind.

same column at 0.5 mm. The first pure material collected was **3**, bp 65–70° (0.9 g), followed by a fraction contaminated with 3-acetoxymesityl oxide, bp 70–80° (1.3 g). The major component was 3,4-diacetoxy-4-methylpentan-2-one, bp 102–112° (9.9 g), purest fraction bp 108–112° (9.1 g).

A. **2,2-Dimethylacetoacetaldehyde** had the following properties: $n^{25}\mathrm{D}$ 1.403; $\nu_{\max}^{\mathrm{CCl_4}}$ 2800, 2700, 1730, 1715, 1365, and 1135 cm^{-1}; $\lambda_{\max}^{\mathrm{EtOH}}$ 283 mμ (log ε 1.60), shoulder 235 mμ (log ε 1.94); $\lambda_{\max}^{n\text{-hex}}$ 292 mμ (log ε 1.66); nmr ($CDCl_3$): singlet 1.33 (6 H), singlet 2.17 (3 H), and singlet 9.58 ppm (1 H).

Anal. Calcd for $C_6H_{10}O_2$: C, 63.13; H, 8.83. Found: C, 63.38; H, 8.82.

B. **3-Acetoxy-4-methyl-4-penten-2-one (3)** was obtained in 13.5% yield; $n^{25}\mathrm{D}$ 1.4335; $\nu_{\max}^{\mathrm{CCl_4}}$ 3065, 1735, 1725, 1640, 1365, 1225, 1060, and 915 cm^{-1}; $\lambda_{\max}^{\mathrm{EtOH}}$ 287 mμ (log ε 2.23) and 241 mμ (log ε 2.45); $\lambda_{\max}^{n\text{-hex}}$ 294 mμ (log ε 2.21) and 235 mμ (log ε 2.46); nmr ($CDCl_3$): broad singlet 1.68 (3 H), singlet 2.01 (6 H), quartet J = 2 cps, 4.96 (1 H), broad singlet 5.06 (1 H), and singlet 5.17 ppm (1 H).

Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.75. Found: C, 61.39; H, 7.96.

C. **3-Acetoxymesityl oxide** was collected by vpc from the aforementioned fractions; $n^{25}\mathrm{D}$ 1.4533; $\nu_{\max}^{\mathrm{CCl_4}}$ 1755, 1700, 1630, 1375, 1280, 1235, and 1135 cm^{-1}; $\lambda_{\max}^{\mathrm{EtOH}}$ 306 mμ (log ε 1.83) and 242 mμ (log ε 2.99); nmr ($CDCl_3$): singlet 1.75 (3 H), singlets 2.10 and 2.13 (6 H), and singlet 2.23 ppm (3 H).

Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.75. Found: C, 61.82; H, 7.89.

D. **3,4-Diacetoxy-4-methylpentan-2-one** showed $n^{35}\mathrm{D}$ 1.4329 [lit.[20] bp 94° (0.1 mm) and 115–120° (0.3 mm); $n^{20}\mathrm{D}$ 1.4384), and other spectral properties in accord with this assignment.

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(20) I. G. Tishchenko, *Uch. Zap. Belorussk. Gos. Univ., Ser. Khim.*, 42, 189 (1958); *Chem. Abstr.*, **55**, 4351*e* (1961); E. Detilleux and J. Jadot, *Bull. Soc. Roy. Sci. Liege*, **29**, 208 (1960;) *Chem. Abstr.*, **55**, 7276*e* (1961).

The Vapor-Phase Thermolyses of 3-Hydroxy-1,5-hexadienes. II. Effects of Methyl Substitution[1a]

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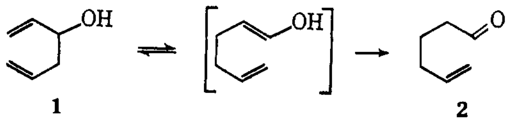
Abstract: The vapor-phase thermolyses of 3-hydroxy-1,5-hexadienes result in rearrangement to Δ^5-unsaturated carbonyl compounds and in the formation of cleavage products. Based on a series of ten methyl-substituted compounds studied, the formation of these products is interpreted on the basis of two competing concerted bond reorganizations both of which proceed through a cyclic six-membered transition state. Production of cleavage products predominates at higher temperatures, whereas the rearrangement is favored at lower temperatures. The thermolysis presents a general method for the preparation of Δ^5-unsaturated carbonyl compounds, although reaction yields are highly susceptible to substituent effects. Substitution in the 1 or 5 position favors the cleavage reaction due to steric and electronic factors, respectively.

We have previously reported[2] the thermal vapor-phase rearrangement of 1,5-hexadien-3-ol (**1**) to 5-hexenal (**2**), a process for which the term "oxy-Cope rearrangement" has been proposed.[3,4] This reaction may be considered a Cope rearrangement, leading to an enol intermediate, irreversible ketonization of which results in the observed carbonyl compound.



1 **2**

The occurrence of an analogous reaction involving two hydroxyl groups was suspected in 1934 in the catalytic pyrolysis of divinyl glycols,[5] although the purely thermal nature of the reaction has only recently been established.[4b,6]

In recent years there has been considerable interest in reactions involving bond reorganizations which are best interpreted on the basis of a cyclic transition state. The well-known Cope rearrangement falls into this category and has been described as an electrocyclic reaction.[7] This rearrangement is a typical "no-mechanism" reaction[8] which is brought about solely by thermal excitation either in solution or in the vapor state. The reaction usually appears as a unimolecular, homogeneous intramolecular process and only in rare instances have there been found intermolecular "crossover" products, resulting from fragmentation–recombination processes. Thus, Huntsman[9] has reported the formation of some 1,5-hexadiene and 2,5-dimethyl-

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(1) (a) Presented in part at the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966. (b) Taken in part from the M.S. Theses of K. K. C. and G. M. G., June 1966. (c) Undergraduate research participant.

(2) A. Viola and L. Levasseur, *J. Am. Chem. Soc.*, **87**, 1150 (1965).

(3) J. A. Berson and M. Jones, Jr., *ibid.*, **86**, 5017, 5019 (1964).

(4) (a) The name "enologenic Cope rearrangement" has now been suggested for this reaction.[4b] It would appear to us that it suffices to recognize the "Cope" rearrangement as a general reaction capable of occurring in a vast number of chemical environs. To attempt a definitive nomenclature for each variation of the reaction must of necessity lead to an undesirable profusion of adjectives. (b) E. Brown, P. Leriverend, and J. M. Conia, *Tetrahedron Letters*, 6115 (1966).

(5) M. Urion, *Compt. Rend.*, **190**, 1512 (1930); *Ann. Chim.*, [11] 1, 5 (1934).

(6) J. Chuche and J. Wiemann, *Compt. Rend.*, **262**, 567 (1966).

(7) R. B. Woodward and R. Hoffman, *J. Am. Chem. Soc.*, **87**, 395, 2511 (1965).

(8) For a review, see S. J. Rhoads in "Molecular Rearrangements," P. de Mayo, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, Chapter 11.

(9) W. D. Huntsman, *J. Am. Chem. Soc.*, **82**, 6389 (1960).