

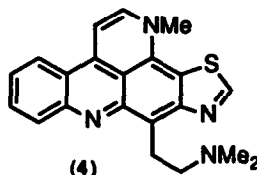
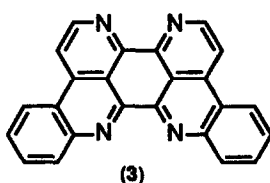
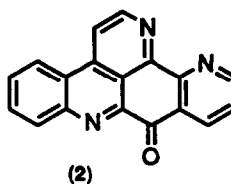
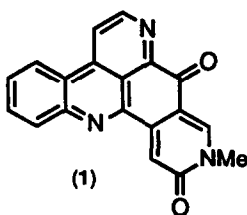
SYNTHESIS OF THE MARINE ALKALOID ASCIDIDEMIN

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Summary: A short synthesis of the pentacyclic marine alkaloid ascididemin (2) is described in which the key step is the photocyclisation of the quinoneimine (7).

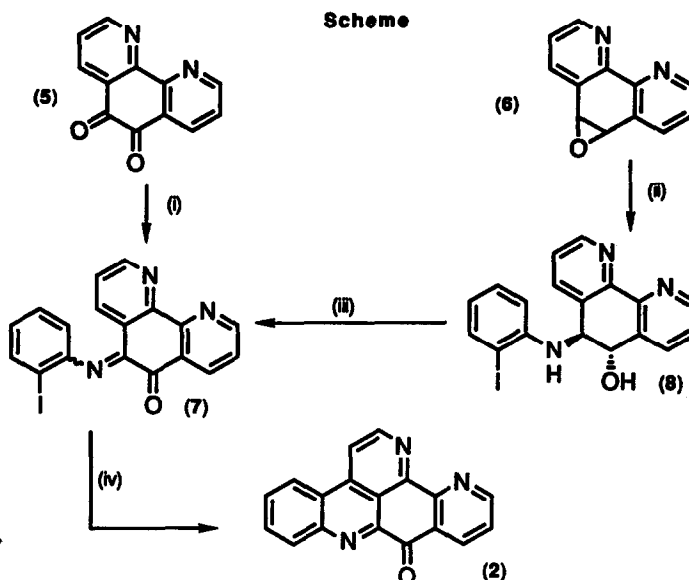
Marine organisms have proved a rich source of novel biologically active natural products, although relatively few alkaloids have been isolated from this source. The largest group of marine alkaloids to have been characterised so far is based on the pyrido[*k*,*l*]acridine skeleton. Examples include amphimedine (1),¹ ascididemin (2),² eilatin (3),³ and the sulphur containing alkaloids such as dercitin (4).⁴ These polycyclic aromatic structures pose an interesting challenge, both in terms of structure determination and synthesis. In continuation of our work in this area,⁵ we now report an extremely short synthesis of ascididemin (2).



Ascididemin, a yellow, high melting alkaloid isolated from the Okinawan tunicate *Didemnum* sp. was assigned the pyridoacridine structure (2) on the basis of extensive NMR studies.^{2a} This structure has been confirmed by a very recent synthesis starting from quinoline-5,8-quinone.^{2b} Our synthesis (Scheme), in which the key intermediate is the quinoneimine (7) is conceptually different and starts from either 1,10-phenanthroline-5,6-quinone (5)⁶ or the phenanthroline-5,6-epoxide (6),⁷ both of which are readily prepared from 1,10-phenanthroline, and the quinone is commercially available.

Quinoneimine (7), m.p. 124 °C decomp., could be prepared in a single step from quinone (5) by a novel aza Wadsworth - Emmons reaction⁸ using the sodium salt of diethyl N-(2-iodophenyl)-phosphoramidate, prepared for this purpose from diethyl phosphorochloridate and 2-iodoaniline (97 %). However the yield of (7) was low (10 %), and therefore a two-step route from the epoxide (6) was preferred. Thus the epoxide was opened with 2-iodoaniline in the presence of

triethylaluminium⁹ to give the amino alcohol (8), m.p. 128 - 130 °C (79 %); the Lewis acid is essential for the success of this reaction. The alcohol (8) was readily oxidised with barium manganate to the purple quinoneimine (7) (83 %). Finally photocyclisation¹⁰ of the quinoneimine in concentrated sulphuric acid (Phillips HPK-125 high pressure mercury lamp, quartz filter, water cooling) and the only chromatography needed in this route, gave ascididemin (2) (32 %), with spectroscopic properties identical to those of the natural product.² As far as we are aware, this is the first azastilbene photocyclisation of a quinoneimine.



Reagents: (i) 2-IC₆H₄NHP(O)(OEt)₂, NaH, glyme; (ii) 2-IC₆H₄NH₂, Et₃Al, CH₂Cl₂; (iii) BaMnO₄, CH₂Cl₂; (iv) hv, H₂SO₄.

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