Tetrahedron Letters No.53, pp. 5497-5500, 1968. Pergamon Press. Printed in Great Britain.

THE STRUCTURE OF COLLETODIOL, A MACROCYCLIC DILACTONE FROM COLLETOTRICHUM CAPSICI

J. MacMillan and R.J. Pryce
Department of Organic Chemistry
The University, Bristol.

(Received in UK 12 September 1968; accepted for publication 1 October 1968)

A preliminary investigation (1) of the structure of colletodiol, $C_{14}H_{20}O_6$, a metabolite of Colletotrichum capsici, indicated a monocyclic di-αβ-unsaturated ester or lactone containing two hydroxyl groups. We now deduce structure (I) by analysis of the n.m.r. spectrum of colletodiol and by alkaline hydrolysis to the C_6- and C_8- acids, (II) and (III) respectively. To our knowledge colletodiol is the first naturally-occurring macrocyclic dilactone derived from two different ω-hydroxy acids.

The chemical shifts observed at 220 MHz (Fig. 1) and comprehensive decoupling experiments at 100 MHz allowed a complete analysis of the n.m.r. spectrum of colletodiol in $CDCl_3$ solution. The results are shown diagrammatically in (IV) and (V) where the τ-values of the protons labelled in (I) by capital letters are shown in brackets and the coupling constants are expressed in Hz. The broad signal at 6.96τ (Fig. 1) is removed by D_2O, and is due to protons H_E and H_F. Diagrams (IV) and (V) clearly show the presence of two distinct and isolated sets of contiguous protons which uniquely define structure (I). The 100 MHz spectrum of the dibenzoate (1) of colletodiol was similarly analysed; here the methyl signals were non-equivalent overlapping doublets.

Mild alkaline hydrolysis of colletodiol gave two acids whose structures (II) and (III) were deduced on spectroscopic evidence. The less polar liquid acid (II) showed $\lambda_{max.}^{EtOH}$ 211 mμ (ε 10400) and $\nu_{max.}^{CHCl_3}$ 3600, broad absorption down to 2100, 1702, 1660 and 986 cm.$^{-1}$. Decoupling experiments on the 100 MHz spectrum of acid (II) in $CDCl_3$ solution allowed the assignments shown diagrammatically in (VI); the lower case letters in (VI) and (II) correspond to the capital letters used to identify the protons in colletodiol (I). The i.r. spectrum of our acid (II) does not agree with that reported (2) for synthetic trans-5-hydroxyhex-2-enoic acid.

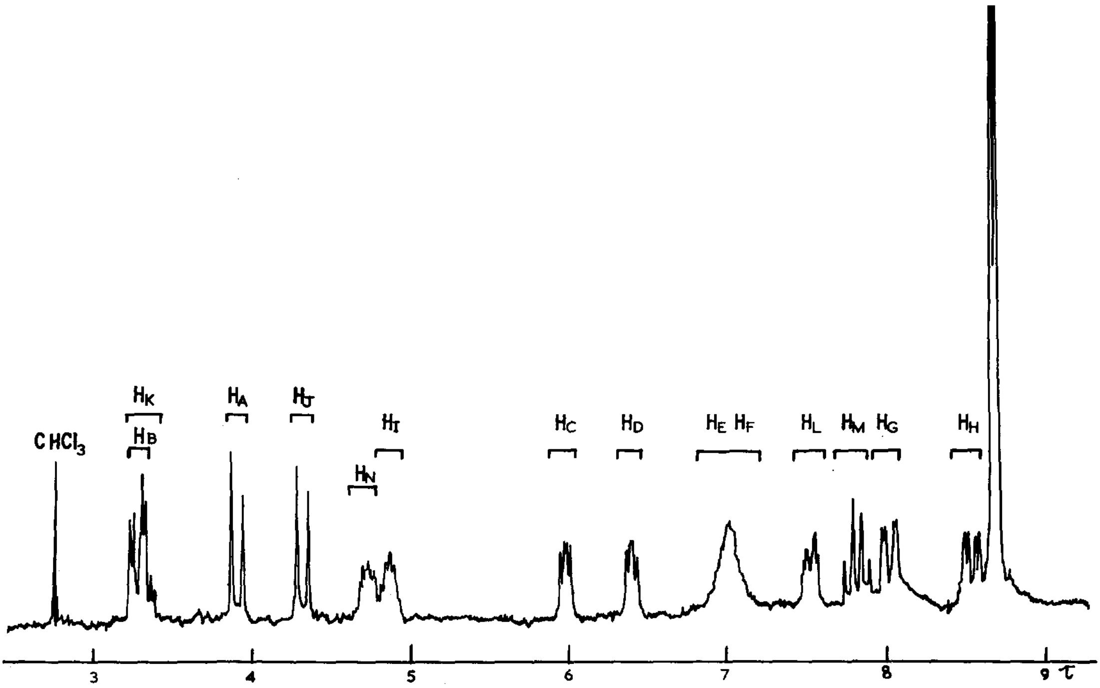
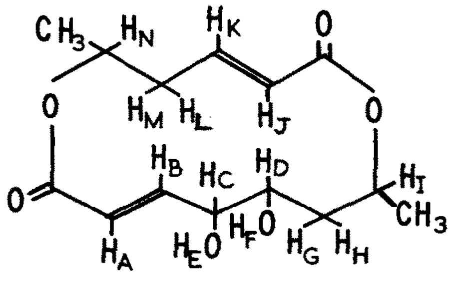


FIG. 1

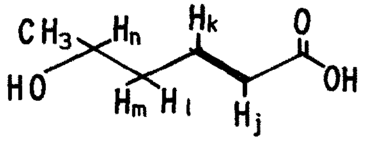
220 MHz n.m.r. spectrum of colletodiol in $CDCl_3$ solution.

The more polar acid (III), m.p. 110.5 - 112°, obtained by hydrolysis of colletodiol (I), had $\lambda_{max.}^{EtOH}$ 211 mμ (ε 9700) and $\nu_{max.}^{nujol}$ 3600, broad absorption down to 2300, 1720, 1652, and 1087 $cm.^{-1}$. The n.m.r. spectrum was interpreted on the basis of structure (III) as shown in diagram (VII) where the lower case letters correspond to the capital letters used in (I).

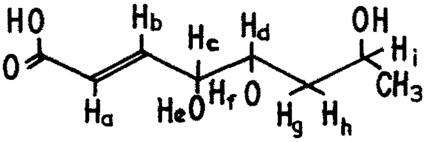
High resolution mass spectra of colletodiol (I), its bis-trimethylsilyl ether, and its hydrolysis products (II) and (III) which will be detailed in a full paper are in agreement with the proposed structures. For example the base peak, $C_7H_{15}OSi$, of the bis-trimethylsilyl ether is accounted for by McLafferty rearrangement to (VIII, R = $SiMe_3$) followed by cleavage at <u>a</u> to the ion (IX, R = $SiMe_3$). The low resolution mass spectrum of the bis-trimethylsilyl ether, obtained by combined gas chromatography-mass spectrometry, showed a peak at $^{m}/e$ 147



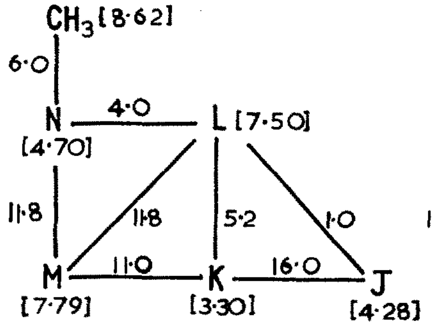
I



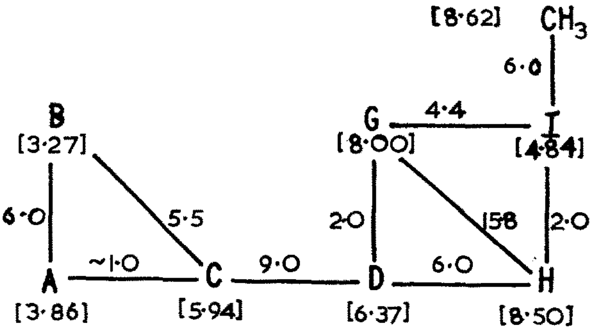
II



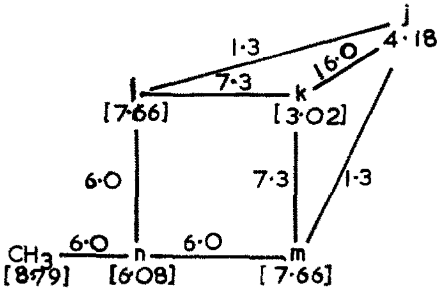
III



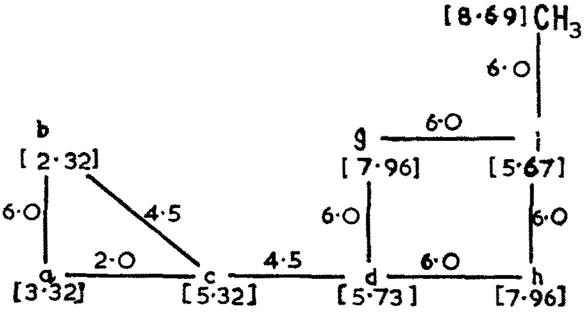
IV



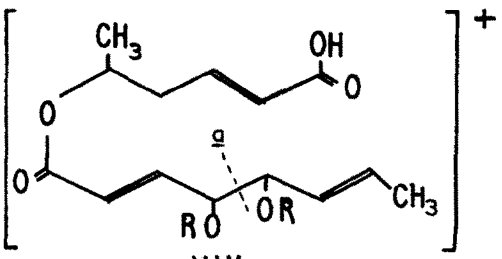
V



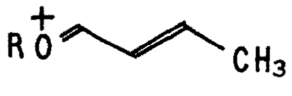
VI



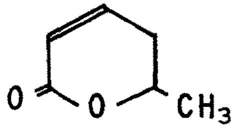
VII



VIII



IX



X

probably due to the ion $Me_2Si = \overset{+}{O}{-}SiMe_3$ and characteristic of vicinal bis-trimethylsilyl ethers (3,4).

The trans-stereochemistry of both double bonds in colletodiol is supported by the large vinylic coupling constants in the n.m.r. spectra of colletodiol, its dibenzoate, and the acids (II) and (III). The trans-stereochemistry of the acid (II) is further supported by its failure to form a lactone on distillation; distillation of the corresponding cis-acid gives (5) the lactone (X). The conformation of colletodiol will be discussed in the full paper; the absolute stereochemistry is in progress.

We thank the S.R.C. for a Research Studentship (R.J.P.) and the Polymer and Petrochemical Laboratory, I.C.I. Ltd., for the 220 MHz n.m.r. spectrum of colletodiol, obtained under the S.R.C. Universities evaluation scheme.

REFERENCES

1. J.F. Grove, R.N. Speake, and G. Ward, J. Chem. Soc. (C), 230 (1966).
2. S. Dolezal, Coll. Czech. Chem. Comm. **30**, 2638 (1965).
3. R. Binks, J. MacMillan, and R.J. Pryce, Phytochemistry, in press.
4. J. Diekman, J.B. Thomson, and C. Djerassi, J. Org. Chem. **33**, 2271 (1968).
5. U. Eisner, J.A. Elvidge, and R.P. Linstead, J. Chem. Soc. 1372 (1953).