

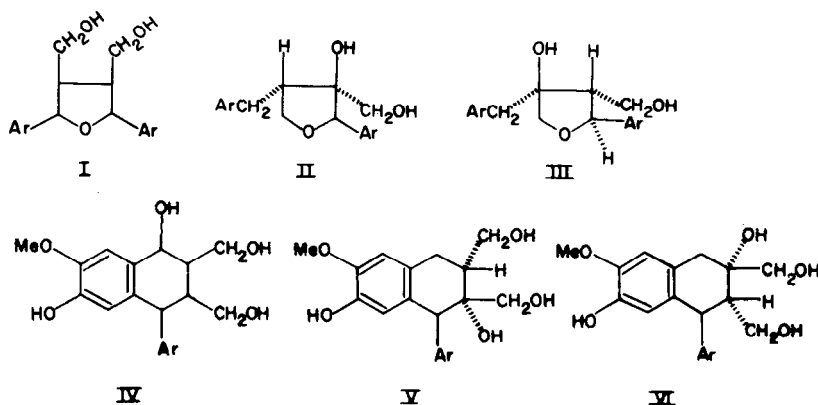
(-)-OLIVIL AND (+)-CYCLOOLIVIL

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(Received 19 December 1963)

THREE possible structures for olivil (I, II, III) have
been mentioned in recent work (1,2);



Ar = 4-hydroxy-3-methoxyphenyl

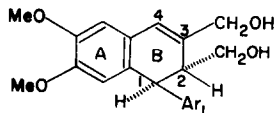
of these, structure III has been established (2) by proton magnetic resonance spectroscopy, leading to VI, rather than IV or V, for cycloolivil. Chemical evidence of structure is conflicting, II being favoured by Freudenberg and Weinges (1) as the dimethyl ether underwent fission with lead tetraacetate. The presence of a hindered hydroxyl group (II, III) is indicated, since the triol obtained by hydrogenolysis of

olivil dimethyl ether could only be di-acetylated (3) although dimethyl cycloolivil, formed by acid-catalysed rearrangement, has been reported (4) to give a triacetate.

The lead tetraacetate fission may have resulted from acetylium ion catalysis of the dimethylolivil rearrangement during reaction, for structure VI is also labile: this is supported by the observation (5) that both alkyl olivils and cycloolivils afford diacetates on treatment with acetic anhydride. We found that dimethylolivil did not react with periodic acid at pH 4-5 but regard this as inconclusive, since hindered vicinal diols are often unaffected by the reagent (6): steric hindrance of one -OH group accounts for the isolation of only the mono-toluene-p-sulphonate, m.p. 51-2°, by prolonged treatment with the sulphonyl chloride in pyridine. This observation was contrary to I for olivil and IV for cycloolivil (7), as also was the finding that reaction with boron trifluoride/borohydride effected a high yield conversion of dimethylolivil into dimethylcycloolivil without isolation of a desoxy compound, although benzyl alcohols are normally hydrogenolysed under these conditions (8). The product was identical (i/r spectrum, m.p. and optical rotation) with the dimethyl ether prepared from a sample of cycloolivil kindly supplied by Professor Hasegawa. It was noted that dimethyl olivil was unchanged following treatment with diborane/tetrahydrofuran alone and with boron trifluoride/tetrahydrofuran alone.

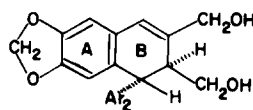
Support for cycloolivil as VI was obtained by the following sequence: the dimethyl ether was converted into a diacetate, m.p. 141-142°, but no further acetylation

occurred in acetic anhydride/pyridine; the remaining -OH group (i/r spectrum) was eliminated by toluene-p-sulphonic acid in acetone, affording the diacetate of dimethyl anhydro-cycloolivil, m.p. 125-127°, which was hydrolysed to the diol (VII), m.p. 90-92°. Alternatively, the anhydro-diacetate was obtained in one step by treatment of dimethyl cycloolivil with perchloric acid/acetic acid.



(VII)

$Ar_1 = 3,4\text{-dimethoxyphenyl}$

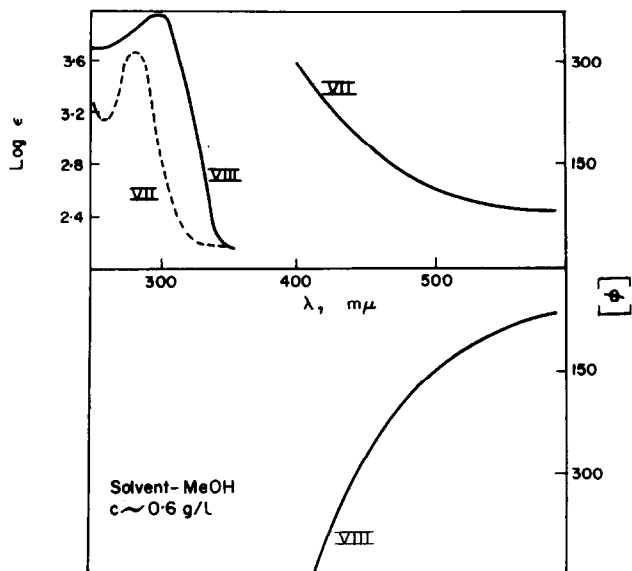


(VIII)

$Ar_2 = 3,4,5\text{-trimethoxyphenyl}$

The ultra-violet absorption of dimethylanhydrocycloolivil is consistent with a conjugated double bond in the 3-4 position (VII) and excludes unsaturation at the 1-2 position, which leads to a large bathochromic shift in the anhydrocompounds of the picropodophyllin series (9). The absolute configuration of dimethylanhydrocycloolivil at C2 follows from the conversion (3) of (-)olivil into (-)guaiaretic acid and also from its correlation (10) with gmelinol. The optical rotatory dispersion of VII was compared with that of the diol VIII, m.p. 92-93°, obtained by lithium aluminium hydride reduction of α -apopicropodophyllin of known (11) configuration. At longer wavelengths the two curves are related as object and mirror image in the 'x' axis: the two compounds are therefore enantiomeric with respect to ring B and a trans configuration is indicated at

01:2 in cycloolivil.



This technique of assigning configuration has been shown (11) to be independent of the alkoxylation pattern in lignans for measurements at the D line, the deviation shown (Fig.) at shorter wavelengths is ascribed to the bathochromic displacement of the absorption maximum in VIII with respect to VII.

We thank Professor Birch for sending us information in advance of publication and Mr. A. G. Kenyon of the Tropical Products Institute, D.S.I.R. for a supply of olive tree resin.

References

- (1) K. Freudenberg and K. Weinges, Tetrahedron Letters, 1077, (1962).
- (2) M. Smith, ibid., 991, (1963).
- (3) G. Traverso, Gazz. Chim. Ital., 90, 792 (1960).
- (4) M. Hasegawa and T. Shirato, J. Jap. For. Soc., 41, 1 (1959).
- (5) G. Traverso, Gazz. Chim. Ital., 88, 851 (1958).
- (6) C. A. Bunton and M. D. Carr, J. Chem. Soc., 770, (1963).
- (7) B. L. Vanzetti, Acad. d'Italia, Mem. Classe Sci., 13, 411 (1937).
- (8) D. C. Ayres, B. Green, P. Hofer, P. J. S. Fauwels and G. R. Pettit, Proc. Chem. Soc., 357, (1962).
- (9) A. W. Schrecker and J. L. Hartwell, J. Amer. Chem. Soc., 74, 5676, (1952).
- (10) A. J. Birch and M. Smith, J. Chem. Soc., in the press.
- (11) J. L. Hartwell and A. W. Schrecker, J. Amer. Chem. Soc., 77, 432, (1955).