STUDIES IN ANTIMALARIALS

Biguanido-aryl-sulphides and sulphones

FOLLOWING the discovery of the unique antimalarial properties of Paludrine[1], many attempts have been made to improve upon the activity of the parent drug.[2,3,4,5,6,7,8,9,10] Considering that a suitable substituted biguanide system may be sufficient for antimalarial activity,[11] we have prepared a series of N^1-N^5-aryl substituted biguanides as possible antimalarials, by replacing the isopropyl group in paludrine and its bromoanalogue with chemotherapeutically active residues of 4-nitro-4'-amino diphenyl sulphide, 4-nitro-4'-amino diphenyl sulphone, 4, 4'-diamino diphenyl sulphide and 4, 4'-diamino diphenyl sulphone.[12,13,14,15]

TABLE A

N'—N⁵—diaryl biguanides

RNH—C (=NH)—NH—C (=NH)—NHR', HCl

No.	R	R'	M.P. °C.
I	p-NO_2-C_6H_4-S-C_6H_4-	H	236-87
II	do	p-Cl·C_6H_4--	224-26
III	do	p-Br·C_6H_4--	220-22
IV	p-NO_2-C_6H_4-SO_2-C_6H_4-	H	238-39
V	do	p-Cl-C_6H_4	207-8
VI	do	p-Br-C_6H_4-	223-25

TABLE B

4, 4'-Di (N'—aryl) biguanido diphenyl sulphide and sulphone

$$\begin{matrix} \text{RNH—C (=NH)—NH—C (=NH)—NH} \\ \text{RNH—C (=NH)—NH—C (=NH)—NH} \end{matrix} > R'$$

where R' = —C_6H_4—S—C_6H_4——and —C_6H_4—SO_2—C_6H_4—

No.	R	R'	M.P. °C.
I	H-	-C_6H_4-S-C_6H_4-	244
II	p-Cl-C_6H_4-	do	224-26
III	p-Br-C_6H_4-	do	232-33
IV	C_6H_5-	do	252-53
V	p-CH_3-C_6H_4-	do	192-93 (base)
VI	H-	-C_6H_4-SO_2-C_6H_4-	252 (deeomp.)
VII	p-Cl·C_6H_4-	do	above 325
VIII	p-Br-C_6H_4	do	278

Table A lists the products of condensation of arylcyanoguanidines with the appropriate arylamine hydrochloride by heating in equimolecular proportions in dimethylaniline at 120-40° C. for 2-4 hrs. The reaction products crystallised out as hydrochloride from the hot solvent. For the synthesis of compounds given in Table B, pyridine was used in place of dimethylaniline as solvent.

The chemotherapeutic activities (antimalarial and antitubercular properties) of the compounds are being tested.

Full details will be published elsewhere.

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