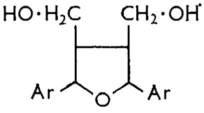
657. *Lignans. Part V.*[1] *(−)-Olivil and (+)-Cyclo-olivil*

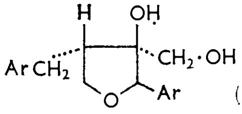
By D. C. Ayres and S. E. Mhasalkar

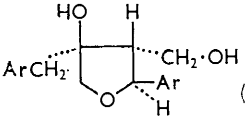
Evidence for a revised structure of (−)-olivil and (+)-cyclo-olivil is presented, and the assignment of a configuration to cyclo-olivil is completed by optical rotatory dispersion studies.

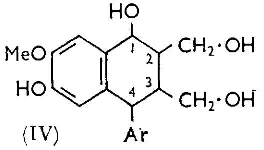
A polymer of the solvent tetrahydrofuran was detected in the products of a hydrogenolysis experiment.

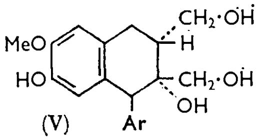
Three possible structures for olivil (I)—(III), have been mentioned in recent work, leading to corresponding structures (IV)—(VI) for the acid-catalysed-rearrangement product, cyclo-olivil:

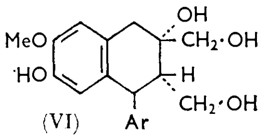

(I)


(II)


(III)


(IV)


(V)


(VI)

(Ar = 4-hydroxy-3-methoxyphenyl)

In a reappraisal [2] of the evidence, we referred to the likelihood of the rearrangement being catalysed by the acetylium ion, and were encouraged to believe that this was correct by the observation of marked changes in optical rotation when dimethylolivil was warmed in acetic anhydride. Since a distinction between structures (II) and (III) would be invalidated by rearrangement of the latter, a test for a vicinal diol was made with periodic acid at pH 4—5, but no fission was detected. This did not exclude structure (II), since the test may fail for hindered diols,[3] and one hydroxy-group in dimethylolivil is resistant to tosylation in pyridine solution. Further, dimethylcyclo-olivil could only be diacetylated in pyridine, and the residual OH group (infrared spectrum) was eliminated by treatment with toluene-*p*-sulphonic acid in acetone, affording the diacetate of dimethyl α-apocyclo-olivil (VII), m. p. 129—130°, which was also obtained in one step on reaction with perchloric acid–acetic acid and was hydrolysed to the diol, m. p. 90—92°. The position of the double

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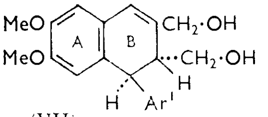
[1] Part IV, D. C. Ayres and P. J. S. Pauwels, preceding Paper.

[2] D. C. Ayres and S. E. Mhasalkar, *Tetrahedron Letters*, 1964, 335.

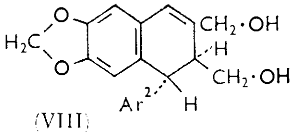
[3] C. A. Bunton and M. D. Carr, *J.*, 1963, 770.

bond in this compound follows from its ultraviolet absorption spectrum (see Figure), which is typical of 1,2-conjugation and excludes 3,4-unsaturation which leads to a large bathochromic shift in γ-apo-compounds of the picropodophyllin series.[4] Formation of an α-apo compound would also be expected from structure (IV) or (VI), but the former cannot account for the low reactivity of one OH group or for the behaviour of dimethylolivil with boron trifluoride–borohydride; here, rearrangement to dimethylcyclo-olivil occurred without the subsequent hydrogenolysis typical of benzyl alcohols. A second product, however, was isolated, as a waxy solid, m. p. 37—38°, freely soluble in organic solvents; analytical evidence showed that this was a polymer of tetrahydrofuran with a molecular weight corresponding to 14 units. No end-groups were sought in this material although it must have been generated by cationic polymerisation[5] and, further, the dissolved alcohol functioned as a co-catalyst, for very little polymer was formed under identical conditions in the absence of dissolved substrate. This polymerisation was faster than the previously described reaction[6] between diborane and tetrahydrofuran, which afforded n-butyl borate.

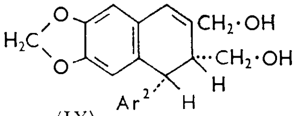


(VII)

(Ar¹ = 3,4-dimethoxyphenyl)

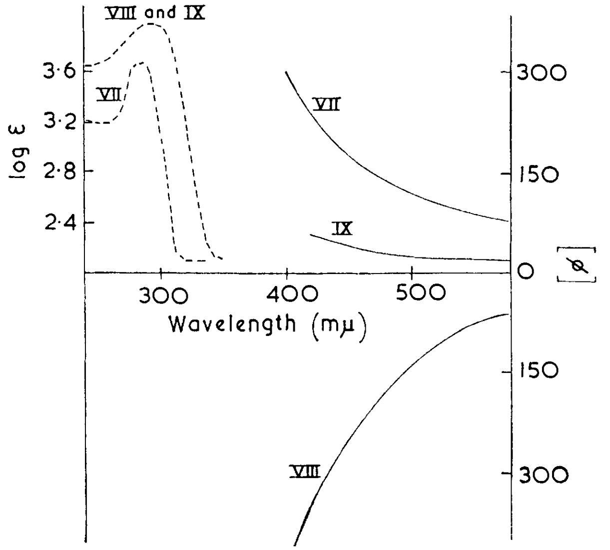


(VIII)



(IX)

(Ar² = 3,4,5-trimethoxyphenyl)



Ultraviolet spectra (– – – –) and optical rotatory dispertion curves (———) of compounds (VII)—(IX)

At this point, we were able to account for the fission by lead tetra-acetate of dimethylolivil[7] [indicating structure (II) for olivil], following the isolation of dimethyl α-apocyclo-olivildiacetate as the ultimate product of its reaction in acetic anhydride; this was clearly obtained by rearrangement to dimethylcyclo-olivil, [(III) $\longrightarrow$ (VI), Ar = 3,4-dimethoxyphenyl], which is labile, followed by elimination.

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[4] A. W. Schrecker and J. L. Hartwell, *J. Amer. Chem. Soc.*, 1952, **74**, 5676.

[5] J. B. Rose in " The Chemistry of Cationic Polymerisation," ed. P. M. Plesch, Pergamon, Oxford, 1963, p. 433.

[6] J. Kollonitsch, *J. Amer. Chem. Soc.*, 1961, **83**, 1515.

[7] K. Freudenberg and K. Weinges, *Tetrahedron Letters*, 1962, 1077.

A *trans*-configuration at the 3,4-position in dimethylcyclo-olivil * was established by a comparison (Figure) of its optical rotatory dispersion with those of α-apopicropodophyllol (VIII) and α-apopodophyllol (IX).[1] The absolute configurations of all three compounds are known [2] and, at longer wavelengths, the curve for compound (VII) is the mirror image, with respect to the x-axis, of compound (VIII), and the two are therefore enantiomeric with respect to ring B; there is some deviation at shorter wavelengths, which may be attributed to the bathochromic displacement of the absorption maximum in compound (VIII) with respect to compound (VII). The assignment is confirmed by the very different rotatory dispersions of compound (VII) and α-apopodophyllol, (IX), which have the same absolute configuration and where the latter is 3,4-*cis*-substituted.

EXPERIMENTAL

Analyses were by Mr. B. T. Saunderson.

Isolation of Olivil.[8]—The powdered resin (100 g.) of *Olea europa* was continuously extracted with methanol to give the crude material (48 g.); the pure material (45 g., 45%), m. p. 118—120°, was obtained on crystallisation from methanol, α_D^{20} $-127°$ (Found: C, 61·2; H, 6·9. Calc. for $C_{20}H_{24}O_7$,MeOH: C, 61·7; H, 6·9%).

Dimethylolivil.—Dimethylolivil was obtained in 53% yield by the methylation of olivil (2·00 g.) with methyl sulphate; the yield was not improved by the use of methyl iodide–silver oxide in dimethyl sulphoxide.[9] The product had m. p. 155—156° (MeOH), $[\alpha]_D$ $-35°$ (Found: C, 65·0; H, 6·9. Calc. for $C_{22}H_{28}O_7$: C, 65·3; H, 6·9%).

*Toluene-*p*-sulphonate of Dimethylolivil.*—Dimethylolivil (200 mg.) and the sulphonyl chloride (500 mg.) were dissolved in pyridine (2 ml.) and the solution was kept in the refrigerator for 7 days. When the solution was poured into ice–water an oil separated, and this was washed successively with sodium hydrogen carbonate solution, dilute hydrochloric acid, and water. The residue was dried in a desiccator and solidified after triturating with light petroleum (b. p. 40—60°). The crude material (200 mg., 80%), m. p. 49—50°, was crystallised from aqueous ethanol, which raised the m. p. to 51—52° (Found: C, 62·3; H, 6·3; S, 5·1. $C_{27}H_{26}O_9S$ requires C, 62·4; H, 6·1; S, 5·7%).

Dimethylolivil and Periodic Acid.—Solutions of dimethylolivil in water and dioxan–water [10] were treated with sodium metaperiodate solution at pH 4·0—5·0 in the presence of dimedone.[11] There was no evidence of glycol fission and the starting material was recovered in good yield.

Reaction of Dimethylolivil with Boron Trifluoride–Sodium Borohydride.—The dimethyl ether (500 mg.) and boron trifluoride etherate (8 ml.) were dissolved in tetrahydrofuran (30 ml.) and slowly added, with stirring, to sodium borohydride (0·5 g.) suspended in tetrahydrofuran (20 ml.). Addition was complete in 30 min., and stirring was continued for a further 30 min. at room temperature and for 1 hr. at 50°. The mixture was then acidified with 2N-hydrochloric acid, diluted with water (10 ml.), and extracted with chloroform (3 × 20 ml.). The combined extracts were washed with sodium hydrogen carbonate solution, dried ($MgSO_4$), and evaporated to give a yellow semisolid, which was dissolved in hot benzene (20 ml.) and afforded crystalline material (365 mg., 73%), m. p. 180—181° on standing overnight. This product was identified as dimethylcyclo-olivil by comparison (infrared spectrum and optical rotatory dispersion) with an authentic specimen,[8] m. p. 183°.

Isolation of Polymerised Tetrahydrofuran.—Polymerised tetrahydrofuran was isolated when the benzene liquor from the crystallisation of dimethylcyclo-olivil was evaporated. The oil obtained was dissolved in hot methanol, and filtered from insoluble material; a white solid (200 mg.) separated when the filtrate was cooled. An analytical sample, m. p. 37—38°, was obtained by washing the product with cold methanol and recrystallising it from the same solvent (Found: C, 66·9; H, 11·0. $C_{4n}H_{8n}O_n$ requires C, 66·7; H, 11·1%). The molecular weight of the product was 1017, as determined ebullioscopically in benzene, whence $n = 14$.

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* In a recent Paper Kato [8] has published n.m.r. evidence for this configuration.

[8] G. Koerner and B. L. Vanzetti, *Atti R. Accad. Lincei, Rend.*, 1903, [5], **12**, i, 122.
[9] R. Kuhn, H. Trischman, and I. Löw, *Angew. Chem.*, 1955, **67**, 32.
[10] N. G. Brink, F. A. Kuehl, E. H. Flynn, and K. Folkers, *J. Amer. Chem. Soc.*, 1948, **70**, 2090.
[11] D. Spencer and T. Henshall, *J. Amer. Chem. Soc.*, 1955, **77**, 1943.

Dimethylcyclo-olivil Diacetate.—Dimethylcyclo-olivil (250 mg.) was dissolved in pyridine (12 ml.), acetic anhydride (1·5 ml.) added, and the solution kept at room temperature for 5 days. The excess of acetic anhydride was decomposed with methanol (2 ml.), and when the solvent was removed the *diacetate* (255 mg., 85%) was isolated and crystallised from 10% aqueous ethanol and finally from ethanol, m. p. 141—142° (Found: C, 63·5; H, 6·5; $C_{26}H_{32}O_9$ requires C, 63·9; H, 6·5%).

The starting material, m. p. 181—182°, was obtained in 82% yield on hydrolysis [1] of the diacetate (35 mg.) with potassium hydroxide–ethanol.

Dimethyl-α-apocyclo-olivil Diacetate.—(*a*) Dimethylcyclo-olivil diacetate (35 mg.) was refluxed in dry acetone (15 ml.) with toluene-*p*-sulphonic acid (20 mg.). The oil obtained on evaporation of solvent was dissolved in chloroform (10 ml.), washed with 0·1N-sodium hydroxide solution and water, dried ($MgSO_4$), and evaporated to yield a residue (22 mg., 65%), which solidified on trituration with light petroleum (b. p. 40—60°) and crystallised from aqueous ethanol, m. p. 129—130°.

(*b*) Dimethylcyclo-olivil (200 mg.) was dissolved in glacial acetic acid (15 ml.) containing perchloric acid (12 drops, 60%) and set aside for 8 days at room temperature. The resulting purple solution was cooled in ice and made just alkaline with concentrated potassium hydroxide solution; the whole was then extracted with chloroform (3 × 15 ml.) and the extracts were washed with water, dried ($MgSO_4$), and evaporated. The residue (158 mg., 68%) solidified under light petroleum (b. p. 40—60°) and, after recrystallisation from aqueous ethanol (5%), was identified with the product from (*a*) above by mixed m. p.; comparison of infrared spectra ($\nu_{max.}$ 1740, 1710, 1610 cm.$^{-1}$) and optical rotatory dispersions

λ	5794	4916	4358
φ	180	228	273

Analytical figures for these products were variable because of solvation (infrared spectrum); the products were therefore characterised by hydrolysis [1] to the *α-apo-diol*, which was also derived from dimethylcyclo-olivil as follows. Dimethylcyclo-olivil (46 mg.) was treated with toluene-*p*-sulphonic acid (20 mg.) in acetone as above and the crude solid product (33 mg., 75%) was crystallised from ethanol affording *dimethyl-α-apocyclo-olivil*, m. p. 92—93° (Found: C, 68·0; H, 7·0. $C_{22}H_{26}O_6$ requires C, 68·4; H, 6·7%).

Reaction Between Dimethylolivil and Acetic Anhydride.—Dimethylolivil (250 mg.) was dissolved in acetic anhydride (8 ml.) and the optical rotation was measured at intervals at a concentration of 150 mg./l., when a progressive change was observed; a constant reading was finally obtained after 1·5 hr. reflux.

	$[\alpha]_{\lambda}^{20}$		
λ	After 3 hr./20°	32 hr./20°	Further 1·5 hr./reflux
D line	−0·068	−0·043	+0·012
4358 Å	−0·148	−0·115	+0·018

The resulting solution was poured into ice–water and the oil that separated was stirred in sodium carbonate solution (5%), washed with water, and left under light petroleum (b. p. 40—60°) to solidify. Crude material (100 mg., 35%) was crystallised from ethanol–water and identified with the products described in (*a*) and (*b*) above.

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