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A REVISED STRUCTURE OF PEDERIN[1)]

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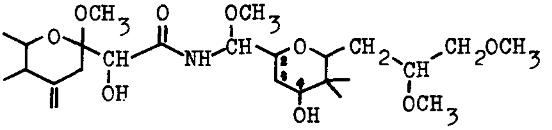
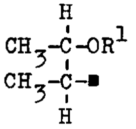
A structural formula 1 has been assigned to the insect poison pederin, $C_{25}H_{45}O_9N$, by Cardani et al.[2)] However, spectroscopic evidence indicates that it should be represented rather by a revised structure 2.



1 OH at C-3 instead of C-4.

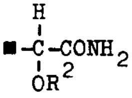
2 revised structure; OH at C-4.

Pederin affords on mild acid hydrolysis an acid amide $C_{11}H_{19}O_4N$, m.p. 147.5 - 148.5°, m/e 229 (M^+), ν max (nujol) 3480, 3360 (OH, NH), 1680, 1575 ($CONH_2$), 1650, 888 cm^{-1} ($>C=CH_2$). The n m r spectrum (Fig. 1) of this compound demonstrates the presence of following groups 3 - 6.



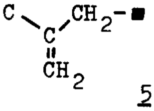
$CH_3-\overset{H}{\underset{}{C}}-OR^1$, $CH_3-\underset{H}{C}-\blacksquare$

3



$\blacksquare-\overset{H}{\underset{OR^2}{C}}-CONH_2$

4



$C\diagdown\underset{\underset{CH_2}{\|}}{C}\diagup CH_2-\blacksquare$

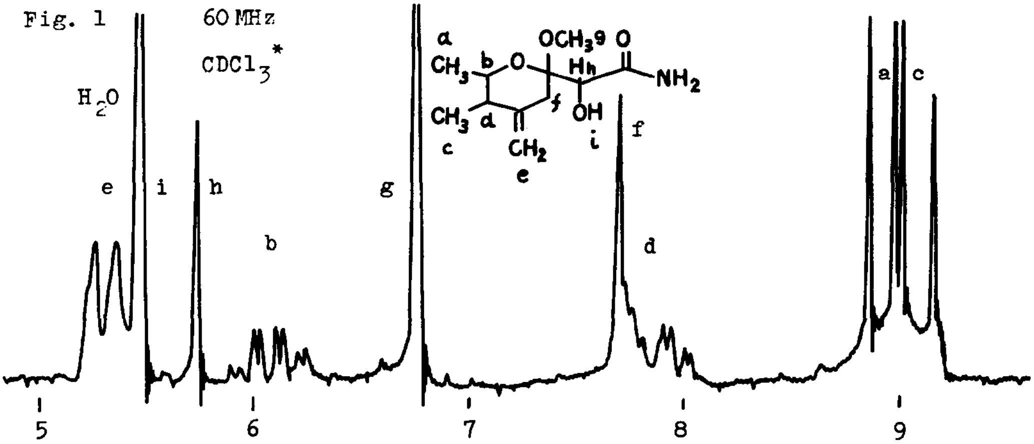
5

$\blacksquare-OCH_3$

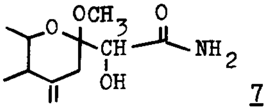
6

■ indicates carbon with no hydrogen atom.

The partial structures 4 and 5 are inferred respectively by the low line position (τ 5.70) of carbinyl proton of sec. hydroxyl (or alkoxyl) group and by the long range coupling between methylene group and terminal methylene group. Comparison of the spectrum with that of pederin itself shows that no structural change had occurred in this moiety on hydrolysis. Since the singlet peak corresponding to h (Fig. 1) of pederin is displaced to downfield in that of diacetyl pederin[1,2)] (τ 4.68) while the multiplet corresponding to b remains practically unchanged, R^1 in 3 and R^2 in 4 are alkyl and hydrogen respectively. Examination of possible modes of combination of the fragments 3 - 6 shows the amide to be expressed by 7. The two most intense peaks in the mass spectrum of the amide, m/e 95 and 155, corresponding to 8 and 9 respectively, are also consistent with this formulation. The doublet line at τ 4.55 (1H) in



the n m r spectrum of D_2O treated pederin appears in the undeuterated sample as a quartet and the characteristic low line position remains essentially unchanged in the diacetate, which contains no hydroxyl group. These results indicate that the doublet arises from H_A of part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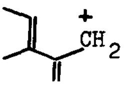
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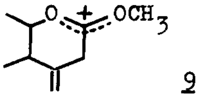
9

formula 10, where R^1 represents an alkyl group. The doublet is decoupled on being irradiated at a position higher by 159 Hz, where the signal due to H_B appears as an unresolved peak (Fig. 2).

Extensive double resonance experiments enabled us to interpret the signals in τ 6 and 8 region as shown in Fig. 2 and 3.** The results show the presence of 10 and 11 in the amine moiety and clearly contradict with the proposal of Italian workers.[2] Since the quartet line (10, 4 Hz) due to H_E is displaced to down field in the spectrum of the acetate, R^3 must be a hydrogen atom.

In the spectrum of pederin in pyridine solution (Fig. 4, only the τ 5 - 7 region is shown), the quartet line (10, 4 Hz) due to H_E appears at τ 5.90 and is overlapped by another set of four lines (7, 3 Hz). Therefore pederin contains an additional partial structure 12 or

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* A small amount of pyridine was added as stabilizer.[1]

** All chemical shifts and coupling constants are obtained by first order analysis, and are only approximate values. However these values are sufficiently useful for the following discussions.

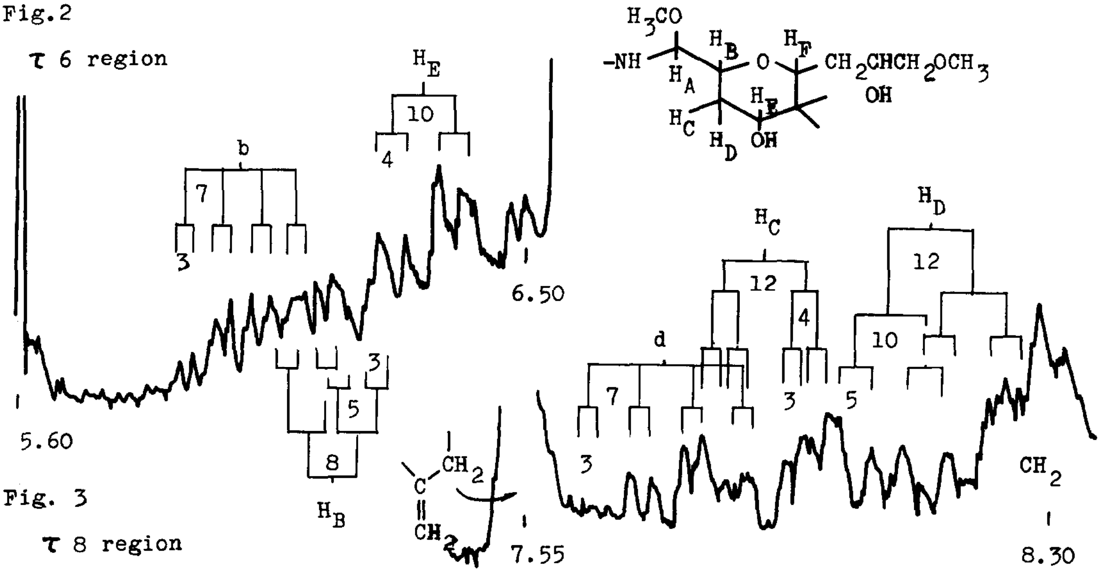


Fig.2

τ 6 region

Fig. 3

τ 8 region

13. The pattern of the signals near τ 6.25 due to about two protons and the peak area near τ 6.15 show the presence of an AB_2 or ABC system,* which can also be seen in the spectrum of the diacetate. With this the partial structure 14 or 15 is indicated. Since in the above partial formulas 10 - 15 the presence of at least six C-O linkages in the amine moiety was demonstrated and out of five oxygen atoms contained in this moiety three are present as methoxyl groups (n m r) and one as a hydroxyl group, the remaining one must form a cyclic ether. The presence of seven C-O bonds then becomes impossible and the partial formula 15 can be excluded. The amine moiety possesses, in addition, two tert. methyl groups 16 and 17 (n m r).

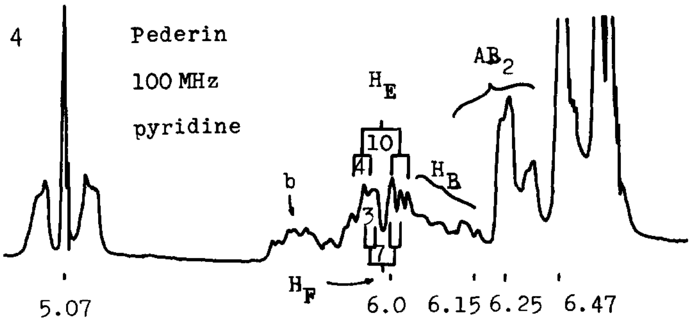
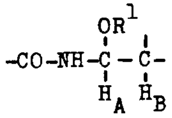
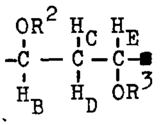


Fig. 4



$$-CO-NH-\underset{H_A}{\overset{OR^1}{C}}-\underset{H_B}{C}-$$

10



$$-\underset{H_B}{\overset{OR^2}{C}}-\underset{H_D}{\overset{H_C}{C}}-\underset{OR^3}{\overset{H_E}{C}}-$$

11

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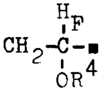
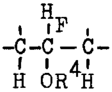
* Peaks due mainly to the A part (near τ 6.15) are further split to form a multiplet.



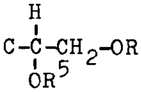
$$CH_2-\underset{OR^4}{\overset{H_F}{C}}-\blacksquare$$

12



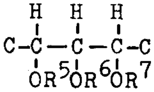
$$-\underset{H}{C}-\underset{OR^4}{\overset{H_F}{C}}-\underset{H}{C}-$$

13



$$C-\underset{OR^5}{\overset{H}{C}}-CH_2-OR$$

14



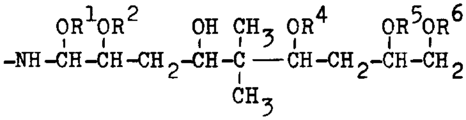
$$C-\underset{OR^5}{\overset{H}{C}}-\underset{OR^6}{\overset{H}{C}}-\underset{OR^7}{\overset{H}{C}}-C$$

15

$\blacksquare -CH_3$ 16

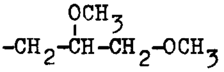
$\blacksquare -CH_3$ 17

Since the moiety must have a skeleton with only eleven carbon atoms, it should contain 12 rather than 13 and the quarternary carbon atom in 11, 12, 16 and 17 should be identical. The partial formula is thus extended to 18. Further, since in the mass spectrum of pederin,



$$-NH-\overset{OR^1}{CH}-\overset{OR^2}{CH}-CH_2-\overset{OH}{CH}-\underset{CH_3}{\overset{CH_3}{C}}-\overset{OR^4}{CH}-CH_2-\overset{OR^5}{CH}-\overset{OR^6}{CH_2}$$

18



$$-CH_2-\overset{OCH_3}{CH}-CH_2-OCH_3$$

19

the dominant peaks at m/e 439 (M-2xMeOH), 394 (M-2xMeOH-CH_2OCH_3) and 336 (M-2xMeOH-19) in the high mass region point to the presence of 19 and R^1 has been shown to be methyl,[2)] the structure 2 is concluded as the most possible expression for pederin.[3)]

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1) Previous paper: T. Matsumoto, M. Yanagiya, S. Maeno, S. Tsutsui and S. Yasuda, Bull. Chem. Soc. Japan, **37**, 1892 (1964).

2) C. Cardani, D. Ghringhelli, R. Mondelli and A. Quilico, Tetrahedron Letters, **1965**, 2537; Gazz. Chim. Ital. **96**, 3 (1966).

3) The structure 2 was first suggested by one of us (T. M.) on the basis of spectroscopic evidence at the 9th Symposium of the Chemistry of Natural Products, Osaka, Japan, 1965, Abstracts of Papers. p. 67.