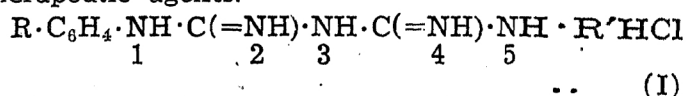


### STUDIES IN ANTIMALARIALS—SOME SULPHA-BIGUANIDE DERIVATIVES

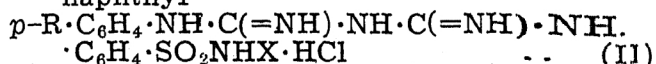
AMONG sulphanilamides<sup>1-3</sup> sulphadiazine is the most effective and possesses a slight but definite prophylactic action<sup>4</sup> in malaria. Meta-chloridine,<sup>3</sup> a recent suppressive antimalarial drug of the sulpha-group, is also a pyrimidine derivative.

Considering the activity of sulphadiazine, Curd and Rose<sup>5</sup> prepared at first its sulphur-free analogues of phenyl-substituted pyrimidine type and their later work culminated in the discovery of paludrine,<sup>5,7</sup> which is a substituted biguanide derivative.

Compounds of the type (I) have not shown appreciable antimalarial activity<sup>6</sup> which might be partly due to lack of any potential substituent in the aromatic nucleus at N<sup>5</sup>-position of the biguanide molecule. Hence it was thought of interest to prepare compounds of type (II) where "SO<sub>2</sub>NH<sub>2</sub>" or substituted "SO<sub>2</sub>NH<sub>2</sub>" radical is introduced in the aromatic nucleus at N<sup>5</sup>-position, and for this purpose only potent sulpha compounds, sulphanilamide, sulphathiazole and sulphadiazine were selected. It may be mentioned that compounds of the type (III) have already been patented<sup>8,9</sup> as therapeutic agents.



R = alkyl, halo, nitro. etc. R' = phenyl or naphthyl

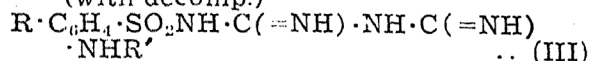


(a) X=H and R=H, m.p. 228°; R=Cl, m.p. 233°; R=Br, m.p. 245-6°; R=NO<sub>2</sub>, m.p. 217°; R=CH<sub>3</sub>, m.p. 231°; R=CH<sub>3</sub>O, m.p. 234°.

(b) X=2-thiazolyl and R=H, m.p. 225°; R=Cl, m.p. 219°; R=Br, m.p. 197° (with

decomp.); R=NO<sub>2</sub>, m.p. 267°; R=CH<sub>3</sub>, m.p. 189-190° (with decomp.); R=CH<sub>3</sub>O, m.p. 176° (with decomp.).

(c) X=2-pyrimidyl and R=H, m.p. 238°; R=Cl, m.p. 189°; R=Br, m.p. 202°; R=NO<sub>2</sub>, m.p. 246°; R=CH<sub>3</sub>, m.p. 232° (with decomp.); R=CH<sub>3</sub>O, m.p. 210-212° (with decomp.)



R=NO<sub>2</sub>, AcNH, NH<sub>2</sub>, etc. R'=H, alkyl or aryl.

The eighteen new compounds indicated above have been synthesised by the interaction of the hydrochloride of the required sulpha-derivative and the corresponding para-substituted-phenylcyanoguanidine in boiling aqueous dioxan medium. The compounds were obtained as their hydrochloride salts and crystallised from dilute alcohol or water. The substituted phenylcyanoguanidines were obtained after denitrogenating the corresponding substituted phenylazocyanoguanidines and the report of a systematic study of the denitrogenation of similar triazines will be communicated later. These compounds which are fairly soluble in water and bitter in taste are being tested against bird malaria (*P. gallinaceum*) for their activity as antimalarials.

Further work on substituted biguanides as possible antimalarials is in progress. Full paper will be published elsewhere.

One of the authors (H. L. Bami) wishes to thank the Indian Research Fund Association for the award of a research fellowship which enabled him to undertake this work.

H. L. BAMBI.  
B. H. IYER.  
P. C. GUHA.

Organic Chemistry Labs.,  
Dept. of Pure & Applied Chemistry,  
Indian Institute of Science,  
Bangalore,  
July 25, 1947.

---

1. Diaz de Leon, *Public Health Reports, Washington*, 1937, **52**, 1460. 2. Curd, *Ann. Trop. Med. and Parasitol.*, 1943, **37**, 115. 3. Bami, Iyer and Guha, "Recent advances in the chemistry of synthetic antimalarials," *Science and Culture*, 1947, **13**, 18-26. 4. Curd, *Ann. Trop. Med. and Parasitol.*, 1945, **39**, 147. 5. Curd and Rose, *J.C.S.*, 1946, 343. 6. —, *Ibid.*, 720. 7. Bami, Iyer and Guha, *J. Indian Inst. Sci.*, 1946, **29A**, 1-8. *cf. Science and Culture*, 1946, **12**, 448. 8. Rose, B.P., 550538, 1943. 9. Winnek, U.S.P., 2295884, 1943.

---