

The Synthesis of Indole Subunits for CC-1065

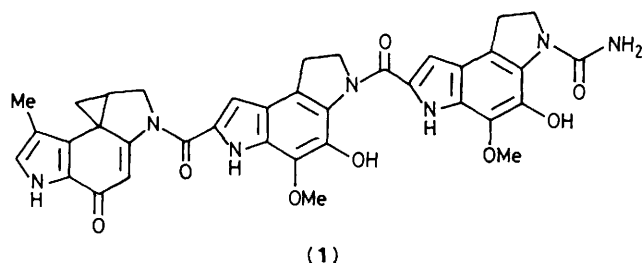
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A four-step preparation of the benzodipyrroles (**5**) and (**7**) from the quinone di-imine (**2**) is described.

The cytotoxic agent CC-1065 (**1**) was isolated from *Streptomyces zelensis* by Martin and co-workers.¹ Its novel structure

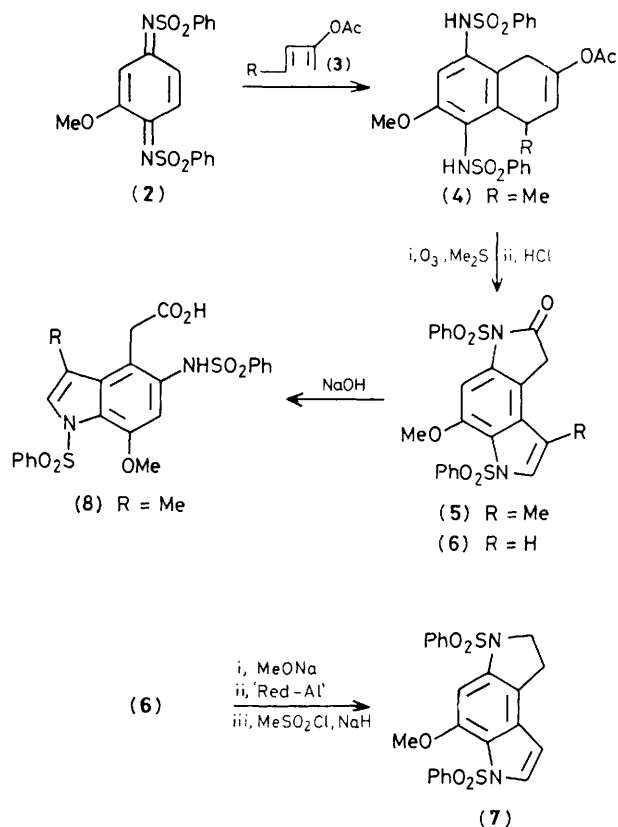
and potent inhibitory activity against L1210 and P388 leukemias in mice combine to make (**1**) a significant synthetic



objective. Wierenga² has reported a route to the left-hand portion and Umezawa³ has synthesized the central and right-hand portions. Recently Magnus and Or⁴ have reported an expedient route to an intermediate for the preparation of the left-hand portion. We now report an approach which is quite different from either the Wierenga or Magnus routes. We set out to construct *each portion* from (2) by use of the requisite diene. The benzodipyrrole (5), an intermediate for the construction of the left-hand portion, was prepared as illustrated in Scheme 1. The reaction of (2)⁵ with 2-acetoxypenta-1,3-diene (3; R = Me) (4 days, room temp.) afforded the enol acetate (4) in 75% yield. Ozonolysis (O₃, -78 °C, then Me₂S) followed by acid mediated aromatization (HCl, dioxane) furnished compound (5) in 88% yield.† The intermediate for the central and right-hand portions was synthesized from (2) and 2-acetoxybutadiene (3; R = H) (10 days, room temp.). Ozonolysis and acid-catalysed aromatization afforded the benzodipyrrole (6). The carbonyl group could be removed by a three-step procedure involving lactam reduction followed by cyclization of the resulting alcohol. Compound (7) was produced in *ca.* 29% yield from (2).

The benzodipyrroles (5) and (7) possess the requisite functionality for ready conversion into units which can be coupled to produce (1). The approach described above is both direct and flexible. Other heterocyclic analogues of (1) could be similarly produced.

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Scheme 1

work. We also thank Drs R. A. Jacobson and J. Benson for a crystal structure determination.

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References

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- 3 N. Komoto, Y. Enomoto, N. Miyagaki, Y. Tanaka, K. Nitani, and H. Umezawa, *Agric. Biol. Chem.*, 1979, **43**, 557.
- 4 P. Magnus and Y-S. Or, *J. Chem. Soc., Chem. Commun.*, 1983, 26.
- 5 This could be synthesized from commercially available 2-methoxy-*p*-phenylenediamine·H₂SO₄ by reaction with KOH-PhSO₂Cl followed by oxidation with Pb(OAc)₄ in HOAc (90% yield). For the reaction of quinone di-imines with dienes see R. Adams and W. P. Samuels, *J. Am. Chem. Soc.*, 1955, **77**, 5383.

† Compound (5) was readily hydrolysed to the acid (8) with NaOH. A single crystal X-ray study confirmed the structure.