

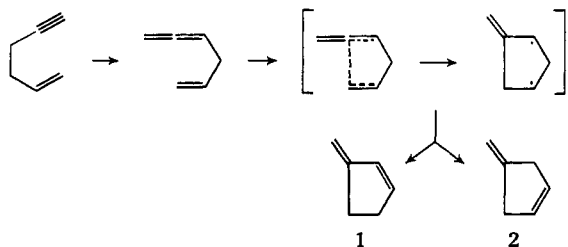
# The Vapor Phase Acetylenic Oxy-Cope Reaction of 5-Hexen-1-yn-3-ol. The Chemistry of an Allenol Intermediate<sup>1</sup>

Alfred Viola and John H. MacMillan

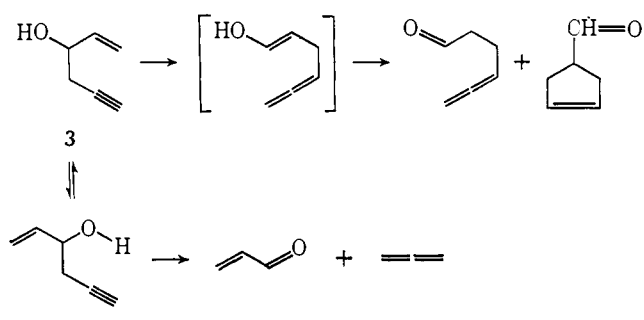
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**Abstract:** The vapor phase thermolysis of 5-hexen-1-yn-3-ol affords 2- and 3-cyclopentenecarboxaldehydes, *trans*-2,5-hexadienal, and sorbaldehyde in varying amounts dependent upon temperature and contact time. Since the  $\beta$ -hydroxyolefin cleavage which normally competes with oxy-Cope processes is completely absent, kinetic parameters could be determined. The Arrhenius energy of  $30 \pm 2$  kcal/mol and  $\Delta S^\ddagger$  of  $-14$  eu are indicative of a concerted mechanism and suggest that the participation of triple bonds in electrocyclic reactions leads to increased rates in comparison with the corresponding olefinic structures. The kinetic data obtained, the effects of temperature and contact time upon product distribution, and the results of a deuterium tracer indicate the intermediacy of the primary oxy-Cope product in the formation of all observed products. The latter, therefore, represent various reactions of the allenol, 1-hydroxy-1,2,5-hexatriene.

As a part of our continuing study of the thermolytic behavior of 3-hydroxy-1,5-hexadienes,<sup>2</sup> the oxy-Cope reaction,<sup>3</sup> the effects due to triple bond participation have been further<sup>4</sup> investigated. Only a few examples of triple bond participation in Claisen<sup>5</sup> or Cope<sup>4,6-9</sup> reactions have been reported. Huntsman<sup>7</sup> reported the parent acetylenic Cope system, 1-alken-5-ynes, to produce 1,2,5-alkatrienes, followed by a secondary thermal cyclization of the allenic products, *via* the diradical pathway indicated, to form **1** and **2**.



We have previously reported<sup>4</sup> the vapor phase thermolysis of 1-hexen-5-yn-3-ol (**3**) to produce the



(1) (a) Paper IV. For paper III, see ref 4. (b) Presented in part at the 157th National Meeting of the American Chemical Society, Minneapolis, Minn., April 1969.

(2) A. Viola, E. J. Iorio, K. K. Chen, G. M. Glover, U. Nayak, and P. J. Kocienski, *J. Amer. Chem. Soc.*, **89**, 3462 (1967).

(3) J. A. Berson and M. Jones, Jr., *ibid.*, **86**, 5017, 5019 (1964); A. Viola and L. Levasseur, *ibid.*, **87**, 1150 (1965).

(4) A. Viola and J. H. MacMillan, *J. Amer. Chem. Soc.*, **90**, 6141 (1968).

(5) For a recent review, see A. Jefferson and F. Scheinmann, *Quart. Rev. (London)*, **22**, 411 (1968).

(6) D. K. Black and S. R. Landor, *J. Chem. Soc.*, 6784 (1965).

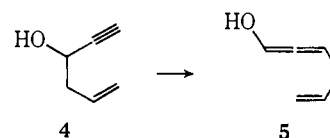
(7) W. D. Huntsman, J. A. DeBoer, and M. H. Woosley, *J. Amer. Chem. Soc.*, **88**, 5846 (1966).

(8) J. W. Wilson and S. A. Sherrod, *Chem. Commun.*, 143 (1968).

(9) J. Chucho and N. Manisse, *C. R. Acad. Sci., Paris, Ser. C*, **267**, 78 (1968).

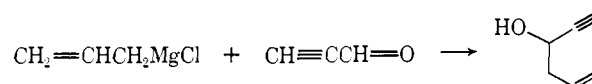
oxy-Cope and  $\beta$ -hydroxyacetylene cleavage products indicated.

The study of the thermolysis of 5-hexen-1-yn-3-ol (**4**) seemed an intriguing extension of our previous report, since the anticipated intermediacy of the Cope product would permit the study of the behavior of the allenol **5**.<sup>10</sup>



## Results

The desired starting material, 5-hexen-1-yn-3-ol (**4**) was prepared by the addition of propargylaldehyde to allylmagnesium chloride at  $-20^\circ$ , in order to avoid side reactions due to the acetylenic hydrogen. The structure of **4** was verified by spectroscopic means, as detailed in the Experimental Section, and by hydrogenation which produced the anticipated mixture of hydrogenation, hydrogenolysis, and disproportionation products.<sup>11</sup>

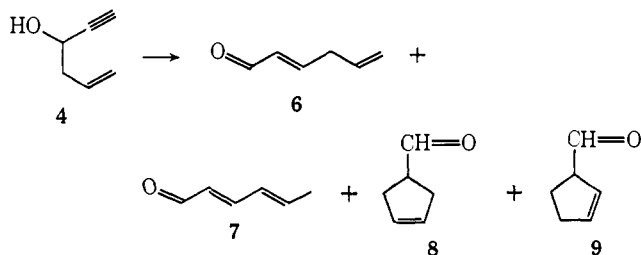


Thermolysis of **4** produced four main products, **6-9**, whose relative amounts depended upon the temperature and the residence time in the thermolysis column. The reaction was accompanied by fragmentation, which ranged from a negligible percentage at  $350^\circ$  to as much as 25% at  $390^\circ$ . The main products were separated by preparative vpc and were identified as follows.

The carbon skeleton of *trans*-2,5-hexadienal (**6**) was established by hydrogenation to hexanal and the positions of unsaturation were assigned on the basis of the ultraviolet, infrared, and nmr spectra as detailed in the Experimental Section. The structure assignment

(10) As an extension of the term "enol," the term "allenol" is proposed for a 1-hydroxy-1,2-diene and will be used for this designation throughout this paper.

(11) For an explanation of hydrogenation data of unsaturated alcohols, see ref 2 and references cited therein.



was further verified by the formation of a 2,4-dinitrophenylhydrazone derivative whose melting point is in excellent accord with that reported.<sup>12</sup> The geometric configuration is based upon the nmr spectrum wherein the splitting constant,  $J_{\alpha,\beta} = 16$  Hz, is indicative of the *trans* configuration as is the strong infrared band at  $975\text{ cm}^{-1}$ .<sup>13</sup>

Sorbaldehyde (7) was identified by comparison of its various properties with those of a commercial sample. Both vpc and the nmr spectrum of the sorbaldehyde fraction indicated the presence of all four geometric isomers with relative abundances which differed from those present in the commercial sample, although the all-*trans* form predominated in both.

Analytical vpc indicated that the two components subsequently identified as  $\Delta^3$ - and  $\Delta^2$ -cyclopentene-carboxaldehydes (8 and 9) could not be completely resolved with a variety of column packings. Although the  $\Delta^3$  isomer always predominated, successive passes through the preparative vpc column eventually afforded a 50:50 mixture of the two components. Quantitative hydrogenation of this mixture afforded a single product which, upon oxidation, gave cyclopentanecarboxylic acid, identified by means of its infrared spectrum which was superimposable on that previously obtained<sup>4</sup> in the study of the thermolysis of 3. The  $\Delta^3$  isomer was identified through the infrared spectrum of an enriched mixture which contained about 80% of this component; the spectrum was essentially superimposable on that previously reported<sup>4</sup> for the same compound. Since the ultraviolet spectrum of the 50:50 mixture of the two isomers consisted of only end absorption above  $220\text{ m}\mu$ , the  $\Delta^1$  isomer was eliminated from consideration. Fortunately there was essentially no overlap of the nmr absorption bands of the two compounds and, since the spectrum of the pure  $\Delta^3$  isomer was known to us,<sup>4</sup> that of the other component of the 50:50 mixture could be ascertained. The  $\Delta^2$ -cyclopentene-carboxaldehyde structure is therefore assigned on the basis of quantitative hydrogenation of the mixture to give only cyclopentanecarboxaldehyde, of the absence of  $\Delta^1$  isomer and of a consistent nmr spectrum.

The formation of propargylaldehyde had been anticipated *via* the  $\beta$ -hydroxyolefin cleavage<sup>14</sup> which has invariably accompanied the oxy-Cope reaction.<sup>2-4,8,9</sup> However, no propargylaldehyde appeared in the thermolysis product, although some low-boiling fragmentation products were observed, as a number of unidentified peaks close to the air peak in the vpc of all

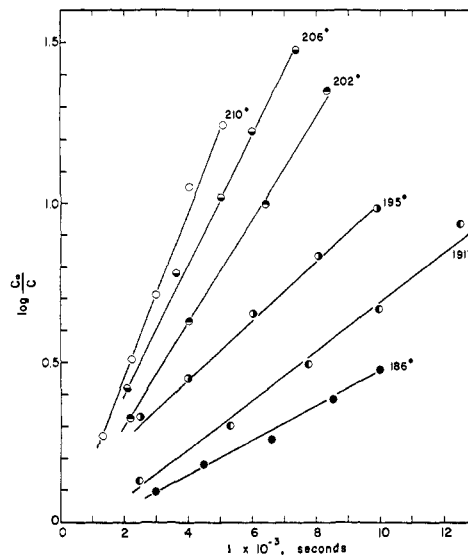


Figure 1. Kinetic data for the disappearance of 4.

thermolyses. Consequently, a sample of propargylaldehyde was passed through the thermolysis column at  $370^\circ$  but no fragmentation products were observed. Similarly, a mixture of  $\Delta^2$ - and  $\Delta^3$ -cyclopentene-carboxaldehydes was recovered unchanged after thermolysis at  $370^\circ$  as was a sample of *trans*-2,5-hexadienal (6). Thermolysis of a sample of commercial sorbaldehyde at  $370^\circ$ , however, produced not only some fragmentation, but also resulted in a change in the relative amounts of the four geometric isomers normally present.

### Reaction Kinetics

Oxy-Cope processes previously reported in the literature were invariably accompanied by the competing  $\beta$ -hydroxyolefin cleavage reaction, a factor which has precluded direct kinetic measurements of the oxy-Cope process. Since the anticipated cleavage was not observed during any of the thermolyses reported herein, the rate of disappearance of 4, in small sealed tubes, was determined over the temperature range of  $186$ – $210^\circ$ . Below this range, the reaction was too slow for accurate analyses and above this range extensive decomposition occurred. The data, summarized in Figure 1, clearly indicate the first-order disappearance of starting material and rule out any intermolecular process. The resulting rate constants afford an Arrhenius plot which indicates  $E_a = 30 \pm 2$  kcal/mol and  $\Delta S^\ddagger = -14 \pm 2$  eu. The excellent linearity of the Arrhenius plot rules out any likelihood of direct formation of the observed products from the starting material by competitive first-order processes.

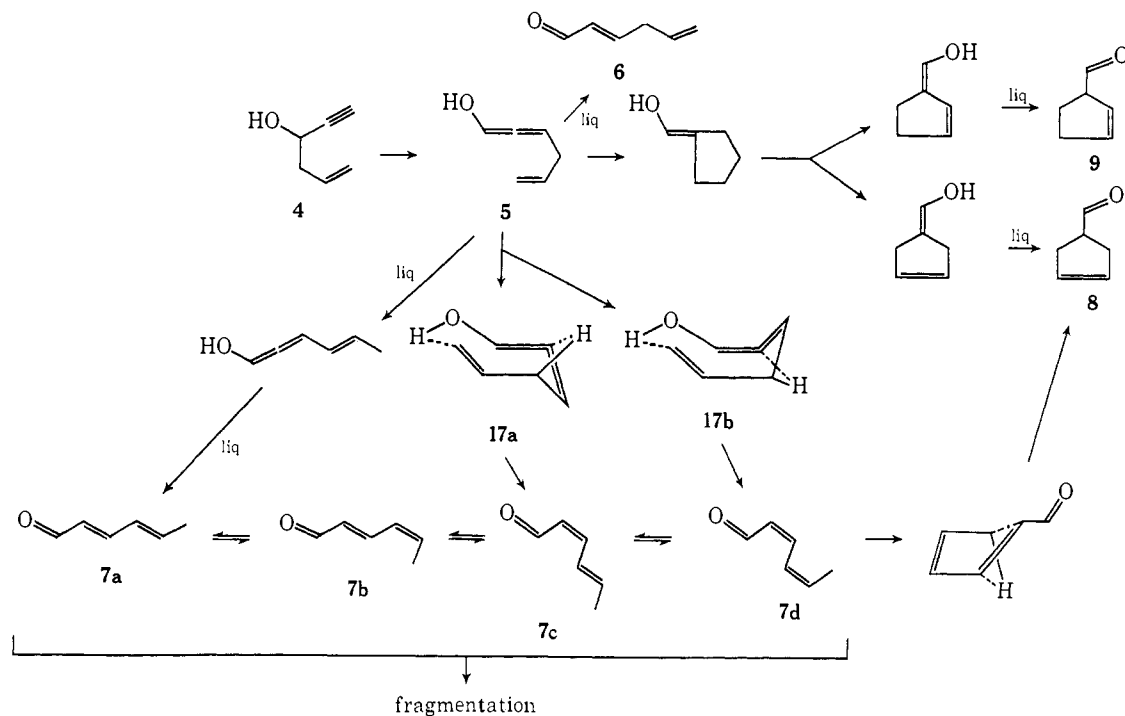
The kinetic parameters strongly suggest a concerted mechanism involving a cyclic transition state. Reported activation energies for concerted Cope processes range from 23 to 36 kcal/mol<sup>15</sup> but the lower end of this range reflects accompanying ring strain relief such as in the reaction of divinylcyclobutane.<sup>15c</sup> The

(12) J. P. Ward and D. A. Van Dorp, *Rec. Trav. Chim. Pays-Bas.*, **85**, 117 (1966).

(13) R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1967.

(14) R. T. Arnold and G. Smolinsky, *J. Amer. Chem. Soc.*, **81**, 6443 (1959); *J. Org. Chem.*, **25**, 129 (1960); G. G. Smith and B. L. Yates, *J. Chem. Soc.*, 7242 (1965).

(15) (a) E. G. Foster, A. C. Cope, and F. Daniels, *J. Amer. Chem. Soc.*, **69**, 1893 (1947); (b) R. G. Aldridge and G. W. Murphy, *ibid.*, **73**, 1158 (1951); (c) G. S. Hammond and C. D. DeBoer, *ibid.*, **86**, 899 (1964); (d) W. von E. Doering and V. Toscano, unpublished results. See footnote 12 of W. von E. Doering, *et al.*, *Tetrahedron*, **23**, 3943 (1967).



value of 36 kcal/mol has been reported<sup>15d</sup> for the pure unperturbed Cope rearrangement of 1,1-dideuterio- $\rightarrow$  3,3-dideuterio-1,5-hexadiene. The perturbation effect of an oxygen on a diradical Cope process has been estimated at 3 kcal/mol,<sup>16</sup> but this effect, if applicable to the propargylic system, is counteracted by the difference in bond dissociation energy between an allylic and propargylic bond, estimated<sup>17</sup> at 3–4 kcal/mol. Possibly, the low  $E_a$  found here results from the cylindrical symmetry of the acetylenic  $\pi$ -electron system, which eases the approach of the terminal methylene in the formation of the requisite transition state and/or decreased proton-proton interactions at the 1–6 positions. We have previously suggested<sup>4</sup> that electrocyclic reactions involving acetylenic bonds may well proceed more readily than their olefinic analogs since both the oxy-Cope and the  $\beta$ -hydroxyacetylene cleavage reported for **3** appeared to proceed at a faster rate than the corresponding reactions of 1,5-hexadien-3-ol.<sup>18</sup> The absence of  $\beta$ -hydroxyolefin cleavage in this system, therefore, stems from the increased rate of the competing Cope process since only the latter involves participation of an acetylenic bond. By contrast, in the thermolysis of **3** both processes involved the acetylenic link.

## Discussion

Chart I summarizes the mechanistic scheme which we propose for the formation of all observed products. This scheme is consistent with the observed data, as discussed below, and actually represents various reactions of the thermally produced allenol **5**. All steps

(16) J. A. Berson and E. J. Walsh, Jr., *J. Amer. Chem. Soc.*, **90**, 4730 (1968).

(17) M. M. Martin and E. B. Sanders, *ibid.*, **89**, 3777 (1967), and references cited therein.

(18) In direct competition experiments at 350°, the amount of surviving 1,5-hexadien-3-ol was *ca.* three times that of **3** and the amount of surviving dienol was *ca.* six times that of **4**. The report of these experiments as well as the kinetic study of  $\beta$ -hydroxyacetylene cleavage will be submitted for publication shortly.

requiring 1,3-hydrogen shifts occur in the liquid state after condensation of the vapor, in agreement with our previously reported findings<sup>2,4</sup> and with the Woodward-Hoffmann rules forbidding thermal, concerted, uncatalyzed 1,3-hydrogen shifts.<sup>19</sup>

The yield data, summarized in Table I, suggest interrelationships in the formation of the observed products. The amount of oxy-Cope product **6** de-

**Table I.** Effect of Temperature and Residence Time<sup>a</sup> on Yields (%)<sup>b,c</sup>

$t$ , °C	$P$ , <sup>a</sup> mm	2,5-Hexadienal <b>6</b>	2,4-Hexadienal <b>7</b>	Cyclopentene-carboxaldehydes <b>8 + 9</b>	Fragmentation <sup>c</sup>
390	20	28	15	31	26
	0.5	46	21	24	10
370	20	32	15	38	15
	0.5	48	37	6	9
350	20	46	16	23	15
	0.5	62	24	6	8

<sup>a</sup> Pressure was monitored at the trap end of the flow system and is not, therefore, a true measure of pressure within the thermolysis zone, but, at constant drop rate, reflects the relative residence time.

<sup>b</sup> Percentages are based on integrated vpc peak areas of condensed products and the weight loss. <sup>c</sup> Fragmentation includes the highly volatile products and the weight loss. Since the latter is due in part to mechanical losses and not solely to noncondensation of the more volatile fragmentation products, all products data in this table reflect a lower limiting value.

creases with increasing temperature and increasing contact time, indicative of the intermediacy of its enolic precursor in the formation of other products. The production of sorbaldehyde (**7**) also decreases with increased residence time but passes through a maximum with increasing temperature, indicative of multiple

(19) R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, **87**, 2511 (1965).

involvement. The formation of the cyclopentenecarboxaldehyde fraction, **8** + **9**, increases with increasing residence time but also passes through a temperature maximum, indicative of the formation of **8** and **9**, as end products, from precursors whose concentration is temperature dependent. The observed fragmentation must result from thermal decomposition of one or more of the end products or their precursors, since competing processes involving decomposition of **4** are ruled out by the reaction kinetics and by the residence time dependency of the amount of fragmentation under conditions where no starting material survives. The participation of free radicals in the rearrangement of **4** is discounted by the kinetic parameters and by the fact that, in agreement with our previously reported findings,<sup>2,4</sup> no evidence for intermolecular coupling could be detected.

The first-order disappearance of **4** indicates the formation of all observed products through a common intermediate, presumably the allenol, **5**. In our previously reported thermolyses,<sup>2,4</sup> all evidence indicated the survival of the enolic intermediate in the vapor phase, with ketonization occurring only after condensation.<sup>4</sup> Similarly, if ketonization of the allenol is restricted to intermolecular collisions in the liquid state after condensation, the formation of thermolysis products other than **6** reflects intramolecular reactions of the allenol.

The diradical pathway suggested by Huntsman for the thermolysis of 1-alken-5-yne led to a slight preponderance of the conjugated cyclic diene **1**.<sup>7</sup> A similar pathway should favor the production of a small excess of the conjugated enolic precursor of **9**, which was not the case. Table II lists the ratios of  $\Delta^3$ - and  $\Delta^2$ -

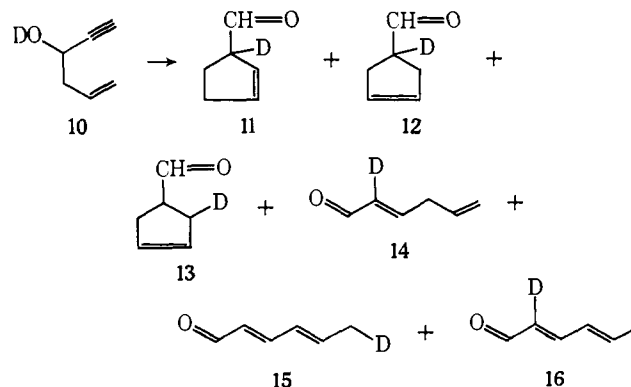
**Table II.** Effect of Temperature and Residence Time<sup>a</sup> on Composition<sup>b</sup> of Cyclopentenecarboxaldehyde Fraction

<i>t</i> , °C	<i>P</i> (mm) <sup>a</sup>	Ratio <b>8</b> : <b>9</b>
390	20	5.5
	0.5	2.5
370	20	6.2
	0.5	2.9
350	20	7.1
	0.5	5.0
370 <sup>c</sup>	20 <sup>c</sup>	1.3 <sup>c</sup>

<sup>a</sup> At constant drop rate, pressure reflects the relative residence time. <sup>b</sup> Data were obtained from partially resolved vpc peak areas. <sup>c</sup> From deuterium tracer study involving thermolysis of **10**.

cyclopentenecarboxaldehydes, **8**:**9**, which were not only substantially larger than unity in all cases, but increased with increased contact time (higher pressure). The fact that increased temperature results in a decreased ratio is indicative of an alternate mechanism for the formation of **8**, with a lower activation energy than the diradical pathway. In order to elucidate further the reaction course, the deuterium-labeled alcohol **10** was thermolyzed and the products were fractionated by means of preparative gas chromatography.<sup>20</sup>

(20) The degree of deuterium scrambling is indicated by the mass spectrum of each fraction. The content of dideuterated species was negligible in the cyclopentenecarboxaldehyde fraction, slightly more in the 2,5-hexadienal, and moderate in the sorbaldehyde. The fact that the dideuterium content parallels the relative vpc retention times of these fractions suggests that deuterium scrambling may occur in the liquid state during the separation process and not necessarily in the vapor during the thermolysis.

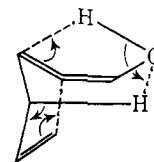


The deuterium distribution was established by nmr. In the cyclopentenecarboxaldehyde fraction, the splitting pattern of the aldehydic proton and the decreased intensities of the bands corresponding to the  $\alpha$  protons clearly indicated the formation of about equal amounts of the  $\alpha$ -deuterated species **11** and **12**, in agreement with the participation of the above diradical pathway. However, decreased intensity of the  $\delta$  2.68 multiplet of the  $\Delta^3$  component shows the remainder of the label to be in the 2 position (**13**). An additional route to the  $\Delta^3$  isomer, **8**, involving eventual transfer of the hydroxylic proton to the 2 position as indicated in **13**, is suggested by the processes for sorbaldehyde formation.<sup>21</sup>

The deuterated sorbaldehyde consists of **15** and, to a lesser degree, **16**. The introduction of the label into the terminal methyl group is evidenced by an altered multiplet pattern and decreased integral for the  $\delta$  1.9 band, whereas the evidence for the  $\alpha$  label consists of a decrease in absorption at  $\delta$  6.06 and also the appearance of a weak broad band in the center of each of the aldehydic doublets. A quantitative evaluation was not possible due to the greater extent of deuterium scrambling in this fraction<sup>20</sup> and to the altered geometric isomer ratio which made spectral comparisons with authentic sorbaldehyde difficult.

Table III lists the geometric isomer distribution in sorbaldehyde from various sources. The thermolysis of commercial sorbaldehyde, which also produced fragmentation, led to the formation of increased amounts of *cis* isomers **7c** and **7d** at the expense of the all-*trans* form, **7a**. However, the sorbaldehyde produced during thermolysis of **4** contains a still larger proportion of *cis* forms. The data are consistent with sorbaldehyde formation from **5** via the cyclic transition

(21) The hydrogen transfers required for the direct formation of the enolic precursor of **13** from the allenol could be accomplished in a concerted process involving a somewhat tortuous tricyclic transition state.



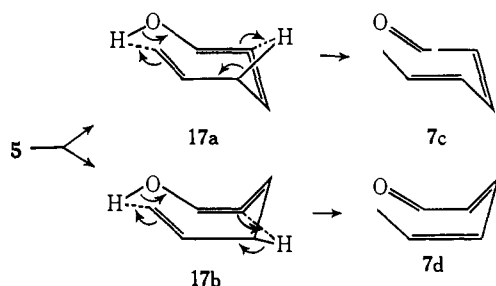
Although such a process could account for the temperature effect on the **8**:**9** ratio, it would not explain the increased amounts of **8** formed with increased contact time. Since this process as well as the intermediary of the diradical involve direct conversion of the allenol via two competitive reactions, the product ratio would have to be independent of contact time in the absence of a highly unlikely  $9 \rightarrow 8$  isomerization. Although the isomerization of their respective enolic precursors is not precluded by the fact that the **8**:**9** ratio remains unchanged upon rethermolysis of a 50:50 mixture of the two cyclopentenecarboxaldehydes, such a process would have to proceed in the direction out of conjugation to afford the observed product ratio.

**Table III.** Distribution (%)<sup>a</sup> of Geometric Isomers in Various Sorbaldehyde Samples

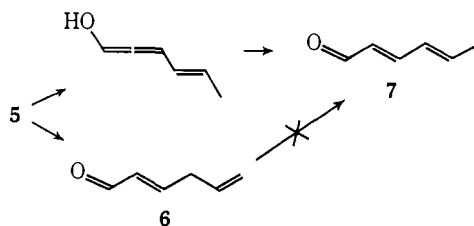
Source	7a <i>trans,trans</i>	7b <i>trans,cis</i>	7c <i>cis,trans</i>	7d <i>cis,cis</i>
Commercial sample	77	19	4	Trace
Thermolyzed <sup>b</sup> commercial	66	18	11	4
From thermolysis <sup>b</sup> of 4	51	36	11	2

<sup>a</sup> Percentages are based on relative areas of the corresponding aldehydic proton nmr peak. Doublets are centered at  $\delta$  9.53, 9.63, 10.19, and 10.23 for the 7a, 7b, 7c, and 7d isomers, respectively. These assignments are based upon isomeric abundance in the commercial sample and are in accord with diamagnetic anisotropy effects. <sup>b</sup> Thermolysis at 370°.

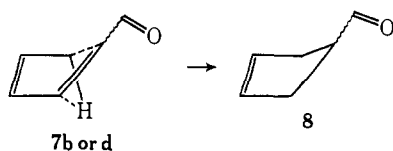
state 17, two configurations of which afford the *cis,trans* and *cis,cis* isomers, 7c and 7d. This process results in deuterium labeling of the terminal methyl



group. Thermal *cis,trans* isomerization in the vapor affords the *trans,trans* isomer as does a liquid state allylic shift in 5. The latter transformation, competitive with ketonization, accounts for the appearance of the deuterium label in the  $\alpha$  position. A direct 6  $\rightarrow$  7 isomerization is excluded by the fact that 6 was recovered unchanged upon recycling through the thermolysis column.



As a consequence of the  $\Delta^4$ -*cis*-sorbalddehydes produced in the thermolysis zone, we suggest the possibility of formation of 8 *via* a thermal 1,2 cycloaddition. This process not only accounts for the appearance of the deuterium label in the 2 position of 8, since it occurs



in the terminal methyl of 7, but also accounts for the increase of 8 produced by increased residence times. Furthermore, the contribution of this pathway to the formation of 8 dictates the isotope effect observed in the thermolysis of deuterated alcohol, 10. Since the rate of formation of 7 *via* the intermediacy of 17 is decreased by deuterium substitution, the decreased contribution of this pathway to  $\Delta^3$ -cyclopentene-

carboxaldehyde formation results in the lowered 8:9 ratio observed (see Table II). Either  $\Delta^4$ -*cis*-sorbalddehyde isomer, 7b or 7d, is sterically capable of formation of the requisite transition state leading to 8. The all-*cis* isomer, 7d, can arise directly *via* 17b, but all geometric forms of 7 are presumably thermally interconvertible. Although the geometric redistribution obtained by thermolysis of commercial 7 may not represent an equilibrium system due to the short contact time, the distribution observed from the thermolysis of 4 seems to represent a higher initial concentration of  $\Delta^4$ -*cis* isomers. A complicating factor is the fragmentation observed in the thermolyses of 4 and of commercial 7, which we suspect occurs largely through the *cis* forms. The greater amount of fragmentation observed during thermolyses of 4<sup>22</sup> then reflects the greater proportion of *cis* isomers of 7 produced initially as compared with commercial 7. The sorbaldehyde produced by thermolysis may therefore undergo further thermal reactions to give internal cycloaddition, geometric redistribution, or fragmentation.

## Experimental Section

Melting points and boiling points are uncorrected. Infrared spectra were obtained with a Beckman IR-5A spectrophotometer on neat liquid samples. Nmr spectra were determined with a Varian A-60A spectrometer in deuterated chloroform solutions with an internal tetramethylsilane standard. Elementary analyses were performed by Dr. Stephen M. Nagy, Belmont, Mass. Ultraviolet spectra were determined with a Bausch and Lomb Spectronic 505 from Spectrograde "Isocetane" solutions. Vapor phase chromatographic analyses were obtained with a F & M Model 500 using 2-ft columns packed with 10% silicone grease or 20% Triton X-305 on Chromosorb P. Relative peak areas were determined with a disc integrator. Preparative vpc was accomplished with a F & M Model 776 using 8 ft  $\times$  1 in. columns packed with 20% Triton X-305 on Chromosorb P.

**Preparation of 5-Hexen-1-yn-3-ol (4).** This compound, previously unreported, was prepared by the addition of allylmagnesium chloride to propargylaldehyde.

In a 1-l. three-necked flask, equipped with mechanical stirrer, condenser, and dropping funnel, were placed 300 ml of absolute ether, 34 g (1.4 g-atoms) of Mg turnings, and a crystal of iodine. A solution of 54 g (0.7 mol) of freshly distilled allyl chloride in 100 ml of absolute ether was added, with stirring, over a period of 2 hr. During the course of the addition, a thick white Grignard complex separated from the solution. The complex was redissolved by adding a few milliliters of anhydrous tetrahydrofuran. After the addition was complete, the flask was immersed in a Dry Ice-acetone bath maintained at  $-25^\circ$ . A solution of freshly distilled propargylaldehyde, 11 g (0.2 mol), prepared by the procedure given in ref 23, in 100 ml of absolute ether was then added, with stirring, over a period of 1.5 hr. During the addition, the bath temperature was maintained at  $-25$  to  $-30^\circ$ . After the addition was complete, the mixture was allowed to warm to room temperature and was then decomposed by pouring onto ice-ammonium chloride. The ether and aqueous layers were separated and the aqueous layer was extracted with two 50-ml portions of ether. The combined ether layers were dried with anhydrous  $MgSO_4$  and the ether was evaporated to yield a light yellow oil. Careful fractionation under reduced pressure yielded 11 g of a homogeneous (vpc) fraction, which represents a yield of 57% based on the amount of propargylaldehyde used, bp  $67-69^\circ$  (35 mm),  $n_D^{25}$  1.4580,  $d_4^{25}$  0.8953.

*Anal.* Calcd for  $C_6H_8O$ : C, 74.97; H, 8.39. Found: C, 74.93; H, 8.42.

(22) Although recyclic experiments show that fragmentation cannot originate from 6, 8, or 9, the possibility remains that one of the respective enols is responsible. We consider the latter unlikely since none of our enolic precursors previously reported, ref 2 and 4, have shown such tendencies, whereas some of the resulting carbonyl compounds have.

(23) J. C. Sauer, "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., John Wiley & Sons, Inc., New York, N. Y., 1963, p 813.

The infrared spectrum of 5-hexen-1-yn-3-ol contained pertinent bands at about 3400 (s), 3300 (spike), 3080 (m), 2900 (m), 2130 (w), 1650 (m), 1435 (m), 1300 (m), 1120 (m), 1030 (s), 990 (s), 955 (m), 920 (s), and 640  $\text{cm}^{-1}$  (s).

The nmr spectrum consisted of a complex multiplet centered at  $\delta$  2.5 (4 H, allylic, acetylenic and hydroxylic) which collapsed to a simpler multiplet (3 H, allylic and acetylenic) on exchange with  $\text{D}_2\text{O}$ , and multiplets centered at  $\delta$  4.43 (1 H, methine),  $\delta$  5.2 (2 H, terminal vinyl), and  $\delta$  5.9 (1 H, internal vinyl).

Hydrogenation of a small amount of the alcohol over Pd-C led to the absorption of 90% of the theoretical amount of hydrogen required for the saturation of three double bonds. Analytical vpc of the hydrogenation product indicated three constituents. The retention time of the major component (73%) was equal to that of 3-hexanone and that of the second component (24%) corresponded to 3-hexanol. The remaining trace component is believed to be hexane. The major constituent, isolated by preparative vpc, had an infrared spectrum superimposable on that of 3-hexanone and formed a 2,4-dinitrophenylhydrazone derivative, mp 135–136° (lit.<sup>24</sup> mp 130°), which showed no melting point depression on admixture with an authentic sample of the same derivative of 3-hexanone.

**Thermal Vapor Phase Rearrangements.** The rearrangements were performed in a flow system which has been described previously.<sup>2</sup>

The condensed products, usually representing a recovery of 85–90%, were subjected to vpc analyses and consisted of mixtures of the following components in varying amounts which depended upon reaction conditions: low-boiling products,  $\Delta^2$ - and  $\Delta^3$ -cyclopentenecarboxaldehyde, *trans*-2,5-hexadienal, various configurational isomers of sorbaldehyde, and traces of unreacted starting alcohol. Thermolyses were performed numerous times under various pressure and temperature conditions. The data are summarized in Table I. A typical experiment follows.

5-Hexen-1-yn-3-ol (3.10 g) was passed through the thermolysis column at 370° and a pressure of 20 mm. A drop rate of 4 drops/min was always maintained. The condensed product, 2.82 g (91% recovery), consisted of 6% low-boiling fragmentation products, 42% of a mixture of  $\Delta^2$ - and  $\Delta^3$ -cyclopentenecarboxaldehydes, 35% *trans*-2,5-hexadienal, and 17% sorbaldehyde. The compounds were identified as follows.

**$\Delta^3$ -Cyclopentenecarboxaldehyde (8) and  $\Delta^2$ -Cyclopentenecarboxaldehyde (9).** Mixtures containing only these two components were obtained by preparative vapor phase chromatography but the two components were not readily separated on any column packing tried. The  $\Delta^3$  isomer was always in excess and was identified in the following manner. The infrared spectra of mixtures consisting of more than 80% of this component were essentially superimposable on the spectrum of the  $\Delta^3$  isomer previously obtained.<sup>4</sup> Vpc retention times of this component were also identical with those of the previously obtained  $\Delta^3$  isomer on both polar and nonpolar columns. Nmr spectra of mixtures of the two components showed all the peaks found in the known  $\Delta^3$  isomer.<sup>4</sup>

The presence of the  $\Delta^2$  isomer, which always appeared as a shoulder on the  $\Delta^3$  isomer peak of the vapor phase chromatogram, was established as follows. Ultraviolet spectra of mixtures of the two components showed only end absorption above 220  $\text{m}\mu$ . Hydrogenation of a small sample of a 1:1 mixture of the two components with Pd-C led to the absorption of 110% of the amount theoretically required for saturation of one double bond. The hydrogenated product was a single entity, as evidenced by vpc on both polar and nonpolar columns. Bubbling a stream of air through a warmed sample of the hydrogenated compound for 5 hr quantitatively converted it to a saturated acid whose infrared spectrum was identical with that published for cyclopentanecarboxylic acid.<sup>25</sup>

The nmr spectrum of the mixture showed little overlap between peaks due to the  $\Delta^2$  and  $\Delta^3$  isomers; therefore nmr assignments for the  $\Delta^2$  isomer can be given.

The spectrum showed a doublet at  $\delta$  9.52 (1 H, aldehydic), multiplets at  $\delta$  6.05 (1 H, vinyl proton at position 2),  $\delta$  5.7 (1 H, vinyl proton at position 3),  $\delta$  3.52 (1 H, methine proton), and a complex of multiplets centered at  $\delta$  2.2 (4 H, aliphatic protons).

(24) "Tables for Identification of Organic Compounds," M. Frankel and S. Patai, Ed., The Chemical Rubber Publishing Co., Cleveland, Ohio, 1960.

(25) B. Trost, "Problems in Spectroscopy," W. A. Benjamin, Inc., New York, N. Y., 1967, Compound No. 111.

***trans*-2,5-Hexadienal (6).** This compound was isolated and purified by means of preparative vpc, bp 141–143°,  $n_D^{25}$  1.4725

*Anal.* Calcd for  $\text{C}_8\text{H}_{14}\text{O}$ : C, 74.97; H, 8.39. Found: C, 74.79; H, 8.54.

The infrared spectrum contained pertinent bands at about 3075 (w), 2990 (w), 2900 (w), 2800 (m), 2700 (m), 1720 (shoulder), 1690 (vs), 1635 (s), 1430 (m), 1310 (w), 1130 (s), 995 (s), 975 (s) and 920  $\text{cm}^{-1}$  (s).

The ultraviolet spectrum consisted of a broad band,  $\lambda_{\text{max}}$  220  $\text{m}\mu$ ,  $\epsilon_{\text{max}}$   $1.1 \times 10^4$ .

The nmr spectrum consisted of a doublet at  $\delta$  9.51 (1 H, aldehydic,  $J = 7$ ), a doublet of triplets at  $\delta$  6.82 (1 H,  $\beta$  vinylic,  $J_{\alpha\beta} = 16$ ,  $J_{\beta\gamma} = 6.5$ ), a doublet of doublets with long-range triplet splitting centered at  $\delta$  6.08 (1 H,  $\alpha$  vinylic,  $J = 7$ , 16), a typical terminal vinyl pattern at  $\delta$  4.9–5.3 and  $\delta$  5.82 (3 H, the latter multiplet consists of a series of triplets,  $J = 6.5$ ), and a triplet with long-range quartet splitting at  $\delta$  3.08 (2 H, methylene).

The compound formed a 2,4-dinitrophenylhydrazone, mp 140–142° (lit.<sup>12</sup> mp 140–142°).

*Anal.* Calcd for  $\text{C}_{12}\text{H}_{12}\text{O}_4\text{N}_4$ : C, 52.17; H, 4.38. Found: C, 52.23; H, 4.51.

Hydrogenation of a small sample of the aldehyde over Pd-C led to the absorption of 100% of the theoretical amount required for saturation of two double bonds. The hydrogenation product, shown to be a single entity by vpc, had an infrared spectrum superimposable on that of authentic hexanal and its 2,4-dinitrophenylhydrazone derivative, mp 105° (lit.<sup>24</sup> mp 104°), showed no melting point depression on admixture with an authentic sample of the same derivative of hexanal.

**2,4-Hexadienal (Sorbaldehyde) (7).** A fraction isolated from the thermolyses by means of preparative vpc consisted of mixtures of all four geometric isomers of sorbaldehyde, but separation of individual isomers could not be effected. The sorbaldehyde was initially identified by its characteristic odor and its presence was confirmed by comparison of its vpc retention times and infrared spectrum with those of a commercial sample. The mixture afforded a 2,4-dinitrophenylhydrazone derivative, mp 188–189° (lit.<sup>26</sup> mp 192°), which showed no melting point depression on admixture with an authentic sample.

*Anal.* Calcd for  $\text{C}_{12}\text{H}_{12}\text{O}_4\text{N}_4$ : C, 52.17; H, 4.38. Found: C, 52.29; H, 4.55.

The nmr spectrum of sorbaldehyde consists of a methyl doublet at  $\delta$  1.9, multiplets in the region of 5.8–6.6 (3 H) and 6.9–7.7 (1 H), and a series of doublets in the aldehydic region. Complete analysis of the spectrum is difficult due to the mixture of geometric isomers always present. The aldehydic region, however, contains four sets of doublets readily assignable to the four isomers (see Table III).

**Preparation and Thermolysis of 5-Hexen-1-yn-3-ol-O-d (10).** A small sample of pure 5-hexen-1-yn-3-ol was stirred overnight with a large excess of 99%  $\text{D}_2\text{O}$ . The alcohol was separated, dried over anhydrous  $\text{MgSO}_4$ , and then subjected to thermolysis at 370° (20 mm). The products were separated by preparative vpc, dissolved in deuteriochloroform, and the resulting solutions were used for the determination of the nmr and mass spectra.

The nmr spectra of the deuterated cyclopentenecarboxaldehyde fraction, consisting of **11**, **12**, and **13**, and of the deuterated sorbaldehyde fraction, **15** and **16**, have been detailed in the Discussion. The spectrum of  $\alpha$ -*d-trans*-2,5-hexadienal (**14**) indicated the deuterium labeling to be in the  $\alpha$  position by virtue of a collapse of the aldehydic doublet at  $\delta$  9.51 into a triplet ( $J = 1$ ), a considerable reduction in absorption at 6.08, and a change in the splitting pattern of the 6.82 multiplet.

The mass spectra of the three fractions were obtained to indicate the amount of deuterium scrambling. The diduterium content, taken as the excess percentage of the  $M + 1$  peak over that normally expected, was considered a measure of the degree of scrambling. The intensity of the  $M + 1$  peak for the cyclopentenecarboxaldehyde fraction, **11** + **12** + **13**, was 9%, for **14** it was 16%, and for **15** it was 23% of the molecule-ion peak intensity. The expected intensity of the  $m/e$  98 peak is 6.7% of that at  $m/e$  97.

**Kinetic Procedures.** A Colora constant-temperature bath with Dow-Corning 210-H Fluid as heating liquid was used for the rate studies. A calibrated thermometer was used for all temperature readings and bath temperatures accurate to  $\pm 0.2^\circ$  were obtained. The rates of disappearance of starting material were determined in sealed capillary tubes 30–50 mm in length. Approximately 5  $\mu\text{l}$  of a

(26) P. Naylor and M. C. Whiting, *J. Chem. Soc.*, 3037 (1955).

solution of **4** in nonane, of known composition, was placed in the capillary tubes. The contents of the tubes were frozen in Dry Ice-acetone, evacuated to pressures of 1 mm or less, and sealed off while frozen. For kinetic runs at each temperature, five sealed capillaries were placed in individual perforated copper casings and immersed in the bath at measured intervals. Reactions were quenched by quickly plunging the tubes into ice water. The contents of the capillaries were analyzed by vpc to determine the ratio of nonane to remaining starting material. A calibration curve prepared from known concentrations of **4** in nonane was used to correct for any nonlinearity in thermal conductivity response. Absence of any pressure or wall effects was established by variations in sample and capillary sizes, none of which affected the linearity of the first-order plots. Nonane had previously been established as an inert carrier in flow experi-

ments. The estimated error limits for evaluation of vpc peak areas are  $\pm 3\%$ . Estimated precision of the rate constants obtained at six temperatures is  $\pm 8\%$  and error limits of the calculated kinetic parameters were assigned accordingly.<sup>27</sup> All needed slopes and intercepts were calculated by the method of least squares.

**Acknowledgments.** We wish to thank Dr. Philip L. Levins for the mass spectral analyses and interpretations and Dr. John L. Roebber for stimulating discussions concerning the determination and interpretation of kinetic data.

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## Steric and Electronic Effects on the Neighboring General Acid Catalyzed Hydrolysis of Methyl Phenyl Acetals of Formaldehyde

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**Abstract:** The hydrolysis of a series of methoxymethyl ethers of substituted phenols has been studied at several temperatures ( $\mu = 1.0$ ) between pH 0.0 and 6.5. The pH-log  $k_{\text{obsd}}$  profiles for those acetals not containing *o*-carboxyl groups are characterized by a straight line of slope  $-1.0$ , in agreement with the expectation of specific acid catalyzed hydrolysis. The pH-log  $k_{\text{obsd}}$  profiles for those acetals possessing *o*-carboxyl groups are characterized by a plateau rate in the acid region, followed by a descending leg of slope  $-1.0$  above pH 3-4. The experimental data for the *o*-carboxyl-substituted acetals is in accord with the kinetically equivalent mechanisms of intramolecular carboxyl group general-acid catalyzed hydrolysis (RCOOH) or specific acid catalyzed hydrolysis of the anionic form of the acetal (RCOO<sup>-</sup> + H<sup>+</sup>). Carboxyl group participation in the reaction is verified on the basis that the log  $k_{\text{H}}$  values ( $k_{\text{H}}$  the calculated specific acid rate constant) for the anionic form of the *o*-carboxyl-substituted acetals exhibit large positive deviations from a Hammett  $\rho\sigma$  plot constructed from the log  $k_{\text{H}}$  values for acetals not possessing *o*-carboxyl groups and for the acetals possessing undissociated carboxyl groups. Juxtapositioning of a second carboxyl group increases the rate constant for intramolecular general-acid catalyzed hydrolysis by the first carboxyl group. It is established that this enhancement in rate is a steric effect and not one of electrostatic stabilization of the transition state for intramolecular general-acid catalyzed hydrolysis. The relationship of the results of this model enzyme study to the mechanism of lysozyme action is discussed.

An impressive array of techniques has been used to elucidate the structure of lysozyme.<sup>3</sup> A recent review by Jolles has summarized the known data for this enzyme.<sup>4</sup>

On the basis of this information, a reasonable model may be constructed for the enzyme-substrate complex which reveals that the only side chains near the site of catalysis and likely to be involved in the hydrolytic mechanism are the carboxyl groups of Glu-35 and Asp-52.<sup>3c,5,6</sup> It has been suggested that, due to the local environments, one of these carboxyl groups is dissociated and one is undissociated at the pH at which lysozyme is most active.<sup>7</sup> The pH-log

$k_{\text{obsd}}$  profile for catalysis by lysozyme describes a bell-shaped curve.<sup>8-11</sup> The simplest interpretation of this behavior considers that there are two acid dissociations, the first of which increases activity and the second of which decreases activity.

Given the probable involvement of the carboxyl groups of Glu-35 and Asp-52 located at the active site, and the presence of an acetamido group in the 2 position of the natural substrate a finite listing of plausible mechanisms for enzymic catalysis may be written.<sup>11,12</sup> These mechanisms take into account the known features of hydrolysis of glycosides, which have been reviewed by Vernon,<sup>13</sup> Long,<sup>14</sup> and Cordes.<sup>15</sup> One common

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