SOME N^1-N^3-DISUBSTITUTED GUANIDINES

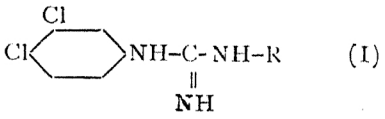
DURING the progress of research on chemotherapeutically active substances, King and Tonkin[1] discovered that *p*-tolyl-guanidine nitrate had a slight retarding action on a sporozoite-induced infection of *Plasmodium gallinaceum* in chicks. A large number of aromatic and aliphatic guanidines were then synthesized by the same authors, the most active among them being *p*-anisyl-guanidine nitrate.

The discovery of *Paludrine* by Curd and Rose[2] led them to synthesize a large number of substituted diguanides related to *Paludrine*, but carrying various mono- and poly-halogeno-phenyl groups in place of *p*-chloro-phenyl.[3] It was noted that the 3 : 4-dihalogeno-derivatives were the most effective and especially the 3 : 4-dichloro-compounds showed markedly higher suppressive activity (roughly 5-10 times) on malarial infections than the corresponding members of the *p*-halogeno-series.

It was, therefore, thought worthwhile to prepare guanidine derivatives of the type (I) carrying 3 : 4-dichlorophenyl group at N^1-position and having alkyl-, aryl-, or sulpha-substituted residues at N^3-, and to study their pharmacological properties. Accordingly, 3 : 4-dichlorophenyl cyanamide (m.p. 134° C.) was prepared

by a modification of Pierron method,[4] and reacted with some aromatic and aliphatic amines, as well as some sulphonamides in pyridine medium and the following 12 compounds have been isolated and characterised.

TABLE



(I)

Sl. No.	R	m. p. °C. (uncorrected)
1	Phenyl	135–136
2	*p*-Chlorophenyl	161–162
3	*p*-Bromophenyl	175–176
4	*p*-Iodophenyl	173–174
5	*p*-Tolyl	150–151
6	*p*-Anisyl	107–108
7	3 : 4-Dichloro-phenyl	173–175
8	3 : 4 : 5-Trichloro-phenyl	168–169
9	Methyl	153–155
10	2-Butyl	92– 94
11	Sulphanilylguanidyl	113–115
12	Sulphanilyl (hydrochloride)	185–186

All the compounds were crystallised in the form of small, shiny, white needles or long plates from water or dilute ethanol. These compounds are awaiting pharmacological investigations.

Further work on substituted guanidines is in progress. Full details of the present work will be published elsewhere.

Organic Chemistry Labs., N. S. JOHARY.
Ind. Inst. of Science, S. S. GUHA.
Bangalore-3, P. C. GUHA.
May 29, 1952.

1. King and Tonkin, *J. Chem. Soc.*, 1946. 1063, 2 Curd and Rose, *Ibid.*, 1946, 729. 3. Crowther, Curd, Davey, Hendry, Hepworth and Rose, *Ibid.*, 1951, 1774, 4. Paul Pierron, *Bull. Soc. Chim.*, 1906, III, **35**, 1197.