# TWO SYNTHESES OF ELLIPTICINE

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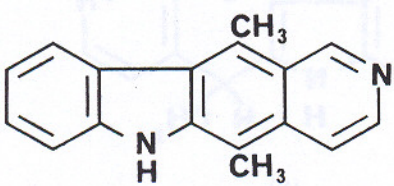
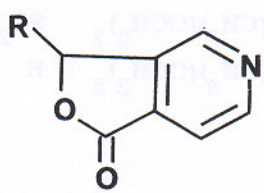
This paper describes two related syntheses of the indole alkaloid ellipticine (1). Both are short and both flexible in having the potential for easily synthesising side-chain-modified analogues of this anti-cancer alkaloid.

Condensation of 2-lithio-1-benzenesulphonylindole with the pyridine lactones (2a) and (2b) gave the keto-alcohols (3a) and (3b) respectively.




(1)

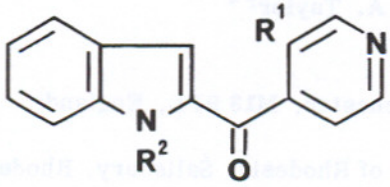



(2) R

a H

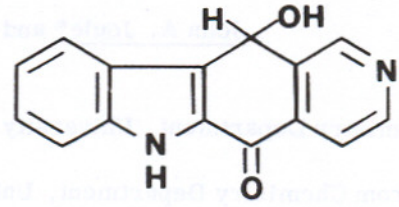
b $CH_3$

The primary alcoholic group of (3a) was oxidised with manganese dioxide and the resulting keto-aldehyde (3c) selectively acetalised to give (3d). Alkaline removal of the $N_a$-protecting group (⟶ (3e)) was followed by hydrochloric acid catalysed removal of the acetal which process also brought about condensation at the indole $\beta$-position. The presumed intermediate (4) was not isolated, however, suffering *in situ* aerial oxidation to the product quinone (5). Three mol equivalents of methyl-

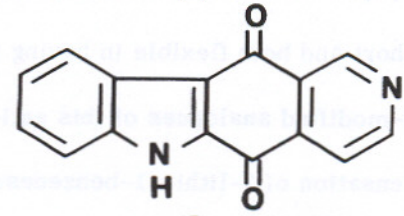


(3)

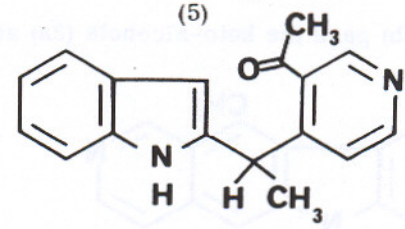
| | $R^1$ | $R^2$ |
|---|---|---|
| a | $CH_2OH$ | $SO_2Ph$ |
| b | $CH(CH_3)OH$ | $SO_2Ph$ |
| c | CHO | $SO_2Ph$ |
| d | $CH(OCH_2)_2$ | $SO_2Ph$ |
| e | $CH(OCH_2)_2$ | H |
| f | $COCH_3$ | $SO_2Ph$ |
| g | $C(CH_3)(OCH_2)_2$ | $SO_2Ph$ |
| h | $C(CH_3)(OCH_2)_2$ | H |



(4)



(5)



(6)

lithium converted this into material which was immediately reduced with lithium aluminium hydride to give ellipticine (1).

The secondary alcohol (3b) was oxidised with manganese dioxide to (3f), selectively acetalised at the methyl ketone and the resulting acetal, (3g), deprotected with alkali (→ (3h)). Wittig reaction with triphenylphosphonium methylide followed by catalytic reduction then gave a substance (6) with the appropriate substitution and oxidation level for conversion to ellipticine, achieved by reaction of (6) with dilute hydrochloric acid at reflux.