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AKLAVINONE

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THE preceding communication[1] describes the identity of rutilantinone (I), the aglycone of the rutilantins,[2] with ε-pyrromycinone,[3] which is

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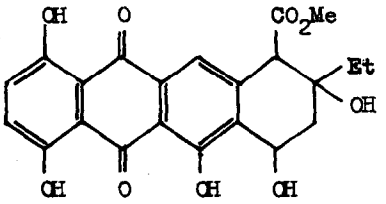
1 H. Brockmann, H. Brockmann jnr., J. J. Gordon, W. Keller-Schlierlein, W. Lenk, W. D. Ollis, V. Prelog and I. O. Sutherland, Tetrahedron Letters No. 8, 25 (1960).

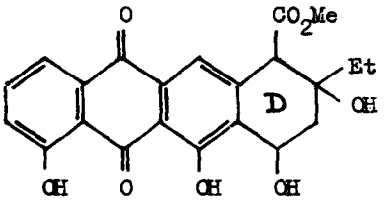
2 W. D. Ollis, I. O. Sutherland and J. J. Gordon, Tetrahedron Letters No. 16, 17 (1959).

3 H. Brockmann and W. Lenk, Chem. Ber. 92, 1880 (1959).

similarly derived from the cinerubins[4] and pyrromycin.[5] We now wish to report on the structural relationship which has been shown to exist between ε-pyrromycinone (rutilantinone)(I) and aklavinone obtained from another antibiotic, aklavin.[6] Aklavinone ($C_{22}H_{20}O_8$) and rutilantinone ($C_{22}H_{20}O_9$) are shown to have closely analogous structures in that aklavinone just lacks one of the phenolic hydroxyl groups present in rutilantinone.



I



II

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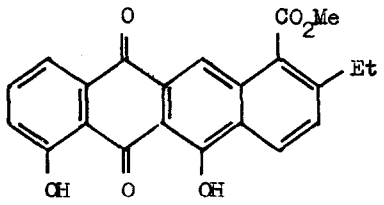
4 L. Ettlinger, E. Gäumann, R. Hütter, W. Keller-Schlierlein, F. Kradolfer, L. Neipp, V. Prelog, P. Reusser and H. Zahner, Chem. Ber. 92, 1867 (1959).

5 H. Brockmann and W. Lenk, Chem. Ber. 92, 1867 (1959).

6 F. Strelitz, H. Flon, U. Weiss and I.N. Asheshov, J. Bacteriol. 72, 90 (1956).



III

Mild acidic hydrolysis of aklavin hydrochloride yielded the aglycone, aklavinone, orange needles, m.p. 170° (Found: C, 64.15; H, 5.12; OMe, 7.47. $C_{22}H_{20}O_8$ requires C, 64.08; H, 4.89; (1) OMe, 7.53%) characterised (acetic anhydride-pyridine) as a tri-acetate, m.p. 198° (Found: C, 62.47; H, 5.16; OMe, 5.69. $C_{28}H_{26}O_{11}$ requires C, 62.45; H, 4.89; (1) OMe, 5.77%). Hydroxyl absorption [ν_{max} 3610 cm^{-1}. (Nujol)] in the infra-red spectrum of the tri-acetate indicated the presence of a tertiary hydroxyl group; and absorption in the carbonyl region was assigned to phenolic (ν_{max} 1785 cm^{-1}.) and alcoholic acetate (ν_{max} 1751 cm^{-1}.) groupings. Aklavinone was weakly acidic [pK_a' 9.9 (90% ethanol)]; it was converted into a dibasic acid [pK_a' 6.85 and 10.6 (90% aqueous acetone)] by alkaline hydrolysis. The presence of an ester group in aklavinone (probably $-CO_2Me$ by analogy with rutilantinone) was confirmed by the infra-red spectra of aklavinone

[ν_{max} 1728, 1740 cm^{-1}. (Nujol)] and its tri-acetate [ν_{max} 1740 cm^{-1}. (Nujol)].

The ultra-violet and visible spectra of aklavin,[6] aklavinone [λ_{max} (ε_{max}) 229 (43,800), 258 (26,700), 288 (11,500), 430 mμ(13,100), λ_{infl} 278 mμ(12,000) (in methanol)] and aklavinone tri-acetate [λ_{max} (ε_{max}) 214 (28,000), 259 (41,900), 340 mμ(7,100) (in ethanol)] were consonant with a 1:8-dihydroxyanthraquinone chromophore.[7] This assignment was further supported by the infra-red spectra of both aklavinone [ν_{max} 1674, 1623, 1575 cm^{-1}. (Nujol)] and its tri-acetate [ν_{max} 1681, 1600 cm^{-1}. (Nujol)].[8] These results led us to consider that aklavinone was a deoxy-rutilantinone and could be represented by structure (II).

Like rutilantinone, aklavinone was converted into a bisanhydro-derivative, orange needles, m.p. 236° (Found: C, 69.86; H, 4.22; OMe, 8.21. $C_{22}H_{16}O_6$ requires C, 70.20; H, 4.29; (1) OMe, 8.25%) by the action of toluenesulphonic acid in refluxing toluene. The spectral properties of this compound [ν_{max} 1740, 1678, 1627, 1602, 1579 cm^{-1}. (Nujol); λ_{max} (ε_{max}) 242 (45,100), 262 (47,400), 279 (19,300), 290 (19,600), 440 (18,900), 462 (14,600), 474 mμ(15,800) (in n-hexane)] are in accordance with its formulation as the 1:11-dihydroxytetracene-5:12-quinone derivative (III), the methoxycarbonyl and ethyl substituents being placed by analogy with bisanhydrorutilantinone and using biogenetic arguments similar to those used for ε-pyrromycinone (rutilantinone). This

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7 J. H. Birkinshaw, Biochem. J. 59, 485 (1955).

8 H. Bloom, L. H. Briggs and B. Cleverley, J. Chem. Soc. 178 (1959).

structure (III) is further supported by the formation of benzene-1:2:3:4-tetracarboxylic acid, characterised as its tetramethyl ester, m.p. 130.5-131.5°, by alkaline permanganate oxidation of bisanhydroaklavinone, thus demonstrating that aklavinone has the structure (II).

The nuclear magnetic resonance spectrum of aklavinone ($CHCl_3$, 56.4 Mc.) exhibits the following bands (τ-values): 8.90 (3), 8.43 (2), 7.66 (2), 6.30 (3), 5.70 (1), 4.67 (1).* The first two bands show the characteristic pattern of an isolated ethyl group in which the two classes of protons are only slightly non-equivalent. The broad band at 7.66 clearly arises from a methylene group which cannot, however, be attached to an aromatic ring (α-protons in tetralin absorb at 7.30). The band at 6.30 is sharp and corresponds to an ester methyl group. The absorption near 4.67 consists of a broad band. Its position corresponds to the superimposition of two powerful deshielding effects and it must therefore be assigned to a proton attached to a carbon atom bearing both an aromatic ring and a hydroxyl group. The remaining band (5.70) is reasonably sharp and its position is consistent with an assignment to a proton which is simultaneously benzylic and α- to a carbomethoxy group. The lack of fine structure in this band indicates the absence of protons on the two adjacent carbon atoms.

The assignments of the bands of the nuclear magnetic resonance spectrum of aklavinone can only be accommodated by the arrangement of substituents on ring D shown in formula (II). Thus the position of the

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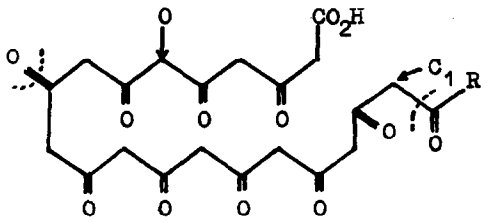
* The figures in parentheses refer to relative integrated intensities.

secondary hydroxyl group in aklavinone is settled and it may be presumed that the corresponding hydroxyl group is similarly located in rutilantinone. The position of the secondary hydroxyl group in t-pyrromycinone (rutilantinone) was suggested previously only on a proposed biosynthetic scheme.[2,3,4]

The biogenetic route leading to aklavinone (see IV) may be considered to be the same as that leading to rutilantinone, except that p-oxidation, which leads to the extra hydroxyl group of rutilantinone, does not occur during the biosynthesis of aklavinone.



IV

Aklavin itself is amphoteric and appears to consist of a basic sugar (possibly $C_8H_{17}NO_4$ isomeric with amosamine[9] and mycaminose[10]) linked glycosidically to the secondary hydroxyl group of aklavinone.

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9 C. L. Stevens, R. J. Gasser, T. K. Mukherjee and T. H. Haskell, J. Amer. Chem. Soc. 78, 6212 (1956).

10 F. A. Hochstein and P. P. Regna, J. Amer. Chem. Soc. 77, 3353 (1955).

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