

Structure of the Substance $C_{27}H_{38}O$ Formed by the Base-Catalyzed Self-Condensation of Isophorone^{1a}

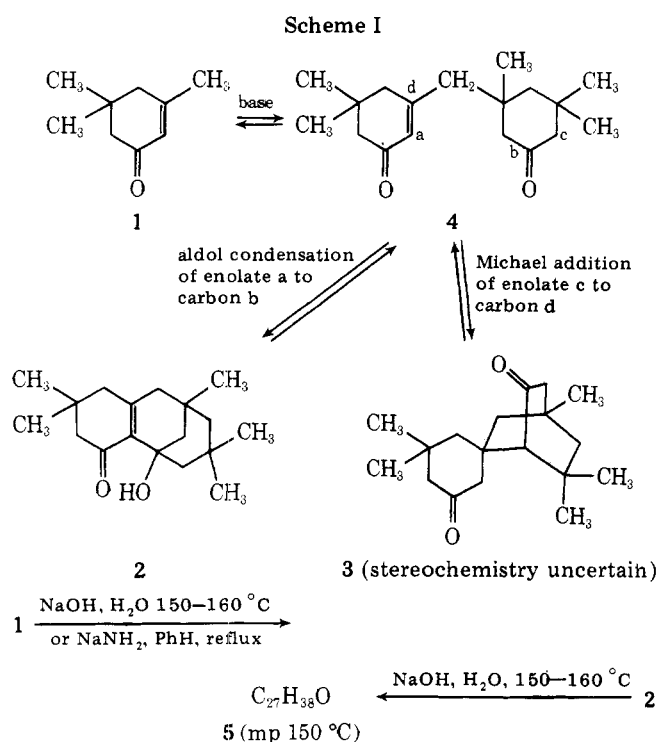
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Received October 12, 1976

The yellow, crystalline product, $C_{27}H_{38}O$, formed by reaction of isophorone (1) with hot concentrated aqueous alkali, has been shown to possess structure 13 both by a total synthesis and by determination of its crystal structure by x-ray diffraction. The synthetic scheme used supports the idea that this trienone 13 is formed by the base-catalyzed dehydration of the isophorone dimer 2 to form an intermediate dienone 9 with a bridgehead double bond. Michael addition of the isophorone enolate 10b to this dienone 9 followed by an aldol condensation provides a reasonable reaction path for the formation of the trienone 13.

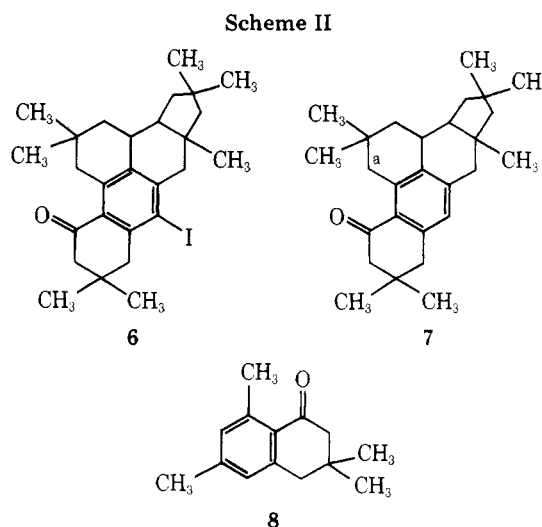
Following two early structural studies,^{2,3} it is now known that many 3-methylcyclohexenone derivatives such as isophorone (1, Scheme I) undergo a base-catalyzed condensation



reaction to form dimeric structures of the types 2 and 3.^{4,5} These dimers 2 and 3 are presumably formed via the Michael adduct 4 followed either by an aldol condensation to form the ketol 2 or by a second Michael addition to form the diketone 3. Although both dimerization processes have been shown to be reversible, generally the use of a metal hydroxide in a protic solvent (e.g., H_2O) favors production of the ketol dimer 2 while use of $NaNH_2$ in an aprotic solvent (e.g., Et_2O , PhH) favors the diketone dimer 3.

In the course of studying the base-catalyzed dimerization of isophorone (1), heating this enone 1 to 155–160 $^\circ\text{C}$ with aqueous $NaOH$ ⁴ or with $NaNH_2$ in boiling PhH⁵ was found also to yield a yellow, crystalline solid 5 (mp 150 $^\circ\text{C}$) with a composition $C_{27}H_{38}O$ corresponding to an isophorone trimer minus two molecules of H_2O . This same product 5 was also formed along with isophorone (1) when the ketol dimer 2 was heated with aqueous $NaOH$ ⁴. Subsequently, a "trimer" with the same composition was obtained by passing isophorone vapor through a tube packed with MgO pellets and heated to 380 $^\circ\text{C}$.⁶ Although these authors gave no melting point or other

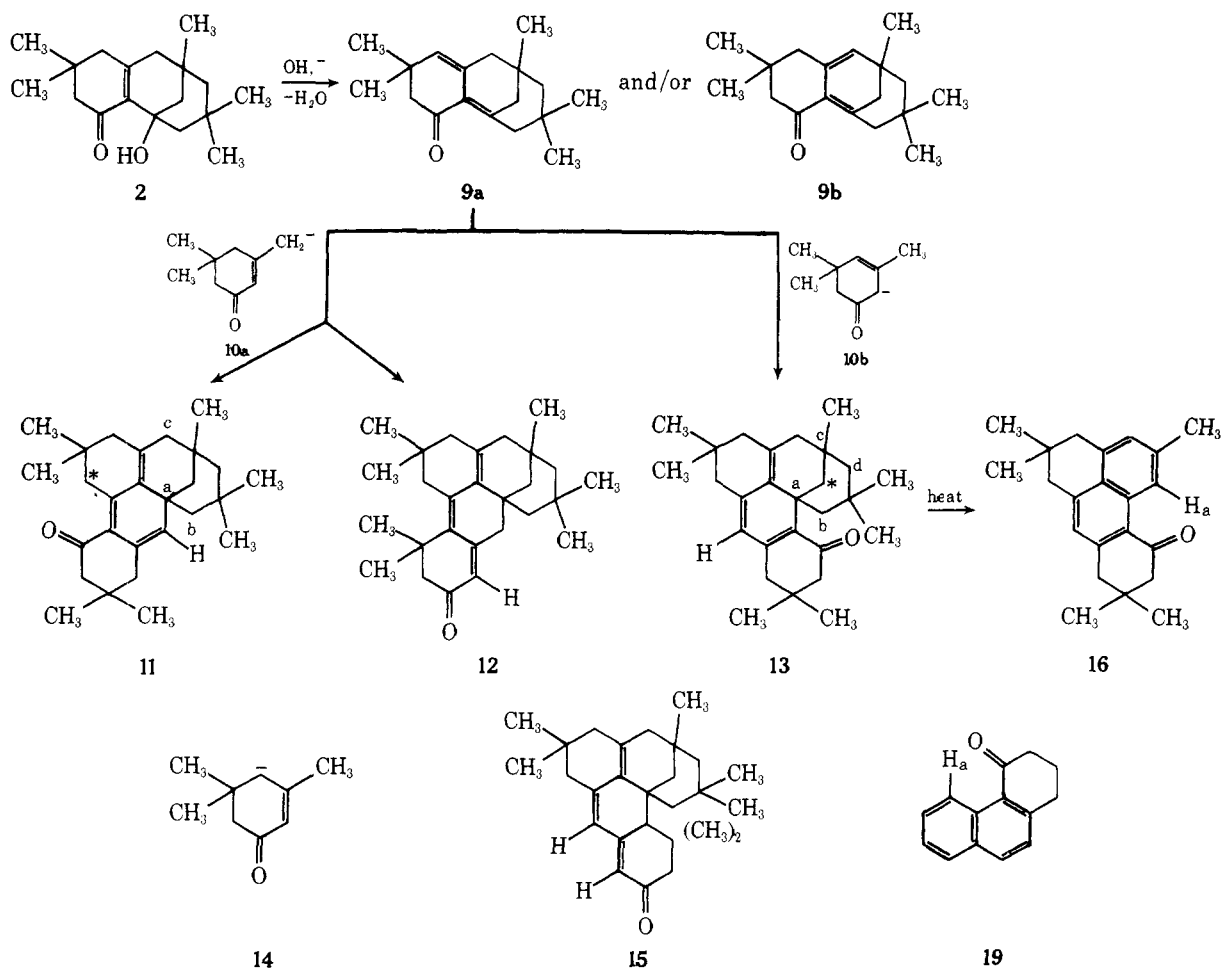
description of the physical properties of their "trimer", the product would appear to correspond to the substance 5 (mp 150 $^\circ\text{C}$) obtained from isophorone and other basic reagents. These workers stated that they had examined the IR, Raman, UV, NMR, and mass spectra of this "trimer" 5 but did not report this spectral data because they regarded the data as inconclusive. Instead, the "trimer" was treated with I_2 and CF_3CO_2Ag in CCl_4 to produce two moniodo derivatives.^{6,7} Since the authors were unsuccessful in obtaining a crystal structure for the major moniodo derivative (melting point not recorded), they determined the crystal structure 6 (617 independent reflections, R factor 11.8%) for the minor moniodo derivative (mp 140–143 $^\circ\text{C}$).⁷ Based upon this structure 6 for the minor moniodo derivative, the structure 7 (Scheme II) was assigned to the isophorone "trimer" 5. Some



support for this structure 7 was obtained by an NMR study with the added lanthanide shift reagent $Yb(DPM)_3$.⁸ This study indicated that two H atoms in the "trimer" 5 were held close to the O atom of the carbonyl group; these H atoms were suggested to be located at the position designated "a" in structure 7.⁸

During the course of other studies in which isophorone (1) was passed over heated metal oxide catalysts,⁹ samples of the "trimer" 5 were again shown to be present in the reaction products and the spectra of the material were determined. Among the salient spectroscopic features were infrared bands at 1642 ($C=O$), 1628 ($C=C$), and 1618 cm^{-1} ($C=C$) and ultraviolet maxima (95% EtOH) at 242 nm (ϵ 12 000) and 390 (8400). The 1H NMR spectrum had distinctive absorption at δ 5.42 (1 H) and 2.92 (1 H, doublet, $J = 12.5$ Hz) and the mass

Scheme III



spectrum exhibited a molecular ion peak at m/e 378 with an intense fragment peak at m/e 307. The natural abundance ^{13}C NMR spectrum (see Table II) exhibited a low field signal at 196.0 ppm ($\text{C}=\text{O}$) with six additional lines in the region 120.2–147.0 ppm attributable to sp^2 hybridized C atoms. Only one of these signals (120.2 ppm) exhibited multiplicity in an off-resonance decoupling experiment indicating a C–H grouping. The remaining 20 ^{13}C NMR lines were in the aliphatic region (25.4–53.4 ppm); some of the lines were sufficiently close together that their multiplicities in off-resonance decoupling measurements were ambiguous (see Table II).

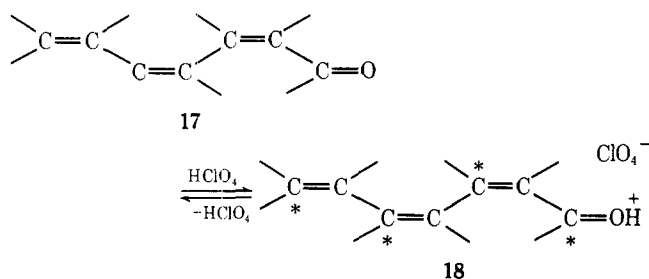
Although certain of these spectral data are compatible with structure **7**, other data are difficult to reconcile. In particular, the ^1H NMR signal at δ 5.42 seems more appropriate for a vinyl CH grouping rather than the aryl CH grouping (typically at δ 6.8–7.5) present in structure **7** and the intense ultraviolet maximum at 390 nm (responsible for the bright yellow color of the “trimer” **5**) seems inappropriate for structure **7**. For comparison, the tetralone **8** (a reasonable spectral model for structure **7**) exhibits aryl CH ^1H NMR absorption at δ 6.88 with ultraviolet maxima (95% EtOH) at 261 nm (ϵ 14 000) and 300 (2000). In addition to the above difficulties with spectral data, any mechanistic scheme we were able to devise to account for the formation of structure **7** from isophorone (**1**) in a base-catalyzed process required some rather bold mechanistic proposals.

The above observations caused us to question the assignment of structure **7** to the isophorone “trimer” **5** and to consider other possible structures. A particularly appealing idea arose from the possibility that β -hydroxy ketone dimer **2** might undergo the characteristic base-catalyzed dehydration when treated with base to form one of the dienones **9** (Scheme III). Although these conjugated systems **9** possess a bridge-

head double bond and will be strained, it is clear from other studies¹⁰ that these intermediates are capable of existence. The Michael addition of one of the isophorone enolate anions **10** to the strained $\text{C}=\text{C}$ of one of these enone systems **9** followed by an intramolecular aldol condensation could lead to three isomeric structures **11**, **12**, and **13**, each of which is compatible with the IR and NMR data observed for the “trimer” **5**. A fourth structure **15**, formed by Michael addition of the enolate **14** to enone **9**, can be excluded because this structure **15** has two vinyl CH groups. The ultraviolet maximum calculated for structure **12** (397 nm) is in better agreement with the observed value (390 nm) than the value calculated for structure **13** (417 nm); since structure **11** contains a cross-conjugated system, a simple prediction of its ultraviolet maximum is not possible. In any event, any one of these structures **11**–**13** is more compatible with the observed UV absorption for the “trimer” **5** than is structure **7**. In both structures **11** and **13** (but not **12**) there is one CH_2 group (designated*) that is held close to the O atom of the carbonyl group and could account for both the unique low-field ^1H NMR signal (doublet at δ 2.92) that we observed and the earlier lanthanide shift reagent results.⁸ It is also of interest to note that if an intermediate formed by addition of $\text{CF}_3\text{CO}_2\text{I}$ to structure **11** were to ionize, the resulting carbonium ion might fragment at bond a–b in structure **11** and then undergo suitable double bond migration and recyclization to form a new bond b–c (see structure **11**). Such a sequence could account for the formation of the monoiodo derivative **6** from structure **11**.

Two additional observations tended to reinforce our belief in the foregoing analysis and to give us a distinct preference for structure **13** as the correct structure for isophorone “trimer” **5**. When a solution of the yellow “trimer” **5** in CH_2Cl_2

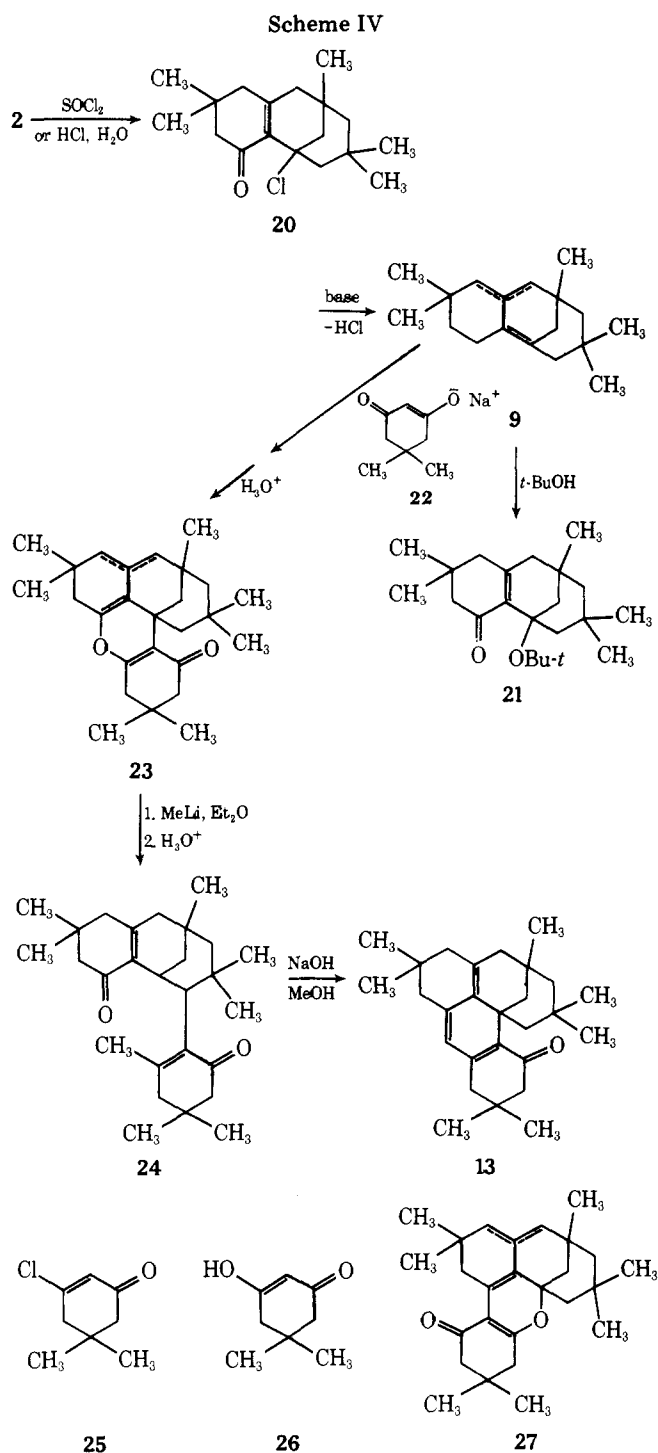
was treated with aqueous 70% HClO_4 , a deep red solution was formed from which a red solid could be isolated; treatment of this red solid with aqueous acetone regenerated the starting "trimer" **5**. The ^{13}C NMR spectrum of a CDCl_3 solution of the red solid (see Table II) was similar to the ^{13}C NMR of the "trimer" **5** except that the carbonyl carbon signal had been shifted upfield by 3 ppm and three of the six vinyl C atom signals had been shifted downfield by ca. 20–30 ppm. These observations are most compatible with the presence in the



"trimer" **5** of a linearly conjugated trienone system **17** that is converted reversibly to its perchlorate salt **18**. In the cation **18**, the bulk of the positive charge would be centered on the designated (*) C atoms accounting for a distinct downfield shift of only three of the six vinyl C atoms. It will be noted that structures **12** and **13** (but not **11**) possess such a linearly conjugated trienone system **17**.

The fact that the mass spectrum of the "trimer" **5** exhibited a molecular peak (m/e 378) and one major fragment peak (m/e 307, $\text{M}^+ - 71$) indicated that the "trimer" **5** had a strong tendency to lose one or more fragments of total mass 71 corresponding to C_5H_{11} . We were, therefore, prompted to heat a sample of the "trimer" **5** to its boiling point at which time vigorous gas evolution was observed. A new ketone ($\text{C}_{22}\text{H}_{26}\text{O}$, mol wt 306) was isolated from this mixture in 34% yield. The various spectral properties of this product (see Experimental Section) indicated it to be a naphthyl ketone. One especially low-field ^1H NMR signal at δ 9.18 indicated that one aryl CH group was uniquely deshielded by the carbonyl function as has been observed previously¹¹ for a proton H_a in the naphthyl ketone **19** (Scheme III). Among the structures **11**–**13** being considered, it is apparent that cleavage of bonds a–b and c–d in structure **13** accompanied by loss of two H atoms can produce a naphthyl ketone **16** that would possess an aryl proton H_a with such a unique NMR signal. Thus, the data available at this stage of our investigation clearly favored formula **13** as the structure of the "trimer" **5**.

To make these assignments more secure we embarked upon a combination of a total synthesis of structure **13** and an x-ray crystal structure determination on the "trimer" **5** in order to avoid the possibility of a molecular rearrangement that might accompany the preparation of a heavy-atom derivative. Our synthetic plan utilized the observation⁴ that the ketol dimer **2** could be converted to the chloro ketone **20** (Scheme IV) by reaction with either SOCl_2 or aqueous 12 M HCl . Our expectation that this chloro ketone **20** would undergo base-catalyzed elimination to form the bridgehead dienone **9** was readily supported by reaction of the chloro ketone **20** with *t*-BuOK in *t*-BuOH to form the *tert*-butyl ether **21**. Since the chloro ketone **20** is stable in boiling *t*-BuOH in the absence of base, it is clear that the ether **21** is not being formed by a solvolytic $\text{S}_{\text{N}}1$ reaction and the structure of the chloro ketone **20** precludes the possibility that the ether is formed in an $\text{S}_{\text{N}}2$ reaction. Thus, the elimination–addition sequence $\mathbf{20} \rightarrow \mathbf{9} \rightarrow \mathbf{21}$ is the only reasonable pathway for the formation of the ether **21**. Treatment of the chloro ketone **20** with NaH in DMF containing the enolate **22** of dimedone (**26**) yielded an initial base-soluble product that formed the keto enol ether **23** upon treatment with acid. The ^{13}C NMR spectrum of this synthetic



intermediate was used to confirm the idea that this substance possessed structure **23** rather than a possible alternative structure **27**. The ^{13}C NMR spectrum exhibited two low-field signals (165.2 and 142.5 ppm) attributable to the two sp^2 carbon atoms bound to oxygen in structure **23**; structure **27** has only one carbon atom of this type. Furthermore, the spectrum lacked a signal at about 70 ppm (e.g., 70.9 ppm in the spectrum of ketol **2**) expected for an sp^3 carbon atom bound to one oxygen atom and three alkyl groups; this structural feature is present in structure **27** but not in structure **23**. After addition of MeLi to the carbonyl group of the keto enol ether **23**, acid-catalyzed hydrolysis produced the diketone **24** and a subsequent base-catalyzed aldol condensation yielded the trienone **13**. This product was identical in all respects with the "trimer" **5** formed from isophorone and aqueous NaOH .

As alternative synthetic routes to the trienone **13**, we also

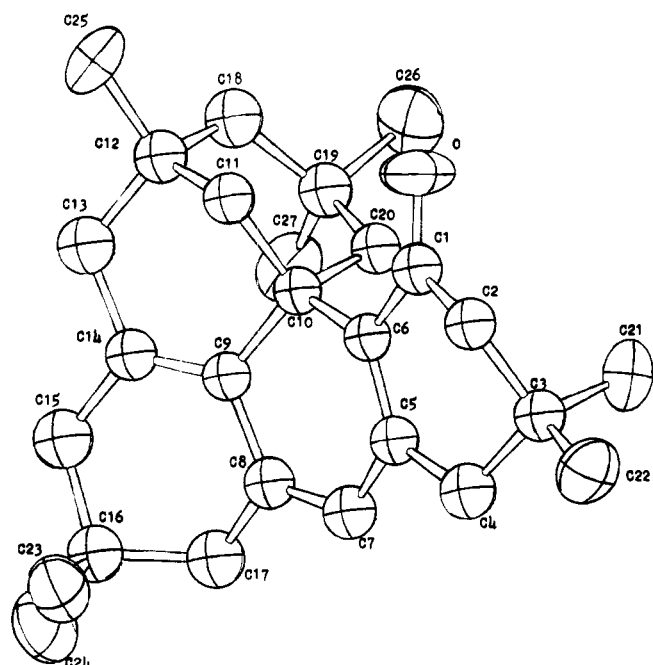


Figure 1. A perspective view of the molecular structure of the trienone 13.

explored briefly the reaction of the chloro ketone **20** with the β -chloro enone **25** in an effort to form an enol ether precursor to enone **23** and the reaction of the chloro ketone **20** with dimedon (**26**) and AgClO_4 in CH_3NO_3 .¹² The first process led to recovery of the starting materials and the second procedure formed a relatively complex mixture of reaction products that was not investigated further.

The structure of the "trimer" **5**, obtained from a single-crystal x-ray diffraction study, is shown in Figure 1. The list of bond lengths and bond angles is given in Table I; the values are consistent with structure **13**. The estimated standard deviations of the bond lengths and angles are ca. 0.005 Å and 0.4°, respectively.

For the conjugated system extending from the carbonyl group (C1) to C14, the carbon-carbon double bond lengths are 1.353 (C₅-C₆), 1.329 (C₇-C₈), and 1.334 Å (C₉-C₁₄) while the remaining bond lengths are 1.481 (C₁-C₆), 1.452 (C₅-C₇), and 1.450 Å (C₈-C₉). Although these values are reasonable for a delocalized system, there is some distortion from planarity and these distortions may be responsible for the difference in the calculated (417 nm) and observed (390 nm) positions of the ultraviolet maximum. The nature and extent of the distortion is shown by dihedral angle calculations for the three-atom planes at each end of a bond; bonds C₁-C₆, C₅-C₇, and C₈-C₉ all show approximately 15° twists from planarity. Some of this distortion is apparently caused by repulsion between the carbonyl oxygen and a methylene proton at C11; the H11-O distance of 2.32 Å is less than the sum of the van der Waals radii of oxygen and hydrogen (ca. 2.5 Å). This close approach is consistent with the observation of a low-field ¹H NMR signal.

Experimental Section¹³

Preparation of the Trienone 13. A mixture of 200 g (1.45 mol) of the enone **1**, 70 g of NaOH, and 30 mL of H₂O was heated to 150 °C with stirring for 20 h and then cooled and partitioned between Et₂O and H₂O. The ethereal layer was washed with aqueous NaCl, dried, and concentrated to leave 198 g of crude product as a dark red liquid. The relatively volatile materials were removed from this mixture by distillation at 0.3 mm and temperatures up to 170 °C. When an EtOH solution of the residue from this distillation was cooled, the crude trienone **13** separated as a yellow solid, mp 138-144 °C. Recrystallization from EtOH gave 25.1 g (14%) of the trienone **13** as yellow

Table I. Molecular Geometry of the Trienone 13

A. Bond Lengths			
Atoms	Distance, Å (standard deviation)	Atoms	Distance, Å (standard deviation)
O-C1	1.213 (4)	C13-C14	1.495 (5)
C5-C6	1.353 (4)	C14-C15	1.518 (5)
C7-C8	1.329 (5)	C15-C16	1.514 (5)
C9-C14	1.334 (4)	C16-C17	1.523 (5)
C1-C6	1.481 (4)	C8-C17	1.508 (5)
C5-C7	1.452 (5)	C10-C20	1.557 (5)
C8-C9	1.450 (5)	C12-C18	1.534 (5)
C1-C2	1.506 (5)	C18-C19	1.537 (6)
C2-C3	1.524 (5)	C19-C20	1.544 (5)
C3-C4	1.516 (5)	C3-C21	1.520 (5)
C4-C5	1.511 (5)	C3-C22	1.520 (5)
C9-C10	1.526 (5)	C16-C23	1.530 (6)
C6-C10	1.543 (5)	C16-C24	1.517 (6)
C10-C11	1.534 (5)	C12-C25	1.520 (6)
C11-C12	1.529 (5)	C19-C26	1.527 (6)
C12-C13	1.524 (5)	C19-C27	1.529 (6)
B. Bond Angles			
Atoms	Angle, deg (standard deviation)	Atoms	Angle, deg (standard deviation)
O-C1-C2	119.9 (4)	C9-C10-C20	109.9 (3)
O-C1-C6	123.1 (3)	C11-C10-C20	107.8 (3)
C2-C1-C6	117.0 (3)	C10-C11-C12	111.0 (3)
C1-C2-C3	112.5 (3)	C11-C12-C13	107.7 (3)
C2-C3-C4	106.1 (3)	C11-C12-C18	108.7 (3)
C2-C3-C21	110.1 (3)	C11-C12-C25	110.5 (3)
C2-C3-C22	110.5 (3)	C13-C12-C18	113.2 (3)
C4-C3-C21	110.7 (3)	C13-C12-C25	109.1 (3)
C4-C3-C22	110.3 (3)	C18-C12-C25	107.7 (3)
C21-C3-C22	109.2 (4)	C12-C13-C14	116.3 (3)
C3-C4-C5	116.1 (3)	C13-C14-C9	122.6 (3)
C4-C5-C6	123.0 (3)	C13-C14-C15	115.1 (3)
C4-C5-C7	115.8 (3)	C9-C14-C15	122.2 (3)
C6-C5-C7	121.2 (3)	C14-C15-C16	116.7 (3)
C5-C6-C10	119.5 (3)	C15-C16-C17	107.3 (3)
C1-C6-C5	118.2 (3)	C15-C16-C23	110.3 (4)
C1-C6-C10	122.0 (3)	C15-C16-C24	109.3 (4)
C5-C7-C8	121.6 (3)	C17-C16-C23	110.0 (4)
C7-C8-C9	120.6 (3)	C17-C16-C24	110.6 (3)
C7-C8-C17	122.8 (3)	C23-C16-C24	109.3 (4)
C9-C8-C17	116.6 (3)	C16-C17-C8	112.5 (3)
C8-C9-C10	117.4 (3)	C12-C18-C19	119.5 (3)
C8-C9-C14	120.4 (3)	C18-C19-C20	110.8 (3)
C10-C9-C14	122.2 (3)	C18-C19-C26	108.8 (3)
C6-C10-C9	110.8 (3)	C18-C19-C27	111.6 (3)
C6-C10-C11	113.4 (3)	C20-C19-C26	107.9 (3)
C6-C10-C20	106.0 (3)	C20-C19-C27	111.7 (3)
C9-C10-C11	108.9 (3)	C26-C19-C27	105.7 (4)
		C19-C20-C10	116.3 (3)

prisms, mp 147-148 °C. When this material was allowed to crystallize very slowly from EtOH, the trienone **13**, mp 149-150 °C, separated as large yellow prisms (lit.⁴ mp 150-152 °C): IR (CHCl_3) 1642 (conjugated C=O), 1628, and 1618 cm^{-1} (C=C); UV max (95% EtOH) 242 nm (ϵ 12 000) and 390 (8400); ¹H NMR (CDCl_3) δ 5.42 (1 H, broad, vinyl CH), 2.92 (1 H, d, J = 12.5 Hz, aliphatic CH), and 0.8-2.4 (36 H, m, aliphatic CH); mass spectrum m/e (rel intensity) 378 (M^+ , 24), 363 (11), 308 (25), and 307 (100).

Anal. Calcd for $\text{C}_{27}\text{H}_{38}\text{O}$: C, 85.66; H, 10.12. Found: C, 85.70; H, 10.13.

The EtOH mother liquors remaining after the above crystallization of the trienone **13** were concentrated to leave a brown, viscous liquid containing (TLC, silica gel coating with an EtOAc-hexane eluent, 1:4 v/v) two or more rapidly eluted components with R_f values of 0.59

Table II. Natural Abundance ^{13}C NMR Spectra in CDCl_3 Solution of the Trienone 13 and Its Perchlorate Salt

Signal in order of increasing field	Signal for trienone 13, ppm (multiplicity in off-resonance decoupling) ^a	Signal for the salt, ppm (multiplicity in off-resonance decoupling) ^a
1	196.0 (s)	193.4 (s)
2	147.0 (s)	178.3 (s)
3	141.1 (s)	163.3 (s)
4	135.8 (s)	153.8 (s)
5	132.4 (s)	132.0 (s)
6	131.4 (s)	127.7 (s)
7	120.2 (d)	124.5 (d)
8	53.4 (t)	51.8 (t)
9	52.4 (t)	46.5 ^b (t, ?)
10	45.8 (t)	46.4 ^b (t, ?)
11	44.8 ^b (t, ?)	46.4 ^b (t, ?)
12	44.7 ^b (t, ?)	46.3 ^b (t, ?)
13	43.9 (t, ?)	45.0 (t)
14	43.1 (t)	44.0 (t)
15	39.8 ^b (s)	40.3 ^b (s)
16	39.7 ^b (t)	40.3 ^b (?)
17	37.5 (q, ?)	40.2 ^b (?)
18	33.2 (q)	37.3 (q)
19	32.6 (s)	32.8 ^b (s)
20	31.1 (q, ?)	32.7 ^b (?)
21	30.3 ^b (s, ?)	32.1 (?)
22	30.3 ^b (s, ?)	30.4 ^b (?)
23	29.9 (s)	30.3 ^b (?)
24	29.2 ^b (q, ?)	29.9 (?)
25	28.9 ^b (q, ?)	29.5 (?)
26	26.6 (q)	26.9 (q)
27	25.4 (q)	25.2 (q)

^a Where the multiplicity designation is accompanied by a question mark, the close spacing of two or more lines made the splitting pattern ambiguous. ^b Only partial resolution of these closely spaced peaks was attained.

(corresponds to the trienone 13) and 0.62 as well as several more polar components with smaller R_f values. A portion of this crude mixture was subjected to a preparative TLC separation to obtain a sample of the materials with R_f values of 0.59 and 0.62. GLC analysis (silicone DC-710 on Chromosorb P) of the sample indicated the presence of comparable amounts of four components with the following retention times: 26.6, 31.0 (corresponds to the trienone 13), 38.0, and 48.4 min. Thus, this base-catalyzed condensation of isophorone (1) produces components other than the trienone 13 but with similar properties. These by-products may include one or more of the structural isomers 11, 12, and 15.

The natural abundance ^{13}C NMR spectrum of the trienone 13 (CDCl_3 solution) exhibited the peaks listed in Table II. The results of off-resonance decoupling measurements (s, d, t, etc.) are indicated in parentheses beside each peak. In cases where close spacing of two peaks made the splitting pattern ambiguous, the multiplicity is designated with a question mark.

When a solution of 2.25 g (5.95 mmol) of the trienone 13 in 10 mL of CH_2Cl_2 was treated with 5 mL of aqueous 70% HClO_4 , the organic layer immediately became deep red in color. After the mixture had been stirred at 25 °C for 30 min, the organic layer was separated, dried, and concentrated to leave 2.83 g of the crude perchlorate salt of the trienone 13 as a red solid: IR (CHCl_3) a series of weak bands in the 6- μ region at 1642, 1605, and 1585 cm^{-1} (C=C); UV max (CH_2Cl_2) 272 nm (ϵ ca. 11 000), 329 (ca. 2900), and 511 (ca. 15 000); ^1H NMR (CDCl_3) δ 6.09 (1 H, broad, vinyl CH) and 0.8-3.0 (37 H, m, aliphatic CH). The natural abundance ^{13}C NMR data obtained for a CDCl_3 solution of this crude salt are summarized in Table II; in some cases, designated (?), we were unable to discern the splitting patterns obtained with off-resonance decoupling. When a solution of 104 mg of this crude salt in 5 mL of acetone was treated with H_2O , the red color was discharged to leave a yellow solution. After this solution had been partitioned between H_2O and CH_2Cl_2 , the organic layer was dried and concentrated to leave 83 mg of the crude trienone 13, mp 143.5-144.5 °C, that was identified with the starting trienone 13 by comparison

Table III. Natural Abundance ^{13}C NMR Spectrum of Ketone 16 in CDCl_3 Solution

Signals in order of increasing field	^{13}C NMR signal, ppm (multiplicity in off-resonance decoupling measurement)
1	199.1 (s)
2	143.9 (s)
3	141.7 (s)
4	137.7 (s)
5	134.2 (s)
6	131.0 (s)
7	126.5 (d)
8	126.4 (s)
9	124.9 (d)
10	123.5 (s)
11	123.2 (d)
12	54.5 (t)
13 and 14	45.2 (t)
15	44.7 (t)
16	33.3 (s)
17	30.5 (s)
18, 19, 20, and 21	27.8 (q)
22	22.1 (q)

of IR and UV spectra. Recrystallization from EtOH raised the melting point of the recovered trienone 13 to 148-149 °C; a mixture melting point determination of the starting and recovered trienone samples was not depressed.

Pyrolysis of the Trienone 13. A 2.00-g (5.29 mmol) sample of the trienone 13 was heated to boiling (ca. 320-330 °C) under an N_2 atmosphere during 30 min and then maintained at this temperature for 50 min. A solution of the product, a viscous brown liquid, in CH_2Cl_2 was filtered through a bed of silica gel and then chromatographed on silica gel with a PhH-hexane eluent (3:1 v/v). After removal of the early fractions containing 1.13 g of viscous yellow liquid, subsequent fractions contained an oily solid that was triturated with pentane to leave 564 mg (34%) of the ketone 16 as a pale green solid, mp 141-143 °C. Recrystallization from EtOH afforded 475 mg of the pure ketone 16 as pale yellow-green needles, mp 143-144 °C, and an additional recrystallization raised the melting point to 143.5-145 °C: IR (CHCl_3) 1660 cm^{-1} (conjugated C=O); UV max (95% EtOH) 218 nm (ϵ 31 000), 258 (22 000), and 343 (8000); ^1H NMR (CDCl_3) δ 9.18 (1 H, broad s, aryl CH), 7.07 (1 H, broad s, aryl CH), 6.93 (1 H, broad s, aryl CH), 2.93 (2 H, s, benzylic CH_2), 2.83 (4 H, s, benzylic CH_2), 2.57 (2 H, s, benzylic CH_2), 2.49 (3 H, s, aryl CH_3), 1.09 (6 H, s, CH_3), and 0.99 (6 H, s, CH_3); mass spectrum m/e (rel intensity) 306 (M^+ , 100), 250 (53), 222 (10), 207 (13), and 192 (10).

Anal. Calcd for $\text{C}_{22}\text{H}_{26}\text{O}$: C, 86.23; H, 8.55. Found: C, 86.04; H, 8.59.

The natural abundance ^{13}C NMR spectrum of a CDCl_3 solution of the ketone 16 exhibited the peaks listed in Table III.

Preparation of the Hydroxy Ketone 2. Following a previous procedure,² a mixture of 117 g (0.849 mol) of isophorone (1), 20 g of NaOH, and 10 mL of H_2O was heated to 100-125 °C with stirring for 2 h. After the reaction mixture had been partitioned between CHCl_3 and aqueous 3 M HCl, the organic layer was washed with aqueous NaCl, dried, and concentrated. The residual liquid was fractionally distilled to separate 14.3 g of pale yellow liquid, bp 100 °C (15 mm), and 86.63 g of a viscous yellow liquid fraction, bp 110-133 °C (0.3 mm), that solidified on standing. Repeated recrystallization of this material from hexane separated 51.8 g (44%) of the pure ketone 2 as colorless prisms: mp 83-84 °C (lit. mp 84-85,⁵ 86-88 °C⁴); IR (CCl_4) 3470 (OH), 1656 (shoulder), 1650 (conjugated C=O), and 1632 cm^{-1} (C=C); UV max (95% EtOH) 250 nm (ϵ 8300); ^1H NMR (CCl_4) δ 4.76 (1 H, broad, OH), 1.1-2.2 (12 H, m, CH_2), 1.03 (6 H, s, CH_3), 0.98 (3 H, s, CH_3), 0.92 (3 H, s, CH_3), and 0.72 (3 H, s, CH_3); mass spectrum m/e (rel intensity) 276 (M^+ , 2), 261 (6), 206 (16), 205 (100), 163 (22), and 121 (19). The natural abundance ^{13}C NMR spectrum of the ketone 2 in CDCl_3 solution is summarized in Table IV.

Preparation of the Chloro Ketone 20. A solution of 9.78 g (35.4 mmol) of the ketone 2 in 50 mL of CHCl_3 (EtOH free) was treated with 4.9 g (41 mmol) of SOCl_2 and the resulting solution was stirred at 25 °C for 16 h. After the resulting solution had been washed successively with H_2O and with aqueous NaHCO_3 it was dried and concentrated to leave 10.6 g of the crude chloro ketone 20 as an orange solid. Recrystallized from MeOH afforded 8.02 g of pure chloro ketone 20 as

Table IV. Natural Abundance ^{13}C NMR Spectrum of Ketol 2 in CDCl_3 Solution

Signals in order of increasing field	^{13}C NMR signal, ppm (multiplicity in off-resonance decoupling measurement)
1	199.4 (s)
2	156.3 (s)
3	134.7 (s)
4	70.9 (s)
5	51.9 (t)
6	51.5 (t)
7	50.1 (t)
8	46.4 (t)
9	45.5 (t)
10	44.4 (t)
11	36.9 (q)
12	32.5 (q)
13	32.2 (s)
14	32.0 (s)
15	31.2 (s)
16	29.5 (q)
17	28.1 (q)
18	26.6 (q)

pale orange prisms, mp 137–138.5 °C (lit.⁴ mp 135–136 °C), as well as 0.97 g of less pure product: mp 136–138 °C (total yield 8.99 g or 86%); IR (CCl_4) 1688, 1678 ($\text{C}=\text{O}$), and 1627 cm^{-1} ($\text{C}=\text{C}$); UV max (95% EtOH) 244 nm (ϵ 8000); NMR (CCl_4) δ 1.1–2.8 (12 H, m, CH_2), 1.08 (3 H, s, CH_3), 1.00 (6 H, s, CH_3), 0.93 (3 H, s, CH_3), and 0.73 (3 H, s, CH_3); mass spectrum m/e (rel intensity) 296 (M^+ , 2), 294 (M^+ , 5), 258 (40), 243 (33), 203 (25), 202 (40), 201 (100), 187 (30), 119 (24), 55 (25), and 41 (38).

Preparation of the *tert*-Butoxy Ketone 21. To a boiling solution of 700 mg (2.38 mmol) of the chloro ketone **20** in 5 mL of *t*-BuOH was added, dropwise and with stirring during 5 min, 5 mL of a *t*-BuOH solution containing 2.69 mmol of *t*-BuOK. During this addition the solution turned deep red and a fine precipitate (presumably KCl) separated. After the reaction mixture had been refluxed for 30 min, it was neutralized by addition of 0.5 g (9 mmol) of solid NH_4Cl and then diluted with Et_2O , filtered, and concentrated. The residue was partitioned between pentane and H_2O and the pentane solution was dried and concentrated to leave 687 mg of the crude product as a light orange solid, mp 110–118 °C. Chromatography on silica gel with an EtOAc–hexane eluent (1:9 v/v) separated 484 mg (61%) of the *tert*-butoxy ketone **21**, mp 126–129 °C. Recrystallization from an EtOH– H_2O mixture afforded the pure *tert*-butoxy ketone **21** as colorless needles: mp 131–132 °C; IR (CCl_4) 1671, 1680 (conjugated $\text{C}=\text{O}$), 1630, and 1620 cm^{-1} (weak, conjugated $\text{C}=\text{C}$); UV max (95% EtOH) 248 nm (ϵ 6500); NMR (CCl_4) δ 1.3–2.5 (10 H, m, aliphatic CH) and 0.6–1.3 [26 H, m, aliphatic CH including singlets at 1.17 (*t*-BuO), 1.05 (CH_3), 0.98 (two CH_3), 0.81 (CH_3), and 0.74 (CH_3)]; mass spectrum m/e (rel intensity) 302 (2), 258 (12), 243 (10), 231 (10), 205 (30), 187 (15), 146 (14), 56 (39), 55 (28), 41 (100), and 39 (35).

Anal. Calcd for $\text{C}_{22}\text{H}_{36}\text{O}_2$: C, 79.46; H, 10.92. Found: C, 79.44; H, 10.93.

In a similar experiment, a solution of 800 mg (2.72 mmol) of the chloro ketone **20** in 5 mL of THF was added to 5 mL of a *t*-BuOH solution containing 3.67 mmol of *t*-BuOK. The mixture, which turned red and deposited a white precipitate (KCl), was stirred at 25 °C for 12 h and then subjected to the previously described isolation and purification procedures. The yield of the *tert*-butyl ether **21**, mp 130–132 °C, was 581 mg (64%).

As a control experiment, a solution of 150 mg (0.51 mmol) of the chloro ketone **20** in 2 mL of *t*-BuOH was refluxed for 25 min and then concentrated under reduced pressure. The recovered chloro ketone **20** (150 mg, mp 137–138.5 °C) was identified with an authentic sample by comparison of IR spectra.

Preparation of the Chloro Ketone 25. Following a previously described procedure,¹⁵ a suspension of 20.0 g (0.14 mol) of dimesone **26** in 40 mL of CHCl_3 (EtOH free) was treated with 6.7 g (0.049 mol) of PCl_3 and the resulting mixture was refluxed for 2.2 h. After the reaction mixture had been concentrated under reduced pressure, the residue was partitioned between Et_2O and aqueous 10% NaOH and the ethereal phase was dried and concentrated. Fractional distillation of the crude organic product afforded 13.6 g (61%) of the chloro ketone **25** as a colorless liquid: bp 99–100 °C (16 mm); n_D^{25} 1.4943 [lit. bp 72

Table V. Natural Abundance ^{13}C NMR Spectrum of the Ketone 23 in CDCl_3 Solution

Signals in order of increasing field	^{13}C NMR signal, ppm (multiplicity in off-resonance decoupling measurement) ^a
1	197.0 (s)
2	165.2 (s)
3	142.5 (s)
4	132.0 (d)
5	129.8 (s)
6	116.5 (s)
7	114.4 (s)
8	53.0 (t)
9 and 10	49.3 (2t)
11	43.8 (t)
12	42.1 (t)
13 and 14	40.7 (2t)
15	37.1 (q)
16	33.9 (s)
17	33.0 (s)
18	31.4 (s)
19, 20, 21, and 22	30.2 (2s, 2q, ?)
23 and 24	29.5 (2q, ?)
25	27.2 (q)
26	26.1 (q)

^a Where the multiplicity designation is accompanied by a question mark, the close spacing of two or more lines made the splitting pattern ambiguous.

°C (5 mm),¹⁶ 105 °C (20 mm),¹⁷]; IR (CCl_4) 1700 (shoulder), 1682, 1670 (shoulder, conjugated $\text{C}=\text{O}$), and 1615 cm^{-1} ($\text{C}=\text{C}$); UV max (hexane) 233 nm (ϵ 13 000); NMR (CCl_4) δ 6.13 (1 H, t, $J = 1.5$ Hz, vinyl CH), 2.55 (2 H, d, $J = 1.5$ Hz, allylic CH_2), 2.18 (2 H, s, CH_2CO), and 1.10 (6 H, s, CH_3); mass spectrum m/e (rel intensity) 160 (M^+ , 9), 158 (M^+ , 25), 143 (6), 104 (33), 102 (100), 67 (28), and 39 (16).

Properties of the Tetralone 8. As a spectroscopic model for the structure **7**, a sample of the tetralone **8** was prepared from acetone by a previously described procedure.¹⁸ The product was obtained as colorless prisms: mp 56–57 °C (lit. mp 56.5–57,^{18b} 54–55 °C^{18c}); IR (CCl_4) 1670 cm^{-1} (conjugated $\text{C}=\text{O}$); UV max (95% EtOH) 261 nm (ϵ 14 000) and 300 (2000); NMR (CDCl_3) δ 6.88 (2 H, broad s, aryl CH), 2.76 (2 H, s, CH_2), 2.60 (3 H, s, aryl CH_3), 2.41 (2 H, s, CH_2), 2.28 (3 H, s, aryl CH_3), and 1.00 (6 H, s, CH_3); mass spectrum m/e (rel intensity) 202 (M^+ , 34), 146 (100), and 118 (9).

Preparation of the Keto Enol Ether 23. To a cold (0 °C) suspension of 21 mmol of NaH (from 956 mg of a 52% dispersion that was washed with pentane) in 5 mL of DMF was added, dropwise and with stirring, a solution of 1.39 g (9.94 mmol) of dimesone (**26**) in 5 mL of DMF. After the addition was complete, during which time the temperature of the mixture rose to 5 °C, a solution of 1.40 g (4.76 mmol) of the chloro ketone **20** in 10 mL of DME was added dropwise and with stirring during 5 min. During this addition the mixture became red-brown in color and gas was evolved. The resulting mixture was stirred at 5 °C for 20 min and at 25 °C for 80 min. The resulting mixture was diluted with H_2O and then partitioned between Et_2O and aqueous 1 M HCl. After the ethereal solution had been washed with H_2O , dried, and concentrated, the residual crude product (2.00 g of viscous yellow liquid) was dissolved in 20 mL of THF containing 0.2 mL of aqueous 70% HClO_4 and stirred at 25 °C for 1.5 h. The resulting mixture was partitioned between Et_2O and aqueous 5% NaOH and the ethereal layer was washed with water, dried, and concentrated. Recrystallization of the residual crude product (1.39 g of tan solid, mp 140–150 °C) from EtOH separated 956 mg (53%) of the ketone **23** as colorless prisms, mp 160–162 °C. An additional recrystallization gave the pure ketone **23**: mp 161–162 °C; IR (CCl_4) 1680 (enol ether $\text{C}=\text{C}$), 1661 (conjugated $\text{C}=\text{O}$), and 1610 cm^{-1} (conjugated $\text{C}=\text{C}$); UV max (95% EtOH) 240 nm (ϵ 18 000) and 318 (2300); NMR (CCl_4) δ 5.15 (1 H, s, broad vinyl CH), 2.71 (1 H, d, $J = 12$ Hz, aliphatic CH), 1.2–2.5 (13 H, m, aliphatic CH), and 0.7–1.2 (21 H, m, CH_3); mass spectrum m/e (rel intensity) 380 (M^+ , 9), 365 (14), 310 (14), 309 (100), 83 (10), 55 (10), 43 (9), and 41 (9).

Anal. Calcd for $\text{C}_{26}\text{H}_{36}\text{O}_2$: C, 82.06; H, 9.54. Found: C, 81.98; H, 9.55.

The natural abundance ^{13}C NMR spectrum of the ketone **23** (CDCl_3 solution) exhibited the peaks listed in Table V.

Table VI. Natural Abundance ^{13}C NMR Spectrum of the sp^2 Carbon Atoms in Diketone 24

Signals in order of increasing field	^{13}C NMR signal, ppm (multiplicity in off-resonance decoupling measurement)
1	200.3 (s) ^a
2	198.7 (s) ^b
3	196.6 (s) ^b
4	194.6 (s) ^a
5	152.2 (s) ^a
6	149.8 (s) ^b
7	144.4 (s) ^b
8	143.6 (s) ^a
9	140.8 (s) ^b
10	139.9 (s) ^a
11	137.4 (s) ^b
12	137.1 (s) ^a

^a Less intense signal. ^b More intense signal.

Preparation of the Diketone 24 and the Trienone 13. To 3.1 mL of a cold (0 °C) ethereal solution containing 2.26 mmol of MeLi was added a solution of 588 mg (1.55 mmol) of the keto enol ether **23** in 7 mL of Et₂O. After the resulting mixture had been stirred at 25 °C for 20 min, it was partitioned between Et₂O and H₂O. The ethereal solution was dried and concentrated to leave a colorless, viscous liquid that was dissolved in 10 mL of cold (0 °C) THF. This cold solution was treated with 2 mL of aqueous 12 M HCl in 5 mL of THF and the resulting solution was stirred at 25 °C for 1.5 h. The resulting yellow solution was partitioned between aqueous NaCl and Et₂O. The ethereal layer was washed successively with aqueous NaHCO₃ and with aqueous NaCl, dried, and concentrated to leave 614 mg of viscous yellow liquid containing (TLC, silica gel with an EtOAc-hexane eluent, 1:9 v/v) the diketone **24** (*R_f* 0.32), the keto enol ether **23** (*R_f* 0.52), the trienone **13** (*R_f* 0.56), and two unidentified components (*R_f* 0.64 and 0.75). Chromatography on silica gel with an EtOAc-hexane eluent (2:23 v/v) separated the crude diketone **24** as a colorless liquid that solidified on standing. Recrystallization from MeOH separated 353 mg (57%) of the diketone **24** as colorless prisms, mp 99–100 °C. An additional recrystallization from H₂O-EtOH raised the melting point to 99.5–100.5 °C: IR (CCl₄) 1665 (conjugated C=O), 1632, and 1600 cm⁻¹ (C=C); NMR (CCl₄) δ 1.2–2.6 (19 H, m, aliphatic CH) and 0.6–1.2 (21 H, m, CH₃); UV max (95% EtOH) 256 nm (ε 13 000); mass spectrum *m/e* (rel intensity) 396 (M⁺, 100), 381 (47), 340 (32), 325 (59), 307 (45), 201 (30), 141 (49), 83 (49), 69 (36), 55 (52), 43 (48), and 41 (61).

Anal. Calcd for C₂₇H₄₀O₂: C, 81.76; H, 10.17. Found: C, 81.73; H, 10.03.

After a solution of 200 mg (0.51 mmol) of the diketone **24** and 650 mg (16 mmol) of NaOH in 8 mL of MeOH had been refluxed for 15 h under an N₂ atmosphere, the resulting dark yellow reaction mixture was concentrated and then partitioned between Et₂O and H₂O. The ethereal layer was dried and concentrated to leave 180 mg of the crude product as a yellow solid, mp 144–147 °C; this material contained (TLC, silica gel coating with an EtOAc-hexane eluent, 1:9 v/v) the trienone **13** (*R_f* 0.49) and a minor identified impurity (*R_f* 0.53) but none of the starting diketone **24** (*R_f* 0.25) was detected. Recrystallization from MeOH separated 154 mg (81%) of the trienone **13** as yellow prisms, mp 147–149 °C. This product was allowed to crystallize from EtOH very slowly to give 90 mg of the pure trienone **13**, mp 149–150 °C, that was identified with the previously described sample by a mixture melting point determination and by comparison of IR, UV, and NMR spectra.

When the natural abundance ^{13}C NMR spectrum of the diketone **24** was determined in CDCl₃ solution at ca. 40 °C, the six lines expected for the sp^2 carbon atoms in structure **24** (Table VI) were accompanied by six additional less intense lines corresponding to a second conformer of structure **24**. Because of the presence of two rotational isomers with different ^{13}C NMR signals, we were unable to resolve satisfactorily the complex multiplet from the sp^3 carbon atoms in this spectrum. To establish that these extra NMR signals arose from two slowly equilibrating conformers (presumably caused by restricted rotation about the C–C bond joining the two ring systems in structure **24**), the ^1H NMR spectrum of the diketone **24** in PhCl solution was examined at ca. 35 °C and at 95 °C. At ca. 35 °C, the highest field CH₃ signal appeared as a less intense singlet at δ 0.68 and

a more intense singlet at δ 0.74. When this solution was warmed to 95 °C, the two signals collapsed to a single line at δ 0.77; upon cooling this solution to ca. 35 °C the original spectrum was obtained.

Structure Determination of "Trimer" 5. A platelike crystal fragment with approximate dimensions 0.5 × 0.7 × 0.3 mm was mounted on a glass fiber with epoxy cement. Unit cell parameters and the orientation matrix were determined on a Syntex P2₁ four-circle diffractometer equipped with a graphite monochromator (Bragg 2θ angle 12.2°) using Mo Kα radiation at a takeoff angle of 6.5°. Fifteen reflections whose 2θ values ranged from 11.72° to 21.90° were machine centered and used in least-squares refinement of the lattice parameters and orientation matrix. Unit cell parameters obtained were¹⁹ *a* = 12.196 (2) Å, *b* = 11.247 (3) Å, *c* = 10.740 (2) Å, α = 94.45 (2)°, β = 110.76 (2)°, γ = 119.04 (2)°, and *V* = 1146.9 (4) Å³. The calculated density of 1.10 g cm⁻³ for two molecules per unit cell agrees with the experimental density of 1.09 (1) g cm⁻³ measured by the flotation method using aqueous zinc chloride solution at room temperature. Omega scans of several low 2θ angle reflections gave peak widths at half-height of less than 0.30°, indicating a satisfactory mosaic spread for the crystal.

Intensity data were collected using θ–2θ scans with x-ray source and monochromator settings identical with those used for determination of the unit cell parameters. A variable scan rate of from 4.88 to 29.3°/min was used and a scan width of 2.3° was sufficient to collect all of the peak intensity. Stationary background counts were measured at the beginning (bgd1) and at the end (bgd2) of each scan with a total background to scan time ratio of 1.0. No significant fluctuations were observed in the intensities of three standard reflections (-3,-3; 4,-4,-4; 2,2,-2) monitored every 97 reflections. Intensities (*I*) were calculated by subtracting the sum of the two background counts (bgd1 + bgd2) from the total scan count (CT). Standard deviations were assigned to the intensities according to the formula

$$\sigma(I) = (\text{CT} + \text{bgd1} + \text{bgd2})^{1/2}$$

From a total of 4274 reflections collected in a complete hemisphere (*h* ≥ 0) of data out to 2θ = 50°, 2223 were accepted as statistically above background [*I* ≥ 3σ(*I*)]. Lorentz and polarization corrections were made in the usual way; no corrections were made for absorption.

The structure was solved²⁰ by direct methods utilizing the program MULTAN to generate phases. *E* values were calculated for all nonzero reflections and the 336 largest *E* values were used as input for MULTAN. When the program was allowed to choose three origin-fixing reflections, it was unable to produce a set of phases that led to a solution. Three alternate origin-setting reflections chosen manually produced a set of phases with an absolute figure-of-merit of 1.152 and Ψ₀ of 0.29 × 10³; the resulting *E* map revealed the positions of all nonhydrogen atoms. After three cycles of full-matrix least-squares refinement, a difference Fourier revealed positions of all nonmethyl hydrogens. Further refinement, followed by another difference Fourier, located methyl hydrogen positions. After three additional cycles of least-squares refinement, varying a scale factor, coordinates of all atoms, anisotropic temperature parameters for the oxygen and methyl carbons, isotropic temperature factors for all other carbon atoms, and fixing the isotropic temperature parameters of all hydrogen atoms at 4.0, the refinement converged²⁴ to *R* = 0.064 and *R_w* = 0.055 (262 variables, 2223 reflections). Final positional and thermal parameters and a list of calculated and observed structure factors are available as supplementary material.

Registry No.—1, 78-59-1; 2, 6244-16-2; 8, 5409-55-2; 13, 61528-42-5; 13 HClO₄, 61528-43-6; 16, 61528-44-7; 20, 6244-19-5; 21, 61528-40-3; 23, 61528-46-9; 24, 61528-41-4; 25, 17530-69-7; 26, 3471-13-4; *t*-BuOH, 75-65-0; PCl₃, 7719-12-2.

Supplementary Material Available. Tables of atomic coordinates and isotropic temperature factors (Table VII), anisotropic thermal parameters (Table VIII), and observed and calculated structure amplitudes (Table IX) (15 pages). Ordering information is given on any current masthead page.

References and Notes

- (1) (a) This research has been supported in part by Public Health Service Grant RO1-GM-20197 from the National Institute of General Medical Science. The execution of this research was also assisted by Institutional Research Grants from the National Science Foundation for the purchase of a mass spectrometer and a Fourier transform NMR spectrometer. (b) Georgia Institute of Technology. (c) Union Carbide Corp.
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 (20) All computations were carried out on the CDC Cyber 74 system. Standard programs utilized included: Germain, Main, and Woolfson's MULTAN, Zalkin's FORNAP, Ibers' NUCLS modification of Busing, Martin, and Levy's least-squares program, Busing and Levy's ORFFE, and Johnson's ORTEP. Scattering factors were taken from Cromer and Waber's tabulation²¹ for carbon and oxygen; Stewart's hydrogen atom scattering factors²² were used. Anomalous dispersion factors employed were those given by Cromer.²³
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Total Synthesis of (±)-Acorone

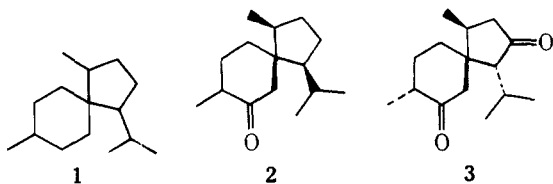
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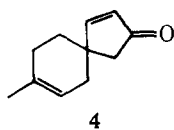
Received September 28, 1976

(±)-Acorone (**3**) has been synthesized by an efficient sequence beginning with 4-methyl-3-cyclohexenecarboxaldehyde (**5**). The imine of the aldehyde was alkylated with trimethylsilylpropargyl bromide. The acetylene moiety was hydrated with dilute acid and mercuric sulfate which also removed the trimethylsilyl group to give 1-(2-oxopropyl)-4-methyl-3-cyclohexenecarboxaldehyde which was cyclized with base to 8-methylspiro[4.5]deca-1,7-dien-3-one (**4**). Base-induced condensation of **4** with ethyl formate followed by acetic anhydride yielded 1-(anti-acetoxymethylene)-8-methylspiro[4.5]deca-3,7-dien-2-one (**14**). Two successive treatments of **14** with lithium dimethylcuprate followed by hydroboration and oxidation afforded a mixture consisting almost entirely of (±)-acorone and (±)-isoacorone (**21**) from which pure (±)-acorone could be isolated by crystallization.

The acorane skeleton (**1**) has recently been subjected to intense synthetic scrutiny.¹ Notable results have been achieved, especially with acorenone **B** (**2**).² Acorone (**3**), itself, has been approached less successfully. The synthesis of Pinder et al.^{3a} failed in the penultimate step, while Marx and Norman^{3b} were successful in producing the enantiomer of natural (+)-acorone.



Spirocyclopentenone (**4**) appeared to be a very attractive intermediate. Indeed, we have synthesized crystalline (±)-acorone via **4** without a single chromatographic separation. A problem in preparing **4** is that most methods of cyclopen-



tenone construction are not sufficiently versatile to incorporate the quaternary carbon necessary for a spiro skeleton.⁴

Regiospecific hydration of an acetylenic carbonyl compound to generate the 1,4-dicarbonyl precursor avoids this problem. Alkylation of the appropriate enolate anion with a propargyl halide should provide the quaternary carbon readily. A communication by Stork and Borch^{5a} appeared in 1964 describing the regiospecific hydration of acetylenic ketones. Both 1,4 and 1,5 diketones were prepared, and a synthesis of *cis*-jasmone was delineated.^{5b} We have begun an extended study of this reaction, with special regard for its synthetic utility.⁶

The synthesis (Scheme I) was begun with 4-methyl-3-cyclohexene-1-carboxaldehyde (**5**).^{7a,b} Lewis acid catalyzed Diels-Alder reaction of isoprene and acrolein gave **5**, accompanied by the symmetrical trioxane (**6**) which was pyrolyzed in the presence of acid to regenerate **5**. The poor yield obtained at our hands (32%) was mitigated by the ready availability of the starting materials. As reported earlier,^{7b} the expected 3-methyl isomer (**7**) could not be separated by GLC nor was it distinguishable by NMR, and was assumed to comprise $\leq 5\%$ of the product.

The *tert*-butyl imine (**8**) was generated in 76% yield without incident. Alkylation was accomplished using the imine alkylation procedure of House.^{8,9} Treatment of imine **8** with *n*-butyllithium in dimethoxyethane (DME) to form the anion followed by addition of 3-bromo-1-trimethylsilyl-1-propyne (**9**)¹⁰ and then by acid hydrolysis gave the alkylated aldehyde **10** (76%).