

**Table V.**  $k_{\text{obsd}}$  Values for Reaction of Chlorobenzene with Excess TTFA in TFA

Temp, °C	Concn, [C <sub>6</sub> H <sub>5</sub> Cl]	[TTFA], mol/l.	$k_{\text{obsd}}$ , sec <sup>-1</sup>
25	0.043	0.222	$3.19 \times 10^{-6}$
	0.043	0.446	$3.34 \times 10^{-5}$
30	0.043	0.561	$3.98 \times 10^{-5}$
	0.043	0.222	$0.85 \times 10^{-4}$
	0.043	0.446	$0.96 \times 10^{-4}$
35	0.043	0.561	$3.51 \times 10^{-4}$
	0.043	0.222	$1.05 \times 10^{-4}$
	0.043	0.446	$3.61 \times 10^{-4}$
	0.043	0.561	$4.52 \times 10^{-4}$

and again evaporated. Recrystallization of the residue from petroleum ether gave 62 mg (15.2%) of 2-methyl-5-phenylphenylacetic acid, mp 115–120°. Two more recrystallizations from the same solvent raised the mp to 127–128°.

*Anal.* Calcd for C<sub>13</sub>H<sub>14</sub>O<sub>2</sub>: C, 79.62; H, 6.24. Found: C, 79.22; H, 6.26.

Its nmr spectrum (CDCl<sub>3</sub>) showed a singlet at  $\tau$  7.68 (3 H), a singlet at 6.34 (2 H), and a multiplet for the aromatic protons (8 H);  $\nu$  3250–2500 (broad), 1700, 765 (both strong), 1240, 1225 (both medium), 1335, 1305, 935, 830, 730, 695, and 685 cm<sup>-1</sup> (all weak).

**Determination of the Energy of Activation for Thallation of Chlorobenzene.**<sup>27</sup> Chlorobenzene was employed as aromatic substrate,<sup>28</sup> pure, dry TFA as solvent, and pure recrystallized TTFA as reagent. Aliquots were withdrawn from the reaction mixture (see Table V) at appropriate time intervals and added to an excess of an aqueous solution of potassium iodide. A calculated amount of a standard solution of pure *p*-iodotoluene in benzene was then

(27) An indirect method was employed in which the extent of thallation was estimated by quenching of the reaction mixture with aqueous KI; the amount of iodoaromatic thus formed was assumed to be equal to the amount of arylthallium ditrifluoroacetate in the reaction mixture [A. McKillop, J. S. Fowler, M. J. Zelesko, J. D. Hunt, E. C. Taylor, and G. McGillivray, *Tetrahedron Lett.*, 2427 (1969)].

(28) Thallation of benzene and alkylbenzenes was so rapid under the pseudo-first-order conditions described that no suitable technique for kinetic evaluation could be developed. The reaction is slower in aqueous TFA and in TFA containing acetic acid, but erratic results were obtained (*cf.* J. M. Briody and R. A. Moore, *Chem. Ind. (London)*, 803 (1970)).

added and the resulting mixture shaken vigorously for 12 hr to ensure complete partition of the iodoaromatics between the aqueous and benzene phases. The benzene layer was analyzed by glc, and the relative areas of the peaks due to *p*-chloriodobenzene and *p*-iodotoluene were determined. Prior to the kinetic runs, it was established by using mixtures of the two iodoaromatics of known concentrations that the concentration of *p*-chloriodobenzene present was directly proportional to the ratio of the area of its peak in the glc trace to that of the standard, *p*-iodotoluene. This ratio therefore gave a direct reading of the concentration of *p*-chloriodobenzene.

The data obtained for the reaction of chlorobenzene with an equimolar amount of TTFA were inconsistent with simple first- and second-order kinetic expressions; a 10 molar excess of TTFA was therefore employed. The data obtained under these conditions were fully consistent with eq 1,

$$\ln \left( \frac{x_e}{x_e - x} \right) = t \{ k_1 [\text{TTFA}] + k_{-1} [\text{TFA}] \} \quad (1)$$

where  $x$  = concentration at time  $t$  and  $x_e$  = concentration at equilibrium, which was adapted from an expression derived to account for pseudo-first-order kinetics in a reversible reaction.<sup>29</sup> Equation 1 can be simplified to eq 2, since TTFA was present in excess, TFA was employed as solvent, and the concentration  $x$  is proportional to the ratio  $r$  of the areas of the glc peaks for *p*-chloriodobenzene and *p*-iodotoluene

$$\ln \left( \frac{r_e}{r_e - r} \right) = k_{\text{obsd}} t \quad (2)$$

where  $r$  = ratio at time  $t$  and  $r_e$  = ratio at equilibrium. For kinetic runs at 25, 30, and 35°, straight line plots were obtained for each concentration of TTFA;  $k_{\text{obsd}}$  values are listed in Table V. From eq 3, derived from eq 1 and 2, values for  $k_1$  at 25, 30, and 35°

$$k_{\text{obsd}} = k_1 [\text{TTFA}] + k_{-1} [\text{TFA}] \quad (3)$$

were calculated by plotting  $k_{\text{obsd}}$  against [TTFA],  $k_1$  being given by the slope of the plot, and were found to be, respectively,  $2.36 \times 10^{-4}$ ,  $7.88 \times 10^{-4}$ , and  $10.24 \times 10^{-4}$  sec<sup>-1</sup>. From these data, the computed<sup>30</sup> energy of activation was found to be 27 kcal/mol.

(29) D. Bethell and A. F. Cockerill, *J. Chem. Soc.*, 920 (1966).

(30) Program written in Fortran IV for ICL 1905 E, based on H. Eyring, *J. Amer. Chem. Soc.*, 73, 5628 (1951).

## The Structure of the "Symmetrical Cedrone"

J. A. Beisler, J. V. Silverton, A. Penttila,<sup>1a</sup>  
D. H. S. Horn,<sup>1b</sup> and H. M. Fales\*

*Contribution from the Laboratory of Chemistry, National Institute of Arthritis and Metabolic Diseases, and Laboratory of Chemistry, National Heart and Lung Institute, Bethesda, Maryland 20014. Received November 9, 1970*

**Abstract:** The structure of the symmetrical form of cedrone has been determined by X-ray analysis. On this basis the structures of the three acetates of cedrone have been deduced. Cedrone and its monoacetate appear to exist in tautomeric forms in solution.

Several years ago, during a study of the oxidative dimerization of acylphloroglucinols,<sup>2</sup> *e.g.*, **1** + **2** → **3**, we became aware of the presence of, but did not report, substances corresponding to the abstraction of

(1) (a) Visiting Scientist from OY Medica AB, Helsinki, Finland; (b) Division of Applied Chemistry, C. S. I. R. O., Melbourne, Australia.

(2) (a) A. Penttila and H. M. Fales, *J. Amer. Chem. Soc.*, **88**, 2327 (1966); (b) A. Penttila and H. M. Fales, *Chem. Commun.*, **18**, 656 (1966).

4 hydrogen atoms from 2 mol of **1**. In the interim, these compounds have been extensively studied by Erdtman and his coworkers,<sup>3</sup> who very reasonably assigned them tricyclic structures such as **4** based on chemical degradations.

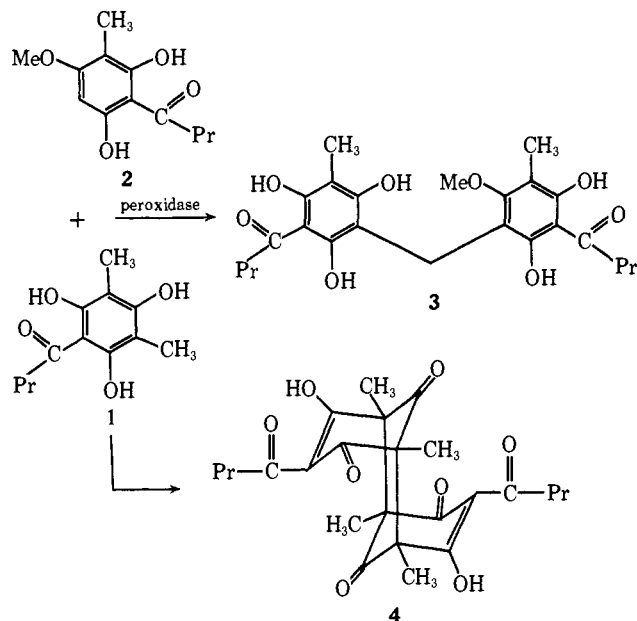
(3) H. Davies, H. Erdtman, and M. Nilsson, *Tetrahedron Lett.*, 2491 (1966); G. E. Moussa, *Acta Chem. Scand.*, **22**, 3329 (1968).

Table I. Nmr Data for Cedrone and Derivatives<sup>a</sup>

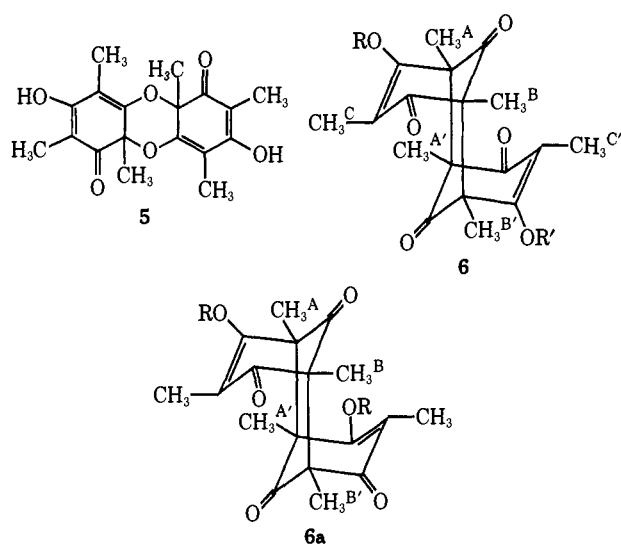
Cedrone (DMSO)		Monoacetate (CDCl <sub>3</sub> )		Diacetates (CDCl <sub>3</sub> )	
"Unsymmetric"	"Symmetric"	Enol acetate side	Aldol side	α	γ
1.05 (6)	0.89 (12)	1.21 (3)	1.08 (3)	1.24 (6)	0.90 (12)
1.12 (6)	1.18 (6)	1.26 (3)	1.18 (3)	1.45 (6)	1.42 (6)
1.19 (3)		1.67 (3)	1.43 (3)	1.66 (6)	
1.69 (3)		2.31 (3, OAc)	7.36 (1, OH)	2.30 (6, OAc)	2.11 (6, OAc)

<sup>a</sup> Shifts are given in parts per million relative to tetramethylsilane  $\delta = 0.00$ .

An analogous compound was obtained from the ferric chloride oxidation of trimethylphloroglucinol many years ago<sup>4,5</sup> and called "cedrone" because its hydrogen iodide cleavage products exhibited a cedar-like odor.<sup>6</sup>



An early structure (5) proposed by Erdtman<sup>7</sup> was clearly incompatible with modern spectral data and Erdtman, *et al.*,<sup>8</sup> have recently proposed the tricyclic



structure 6 or 6a ( $R = R' = H$ ) analogous to the acylphloroglucinol dimers.

We have found that cedrone is also formed by the action of horseradish peroxidase and hydrogen peroxide. During a routine analysis of its nmr spectrum

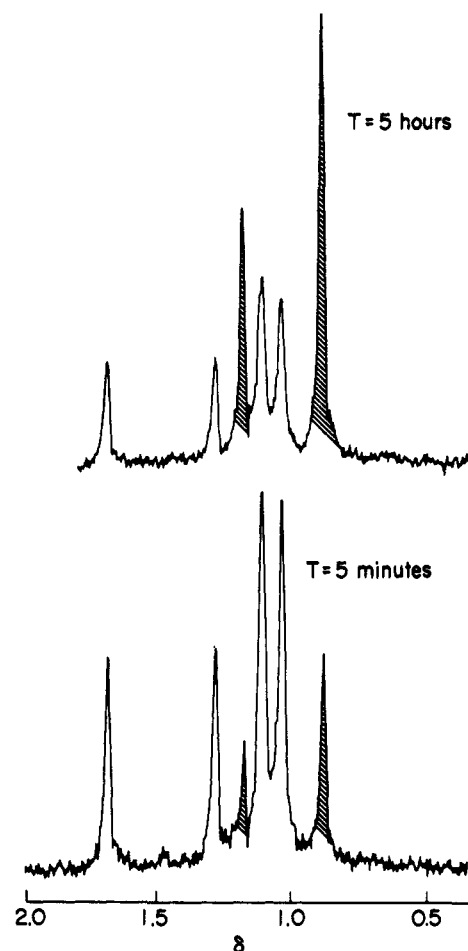


Figure 1. Nmr spectrum of cedrone in deuteriodimethyl sulfoxide showing changes effected by time.

in deuteriodimethyl sulfoxide (DDMS), discussed previously by Erdtman,<sup>8</sup> we were intrigued to find that the ratio between the peaks assigned to the dienolic "symmetric form" 6 ( $R = R' = H$ ) and the dienolic "asymmetric form" 6a ( $R = R' = H$ ) changed with time (Figure 1 and Table I), finally (48 hr) reaching a ratio of 3.5:1 in favor of the "symmetric form." Furthermore, several features of the spectrum appeared to us to argue against interpretation of the spectrum as being

and 8.67 for cedrone in pyridine in Table II and the text, p 2517, are in error and should be reversed. Thus, we find that the low-field signal in this solvent contains two methyl groups and the high field signal four methyl groups.

- (4) H. Weidel, and F. Wenzell, *Monatsh.*, **19**, 259 (1898).  
 (5) R. Boehm, *Justus Liebigs Ann. Chem.*, **302**, 184 (1898).  
 (6) J. Cecelsky, *Monatsh.*, **20**, 779 (1899).  
 (7) H. Erdtman, *Svensk. Kem. Tidskr.*, **46**, 226 (1934).  
 (8) H. Erdtman, G. Moussa, and M. Nilsson, *Acta Chem. Scand.*, **23**, 2515 (1969). Apparently the integrals assigned to the peaks at  $\tau$  8.98

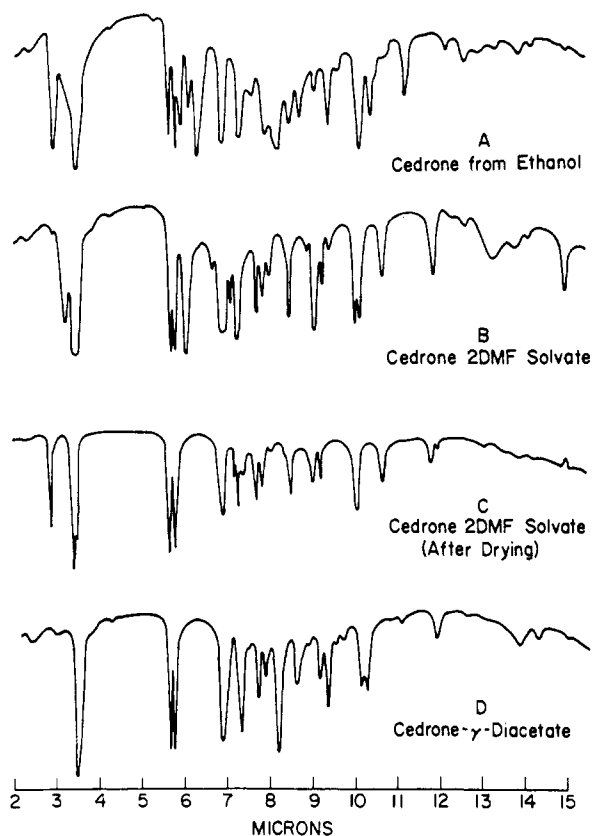


Figure 2. Infrared spectrum (Nujol mulls) of cedrone and its solvates and derivatives.

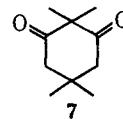
due to forms such as **6** and **6a**. Thus there appeared to be no simple explanation for the upfield shift of the peaks assigned to the "symmetric form" relative to those assigned to the "unsymmetric form," particularly with regard to the peaks which might logically be assigned to methyl groups C or C' on the double bond. More importantly, perusal of the proposed structures reveals that **6** and **6a** should *both* show two peaks for the bridgehead methyls, *i.e.*, A = B' and A' = B in the case of **6**, and A = A' and B = B' in **6a**, although the environment of the two pairs may be more nearly alike in the former.

Supporting the existence of the dienolic structures **6** and **6a** were the nmr (Table I, see also ref 8) and ir spectra<sup>8</sup> of the different enol ethers (**6** and **6a**, R = R' = CH<sub>3</sub>) easily prepared from cedrone by treatment with diazomethane. Glc reveals that these are formed in exactly equal amounts. It is noteworthy that, in accord with the above expectations, in both cases *two* bands may be found for the bridgehead methyl groups. In one case, presumably the "symmetric form" **6** (R = R' = CH<sub>3</sub>), mp 257°, they are considerably closer together ( $\Delta = \delta 0.08$ ) than in the other ( $\Delta = \delta 0.26$ ).

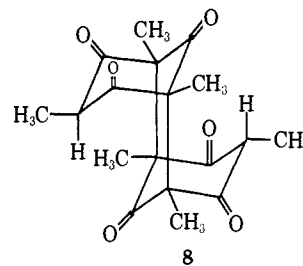
The nmr spectrum of cedrone in deuteriodimethylformamide-*d*-6 (DDMF) showed an unchanging ratio of 5:1 in favor of the symmetric form immediately on mixing, and on standing for several hours a crystalline precipitate appeared in the nmr tube. After losing solvent (see below) by being heated under vacuum or on standing at room temperature the material exhibited the same nmr phenomenon indicating that the multiplicity of peaks was due to the establishment of an

equilibrium between two forms. The crystalline precipitate was prepared again with ordinary DMF; its combustion analysis and ir spectrum displaying an intense peak at 1661 cm<sup>-1</sup> (Figure 2B) showed it to be a solvate containing two molecules of DMF. On this basis, it seemed reasonable to assign the two most intense nmr bands to the form finally isolated as the DMF solvate and this was presumed to be the DMF solvate of Erdtman's "symmetric form" **6**.

The ir spectrum (Nujol mull) of this solvate (Figure 2B) is considerably different from unsolvated cedrone (Figure 2A) as obtained through recrystallization from ethanol. The latter (Figure 2A) is more complex in the carbonyl region and exhibits a broad band at 1650 cm<sup>-1</sup> characteristic of 1,3-diketones in the enolic form in the crystalline state<sup>9</sup> (*e.g.*, dimedone). The DMF solvate showed strongly bonded hydroxyl absorption at 3100 cm<sup>-1</sup> and a DMF carbonyl band at 1661 cm<sup>-1</sup> besides two carbonyl bands at the unusually high frequencies 1725 and 1756 cm<sup>-1</sup>. When the DMF was removed by heating to 76° under vacuum, a very sharp "free" hydroxyl band appeared at 3450 cm<sup>-1</sup>, but the carbonyl bands were unaltered (Figure 2C) except for the loss of the DMF band at 1661 cm<sup>-1</sup>. These bands are totally unexpected for enolic structures such as **6** or **6a** but rather suggest ketones in a strained ring. Their doublet nature is interesting when compared with 2,2,5,5-tetramethylcyclohexane-1,3-dione (**7**) fixed in the keto form which is reported<sup>9</sup> to exhibit a similar doublet at 1688 and 1717 cm<sup>-1</sup>



presumably due to asymmetric and symmetric stretching modes. This fact, together with the high degree of symmetry reflected in the nmr spectrum of the "symmetric form," suggested that the hexaketonic structure **8** be considered, perhaps fixed in this form by unusual steric factors. Such a structure does not account for the presence of hydroxyl groups in the ir. Further, the absence of coupling between methyl groups C, C' and the adjacent protons argue against it. The only other



absorption visible in DDMSO or DDMF was that due to two protons at  $\delta$  6.38 which resembled hydrogen bonded OH more than CH protons, especially since their absorption was lost on addition of deuterium oxide.

At this point it was felt that an X-ray crystallographic investigation was justified and the DMF solvate of the "symmetric form" was chosen because it formed well-

(9) K. Nakanishi, "Infrared Absorption Spectroscopy-Practical," Holden-Day, San Francisco, Calif., 1962, p 66.

defined crystals which proved stable when sealed in a thin Pyrex capillary. Precession photographs showed  $2/m$  diffraction symmetry and systematic absences characterizing space group  $P2_1/c$  ( $C_{2h}^5$ ). The cell dimensions, from least squares refinement of diffractometrically measured  $2\theta$  angles, are  $a = 9.322$  (0.003) Å,  $b = 8.250$  (0.002) Å,  $c = 15.804$  (0.004) Å,  $\beta = 101.86$  (0.03)°; standard deviations are in parentheses. The measured density (estimated error: 0.01 g/cc) was 1.346 g/cc and the density calculated on a basis of two molecules of cedrone and four molecules of DMF was 1.335 g/cc. Since there are four asymmetric units in  $P2_1/c$ , it was necessary that the cedrone molecule possess a center of symmetry.

X-Ray intensity data were collected by the stationary crystal-stationary counter technique with Mo  $K\alpha$  X-radiation (Zr-filtered,  $\lambda = 0.7107$  Å). The maximum  $\sin \theta/\lambda$  was  $0.595 \text{ \AA}^{-1}$ . A reflection whose intensity, corrected for background, was greater than twice its statistical standard deviation was considered "observed." On this basis 1730 reflections were regarded as observed and 366 unobserved.

After application of the usual corrections,  $E$  values were calculated and the symbolic addition method of Karle and Karle<sup>10</sup> was applied manually by two of the authors independently starting with different origins. Both reached the same single solution. A computer approach<sup>11</sup> was also used and this indicated four probable solutions, the apparently least probable of which proved to be the same as the manual solution.

An  $E$  map<sup>12</sup> using the manual solution gave peaks showing atoms at reasonable bonding distances although the indicated structure was different from that suggested by Erdtman. Nevertheless, all the atoms in the asymmetric unit, apart from two ambiguous indications in the DMF molecule, could be accounted for.

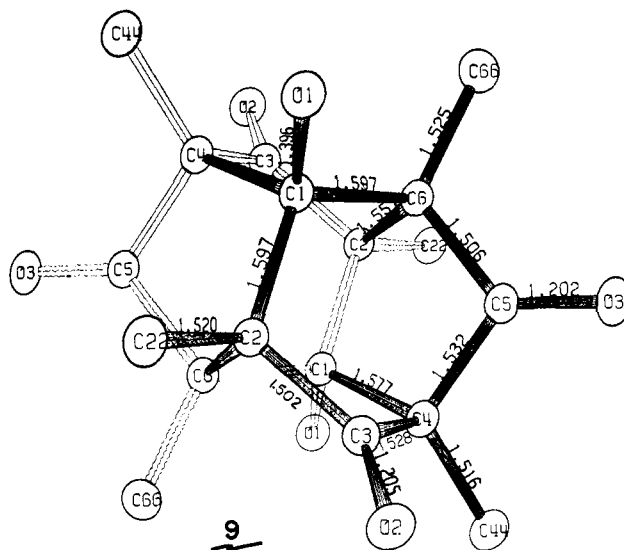
Least squares refinement followed by a difference map gave the missing atoms and the structure was refined with isotropic temperature factors to an  $R$  factor (calculated on observed reflections only) of 0.133. Introduction of anisotropic temperature factors followed by two cycles of refinement reduced the  $R$  factor to 0.094. A difference map then indicated all the hydrogen atoms. The hydrogen atoms were assigned isotropic temperature factors two units greater than the isotropic factors of the heavy atoms to which they were attached. Hydrogen atom temperature factors were not refined since it is the experience of the authors that such refinement is probably not significant, given the estimated errors in the X-ray data. Two cycles of full-matrix least squares refinement on all parameters of the heavy atoms and positional parameters of the hydrogen atoms reduced the  $R$  factor to 0.058. A difference map, calculated after the refinement, was essentially featureless.

The resulting structure and bond lengths are indicated in **9** or schematically **9a** for which the IUPAC name is 2,4,6,8,10,11-hexamethyl-3,7,9,12-tetraketo-1,9-dihydropentacyclo[6.3.0.1<sup>4,11</sup>.0<sup>2,6</sup>.0<sup>5,10</sup>]dodecane. The estimated deviations of bond lengths were *ca.* 0.003 Å. Each dimer molecule is hydrogen bonded *via*

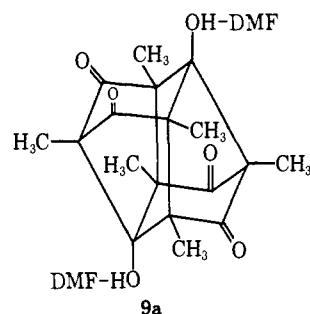
(10) J. Karle and I. L. Karle, *Acta Crystallogr.*, **21**, 849 (1966).

(11) J. F. Cannon, private communication, 1970.

(12) I. L. Karle, H. Hauptman, J. Karle, and A. B. Wing, *Acta Crystallogr.*, **11**, 257 (1958).



the  $-\text{OH}$  groups to the carbonyl oxygen of two symmetrically related DMF molecules. The hydrogen bond has a length of 2.668 Å. No other intermolecular contacts are significantly shorter than usual.



While it is intended to discuss crystal and molecular structure in greater detail at a later date, certain points are relevant to the present discussion. The four bonds formed between the two trimethylphloroglucinol residues result in the production of four cyclically fused five-membered rings. The structure seems relatively strained and most of the strain appears to be taken up by bonds to the carbon atom which is also attached to the hydroxyl group. The five-membered rings are far from planar, and the molecule probably possesses more long carbon-carbon bonds than any other cage compound known. The longest of the carbon-carbon bonds, with lengths of 1.597 Å, are among the longest on record for tetravalent carbon. The six-membered rings formed by the original phloroglucinol atoms are in rather distorted chair forms.

It is apparent that **9** is the double aldol product resulting from further intramolecular condensation of **6** or **6a**. Clearly, this structure satisfies the requirements of its nmr spectrum (Figure 1), all bridgehead methyls now being symmetrically disposed and the slight downfield shift of methyls B and B' brought about by the combined inductive effects of the adjacent C-O bonds. As mentioned above, the infrared bands of the carbonyl groups in **9** resemble those of the model compound of **7** but reflect through their higher frequencies the additional strain disclosed by the X-ray analysis.

The driving force for formation of **9** from **6** or **6a**, besides the formation of a new C-C bond, may involve

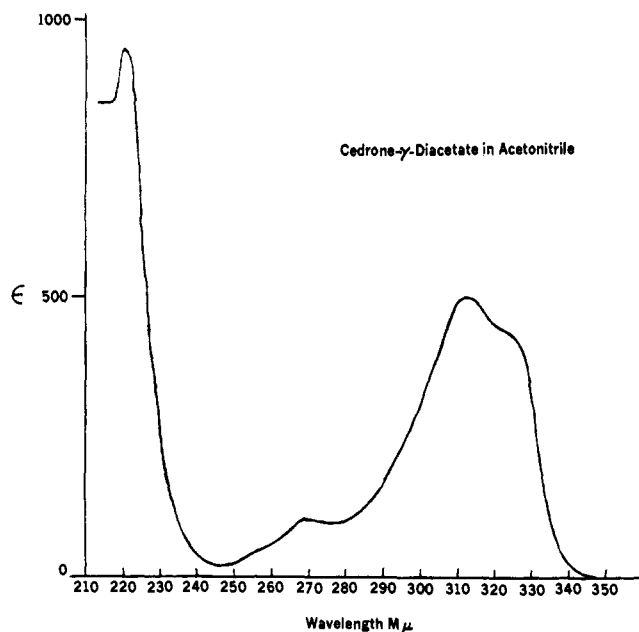


Figure 3. Ultraviolet spectrum of cedrone  $\gamma$ -diacetate in acetonitrile.

the strong hydrogen bonds between the newly formed peri hydroxyl groups and DMF or DMSO.

The situation with regard to the structures of the acetates of cedrone is by no means as clear. Erdtman has found<sup>8</sup> that the acetate, mp 203–205°, reported earlier to be a diacetate<sup>13</sup> is in fact a monoacetate. Two other diacetates have been reported: one, mp 267–268°,<sup>13</sup> referred to here as the  $\alpha$ -diacetate is obtained at room temperature with pyridine-acetic anhydride, and the other (referred to here as the  $\gamma$ -diacetate) shows the unusually high melting point of 338° and is isolated only on prolonged acetylation under relatively strenuous conditions.<sup>8</sup>

We have isolated anew these three compounds and further investigated by glc-mass spectrometry (glc-ms) the behavior of cedrone on acetylation. At room temperature with pyridine-acetic anhydride three peaks are produced in approximately equal amounts: monoacetate (retention time (r.t.) 8.3 min),  $\alpha$ -diacetate (r.t. 11.8 min), and a previously undiscovered diacetate referred to here as the  $\beta$ -diacetate (r.t. 12.7 min). The first and second are identified by having retention times identical with those of the isolated monoacetate and diacetate (mp 267–268°). Furthermore, when introduced directly from the glc, their mass spectra exhibit molecular ions of the expected molecular weight. The previously unidentified  $\beta$ -diacetate has a mass spectrum identical with that of the  $\alpha$ -diacetate and the two are therefore regarded as being structurally very similar. Attempts to isolate the  $\beta$ -diacetate originally present in the reaction mixture in quantities equal to the  $\alpha$ -diacetate were of no avail and glc of the filtrates revealed that it was undergoing transformation to the  $\alpha$ -diacetate as the latter was removed by crystallization.

We therefore assign the  $\alpha$ - and  $\beta$ -diacetates structures **6** and **6a** ( $R = R' = \text{Ac}$ ). If the  $\beta$ -diacetate is converted to its  $\alpha$ -stereoisomer for steric reasons, it follows that the  $\alpha$ -isomer is represented by **6** rather

(13) J. Heuzig and F. Wenzel, *Monatsh.*, **35**, 63 (1914).

than **6a**, although the mechanism for the interconversion is not obvious. The  $\alpha$ -diacetate exhibits ir and nmr spectral properties in good accord with structure **6** (or **6a**).<sup>8</sup> Further, it possesses intense uv absorption ( $\epsilon_{245}^{\text{max}}$  9040) as expected for enol esters.

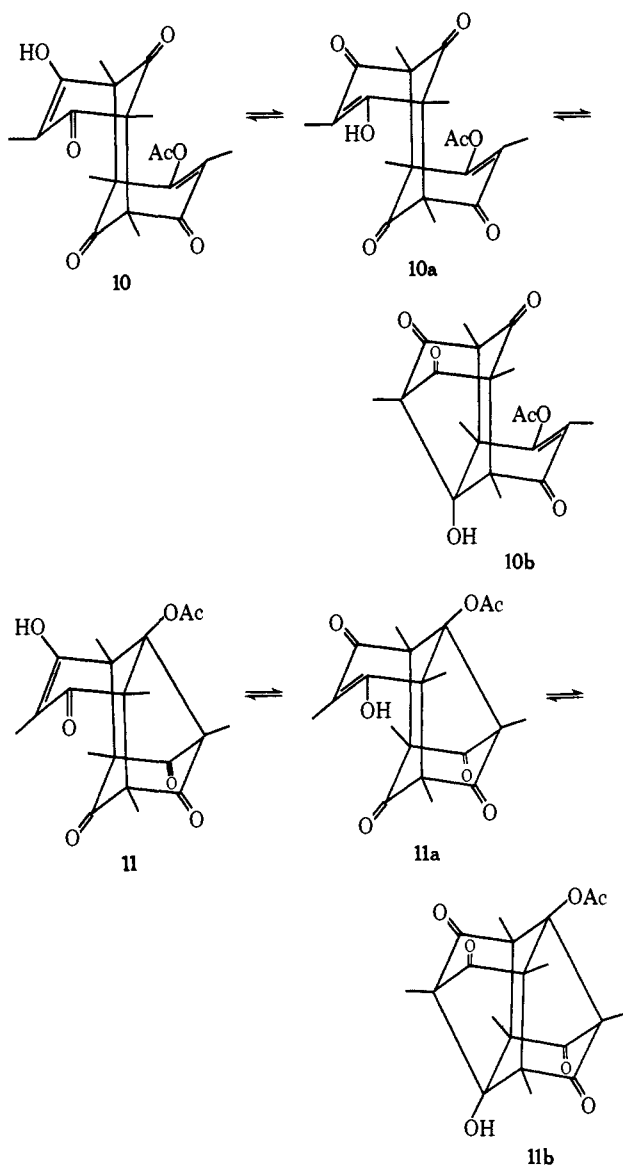
When the acetylation mixture was heated to reflux, a fourth glc peak slowly appeared having a much longer retention time, 15.7 min, and this was found to be due to the high melting  $\gamma$ -isomer of cedrone diacetate assigned by Erdtman<sup>8</sup> the "symmetric form" **6** ( $R = R' = \text{Ac}$ ). Glc-ms showed the molecular weight to be correct but the fragmentation pattern was very different from the  $\alpha$  or  $\beta$  isomers. The nmr of the  $\gamma$ -diacetate shows only one band for the bridgehead methyl groups, a fact taken by Erdtman to support structure **6** ( $R = R' = \text{Ac}$ ). However, as in the case of the enols **6** and **6a** ( $R = R' = \text{H}$ ), neither structure is in fact totally symmetrical with regard to the bridgehead methyl groups.

A more revealing characteristic of the  $\gamma$ -diacetate, also noted by Erdtman,<sup>8</sup> is its lack of enol acetate bands in the ir (Figure 2D) where it absorbs only at 1743 and 1778  $\text{cm}^{-1}$  reminiscent of both the cedrone-DMF solvate and its solvate-free form (Figures 2B and 2C, respectively). Furthermore, the uv (Figure 3) shows only a rather weak absorption band,  $\epsilon_{312}^{\text{max}}$  500 ( $\text{CH}_3\text{CN}$ ), resembling a saturated polyketone<sup>14</sup> and in contrast to the enol of the  $\alpha$ -diacetate. For these reasons, we consider that cedrone  $\gamma$ -diacetate is the acetate of the pentacyclic structure **9**. Thus, its symmetry from nmr data, high melting point, high C=O stretching frequency, and lack of strong uv absorption are explained. From the foregoing, the monoacetate may possess structures equilibrating among **10**, **10a**, and **10b** on one hand, or **11**, **11a**, and **11b** on the other.

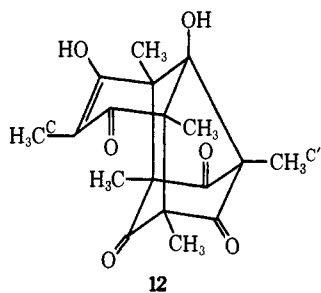
By treatment with diazomethane, the monoacetate forms two different methyl enol ether acetates in equal amounts (glc-ms) showing both the correct molecular weight and identical fragmentation patterns. Therefore **11** and **11a** are eliminated from consideration since only one racemic methyl enol ether would be expected from their reaction. On the other hand, as in the case of the  $\alpha$ - and  $\beta$ -diacetates, the enol ethers of **10** and **10a** would be expected to fragment very similarly and are presumably equally probable in solution prior to methylation. The nmr spectrum of the monoacetate in chloroform (Table I) supports the existence of structure **10b** in chloroform since three bands are found at relatively high field, characteristic of both the  $\gamma$ -diacetate and the "symmetrical form" of cedrone (**9**) and three are also found at lower field as in the case of the  $\alpha$ -diacetate although for obvious reasons the correspondence is not exact. Thus the monoacetate appears to exist in chloroform solution mainly as **10b**, but the equilibrium with **10** and **10a** must be facile to provide the aforementioned methyl ethers with diazomethane.

Examining the nmr spectrum in DMSO of cedrone itself in light of the above observations shows that the low field methyl resonance at  $\delta$  1.69 is adequately explained by **6** or **6a**, although it only accounts for one such group. The next lowest methyl resonance is at

(14) The uv absorption curve (Figure 3) shows some unexplained fine structure and is about twice as intense as expected for a saturated tetraketone; e.g., M. Ramart-Lucas and M. Cornubert [*Bull. Soc. Chim. Fr.*, **53**, 747 (1933)] report 2,2,6,6-tetramethylcyclohexanedione  $\epsilon_{310}^{\text{max}}$  56.



$\delta$  1.29, and this is difficult to rationalize on the basis of either or both structures 6 and 6a. We therefore



propose, by analogy with the monoacetate 10b, that the four bands support structure 12, the monoaldol-monoenol form where the band at  $\delta$  1.69 is due to methyl group C and that at  $\delta$  1.29 is due to methyl group C'. As in the case of the monoacetate, this form appears to be in rapid equilibrium with the enol forms 6 and 6a (or their monomethyl ethers) in order to provide the corresponding dimethyl enol ethers.

A similar enol-aldol tautomerism might occur in the case of the oxidation products (4) of the acylphloroglucinols and it will be interesting to seek evidence for its existence.

### Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 21 spectrophotometer, ultraviolet spectra on a Cary Model 11 MS, nmr spectra on a Varian HA-100 at 100 MHz in solvents as specified with tetramethylsilane as an internal standard  $\delta = 0.00$ . Gc-mass spectra were recorded on an LKB 9000 combined gc-ms instrument; the ionizing voltage was 70 eV, 60  $\mu$ A ionizing current, ion chamber temperature 270°. The gas chromatograph was maintained at 210°, flow rate 20 ml/min on a 1% OV-17 phenylmethylsiloxane polymer on 80-100 mesh Supelcoport F (Supelco, Inc., Bellefonte, Pa.).

The X-radiation used was produced by a Picker constant potential generator (44 kV, 14 mA) and the reflected intensities were measured using a Picker four-circle diffractometer equipped with scintillation counter, ratemeter, scaler, and pulse-height analyzer.

Cedrone was prepared by ferric chloride oxidation of trimethylphloroglucinol as described by Erdtman;<sup>7</sup> recrystallized from ethanol, mp 280-285° dec; ir (Nujol) Figure 2A. It was also prepared by the slow alternate additions of horseradish peroxidase (Calbiochem) and 0.01% hydrogen peroxide to an aqueous solution of trimethylphloroglucinol in phosphate buffer at pH 7.8 over a period of 30 min. Acidification and extraction of the product provided an amorphous residue which contained unchanged trimethylphloroglucinol and cedrone as evidenced by mass spectra obtained as the material volatilized from the direct insertion probe at room temperature and then at 150°.

The DMF-solvate of cedrone was prepared by recrystallizing it several times from DMF, mp 270-90° dec. *Anal.* Calcd for  $C_{24}H_{34}N_2O_8$ : C, 60.24; H, 7.16; N, 5.85. Found: C, 59.91; H, 7.43; N, 5.58 (after heating at 76° under vacuum; N, 0.00).

Cedrone  $\alpha$ ,  $\gamma$ , and monoacetates were prepared as described earlier.<sup>8</sup> The methyl ethers of the monoacetate were formed on addition of ethereal diazomethane but not characterized beyond their gc-mass spectra.

Retention times of the products are listed below relative to *n*- $C_{28}H_{58}$  (10.4 min at 210°, 30 psi inlet, 1% OV-17); cedrone 0.884, monoacetate 0.797,  $\alpha$ -diacetate 1.13,  $\beta$ -diacetate 1.22,  $\gamma$ -diacetate 1.51, monoacetate monoethers 1.07 and 1.16.<sup>15</sup>

**Acknowledgment.** The authors gratefully acknowledge the assistance of Mr. Edward Sokoloski and Mrs. Katherine Warren in instrumental aspects of this work.

(15) NOTE ADDED IN PROOF. It is interesting to note that the same ring system was produced during the preparation for X-ray analysis of a heavy-atom derivative of the anthraquinone dimer rugulosin, *i.e.*, (+)-dibromodehydrotetrahydro rugulosin (N. Kobayashi, Y. Itaka, and S. Shibata, *Acta Crystallogr. Sect. B*, **26**, 188 (1970)).