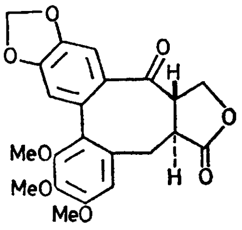
Synthesis of a Steganone Analogue

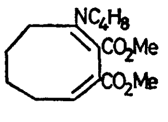
By DAN BECKER
(*Department of Chemistry, Israel Institute of Technology, Technion City, Haifa*)
LESLIE R. HUGHES and RALPH A. RAPHAEL*
(*University Chemical Laboratory, Lensfield Road, Cambridge* CB2 1EW)

Summary A rapid and efficient synthetic approach to attain the structural features characteristic of steganone is described.

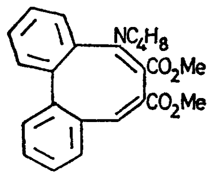
THE interesting antileukaemic constituents of *Steganotaenia araliacea* Hochst.[1] are members of the small group of lignans containing an eight-membered carbocyclic ring.[2] Their structural features are illustrated by the structure of steganone (**1**).



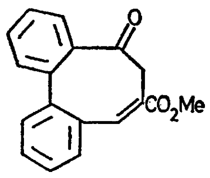
(1)



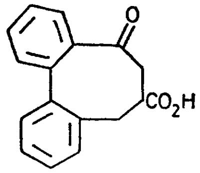
(2)



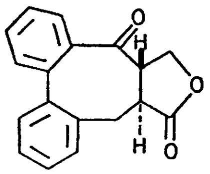
(3)



(4)



(5)



(6)

A relatively rapid route to structures of this type was suggested by the double ring expansion brought about by the interaction of dimethyl acetylenedicarboxylate and 1-pyrrolidinocyclohexene[3] to give the usefully substituted cyclo-octadiene (**2**). Because of the well-known ethylenic properties of the 9,10-double bond of phenanthrene it appeared plausible that 9-pyrrolidinophenanthrenes might exhibit enamine-like properties and undergo an analogous double ring expansion with acetylenic esters.

Heating 9-pyrrolidinophenanthrene itself with dimethyl acetylenedicarboxylate led smoothly to the ring expanded product (**3**) m.p. 155—156°. Hydrolysis with methanolic hydrochloric acid was accompanied by decarboxylation to yield the unsaturated keto-ester (**4**) m.p. 145–149°. Catalytic hydrogenation with Raney nickel gave the corresponding saturated ester which was hydrolysed to the corresponding acid (**5**) m.p. 149—152°. Aldol reaction of the acid (**5**) with aqueous formaldehyde and potassium hydroxide gave as sole product a homogeneous racemic γ-lactone (**6**) m.p. 162—164°. As base-catalysed epimerisation can readily take place at both chiral centres of (**6**) the product represents the thermodynamically more stable of the two possible diastereoisomers. That this was in fact the desired *trans*-fused lactone was strongly suggested by the extremely close correspondence, in the relevant non-benzenoid regions, between the n.m.r. spectrum of (**6**) and steganone itself; both in chemical shift position and complexity of the splitting patterns of the six protons concerned there was virtually complete identity.

We thank Professor S. M. Kupchan for providing the spectrum of steganone, and the S.R.C. for financial support.

(*Received*, 1*st April* 1974; *Com.* 365.)

---

[1] S. M. Kupchan, R. W. Britton, M. F. Ziegler, C. J. Gilmore, R. J. Restivo, and R. F. Bryan, *J. Amer. Chem. Soc.*, 1973, **95**, 1335.

[2] See also Y. P. Chen, R. Liu, H. Y. Hsu, S. Yamamura, Y. Shizuri, and Y. Hirata, *Tetrahedron Letters*, 1973, **4257**, and references therein.

[3] G. A. Berchtold and G. F. Uhlig, *J. Org. Chem.*, 1963, **28**, 1459; K. C. Brannock, R. D. Burpitt, V. W. Goodlett and J. G. Thweatt, *ibid.*, p. 1464; C. F. Huebner, L. Dorfman, M. M. Robison, E. Donoghue, W. G. Pierson, and P. Strachan, *ibid.*, p. 3134.