Total Synthesis of (±)-Bonellin Dimethyl Ester

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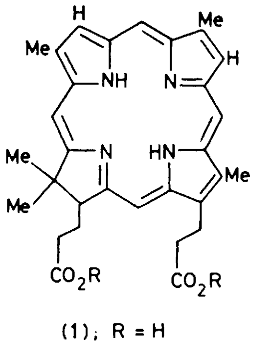
The dimethyl ester of the physiologically active green pigment bonellin from *Bonellia viridis* has been synthesised in racemic form by a sequence in which the macrocycle is formed by a photochemical ring-closure.

Bonellin is the green pigment of *Bonellia viridis*, a marine echurian worm. This pigment is of particular interest because of the remarkable biological changes it brings about in the larvae of *B. viridis*;[1] in addition, the green extracts of this animal show anti-tumour activity.[2] Bonellin has recently been shown[3] to have the novel structure (**1**) and so it is a representative of the class of *C*-methylated chlorins. The biological activity of bonellin made it an important target for synthesis and we now outline the construction of (±)-bonellin dimethyl ester by our photochemical method.[4]

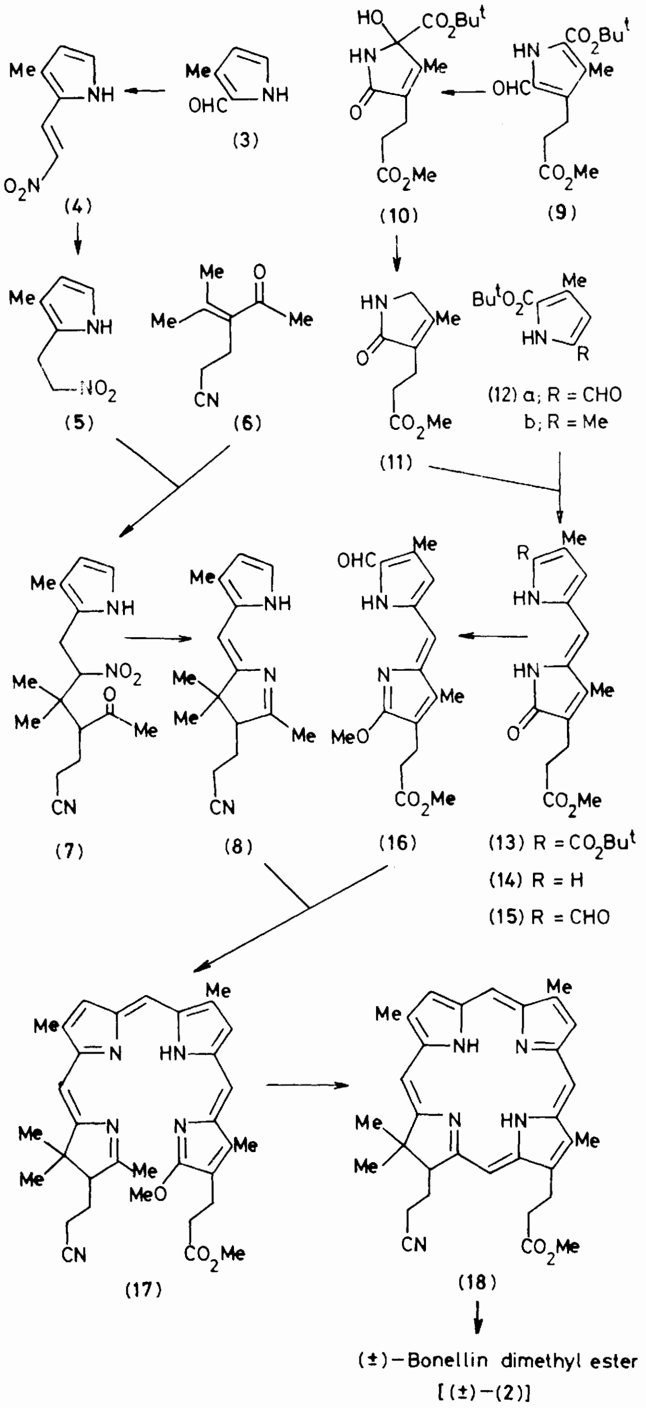


(1); R = H

(2); R = Me

The aldehyde (**3**), prepared photochemically from the *N*-oxide of 4-methylpyridine,[5] condensed with nitromethane to yield the nitro-olefin (**4**) in 88% yield. This was reduced by borohydride to the nitroethylpyrrole (**5**), 90%, which underwent fluoride-ion catalysed Michael addition to the acceptor[6] (**6**). The product was a mixture of diastereoisomers (**7**), combined yield 57%, which was directly converted by sodium methoxide into the nitronate anion ready for reduction with buffered titanium(III) chloride.[7] Ring-closure onto the carbonyl group also occurred during the reductive step; the isolated product, 31% overall, being the unsaturated imine (**8**) required for the western half of bonellin.

The route to the eastern half started with the aldehyde[8] (**9**) which on oxidation by *m*-chloroperbenzoic acid afforded the pyrrolinone (**10**) in 72% yield. Treatment of this with trifluoroacetic acid (TFA) and triethylsilane caused reduction, cleavage of the t-butyl group, and decarboxylation to form the product (**11**), 87%. This was condensed under base catalysis with aldehyde (**12a**) prepared by lead tetra-acetate oxidation of (**12b**),[9] to yield the pyrromethenone (**13**), 89%, which on treatment with methanolic sulphuric acid was converted into the α-free pyrrole (**14**), 51%. Vilsmeier formylation of (**14**), using benzoyl chloride–dimethyl formamide, gave the aldehyde (**15**), 83%. The required imino ether (**16**) was then prepared from (**15**) with trimethyloxonium tetrafluoroborate in the presence of boron trifluoride–diethyl ether; 74% yield.



The two building blocks (**8**) and (**16**) were then combined using TFA catalysis, to generate the seco-system (**17**). This was irradiated in thoroughly degassed tetrahydrofuran in a sealed tube for 14 days with visible light from an array of tungsten lamps (total 1000 W). Chromatographic fractionation then yielded recovered seco-system (**17**) and the chlorin (**18**) in 36% overall yield; ≡ 97% based on unrecovered starting material. Found for (**18**) M^+ 521.2777, $C_{32}H_{35}N_5O_2$ requires M^+ 521.2790. Methanolysis of the nitrile (**18**) with methanolic hydrogen chloride afforded (±)-bonellin dimethyl ester [(±)-(**2**)], 88%. This was shown by ^{1}H n.m.r., u.v.–visible, and mass spectroscopy and t.l.c. to be identical, apart from its racemic nature, with authentic bonellin dimethyl ester prepared from the natural pigment and kindly provided by Dr. J. A. Ballantine (Swansea).

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