SYNTHESIS AND MICROBIOLOGICAL EVALUATION OF SOME NOVEL 10H-PYRROLIZINO(1,2-b)QUINOLINES

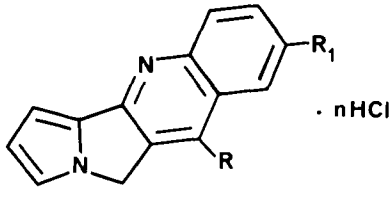
J.A.Box, G.Hall, J.K.Sugden and M.B.Waghela, School of Pharmacy, Leicester Polytechnic, P.O.Box 143, Leicester, LE1 9BH, U.K.

In light of the growing interest in various aspects of pyrrolizine chemistry (Flitsch & Jones 1984; Hall *et al* in press) and the continued search for novel, safe and efficacious chemotherapeutic agents, a number of 10*H*-pyrrolizino[1,2-*b*]quinolines (1) were synthesised and examined for both anti-bacterial and anti-fungal activities.

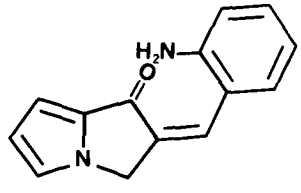
The 10*H*-pyrrolizino[1,2-*b*]quinolines were synthesised in 4 steps from pyrrole, with the exception of 1a which was obtained via its benzylidene intermediate (2). The anti-bacterial and anti-fungal activities were assessed *in vitro*, using overnight grown cell cultures of *E.coli*, *Staph. aureus*, *B. subtilis*, *Ps. aeruginosa*, *C. albicans and S. cerevisiae*, by conventional serial broth dilution and agar plate techniques.

Compounds 1a and 1b were found to inhibit the growth of both *C. albicans* and *S. cerevisiae* at 50 μg ml^{-1}, whereas 1e inhibited the growth of *Staph. aureus*, *B. subtilis*, *Ps. aeruginosa* and *S. cerevisiae*, in the agar plate test, at concentrations greater than 50 μg ml^{-1}. 1a and 1b on further evaluation showed marked inhibition of *A. niger*. 1e completely inhibited *Fusarium* sp. although showing no effect on *A. niger* and *P. notatum*.

It would appear from this study the anti-fungal properties within this series are associated with the 10*H*-pyrrolizino[1,2-*b*]quinoline moiety, as (2) which mimics the tetracyclic ring arrangement of (1), failed to show any activity in either test. It was also noticed that only the water soluble derivatives were active. At the present time, the mode of action is not known, but by analogy with the acridines, these compounds could be disrupting either the structure or function of DNA.



(1)



(2)

	R	R_1	n
a.	H	H	1
b.	Me	H	1
c.	Ph	H	1
d.	Ph	Cl	1
e.	Ph	NH_2	2
f.	2´-FC_6H_4	H	1
g.	4´-MeC_6H_4	H	1

Flitsch, W. and Jones, G. (1984), Adv. Heterocycl. Chem. 37: 2-30.
Hall, G. *et al.* Synthesis in press.