Thujopsene Rearrangements. The Ring System *via* Ring Contraction[1-3]

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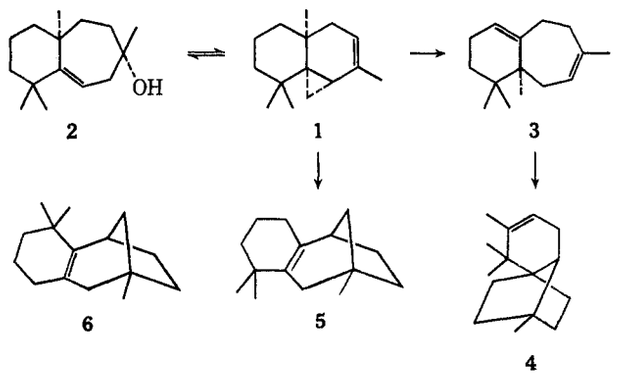
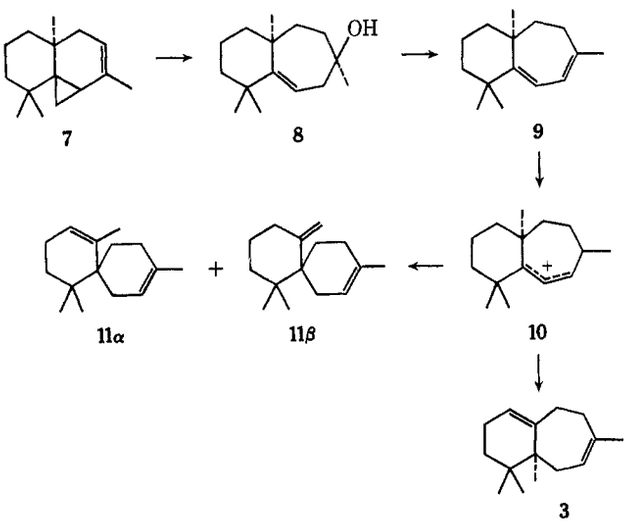
In refluxing acetic acid, *cis*-thujopsene rearranges both to 1,4,11,11-tetramethylbicyclo[5.4.0]undeca-3,7-diene (**3**) and to α- and β-chamigrenes (**11**). When perchloric acid is added, diene **3** is converted to tricyclic olefin **4**. β-Chamigrene, however, is mainly converted to two transitory tricyclic olefins **19** and **20** which, in turn, are transformed into the further rearranged but thermodynamically stable tricyclic olefins **5** and **6**. The structures of **5** and **6** were proven by degradation and partial synthesis. This extensive series of rearrangements is extremely sensitive to the acidic conditions employed and this effect has been studied in detail. The mechanisms of these rearrangements are discussed and the possible biogenetic significance of this process is evaluated.

Part A

Previous studies with *cis*-thujopsene (**1**) showed that under mild acidic conditions (0.02 *M* perchloric acid in 80% aqueous dioxane at reflux) a series of cyclopropylcarbinyl–homoallyl rearrangements first occurred to yield mainly widdrol (**2**) and upon prolonged reaction time the methyl migrated diene **3** was the major product. When *cis*-thujopsene was allowed to react under more acidic conditions (0.02 *M* perchloric acid in acetic acid at reflux) a mixture of olefins of which **3** was the major product was formed very rapidly and upon prolonged heating a final mixture of three compounds in the ratio of 70:18:12 resulted. In an earlier study, the structure of the major hydrocarbon was established[2] to be the tricyclic olefin **4**. In this present investigation, the structures of the two lesser abundant hydrocarbons have been shown to be the tricyclic olefins **5** and **6**. The structures of these two materials were proved by degradation and partial synthesis.



It has been found that under the mild acid conditions which convert *cis*-thujopsene to widdrol and diene **3**, *trans*-thujopsene (**7**) retains its stereochemical integrity and yields, first, mainly epiwiddrol (**8**) and then the diene **9**. When **9** was allowed to react under the more strongly acidic conditions, refluxing 0.02 *M* $HClO_4$ in acetic acid, again the three hydrocarbons **4**, **5**, and **6** were formed but this time in a ratio of 50:30:20. Thus, under these forcing conditions some mixing of the isomeric series occurred but the different ratio of the final products formed from *cis*- and *trans*-thujopsene suggested that **5** and **6** most likely were derived from a precursor more readily formed from *trans*-thujopsene.



The rearrangements in this series of compounds are very sensitive to the experimental conditions and although minor amounts of many materials are formed under most conditions it is usually possible to find a reaction condition which leads to the accumulation of only a few compounds. In earlier studies there were indications, by glpc, that β-chamigrene (**11**β), a naturally occurring hydrocarbon,[5] was formed in the acid-catalyzed rearrangements. In the present investigation, it was found that when *cis*-thujopsene was heated under reflux in glacial acetic acid, 30% of α-chamigrene, 30% of β-chamigrene, and 40% of methylmigrated diene **3** were formed.[6] *trans*-Thujopsene (**7**) under similar conditions yielded these same three materials. Knowing that this trans isomer readily forms diene **9**, it is reasonable that its protonation would yield the allyl cation **10** which, in turn, would rearrange to yield **11** and **3**. Previous studies[2] related to the establishment of the pathway of formation of diene **3** have shown that cation **10** is not on the major pathway for the rearrangement of *cis*-thujopsene. Thus, involvement of cation **10** (or related species) in the rearrangement of *cis*-thujopsene must be minimal. The facile formation of β-chamigrene from diene **9** (and thus from *trans*-thujop-

(1) This work was supported in part by Grant GP-8700, National Science Foundation.

(2) For the previous paper in this study, see W. G. Dauben and L. F. Friedrich, *J. Org. Chem.*, **37**, 241 (1972).

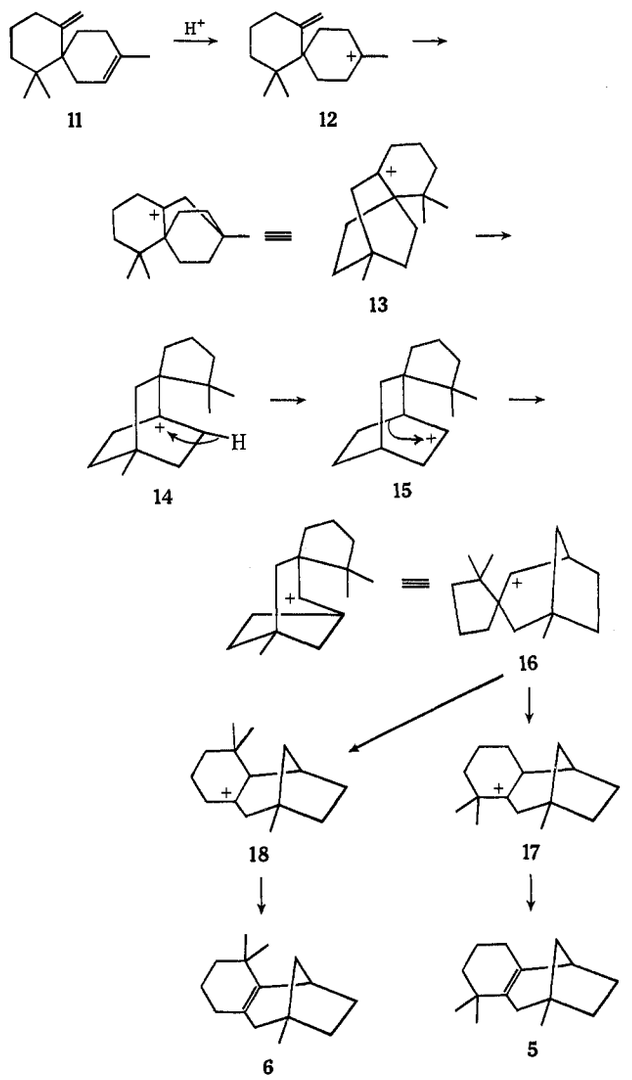
(3) This work was reported at the 14th Symposium of the Chemistry of Natural Products, Fukuoka, Japan, Oct 28–30, 1970, Abstracts, p 220.

(4) National Institutes of Health Predoctoral Fellow, 1967–1970.

(5) In 1960, S. Nagahama [*Bull. Soc. Chem. Jap.*, **33**, 1467 (1960)] reported that *cis*-thujopsene upon reaction with 0.85 *M* oxalic acid in 8% aqueous ethanol yielded widdrol and a new hydrocarbon. During the course of our own related studies, S. Ito [*Chem. Commun.*, 186 (1967)] showed that this new hydrocarbon was the naturally occurring β-chamigrene.

(6) Attention must be given to the analytical method employed since α-chamigrene and diene **3** are only fully separated at 117° using a 500-ft, 0.03-m column coated with PPES plus Igepal.

sene), suggests that the former hydrocarbon is the precursor of **5** and **6**. Indeed, when β-chamigrene (95% pure) was refluxed with 0.02 *M* perchloric acid in acetic acid only olefins **5** and **6** were formed.



With β-chamigrene identified as an intermediate in the formation of **5** and **6**, a reasonable mechanism for their formation can be postulated. Initial protonation of β-chamigrene at the endocyclic double bond to give the carbonium ion **12** is expected since it is known from the chemistry of the hydrocarbon that it is the lesser hindered double bond.[5] Ring closure to the exocyclic double bond yields the bicyclo[2.2.2]octyl cation **13**. This intermediate (or activated complex), upon Wagner–Meerwein rearrangement to **14**, hydride migration to yield **15** to relieve the strain of the bridgehead carbonium ion, and again a Wagner–Meerwein rearrangement, yields the spirano intermediate **16**. This latter cation has two pathways available to it for rearrangements, one giving the ion **17** and subsequently olefin **5** and the other giving ion **18** and subsequently olefin **6**.

This preferred protonation of β-chamigrene at the endocyclic double bond accounts for the inability of the compound to reverse back to cation **10** which could yield the methyl-migrated diene **3**. Therefore, at this β-chamigrene stage the pathway to olefins **5** and **6** is split off from that leading to **3** and subsequently olefin **4**.

Since this postulated mechanism involves an extensive number of steps, it might be expected that by controlling the reaction conditions it should be possible to build up intermediates of lesser stability which are separated by a high energy barrier from the thermodynamically stable **5** and **6**.

When *cis*-thujopsene was allowed to react at 25° with 0.02 *M* perchloric acid in acetic acid, the results given in Table I were obtained. It is seen that *cis*-thujopsene is rapidly rearranged to methyl-migrated diene **3** and to α- and β-chamigrene. Under these acidic conditions, these compounds undergo further rearrangement. β-Chamigrene is more reactive than methyl-migrated diene **3** or α-chamigrene and is transformed into two new isomeric hydrocarbons, **19** and **20**.[7,8]

TABLE I

REACTION OF *cis*-THUJOPSENE WITH 0.02 *M* $HClO_4$ IN ACETIC ACID, 25°

Time, min	Yield of compound, %						
	1	3	11α	11β	4	19	20
5	Trace	62	22	16			
15		61	20	15		4	
30		55	18	13	6	8	
240		20	14	4	38	20	4
720				1	69	18	12

These data again show that β-chamigrene does not cross over to the methyl-migrated diene **3** which leads to **4**. Under these room-temperature conditions, **19** and **20** are stable and no **5** or **6** are formed

This effect of the acidity of the media was further investigated and the results are given in Table II. It is apparent from these data that, as the concentration of perchloric acid increased, products **19** and **20** related to β-chamigrene increased at the expense of tricyclic olefins **4** related to methyl-migrated diene **3**. These results again point to the increased tendency of *cis*-thujopsene to yield chamigrenes as the acidity of the media increases.

TABLE II

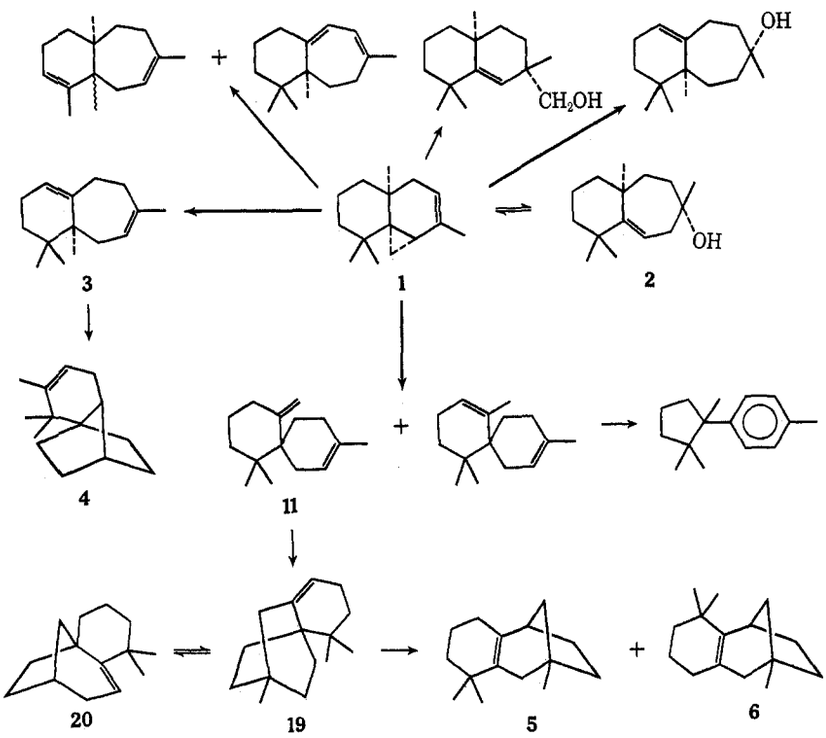
EFFECT OF ACID CONCENTRATION ON *cis*-THUJOPSENE REARRANGEMENT, 40°, 12 HR

Concn of $HClO_4$ in HOAc, *M*	Yield of compounds, %	
	4	19 + 20
0.02	55	35
0.1	40	55
0.5	30	65
1.0	25	70

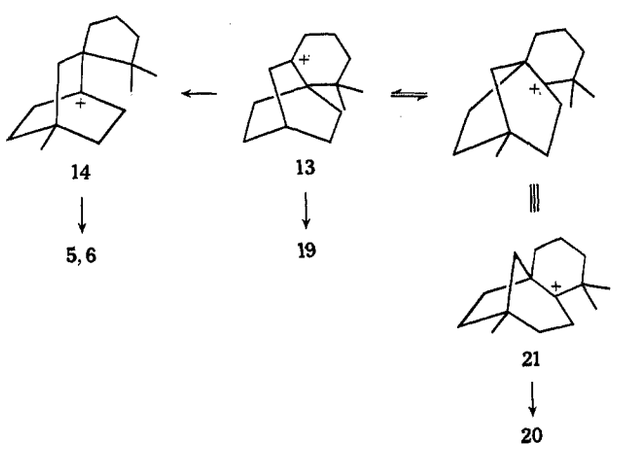
(7) The same two compounds also have been prepared from *cis*-thujopsene by G. C. Kitchens, A. R. Hochstettler, and K. Kaiser (private communication) using different acid conditions. The structure of **19** was established by X-ray crystallography and of **20** by chemical transformations and spectra.

(8) After completion of this work, S. Ito and coworkers [Abstracts of 14th Symposium of the Chemistry of Natural Products, Fukuoka, Japan, Oct 28–30, 1970, p. 174; *Tetrahedron Lett.*, 1149 (1971)] reported of these same two hydrocarbons from a reaction mixture obtained by allowing *cis*-thujopsene to react with a special acidic silica gel (Wako gel Q-50). Their structural assignments were made solely on the basis of mechanistic concepts.

SCHEME I



Recalling that β-chamigrene in refluxing 0.02 *M* perchloric acid–acetic acid only yielded hydrocarbons **5** and **6**, the foregoing data indicate that, as postulated earlier, the new olefins **19** and **20** must be intermediates in the rearrangement of β-chamigrene to **5** and **6**. Indeed, when β-chamigrene was allowed to react at room temperature with 0.02 *M* perchloric acid–acetic acid, first **19** was formed which, in turn, yielded a 60:40 mixture of **19** and **20**, respectively. When this latter mixture of **19** and **20** was heated, **5** and **6** were formed as the major products.



Starting with either pure **19** or **20**, the same 60:40 equilibrium mixture of the two compounds was formed. The intermediate (or activated complex) **13** formed from β-chamigrene has two possible pathways for rearrangement, ring expansion to unstrained **21** or ring contraction to the spiran **14**. This facile interconversion between **19** and **20** followed by slow formation of **5** and **6** *via* **14** clearly points to the higher energy barrier for the formation of the bridgehead cation **14** in the bicyclo[2.2.2]octane system.

As with the formation of tricyclic olefin **4** from bicyclic diene **3**, the thermodynamic stability of **5** and **6** as compared with that of β-chamigrene arises from the fact that the former compounds are tricyclic with one tetrasubstituted double bond as compared with the latter which is bicyclic with a lesser substituted double bond. In general, a cycloalkene is more stable than its acyclic analog by ~20 kcal/mol. The conversion of two relatively unstrained six-membered rings into a bicyclo[3.2.1]octane nucleus has been estimated to involve a strain increase of ~6–7 kcal/mol.[9] Thus the 18–20 kcal/mol energy gained by ring closure to a tricyclic monoolefin overcomes the slight increase in ring strain energy.

Comment should be made on the reasonableness of postulating a bridgehead carbonium ion as an intermediate (or activated complex) in skeletal rearrangements. In this present study, one is concerned with the bicyclo[2.2.2]octane system **14** and in previous work in the formation of the tricyclic olefin **4** with a bicyclo[3.2.1]octane nucleus. Recently, Wiberg,[9] using rates of solvolysis of appropriate bridgehead derivatives, estimated the strain energy of bridgehead carbonium ions of the bicyclo[2.2.1]heptane, bicyclo[2.2.2]octane, and bicyclo[3.2.1]octane systems to be 31.7, 17.3, and 18.7 kcal/mol, respectively. Clearly, bridgehead cations in the latter two systems are of an energy such that it is reasonable that rearrangements may proceed through them.

With this study of the mechanism of formation of hydrocarbons **4**, **5**, and **6**, the study of the major rearrangements of thujopsene under acid conditions is complete. All the major products which appear during the course of the rearrangements have been identified. However, there are many other materials formed in very small amounts and which thus must be viewed as being de-

(9) K. B. Wiberg, private communication.

rived from minor pathways. The rearrangements of thujopsene so far observed by various workers[2,6,7] are summarized in Scheme I.

As can be seen in Scheme I, the rearrangements of *cis*-thujopsene are perhaps the most extensive in scope of any known sesquiterpene. A study of the isomers derived from *cis*-thujopsene has also shown that, under the proper conditions, many bicyclic materials can easily cyclize to give tricyclic compounds. Such results warrant serious consideration and lead to a conclusion that bicyclic sesquiterpenes can, indeed, be precursors of tricyclic sesquiterpenes. It is apparent that *cis*-thujopsene occupies an important place in the search for intermediates in sesquiterpene biogenesis.

Part B

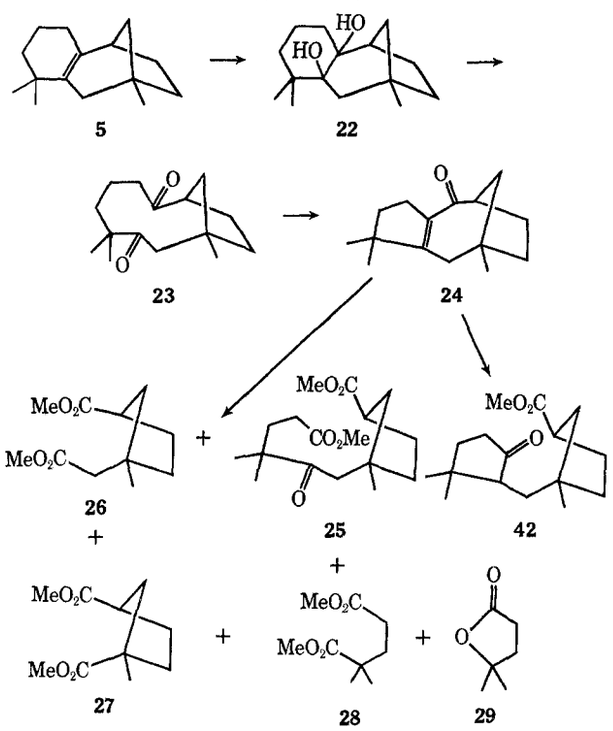
In a typical preparative experiment using 0.02 *M* perchloric acid in acetic acid at reflux temperature, an 85% recovery of hydrocarbons was obtained, the composition of which was 18% of **5**, 12% of **6** and 70% of **4**. The new hydrocarbons **5** and **6** boiled at a lower temperature than **4** and by distillation through a gold-plated spinning band column fractions highly enriched in **5** and **6** were obtained. Subsequent distillation through a Teflon spinning band column yielded **5** in greater than 90% purity. Hydrocarbon **6** was more difficult to purify since its boiling point was between those of **5** and **4** and all fractions were contaminated with one or the other of these latter two compounds. The olefin was best purified by silver nitrate–silica gel chromatography of highly enriched distillation fractions.[10] Analytically pure samples of **5** and **6** were obtained by preparative vpc.

Preliminary investigation of the spectral properties of the two materials indicated a close structural relationship. Since hydrocarbon **5** was more readily available, this material was investigated first. The structure elucidation of the closely related **6** was greatly facilitated by the result obtained with **5**.

Mass spectral and elemental analyses indicated that **5** was isomeric with thujopsene. The infrared spectrum lacked any bands characteristic of a functional group and there was no vinyl absorption in the nmr spectrum. However, the ultraviolet maximum at 197 nm indicated a possibility of a tetrasubstituted double bond and this was confirmed by a strong absorption at 1650 cm^{-1} in the Raman spectrum.[11,12] The extinction coefficients of these latter two absorptions allowed for only one double bond and hence the compound must be tricyclic. Furthermore, from the nmr spectrum, there were only three methyl groups all of which are quaternary, indicating that one of the methyl groups of thujopsene was incorporated into a ring during the transformation.

Since the only functional group present in the molecule was a tetrasubstituted double bond, only a limited degradational scheme could be applied. The following degradation scheme (summarized in Scheme II) was carried out and the fragments of the degradation were

SCHEME II



identified either by unambiguous synthesis or by comparison of the spectral data with those of authentic materials.

The hydrocarbon **5** upon reaction with osmium tetroxide yielded the diol **22**, which was cleaved with lead tetraacetate in benzene to give the diketone **23**. The infrared spectrum of the diketone showed a broad peak at 1705 cm^{-1} indicating the presence of unstrained carbonyl groups. Since no carbon atoms were lost during the cleavage, the original double bond must have been endocyclic. This result, combined with the fact that all the methyl groups are quaternary, requires that one of the methyl groups must be of the angular (or bridgehead) type and the other two must form a *gem*-dimethyl group on a ring.

Treatment of the diketone **23** with aqueous base gave a good yield of a *single* unsaturated ketone. The infrared absorptions at 1650 and 1620 cm^{-1} indicated that the carbonyl group was conjugated and unstrained. The ultraviolet absorption at 254 nm and the absence of vinyl proton resonance in the nmr spectrum confirmed the expected presence of a tetrasubstituted double bond in the conjugated enone **24**.

The enone was ozonized and treated with hydrogen peroxide, and the acidic material was allowed to react with diazomethane to give the keto diester **25**. In addition, lesser amounts of four smaller fragments, **26**, **27**, **28**, and **29**, were isolated, the lactone **29** being isolated from the neutral fraction of the ozonolysis. Formation of the smaller fragments upon ozonolysis was most likely due to the buildup of some peracids from the oxygen in the ozone employed and the peracid, in turn, brought about a Baeyer–Villiger type cleavage. Examples of such anomalous ozonolysis reactions have been reported by other workers.[13]

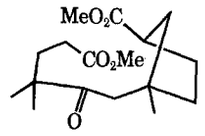
(10) A supply of highly enriched **5** and **6** was kindly supplied by Dr. G. C. Kitchens of the Givaudan Corp.

(11) G. F. Bailey, S. Kint, and J. R. Scherer, *Anal. Chem.*, **39**, 1040 (1967).

(12) The authors wish to thank Dr. J. R. Scherer of the U. S. D. A. Western Regional Research Laboratory, Albany, Calif., for obtaining the Raman spectrum.

(13) (a) P. R. Story and J. R. Burgess, *Tetrahedron Lett.*, 1287 (1968); (b) R. T. Aplin, R. P. K. Chan, and T. G. Halsall, *J. Chem. Soc. C*, 2322 (1969).

Connecting together the smaller fragments of the ozonolysis, the keto diester could be formulated as **25**, **30**, **31**, or **32**. The nmr spectrum did not permit differentiation between these structures. However, **31** and **32** were eliminated on the following basis. The mass spectrum showed a base peak at *m/e* 183; a reasonable assignment of this peak is **33** or **34** which can arise by



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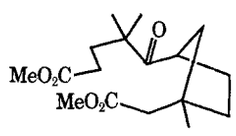

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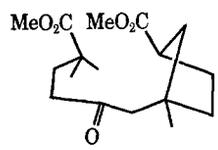

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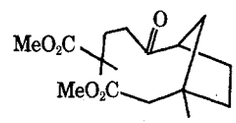

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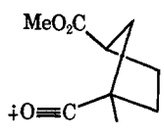

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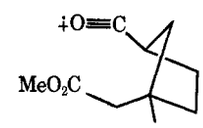

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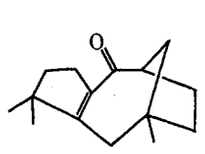
α cleavage of the carbonyl group facilitated by the presence of an α-*gem*-dimethyl group. Compared to the base peak at *m/e* 183, the peak at *m/e* 253, which is due to the loss of a carbomethoxy group, is for all practical purposes not present. Although these spectral interpretations are not conclusive, they support the postulate that the *gem*-dimethyl group is α to the carbonyl group and γ to a carbomethoxy group.



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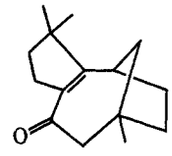

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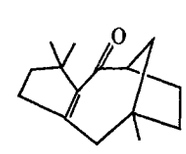

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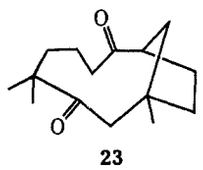

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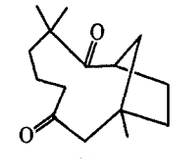

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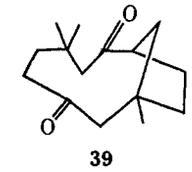

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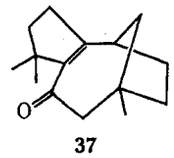

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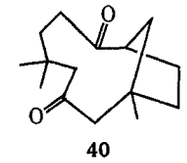

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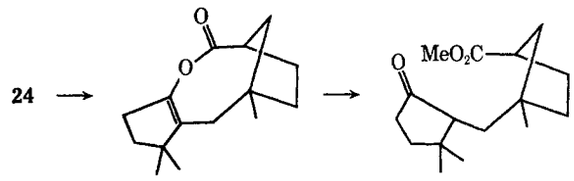
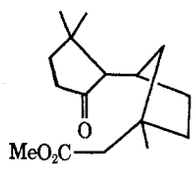
Further evidence for the placement of the *gem*-dimethyl group was found in the formation of a *single* enone from the diketone upon base-induced cyclization. The four possible enones from which the ozonolysis fragments could be obtained are **24**, **35**, **36**, and **37**, which, in turn, could be obtained from the diketones **23**, **38**, **39**, and **40**, respectively. However, **39** and **40** upon cyclization would be expected to yield two enones, since enolization of either carbonyl group can result in ring closure to a bicyclo[3.2.1]octane ring system. On the other hand, **23** and **38**, having the *gem*-dimethyl group next to one carbonyl group, can only yield one such enone; the other would possess a bicyclo[2.2.1]-heptane ring system which would not be expected due to the extra strain of the ring system.

On the basis of the above arguments, keto diesters **31** and **32** need not be considered at this time. To distinguish between **25** and **30** by further degradation was not feasible, since the amount of material available was too limited. Therefore, possible distinctions between enones **24** and **35** were evaluated. The enone was treated with peracetic acid in buffered acetic acid to give an enol lactone **41**, which was opened with a trace of sulfuric acid in methanol to yield the cyclopentanone ester **42**. The infrared spectrum possessed a broad



41 **42**



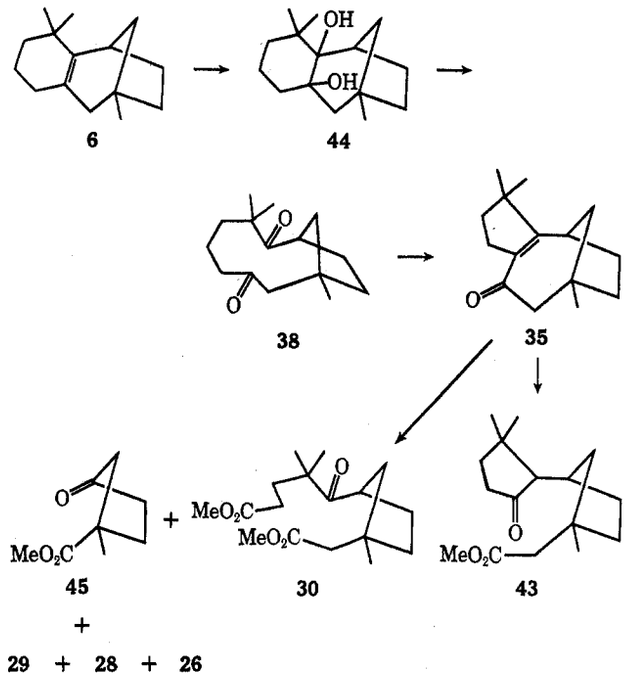
43

band at 1745 cm^{-1} confirming the presence of a cyclopentanone and an ester grouping. The nmr spectrum showed the continued presence of the three methyl groups but more important the presence of a one-proton quintet (J = 8 Hz) at δ 2.8 for a single proton on the cyclopentane ring α to the carbomethoxy group and a broad three-proton band between δ 1.8–2.5 for the protons adjacent to the carbonyl group. The total of four such α protons is commensurate with the structure **42** derived from enone **24** but not with keto ester **43**, which would be derived from enone **35** and demand the presence of five such protons. With this establishment of structure **24**, following back through the foregoing discussion leads to the establishment of structure **5** for the olefinic hydrocarbon derived from thujopsene.

The structure elucidation of hydrocarbon **6** was carried out in an identical manner as described above for isomer **5** and is outlined in Scheme III. The structural similarities of the two materials were clearly evident throughout the degradation. Again, the diketone **38** derived from cleavage of the double bond yielded only one enone **35** upon cyclization, speaking for the placement of the *gem*-dimethyl grouping. The expected products from the ozonization of the enone were obtained but the new fragment **45** was specially significant, since it showed the position of the carbonyl group in the primary ozonolysis product. This product is formed by a Baeyer–Villiger type of cleavage of **30** followed by hydrolysis and oxidation during the ozonolysis.[14] The nmr spectrum of cyclopentanone ester **43** showed the expected five-proton signals assignable to

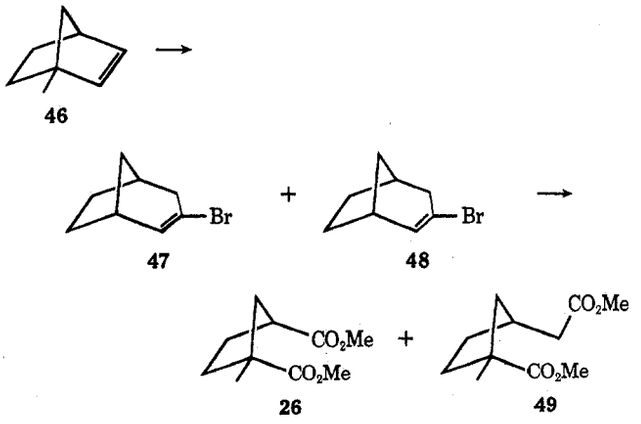
(14) Oxidation of alcohols during ozonolysis has been reported previously; see J. von Euw, A. Lardon, and T. Reichstein, *Helv. Chim. Acta*, **27**, 821 (1944); E. P. Oliveto, H. W. Smith, C. Gerold, R. Raussen, and E. B. Hershberg, *J. Amer. Chem. Soc.*, **78**, 1414 (1952).

SCHEME III

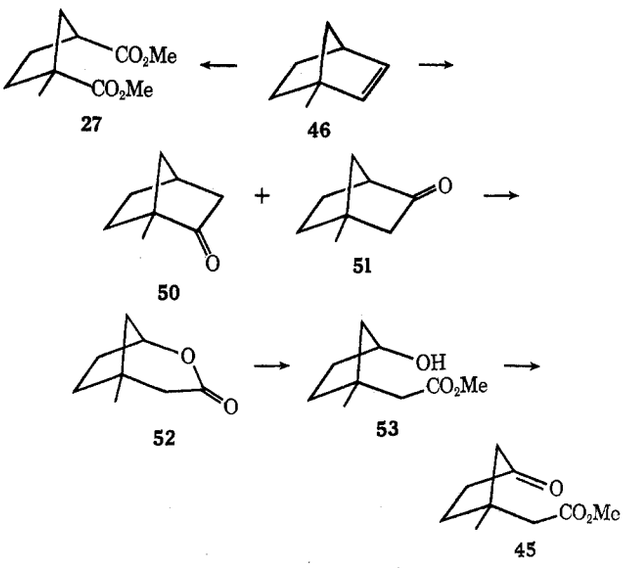


those protons α to the carbonyl and ester groupings. This finding further substantiates the conclusion arrived at with respect to cyclopentanone ester **42**.

The structures of the important smaller fragments from the ozonolysis were first arrived at on the basis of spectral information. The diester **26** was prepared by ozonolysis of bicyclic bromide **48**, which was prepared from 1-methylnorbornene (**46**). Dibromocarbene insertion into **46**[15] followed by lithium aluminum hydride reduction yielded a mixture of bromides **47** and **48** which were not separated, but the mixture was directly ozonized. The resulting diesters **26** and **49** were readily separated and their spectral properties permitted structure assignment.



The diester **27** was prepared by ozonolysis of 1-methylnorbornene followed by esterification of the acid fraction. The cyclopentanone ester **45** also was prepared from this same olefin *via* hydroboration and oxidation to a mixture of ketones **50** and **51**, which upon chromatography was separated into its two components. Peracid oxidation of **51** gave the lactone **52** which was, in turn, converted into hydroxy ester **53** and desired keto ester **45**. Dimethyl α,α-dimethylglutarate was synthesized from 4,4-dimethylcyclohexenone by ozonolysis and esterification and γ,γ-dimethylbutyrolactone was prepared by published procedures.[16]



Experimental Section

Melting points and boiling points are uncorrected. Infrared spectra were obtained with either a Perkin-Elmer Model 137 or 237 spectrometer using CCl_4 as solvent. Ultraviolet spectra were taken on a Beckman DK-2A spectrophotometer. Nmr spectra were taken with Varian Models T-60 or HA-100; carbon tetrachloride was used as the solvent, chemical shifts are given in δ with respect to internal TMS. Mass spectra were recorded with either a Varian M-66 cycloidal mass spectrometer, modified CEC type 21-103 C, or a Finigan quadrupole mass spectrometer. Elemental analysis and high-resolution mass spectra were performed by the Microanalytical Laboratory, College of Chemistry, University of California, Berkeley.

Unless otherwise stated the general work-up of a reaction was as follows: after extraction of the desired materials with organic solvents (ether or hexane), the solution was dried ($MgSO_4$ or Na_2SO_4) and concentrated by rotary evaporation of the solvents.

General Procedure of Ozonolysis.—Ozonolysis was carried out by using the Welsbach ozone generator. For the oxidative work-up of the ozonide, reagent grade ethyl acetate saturated with water was used as the solvent. Ozonolysis was carried out at $-10°$ and the solution of crude ozonide was *partially* concentrated by removing *ca.* three-fourths of the solvent on a rotary evaporator. Water and excess 30% hydrogen peroxide (*ca.* 15-fold excess) were added and the resulting mixture was refluxed for 2 hr, diluted with saturated aqueous sodium bicarbonate solution, and extracted with ether. The ether extract was concentrated to give the neutral material, and the bicarbonate solution was acidified with sulfuric acid. Acidic products were back extracted with ether.

Time Study of Rearrangements. A. Refluxing Acetic Acid.—A 0.5 *M* solution of *cis*-thujopsene in glacial acitic acid under a nitrogen atmosphere was refluxed, and at definite time intervals, 0.1 ml of solution was withdrawn and added to a saturated sodium bicarbonate solution. The organic materials were extracted with hexane, the solvent was removed, and the residue was analyzed on a 500 ft × 0.02 in. capillary column coated with PPE 5 and Igepal.

B. 0.02 *M* $HClO_4$ in Acetic Acid, 25°.—A 0.5 *M* solution of *cis*-thujospene in 0.02 *M* $HClO_4$ in acetic acid was kept at 25° (±1°) under a nitrogen atmosphere. At definite time intervals 0.1 ml aliquots were removed and processed and analyzed as above.

Perchloric Acid–Acetic Acid Treatment of *cis*-Thujopsene.—A solution of 1.34 g (6.56 mmol) of *cis*-thujopsene (**1**) in 14 ml of glacial acetic acid and 20 μl of 70% aqueous perchloric acid was refluxed under nitrogen for 25 hr. The reaction mixture was

(15) C. W. Jefford, S. N. Mahajan, J. Waslyn, and B. Waegell, *J. Amer. Chem. Soc.*, **87**, 2183 (1965).

(16) A. L. J. Beckwith and J. E. Goodrich, *Aust. J. Chem.*, **18**, 1026 (1965).

poured carefully into saturated aqueous potassium carbonate solution, extracted with hexane, and after solvent evaporation the residual oil was chromatographed on Woelm neutral alumina to give 1.1 g (85%) of hydrocarbon mixture. Glpc analysis (5 ft × 0.25 in. KOH, Carbowax 6000, 140°) showed three major materials, **4**, **5**, and **6**, in 13:4:3 ratio. Each compound was purified by preparative glpc for spectra. Hydrocarbon **5**: Raman spectrum 1650 cm^{-1}; nmr 0.91 (s, 3), 0.95 (s, 3), 1.1 (s, 3); uv max (cyclohexane) 197 nm (ϵ 8000); mass spectrum *m/e* (rel intensity) 204 (M^+, 45), 189 (100).

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.97; H, 11.68.

Hydrocarbon **6**: Raman spectrum 1650 cm^{-1}; nmr 0.93 (s, 3), 0.99 (s, 3), 1.06 (s, 3), 2.42 (m, 1); uv max (cyclohexane) 197 nm (ϵ 8900); mass spectrum *m/e* (rel intensity) 204 (M^+, 40), 189 (100).

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.95; H, 11.66.

Oxidation of 5 with Osmium Tetroxide.—A solution of 582 mg (2.85 mmol) of hydrocarbon **5** in 5 ml of reagent grade pyridine was added slowly to 751 mg (2.85 mmol) of osmium tetroxide in 10 ml of pyridine. The reaction mixture was allowed to stand in the dark for 28 days at room temperature, the pyridine was rotary evaporated, and the residue was taken up in 15 ml of benzene and 15 ml of ethanol. To the brown mixture was added a solution of 10 g of potassium hydroxide, 10 g of mannitol, 30 ml of water, and 60 ml of ethanol, and the resulting mixture was refluxed for 6 hr. The reaction mixture was processed in the usual fashion to yield 450 mg of dark brown diol which was recrystallized from the hexane to give 156 mg of diol **22**. Chromatography of the mother liquor on 30 g of Woelm neutral alumina (activity II) gave an additional 98 mg of the diol. The total yield of diol was 254 mg (37.5%): ir 3660, 3590, 1070, 860 cm^{-1}; nmr 0.88 (s, 3), 1.05 (s, 3), 1.13 (s, 3), 2.75 (d, 1, J = 11 Hz); mass spectrum *m/e* (rel intensity) 238 (M^+, 7), 220 (56), 151 (100), 138 (67).

Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.71; H, 11.13.

Diketone 23.—To a solution of 25 mg (0.105 mmol) of diol **22** in 3 ml of dry benzene was added 50 mg (0.113 mmol) of lead tetraacetate, the mixture was stirred under dry nitrogen at room temperature for 1 hr, and 2 ml of quarter saturated aqueous sodium bicarbonate solution was added. The mixture was quickly extracted with ether and the ether solution was dried. Rotary evaporation of ether gave 22 mg (93%) of white crystalline diketone **23**. Tlc (33% ether–hexane) showed only one spot and the diol **22** was absent. Glpc (2% SE-30, 5 ft × 0.125 in., 155°) showed only one peak. A small portion of the diketone was recrystallized twice from hexane: mp 105–106°; ir 1705 cm^{-1}; nmr 0.97 (s, 3), 1.01 (s, 3), 1.31 (s, 3); mass spectrum *m/e* 236 (M^+), 208.

Enone 24.—A solution of 24 mg (0.11 mmol) of diketone **23** and *ca.* 12 mg of potassium hydroxide in 80% aqueous methanol was refluxed under nitrogen for 2.5 hr. The solution was diluted with water and worked up to give 18 mg (75%) of pale brown oil. Glpc (20% DEGS, 5 ft × 0.25 in., 150°) and tlc (20% ethyl acetate–hexane) showed only one major compound. The physical properties were determined on glpc-collected material: ir 1650, 1620 cm^{-1}; nmr 1.03 (s, 6), 1.21 (s, 3); uv max (95% ethanol) 254 nm (ϵ 10,900); mass spectrum *m/e* (rel intensity) 218 (M^+, 90), 203 (100), 190 (25), 175 (33).

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.44; H, 9.97.

Ozonolysis of Enone 24.—A solution of 350 mg (1.6 mmol) of enone **24** in 50 ml of wet ethyl acetate was ozonized as described before. Glpc analysis (5 ft × 0.25 in., 5% SE-30, 180°) of the neutral residue showed only one major peak. This material was purified by preparative glpc. The spectra (ir and nmr) of the glpc collected material was identical with those of authentic γ,γ-dimethylbutyrolactone (**29**).[16]

Crude acidic material from the ozonolysis was esterified with excess diazomethane to give 351 mg of crude esters which were chromatographed on 50 g of Woelm neutral alumina (activity III). Elution with 220 ml of 10% ether–hexane gave 85 mg of a mixture of three major materials in the ratio of *ca.* 40:23:20. These compounds were later identified as **28**, **27**, and **26**, respectively, by comparison of their spectra (ir, nmr, and mass spectrum) with the unambiguously synthesized material. Further elution of the chromatography column with 250 ml of 10% ether–hexane gave 154 mg (30%) of oily keto diester **25**. Glpc examination (10 ft × 0.375 in., 5% SE-30, 225°) of the latter fraction showed only one major peak and the major material was collected from glpc: ir 1740, 1705 cm^{-1}; nmr 1.02 (s, 3), 1.10 (s, 6), 2.52 (s, 2), 2.8 (m, 1), 3.58 (s, 6); mass spectrum *m/e* (rel intensity) 312 (M^+, trace), 249 (12), 183 (100), 155 (24), 95 (52). The absorption peaks in the spectra (ir, nmr) of the glpc collected material are identical with the major absorption peaks in the crude material. The high resolution mass spectrum of the glpc collected material was taken: reference peak 304.9824242, ratio 1.023467, measured peak 312.1943, possible empirical formula $C_{17}H_{28}O_5$, Δm (mmu) +0.6.

Peracid Treatment of Enone 24.—A solution of 100 mg (0.45 mmol) of enone **24** in 0.4 ml of glacial acetic acid saturated with potassium acetate was maintained at room temperature and 70 ml (0.54 mmol) of commercial 40% peracetic acid in acetic acid was added and stirred for 2.5 hr. Water (3 ml) was added and the mixture was worked up under standard conditions to yield 110 mg of crude material (faint odor of acetic acid). Glpc analysis (5 ft × 0.125 in., 2% SE-30, 155°) showed the presence of starting enone **24** and a new product (retention time *ca.* 1.1 times that of the enone). The spectra (nmr and ir) indicated that the major material was the unreacted enone. A small amount of enol lactone **41** (ir 1750 cm^{-1}) was present. The crude material was dissolved in 5 ml of dry methanol, 2 drops of concentrated sulfuric acid were added, and the solution was stirred at room temperature under nitrogen overnight. After work-up, there was obtained 130 mg of crude product. Glpc examination indicated the presence of starting enone but the peak at 1.1 times the retention time of the enone was gone and a new peak appeared at a much longer retention time. The crude material was chromatographed on 15 g of Woelm neutral alumina (activity III) to yield 60 mg of the recovered enone **24** and 28 mg (57% based on the recovered starting material) of the keto ester **42**: ir 1745 cm^{-1} (broad); nmr 0.72 (s, 3), 0.92 (s, 3), 1.14 (s, 3), 2.78 (quintet, 1, J = 2.78), 3.58 (s, 3); mass spectrum *m/e* (rel intensity) 266 (M^+, trace), 251 (22), 219 (34), 191 (27), 142 (35), 125 (100), 109 (54), 95 (46). The high-resolution mass spectrum of this material was taken: reference peak 254.9856198, ratio 1.043936, measured peak 266.1887, possible empirical formula $C_{16}H_{26}O_3$, Δm (mmu) +0.5.

Osmium Tetroxide Oxidation of the Hydrocarbon 6.—A solution of 595 mg (2.92 mmol) of the hydrocarbon **6** and 761 mg (3.0 mmol) of osmium tetroxide in 32 ml of dry ether and 0.75 ml of pyridine was stirred in the dark for 24 days; to the crude osmylation product was added 50 ml of 95% ethanol and 3.0 g (28.8 mmol) of sodium bisulfite ($NaHSO_3$), and the mixture was refluxed for 5 hr. After usual work-up, 605 mg of dark brown residue was obtained. Chromatography of the residue on 60 g of Woelm neutral activity (activity III) gave 396 mg (57%) of the diol **44** which crystallized upon standing. A small portion of the diol was recrystallized from hexane: mp 99–100°; ir 3640, 1005 cm^{-1}; nmr 0.90 (s, 3), 0.98 (s, 3), 1.12 (s, 3), 2.42 (m, 1); mass spectrum *m/e* (rel intensity) 238 (M^+, 1), 220 (40), 151 (100), 138 (69).

Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.85; H, 10.83.

Diketone 38.—Diol **44** (24 mg, 0.104 mmol) was cleaved with lead tetraacetate in a similar manner as described previously for the cleavage of diol **22**. After work-up, 22 mg (90%) of diketone **38** was obtained. The diketone was recrystallized from hexane: mp 132–133°; ir 1710, 1695 cm^{-1}; nmr δ 1.0 (s, 3), 1.25 (s, 3), 1.31 (s, 3), 2.95 (m, 1); mass spectrum *m/e* (rel intensity) 236 (M^+, 17), 218 (6), 208 (8), 193 (22), 154 (78), 126 (100).

Enone 35.—Diketone **38** (20 mg, 0.085 mmol) was treated with base in a similar manner as previously described for the base treatment of diketone **23**. After work-up, 18 mg (97%) of enone **35** (an oil which solidified upon standing) was obtained. The enone was recrystallized from hexane: mp 72–74°; ir 1650, 1620 cm^{-1}; nmr 1.07 (s, 3), 1.10 (s, 3), 2.43 (s, 2), 2.75 (m, 1); uv max (95% ethanol) 258 (ϵ 9500); mass spectrum *m/e* (rel intensity 218 (M^+, 47), 203 (100), 190 (18), 175 (22).

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.73; H, 9.97.

Ozonolysis of Enone 35.—A solution of 123 mg (0.5 mmol) of enone **35** was ozonized as described previously. Wet neutral residue (27 mg) from the ozonolysis contained γ,γ-dimethylbutyrolactone. Acidic material from the ozonolysis was esterified with diazomethane. The crude esters were chromatographed on 30 g of Woelm neutral alumina (activity III). Elution with 50 ml of 10% ethyl acetate–hexane gave 30 mg of a

mixture of diesters. The major diester (*ca.* 80%) was **28**. In addition, small amounts of **26** and **45** were isolated. Further elution with 50 ml of 10% ethyl acetate–hexane gave 42 mg (23%) of the keto diester **30**: ir 1745, 1710 cm^{-1}; nmr δ 1.05 (s, 3), 1.1 (s, 6), 2.35 (s, 2), 3.6 (s, 6); mass spectrum (glpc collected) *m/e* (rel intensity) 312 (M^+, trace), 281 (7), 24.9 (5), 183 (100), 155 (28), 123 (35), 95 (46), 81 (67). The spectra (ir and nmr) of the glpc collected material (5 ft × 0.25 in., 5% SE-30, 220°) were identical in major respect with the spectra of the alumina chromatograph fraction 2. The high-resolution mass spectrum of the glpc collected material was taken: reference peak 304.9824242, ratio 1.023645, measured peak 312.1937, possible empirical formula $C_{17}H_{28}O_5$, Δm (mmu) 0.0.

Peracid Treatment of Enone 35.—Enone **35** (80 mg, 0.37 mmol) was oxidized with peracetic acid in a similar manner as described for the oxidation of enone **24**. After work-up and chromatography, 40 mg (50%) of starting enone **35** was recovered and 15 mg (30% based on recovered starting material) of cyclopentanone ester **43** was obtained: ir 1745 cm^{-1}; nmr 0.99 (s, 3), 1.02 and 1.06 (two s, total 3 H), 1.2 (s, 3), 2.3 (s, 2), 3.6 (s, 3); mass spectrum *m/e* (rel intensity) 266 (M^+, 1), 235 (3), 219 (3), 193 (2), 155 (8), 154 (7), 112 (31), 97 (100), 81 (52); high resolution mass spectrum, reference peak 254.9856198, ratio 1.043935, measured peak 266.1884, possible empirical formula $C_{16}H_{26}O_3$, Δm (mmu) +0.1. The chromatographed material showed only a single spot on tlc and a single peak on glpc (2% SE-30, 5 ft × 0.125 in., 155°).

1-Methylnorbornene (46).—The procedure is similar to that of Jefford.[15] Methylcyclopentadiene dimer (340 g, 2.12 mol) and 10.0 g of sodium bicarbonate were placed in a hydrogenation bomb with glass liner. The bomb was charged with *ca.* 1000 psi of ethylene and heated to 190° while shaking. After 7 hr, heating was stopped, the bomb was cooled, and the mixture was processed. Clear liquids distilling between 100 and 115° were collected (20-cm column) in two fractions (282 g, 64%). The earlier fraction (112 g, 36% **46** and 63% 2-methylnorbornene) was further distilled on a Teflon spinning band column to give 20 g of 1-methylnorbornene (**46**) of greater than 90% purity.

Bromides 47 and 48.—Potassium *tert*-butoxide (16.8 g, 150 mmol) was added slowly in small portions to a solution of 6 g (55 mmol) of 1-methylnorbornene and 13 ml (37.8 g, 150 mmol) of bromoform in 70 ml of olefin-free pentane. The resulting yellow paste was stirred at room temperature for 14 hr, and after work-up, 10.9 g of crude product which contained some *tert*-butyl alcohol and bromoform was obtained. The nmr of the crude product indicated the presence of two dibromides as previously reported.[17] The crude dibromides were dissolved in 50 ml of dry ether and added slowly to a suspension of 27 g (71 mmol) of lithium aluminum hydride in 100 ml of dry ether. The reaction mixture was refluxed under nitrogen for 14 hr, a saturated aqueous solution of sodium sulfate was carefully added, and the mixture was processed to yield 3.5 g (32%) of crude bromides, the nmr of which showed the bromides **47** and **48** in *ca.* 3:2 ratio.

Ozonolysis of the Bromides 47 and 48.—A mixture of bromides **47** and **48** (540 mg, 2.28 mmol) from the preceding experiment was ozonized as described previously. After esterification and work-up, 320 mg (65%) of a mixture of diesters **26** and **49** in *ca.* 3:2 ratio (glpc, 20% DEGS, 5 ft × 0.25 in., 170°) was obtained. The diesters were separated on glpc. Peak I (shorter retention time and present in lesser amount): ir 1745 cm^{-1} (broad); nmr δ 1.2 (s, 3), 2.0–2.5 (m, 4), 3.54 (s, 3), 3.56 (s, 3); mass spectrum *m/e* (rel intensity) 214 (M^+, 1), 183 (5), 155 (88), 141 (82), 123 (63), 81 (100). Peak II: ir 1745 cm^{-1} (broad); nmr 1.04 (s, 3), 2.28 (s, 2), 2.8 (quintet, 1, J = 8 Hz), 3.58 (s, 6); mass spectrum *m/e* (rel intensity) 183 (66), 154 (51), 141 (100), 77 (81), 81 (75).

Anal. Calcd for $C_{11}H_{18}O_4$ (Peak II): C, 61.66; H, 8.47. Found: C, 61.77; H, 8.39.

Diester 27.—1-Methylnorbornene (**46**) (1.0 g, 9.25 mmol) was ozonized as described previously. After esterification and work-up 925 mg of crude diester **27** was obtained. The nmr of the crude product showed the presence of acidic proton (δ 10.2); therefore, the crude material was filtered through 60 g of Woelm neutral alumina (activity II) to give a neutral fraction (497 mg) which was *ca.* 90% in the desired diester **27**. The diester **27** was further purified by preparative glpc (5 ft × 0.25 in., 5% SE-30, 170°): ir 1745 cm^{-1}; nmr 1.22 (s, 3), 2.8 (quintet, 1, J = 8 Hz), 3.48 (s, 3), 3.50 (s, 3); mass spectrum *m/e* (rel intensity) 200 (M^+, trace) 169 (12), 147 (57), 140 (48), 109 (60), 81 (100). The structure of the minor material was not determined, but since the starting material contained a small amount of 2-methylnorbornene, the impurity was thought to arise from this material.

Dimethyl 2,2-Dimethylglutarate (28).—A solution of 1.0 g (8.06 mmol) of 4,4-dimethylcyclohexenone[18] was ozonized as described previously. After esterification and work-up, 0.9 g of crude product was obtained. The glpc analysis (5 ft × 0.25 in., 5% SE-30, 180°) showed two major materials (40 and 44%), a trace of starting material, and *ca.* 5% each of unidentified materials. The two major peaks were collected on glpc. Peak I (shorter retention time and present in 40%): ir 2800, 2700, 1750 cm^{-1}; nmr δ 1.06 (s, 3), 1.78 (s, 2), 2.8 (m, 2), 3.6 (s, 4), 9.36 (s, 1); mass spectrum *m/e* 130 (39), 129 (20), 127 (46), 97 (55), 74 (100), 69 (97). This material was assigned to be 2,2-dimethyl-4-carbomethoxybutylaldehyde on the basis of the spectral data. Peak II (present in 44%) is the desired diester **28**: ir 1745 cm^{-1}; nmr 1.12 (s, 6), 1.6–2.3 (m, 4), 3.56 (s, 3), 3.58 (s, 3); mass spectrum *m/e* (rel intensity) 157 (7), 129 (84), 102 (29), 97 (65), 69 (100).

3-Keto-1-methylnorbornane (51).—To a solution of 4.5 g (41.6 mmol) of 85% pure 1-methylnorbornene (the other 15% was 2-methylnorbornene) in 50 ml of tetrahydrofuran at 0° under nitrogen there was added 60 ml (*ca.* 60 mmol) of *ca.* 1.0 *M* solution of disiamylditborane in tetrahydrofuran. The reaction mixture was stirred at 0° for 30 min and an additional 16 hr at room temperature. Water (20 ml) was added carefully followed by addition of 20 ml of 3 *N* sodium hydroxide and 20 ml of 30% hydrogen peroxide. The reaction mixture was warmed at 50° for 1 hr and worked up in the standard fashion.

The crude alcohols were dissolved in 40 ml of acetone and oxidized with Jones reagent. After work-up, 4.35 g of crude ketone was obtained. Glpc analysis showed the ratio of 3-keto-1-methylnorbornane (**51**) to 2-keto-1-methylnorbornane (**50**) to be *ca.* 4:1.[19] The crude product (4.0 g, 90% of the total crude product) was chromatographed on 400 g of silica gel using an automatic fraction collector and 2% ether–hexane as the eluent. 2-Keto compound **50** was eluted first. 3-Keto-1-methylnorbornane (**51**) was obtained in *ca.* 85% purity after chromatography and was used directly in the next experiment.

Baeyer–Villager Oxidation of 3-Keto-1-methylnorbornane.—To a cooled solution of 611 mg (4.15 mmol, 85% pure) of 3-keto-1-methylnorbornane (**51**) in 2.14 ml of glacial acetic acid and 1.5 ml of concentrated sulfuric acid, there was added 1.04 ml (8.0 mmol) of 40% peracetic acid in acetic acid. The resulting dark solution was stirred at room temperature for 2 hr in the dark, poured into a cold solution of 8.5 g of sodium carbonate in 100 ml of water, and processed to yield 531 mg (91%) of crude lactone **52**. Glpc examination of the crude material indicated the presence of only one major material (91%). The lactone **52** was purified by preparative glpc: ir 1750, 1040, 1028, 1000 cm^{-1}; nmr δ 1.05 (s, 3), 2.35 (s, 2), 4.68 (brd, 1); mass spectrum *m/e* (rel intensity) 140 (M^+, 13), 111 (24), 97 (93), 96 (72), 82 (100).

Similar treatment of the approximate 3:2 mixture of 3-keto- and 2-keto-1-methylnorbornanes gave a crude product whose spectra (ir and nmr) indicated only one major product, that of the lactone **52**. Presumably the lactone formed from 2-keto-1-methylnorbornane is a tertiary butyl type lactone and as such it is unstable in strong acid and opens to an acid which will be lost during alkaline work-up.

Methyl 3-Keto-1-methylcyclopentaneacetate (45).—The crude lactone **52** (450 mg, 3.2 mmol) from the previous experiment was dissolved in 20 ml of reagent-grade methanol and 0.07 ml of concentrated sulfuric acid was added. The reaction mixture was stirred at room temperature for 22 hr, diluted with 30 ml of half-saturated aqueous sodium bicarbonate solution, and processed to yield 410 mg of crude product. The nmr spectrum indicated that the crude product was a mixture of starting lactone **52** and the hydroxy ester **53** in *ca.* 1:2 ratio. The crude material was dissolved in 10 ml of reagent grade acetone and oxidized with Jones reagent at 0°. After the usual work-up, 380 mg of oily material was obtained. Glpc analysis (20% cyanosilicone, 5 ft × 0.25 in., 180°) of crude product showed two materials in *ca.* 68% and 32% yield. They were separated by preparative glpc. The minor component (32%) had a glpc retention time and spec-

(17) C. W. Jefford, S. N. Mahajan, and J. Funsher, *Tetrahedron*, **24**, 2921 (1968).

(18) E. L. Eliel and C. Lukach, *J. Amer. Chem. Soc.*, **79**, 5986 (1957).

(19) Using (+)-diisopinocampheylborane, H. C. Brown and coworkers [*J. Amer. Chem. Soc.*, **86**, 397 (1964)] obtained a ratio of isomers of 88:12.

tra (ir and nmr) identical with those of lactone **52**. The major material (68%) had the following physical properties: ir 1750 cm^{-1} (broad); nmr δ 1.17 (s, 3), 2.06 (AB quartet, 2), 2.33 (s, 2), 3.60 (s, 3); mass spectrum *m/e* (rel intensity) 170 (M^+, 1), 155 (5), 139 (18), 97 (100). This material was identical with one of the ozonolysis product of enone **35**.

Registry No.—**1**, 32435-95-3; **5**, 32435-96-4; **6**, 32435-97-5; **22**, 32435-98-6; **23**, 32435-99-7; **24**, 32436-00-3; **25**, 32436-01-4; **26**, 32436-02-5; **27**, 32436-03-6; **28**, 13051-32-6; **30**, 32436-05-8; **35**, 32436-06-9; **38**, 32460-84-7; **42**, 32436-07-0; **43**, 32436-08-1; **44**, 32436-09-2; **45**, 32436-10-5; **49**, 32436-11-6; **52**, 32436-12-7; 2,2-dimethyl-4-carbomethoxybutylaldehyde, 4007-81-2; perchloric acid, 7601-90-3; acetic acid, 64-19-7.

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Mirestrol. I. Preparation of the Tricyclic Intermediate

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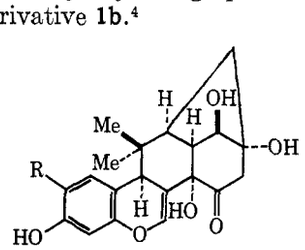
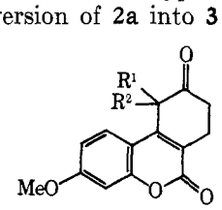
The synthesis of (±)-6aβ,7,8,9,10,10aα-hexahydro-3-methoxy-10,10-dimethyl-6*H*-dibenzo[*b*,*d*]pyran-9-one (**3**) from 3-(β-carbethoxyethyl)-4-methyl-7-hydroxycoumarin (**12a**) through **12b**, **2a**, **15a**, **16**, **17a**, **18**, **19a**, **19b**, and **20** (Schemes II and III) is described. This multistep transformation involved ring closure to the tricyclic unsaturated lactone **2a** and conversion to the cyclic ether **17a** followed by the introduction of two methyl groups at C-10 to give **20**.

Mirestrol (**1a**) was isolated[1] from the tuber of *Pueraria mirifica* which has been used locally in southeast Asia as a rejuvenating drug. The highly potent estrogenic activity of mirestrol was reported,[1a,2] but a limited supply of the natural resource has restricted extensive physiological studies. The structure of mirestrol was elucidated[3] by X-ray crystallographic studies on the monobromo derivative **1b**.[4]

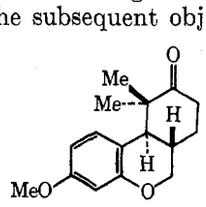


1a, R = H
b, R = Br

This communication deals with the preparation of the A,B,C ring system of mirestrol, which is properly functionalized for eventual conversion into the pentacyclic ring system of the natural product. The tricyclic lactones of type **2** were the first targets and the conversion of **2a** into **3** was the subsequent objective of this study. While all synthetic compounds containing asymmetric carbon are racemic, only one enantiomer is depicted as a matter of convenience.



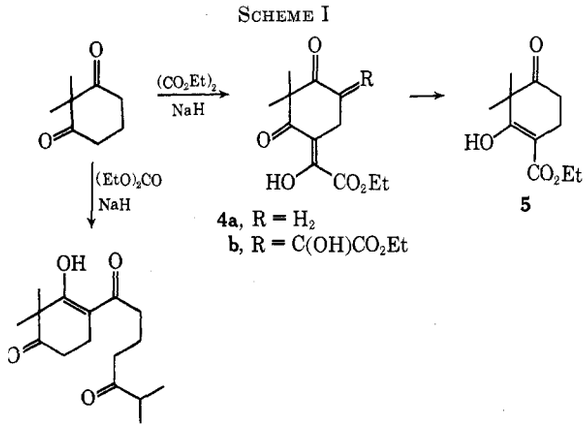
2a, $R^1 = R^2 = H$
b, R^1 = Me, $R^2 = H$
c, $R^1 = R^2$ = Me



3

Preparation of Tricyclic Lactones 2a, 2b, and 2c.—As the most direct approach to obtain **2c**, the Pechmann reaction of resorcinol with **5** was examined. The latter was prepared (Scheme I) by condensation of 2,2-dimethylcyclohexane-1,3-dione[5] and diethyl oxalate to **4a** followed by pyrolysis. A double condensation product **4b** was obtained as a by-product which gave rise to **7** on pyrolysis. Direct carbethoxylation of 2,2-dimethylcyclohexane-1,3-dione with diethyl carbonate in the

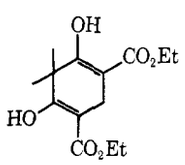
SCHEME I



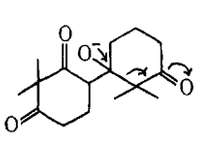
4a, R = H_2
b, R = C(OH)CO_2Et

5

6



7



8

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