Reinvestigation into the Structure of Oroidin, a Bromopyrrole Derivative from Marine Sponge

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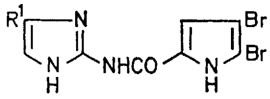
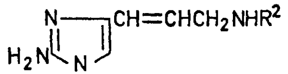
Summary On the basis of the spectral characteristics of a synthetic compound (**4**) it is suggested that the bromopyrrole derivative oroidin, isolated from marine sponge, be reassigned structrue (**3**).

RECENTLY, S. Forenza and his co-workers[1] suggested structure (**1**) for the bromopyrrole, oroidin, isolated from the sponge *Agelas oroides*. Accordingly, the product obtained from acetylation and catalytic reduction of (**1**) was assigned formula (**2**). Upon close examination of the data presented in this communication it was felt that alternative structures for oroidin and its reduction product, namely, (**3**) and (**4**), respectively, would not only accommodate the chemical and physical data presented by these authors but would also be related in a more favourable fashion to the alkaloid dibromophakellin (**5**), isolated from marine sponge and characterized by X-ray analysis.[2] In this communication we report the synthesis of (**4**) and thereby provide evidence for the assignment of structure (**3**) to oroidin.



(1) $R^1 = CH{=}CHCH_2NH_2$
(2) $R^1 = (CH_2)_2CH_2NHAc$
(15) $R^1 = H$



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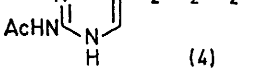
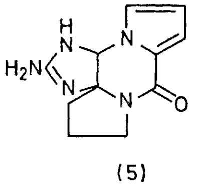


(4)



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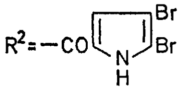
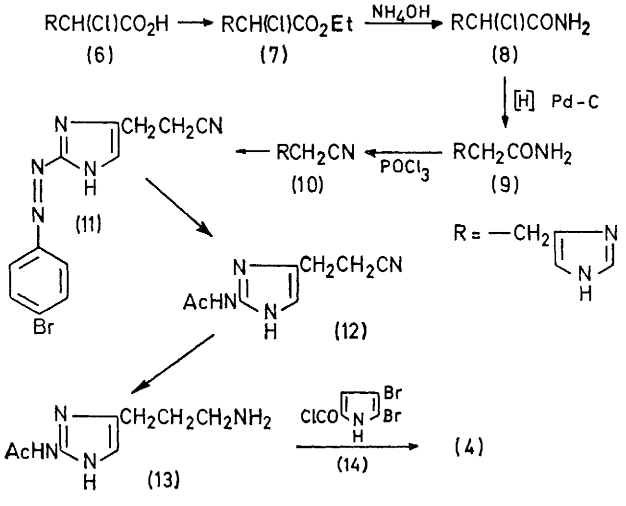
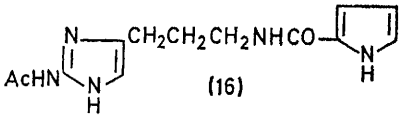


The 4-(5)imidazolepropionitrile (**10**)† was prepared from α-chloro-4(5)imidazolepropionic acid[3] by the sequence (**6**) → (**7**) → (**8**) → (**9**) → (**10**) (Scheme). Compound (**10**) was coupled with diazotized *p*-bromoaniline in alkaline solution to give the 2-substituted phenylazo-derivative (**11**). The azo function of (**11**) was reduced with stannous chloride and the resultant amine directly acetylated to yield the 2-acetamidoimidazole-4(5)-propionitrile, (**12**), m.p. 260—262° (decomp.). Reduction of (**12**) in the presence of palladium on carbon yielded the aminopropylimidazole (**13**), identified as its oxalate salt. Treatment of (**13**) with the acid chloride (**14**) (derived from 4,5-dibromopyrrole-2-carboxylic acid) at 0—5°, in the presence of triethylamine, gave (**4**) in low yield,‡ m.p. 262—265° (decomp.) [m.p. reported[1] for (**2**), 244—247°], *m/e* 431 (M^+), λ_{max} (MeOH) 237 infl. (ϵ 12,900) and 268 nm (19,000). Upon the addition of a trace amount of 0·1N HCl to a solution of (**4**) in alcohol the λ_{max} now appeared at 248 (ϵ 15,700) and 274 nm (14,340). The λ_{max} (MeOH) values reported for (**2**) were 249 (ϵ 14,600) and 276 nm (12,400).[1] In view of these data, it appears that the product obtained by catalytic reduction of oroidin was in all probability contaminated with a trace of hydrogen bromide.§



Thus, in the presence of dilute acid (**4**) exhibits the u.v. absorption anticipated for the individual chromophores of this molecule, *i.e.* the 2-acetamidoimidazole part at 248—249 nm[4] and the dibromopyrrole-2-carboxamide residue at 274—276 nm.[1]

Additional evidence which militates against structure (**2**) was obtained from compound (**15**), m.p. 263—267° (decomp.), λ_{max} (MeOH) 233 (sh.), 298 nm (ϵ 23,400).¶ This substance which was prepared from (**14**) and 2-aminoimidazole, possesses essentially the only chromophore present in (**2**). The discrepancy between the u.v. spectra of (**2**) and (**15**) adds credence to our structural reassignments for oroidin and its reduction product.



Added in proof: After submission of this manuscript a sample of authentic *N*-acetyloroidin was kindly provided by Professor L. Minale. Catalytic reduction of this sample under conditions which were designed to include hydrogenolysis of the bromine atoms gave the same product (**16**) (mixed m.p. and mass spectra), m.p. 240—245° (decomp.), as that obtained by similar reduction of (**4**).

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† All new compounds were characterized by i.r. and n.m.r. spectra and gave combustion analyses or mass spectra in agreement with the reported structures.

‡ This reaction was complicated somewhat by dimerization of (**14**).

§ The extremely rapid hydrogenolysis of bromopyrrole derivatives has been verified in our laboratory.

¶ In the presence of a trace of dilute acid the u.v. maximum of (**15**) was shifted to 300 nm.

[1] S. Forenza, L. Minale, R. Riccio, and E. Fattorusso, *Chem. Comm.*, 1971, 1129.
[2] G. M. Sharma and P. R. Burkholder, *Chem. Comm.*, 1971, 151.
[3] S. Edlbacher and H. von Bidder, *Z. physiol. Chem.*, 1942, **276**, 126.
[4] S. Nakamura, *J. Antibiotics* (*Japan*), 1955, **8A**, 379.