The Synthesis of Indole Subunits for CC-1065

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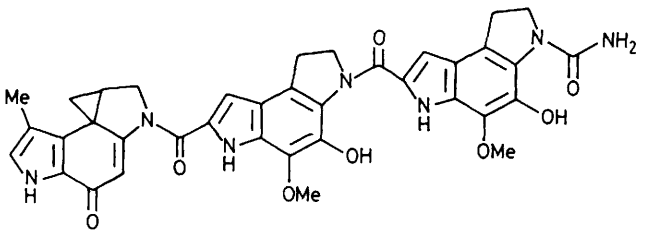
A four-step preparation of the benzodipyrroles (**5**) and (**7**) from the quinone di-imine (**2**) is described.

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



(1)

objective. Wierenga[2] has reported a route to the left-hand portion and Umezawa[3] has synthesized the central and right-hand portions. Recently Magnus and Or[4] 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 (O_3, −78 °C, then Me_2S) 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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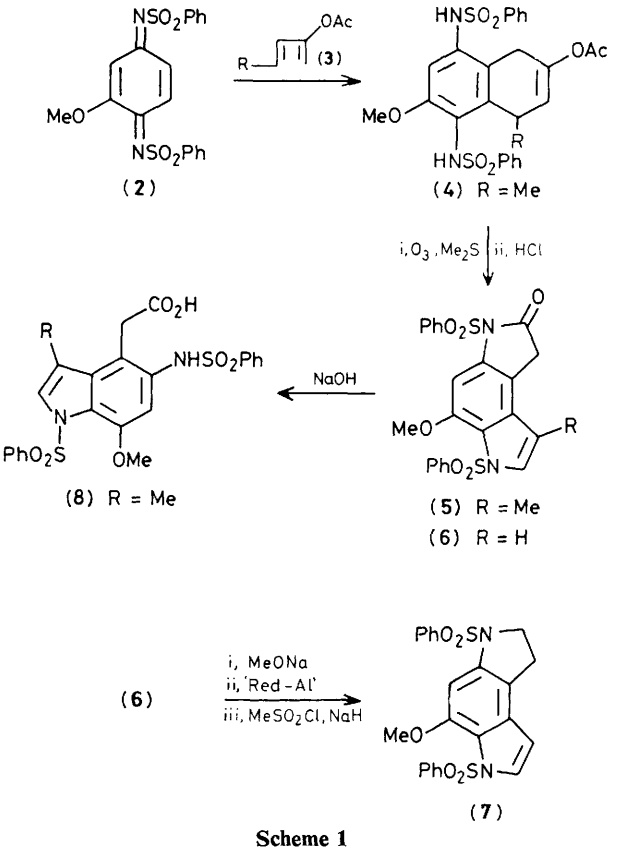

Scheme 1

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

References

1 L. J. Hanka, A. Dietz, S. A. Gerpheide, S. L. Kuentzel, and D. G. Martin, *J. Antibiot.*, 1978, **31**, 1211.
2 W. Wierenga, *J. Am. Chem. Soc.*, 1981, **103**, 5621.
3 N. Komoto, Y. Enomoto, N. Miyagaki, Y. Tanaka, K. Nitanai, 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·H_2SO_4 by reaction with KOH–$PhSO_2Cl$ 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.