

## Phenol Dehydrogenations

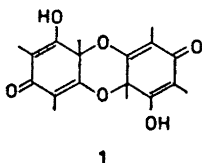
## 13.\* Structure of "Cedrone" — Spectral Evidence

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A spectrometric examination of "cedrone" and its derivatives indicates that this dehydrogenation product of trimethylphloroglucinol has the structure 2 ( $R=CH_3$ ).

Dehydrogenation of 2,4,6-trimethylphloroglucinol gives a dimeric product, "cedrone" ( $C_{18}H_{20}O_8$ ), for which different structures have been proposed.<sup>1,2</sup> The accepted<sup>3</sup> structure (1)<sup>2</sup> accounts for the formation of two dimethyl



ethers and of two "diacetates" (m.p. 195—197° and 267—268°, respectively) — as well as for the facile reductive cleavage to 2,4,6-trimethylphloroglucinol.

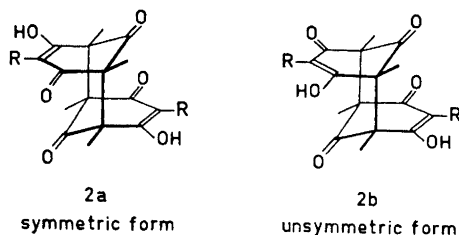
Recent work in this laboratory<sup>4</sup> has shown that dehydrogenation of 3,5-dimethylphloro-acylophenones gives dimers of type 2 ( $R=COCH_3$  or CHO). The structures of these dimers were elucidated by chemical degradations and spectroscopic investigations. Teuber *et al.* have assigned somewhat similar structures to certain dehydrogenation products of pyrogallol and other phenols.<sup>5,6</sup>

It seemed probable that cedrone might have a similar structure (2,  $R=CH_3$ ) and the chemical evidence mentioned above was compatible with both structures. Re-examination of the acetates showed that the alleged<sup>1</sup> low-melting

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diacetate was in fact a monoacetate. The existence of the "high-melting diacetate", m.p. 268° (unsymmetric cedrone diacetate), was confirmed but, in addition, a new high-melting diacetate, m.p. 338° (symmetric cedrone



diacetate), was obtained. The molecular weights of cedrone and the diacetates were checked by mass spectrometry.

Spectral data support structure 2 ( $R = \text{CH}_3$ ) for cedrone. The infrared spectrum shows a band at  $1755 \text{ cm}^{-1}$ , which is retained with some frequency variations in all derivatives (Table 1). It seems to be analogous to the band at

Table 1. Important infrared absorptions ( $\text{cm}^{-1}$ ) of cedrone and its derivatives (in KBr).

Cedrone	Monoacetate	Diacetate m.p. 268°	Diacetate m.p. 338°	Dimethyl ether m.p. 217°	Dimethyl ether m.p. 257°
3438	3490 3315				
	1780	1780	1778		
1755	1738	1735	1743	1730	1730
1715	1715				
	1670 w.sh.	1660		1655	1655
	1660	1626		1600	1600

$1725 \text{ cm}^{-1}$  of the dimethylphloro-acylophenone dimers<sup>4</sup> and is probably due to a non-conjugated carbonyl group though the frequency is rather high. The occurrence of this band rules out structure 1 for cedrone. Also the other bands in the carbonyl region for cedrone and its derivatives are largely consistent with structure 2 ( $R = \text{CH}_3$ ). The unsymmetric diacetate and the dimethyl ethers show bands compatible with conjugated carbonyl groups (near  $1660 \text{ cm}^{-1}$ ) and enol ester/ether double bonds ( $1600\text{--}1626 \text{ cm}^{-1}$ ). Unexpectedly these bands are missing for the symmetric diacetate. All acetates show the expected enol acetate absorption at  $1780 \text{ cm}^{-1}$ .

The ultraviolet spectrum of cedrone in ethanol shows bands at 293, 272 and 207–208 nm ( $\epsilon = 6500, 7600, \text{ and } 5900$ , respectively). The UV spectrum for a solution of cedrone in 0.01 M ethanolic sodium hydroxide showed bands at 282–283 and 215 nm ( $\epsilon = 31\,200 \text{ and } 12\,300$ ) in fair agreement with the

reported<sup>7</sup> absorption of the anion of 2,2,4,4-tetramethylcyclohexane-1,3,5-trione (280 nm,  $\epsilon=28\ 000$ , pH 10). In 0.01 M ethanolic hydrogen chloride cedrone gave no strong absorption at the longer wavelengths, only a band at 211 nm ( $\epsilon=2580$ ) indicating it to be almost completely ketonic in acidic solution.

The NMR data (Table 2) for the diacetates and the dimethyl ethers demonstrate the symmetry properties of these derivatives. They are analogous to

Table 2. NMR data ( $\tau$ -values) for cedrone in pyridine and dimethyl sulphoxide- $d_6$ , (the ratio between the symmetric form (2a) and the unsymmetric form (2b) is 1.6:1), for the diacetate, m.p. 338°, in trifluoroacetic acid and for the other acetates and the dimethyl ethers in deuteriochloroform. Figures in brackets denote number of protons.

Pyridine	Cedrone DMSO		Mono- acetate	Diacetate m.p. 268°	Diacetate m.p. 338°	Dimethyl ether m.p. 217°	Dimethyl ether m.p. 257°	Assign- ments	
	2a	2b							
8.98(6)	9.18(12)	9.1	8.96(3)	8.8 (6)	8.98(12)	8.85(6)	8.75(6)	} CH <sub>3</sub>	
8.67(12)	8.87(6)	8.94		8.86(3)	8.61(6)	8.46(6)	8.59(6)		8.67(6)
		8.76		8.84(3)	8.4 (6)		8.19(6)		8.19(6)
		8.33		8.72(3)					
				8.62(3)					
				8.38(3)					
				7.75(3)	7.75(6)	7.76(6)			
				6.95(1)					
							6.14(6)		6.15(6)

those of the different enolic forms of the dimers of dimethylphloro-acylophenones<sup>4</sup> and show that the cedrone diacetate, m.p. 337–338°, and the dimethyl ether, m.p. 254–257° (*cf.* Experimental) are the symmetric forms while their low-melting isomers are the unsymmetric forms. The NMR spectrum of the cedrone anion (pyridine solution) shows only two types of methyl groups; the low-field signal ( $\tau$  8.67) corresponding to four methyl groups and the other ( $\tau$  8.98) to two methyl groups. In dimethyl sulphoxide- $d_6$  the NMR spectra indicated the presence of the expected two dienolic forms (2a and 2b).

In conclusion: the spectral data rule out structure 1 for cedrone and agree largely with those expected for a compound possessing structure 2 (R=CH<sub>3</sub>).

Further studies on the chemistry of cedrone, and particularly its degradation, are needed in order to establish this structure beyond doubt.

## EXPERIMENTAL

*Dehydrogenation of trimethylphloroglucinol.* Iron(III) chloride (33 g) in water (150 ml) was added dropwise with stirring to trimethylphloroglucinol (12.5 g) dissolved in boiling ethanol (90 ml). After refluxing for 1 h, the mixture was allowed to cool and 50 % hydrochloric acid (100 ml) was added in portions. The mixture was diluted with water (30 ml) and kept in the refrigerator overnight. The precipitate after washing with dilute hydrochloric acid and water was dried and sublimed. Crystallisation from ethanol (butanol or benzonitrile) gave pure cedrone (9.2 g), m.p. 282–285°. Lit.<sup>1</sup> m.p. 280–282°. (Found: M.w.: 332, mass spec. Calc. for C<sub>18</sub>H<sub>20</sub>O<sub>6</sub>: 332).

*Acetylation of cedrone.* A mixture of cedrone (1.5 g), acetic anhydride (9 ml), and pyridine (1 ml) was boiled under reflux 1 h. After 10 h at room temperature it was poured into ice water. The solid obtained was dried and recrystallised from glacial acetic acid to give a product (A), m.p. 245–256° (0.82 g). Further crystallisation from acetic acid and chromatography on silica gel (chloroform-light petroleum, 3:1) gave unsymmetric cedrone diacetate, m.p. 267–268°. (Found: M.w. 416, mass spec. Calc. for  $C_{22}H_{24}O_8$ ; 416). The mother liquor from A was diluted with much water to give a second product, m.p. 190–200° (0.56 g), which was chromatographed on silica gel (chloroform) to give a monoacetate, m.p. 203–205°, as the major product. (Found: C 62.9; H 5.8;  $CH_3CO$  11.6. Calc. for  $C_{20}H_{22}O_7$ ; C 64.2; H 5.9;  $CH_3CO$  11.5).

Similarly cedrone (1.0 g), acetic anhydride (18 ml), and pyridine (2 ml) were refluxed for 1 h and left overnight at room temperature. The crystals deposited (0.1 g) were recrystallised from glacial acetic acid giving symmetric cedrone diacetate, m.p. 337–338°. (Found: C 63.5; H 5.7. M.w. 416, mass spec. Calc. for  $C_{22}H_{24}O_8$ ; C 63.5; H 5.8; M.w. 416).

From the filtrate cedrone monoacetate (m.p. 203–205°) and unsymmetric cedrone diacetate (m.p. 267–268°) were isolated.

When a mixture of cedrone (0.6 g), acetic anhydride (12 ml), and pyridine (1 ml) was boiled for 18 h a practically quantitative yield of symmetric cedrone diacetate, m.p. 337–338°, was obtained. Cedrone monoacetate and unsymmetric cedrone diacetate both yielded symmetric cedrone diacetate, m.p. 338°, on prolonged heating with excess acetic anhydride and pyridine.

*Methylation of cedrone.* Cedrone (2 g) was treated with excess diazomethane in ether and the mixture left in the refrigerator for a few days with occasional shaking. Evaporation gave a brownish product, m.p. 210–240°, which was separated by fractional crystallisation from ethyl acetate into two isomeric cedrone dimethyl ethers, m.p. 254–257° (0.8 g) and 215–217° (0.35 g). Herzig and Wenzel<sup>1</sup> gave m.p. 253–256° and 211–214°, respectively).

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