

in which the isopropyl group in N¹-2:4-Dichlorophenyl-N⁵-isopropyl-biguanide (X) has been replaced by a number of branched chain alkyl groups derived mostly from the different alkyl amines previously reported¹⁴ (XI—XIX).

Table A. N¹-Aryl-N⁵-alkyl-biguanides.
X.NH-C-NH-CNH.R, HCl.

No.	$\begin{array}{c} \\ \text{NH} \\ \end{array} \quad \begin{array}{c} \\ \text{NH} \\ \end{array}$		m.p., ° C.
	X	R	
I	<i>o</i> -Chlorophenyl	Isopropyl	250
II	<i>m</i> -Chlorophenyl	do	227-228
III	<i>p</i> -Chlorophenyl (paludrine)	do	241
IV	<i>p</i> -Fluorophenyl	do	226
V	<i>p</i> -Bromophenyl	do	237-38
VI	<i>p</i> -Iodophenyl	do	234
VII	<i>p</i> -Cyanophenyl	do	231-32
VIII	β -Naphthyl	do	229-30
IX	3 : 4 Dichlorophenyl	do	236
X	2 : 4 Dichlorophenyl	do	240
XI	do	Methyl	215
XII	do	Dimethyl	231
XIII	do	2-Butyl	240
XIV	do	3-pentyl	221-22
XV	do	<i>iso</i> -Pentyl	216-17
XVI	do	β <i>iso</i> Hexyl	217
XVII	do	2-Pentyl	220-221
XVIII	do	Piperidyl	230-31
XIX	do	2-Octyl	224 (Base 150)

STUDIES IN ANTIMALARIALS

N¹- Aryl-N⁵-alkyl-biguanides

FOLLOWING the discovery of Paludrine¹ as a potent antimalarial, sufficient interest was developed in the field of substituted biguanide derivatives as potential antimalarials. The first attempt to improve upon the activity of the parent drug has been to replace its N¹-*p*-chlorophenyl part with phenanthrene and quinoline radicals but all these compounds were found to be inactive when tested against experimental malaria.^{2,4,11} The N⁵-isopropyl group of paludrine has been replaced with 5-and-8-quinolyl,^{5,6} 2-thiazolyl;⁷ *p*-phenyl arsonic acid,^{8,10,11} *m*-phenylsulphonamide and *p*-phenylsulphanomide (substituted or otherwise) groups and the last two have shown antimalarial activity when tested against avian malaria.¹²

Considering that a biguanide system is essential for activity in this type of antimalarials, in addition to the introduction of complex groups (as detailed above) it was thought worthwhile to study the simpler substituents at the either end of a biguanide link. Consequently various isomers and analogues of paludrine were prepared (*vide* table) where the effect of the chlorine atom in the different positions in the phenyl ring I-II, the effect of other halogen atoms and cyano group at the para position of the phenyl ring (IV-VII) and the effect of an extra chlorine atom in the *p*-chlorophenyl group (IX, X) have been studied. The work has been further extended

All these derivatives have been prepared by the interaction of the required arylcyanoguanidines¹³ with the alkyl amines in presence of copper sulphate or with their hydrochlorides by fusion. All the biguanides were isolated as white crystalline hydrochlorides.

Full details will appear elsewhere.

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