

AN INSECT TUMOUR AND OVARIAL HORMONE

SULC¹ was the first to discover a rectal tumour in Fulgorid insects. Buchner² confirmed this, adding that "the most remarkable fact about this organ is that it is always found in the female, a circumstance which escaped Sulc." While at Brünn, in Czechoslovakia, I found *Fulgora europæa* easily available. For over two months, about ten female insects were dissected daily, as a routine, but only once did I come across a specimen where the rectal tumour was absent. When its ovary was examined it was so atrophied as to be considered absent; the genital armature had to be examined to be sure of the sex identity. The above finding established clearly the simultaneous absence of a normal ovary and that of the rectal tumour which thus confirms Buchner's observations and explains the influence of the ovarian hormone on the growth of the rectal tumour.

The brief mention that the rectal tumour was absent would naturally convey the notion that the germ or symbiote, found in the rectal tumour, was altogether wanting from the insect body. From the writings of Sulc it is by no means clear whether each tumour has its special micro-organism. In *Tettigometra obliqua* he finds many tumours but only of three types. One, which he calls the clump-forming tumour, is divided into four units, but represents morphologically the same structure. Thus, according to Sulc, there would be only three symbiotes, one for each type of tumour. In fact, he has illustrated the three germs as morphologically different, in Figs. 51, 53 and 54. In the case of *Fulgora europæa* he has, unfortunately, not given illustrations of the germs in symbiosis with it. He has however done this with *Oliarus cuspidatus*, where Fig. 6 represents the germ found in the rectal tumour and Fig. 9 that in the clump forming tumour. Now Buchner² has subsequently shown that, in *F. europæa*, the germ in the rectal tumour is identical with that found in what Sulc calls, the clump-forming tumour. I have confirmed this observation by isolation. The germ of *F. europæa* is a pigment producer, identical with the yellow colour found within the body of the insect. That of *O. cuspidatus* produces a red pigment, probably β -carotene. What is interesting is that these germs produce zoogloal colonies which unwittingly induced Sulc to give the appropriate term, clump-forming tumour. The absence of rectal tumour thus does not mean the absence of the symbiote, for it is always present in the clump-forming tumour. The formation of the rectal tumour is thus not so much a microbiological phenomenon as a physiological one, being more intimately connected with the function of the female sex hormone.

Now all homopterous insects have tumours on either side of the abdomen. It is equally well known that they are better developed in the female, which thus indicates the share of the female sex hormone. There are germs that directly induce cell multiplication. Mary,³ in the chapter on the Collloid Chemistry of

Tuberculosis, writes that "when we speak of tuberculosis tissue it is not a question of an altered normal tissue. A neoplastic formation is in reality involved for whose formation no bacillus is essential, the agent being always of a toxic nature... (Tissue culture experiments indicate) histological changes of tuberculosis (with) figures showing mitosis." Like the germ of tuberculosis, that of leprosy, also induces new cellular growth. Symbiotic germs of insect tumours probably do the same. That of *Cicadella viridis*,⁴ already isolated, secretes phosphatases which would go to attribute such a property. However, in insects with rectal tumours the new growth is the combined result of bacteria and that of the female sex hormone, where the latter is the leading factor.

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1. *Pub. biol. Ecoles Haut Etudes veter. Brünn.*, 1924, 3. 2. *Zeit. f. Morph. u. Okolog.*, 1925, 4, 3. *Alexander, Colloid Chemistry*, 2, 872-5. 4. *Curr. Sci.*, 1947, 16, 58.

2-THIOL-4:5-DIPHENYLIMIDAZOLE DERIVATIVES

CORRELATING the chemical structure and sympathomimetic activity, Barger and Dale¹ enunciated the " β -phenylethylamine rule" which states that "the optimum constitution of fatty aromatic amine for the production of sympathomimetic action is, ... that which is found in adrenaline itself, viz., a benzene ring and a side chain of two carbon atoms of which the second bears the aminogroup". Imidazole derivatives² have recently come to the forefront as possible sympathomimetics, the 2-*a* naphthylmethylimidazoline (Privine) having already been introduced into medicine. Further, S-methylisothiurea sulphate³ has been reported to overcome fall of blood pressure in spinal anaesthesia.

With a view to studying the pressor activity of compounds possessing all the structural characteristics detailed above, a number of 2-thiol-4:5-diphenylimidazole derivatives (*vide* table) of the type (I) have now been synthesized. Müller⁴ prepared N-aryl derivatives of 2-thiol-4:5-diphenylimidazole by heating benzoin with N-substituted thioureas and alcohol, in sealed tube at about 130-90° C. for 4-5 hrs. Biltz and Krebs⁵ prepared 2-mercapto-4, 5-diphenylimidazole by fusing benzoin and thiourea in the absence of any solvent. Extending the latter method to N-substituted thioureas, compounds 12, 13, 16 and 19 (*vide* table) have been prepared by fusing benzoin with the appropriate thiourea at about 200° C. and purifying the products directly by crystallisation after removing the reactants, or through their alkali salts.

By the action of the corresponding halogen compounds in alcoholic solution on the appropriate 2-thiol, 4, 5-diphenylimidazole, the thioethers Nos. 1 to 11, 14, 15, 17 and 18 (*vide*

TABLE

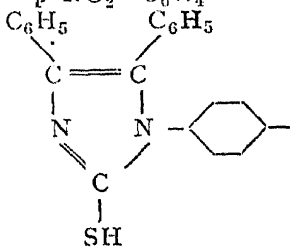
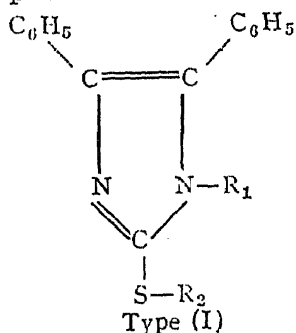
No.	R ₁	R ₂	M.P.° C.
1	H	-CH ₂ -CH ₂ -CH ₃	174
2	H	-CH ₂ -CH=CH ₂	181-2
3	H	-CH ₂ -CO-CH ₃	150-1
4	H	-CH ₂ -CH ₂ -OH	167
5	H	-CH ₂ -COOH	216
6	H	-CH ₂ -C ₆ H ₅	185-6°
7	H	-C ₆ H ₄ -NO ₂ -p	209
8	H	-C ₆ H ₂ -(NO ₂) ₃ 2, 4, 6	186 (decomp.)
9	C ₆ H ₅	-CH ₂ -CO-CH ₃	153-4
10	C ₆ H ₅	-C ₆ H ₃ (NO ₂) ₂ 2, 4	199-200
11	C ₆ H ₅	-C ₆ H ₂ (NO ₂) ₃ 2, 4, 6	205-6 (decomp.)
12	o CH ₃ -C ₆ H ₄	H	288-9 (decomp.)
13	p CH ₃ -C ₆ H ₄	H	319-20 (decomp.)
14	p CH ₃ -C ₆ H ₄	-C ₆ H ₃ (NO ₂) ₂ 2, 4	233
15	p CH ₃ -C ₆ H ₄	-CH ₂ -C ₆ H ₅	191
16	p CH ₃ O-C ₆ H ₄	H	297 (decomp.)
17	p CH ₃ O-C ₆ H ₄	-CH ₂ -C ₆ H ₅	191-2
18	p CH ₃ O-C ₆ H ₄	-C ₆ H ₂ -(NO ₂) ₃ 2, 4, 6	168 (decomp.)
19	p NO ₂ -C ₆ H ₄	H	284 (decomp.)
20			does not melt even at 340

table) have been prepared. Two molecules of benzoin reacted with *p*-phenylene bithiourea to give compound 20.



Full details will be published elsewhere.

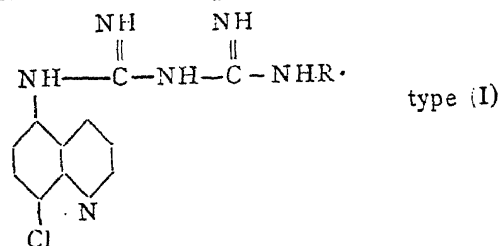
Organic Chemistry Laboratories, M. V. BHATT.
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Bangalore, P. C. GUHA.
April 1, 1948.

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2. Scholz, *J. Ind. and Engg. Chem.*, 1945, **37**, 120-5.
3. Smirk and McGeorge, *Lancet.* 1912, **243**, 301.
4. Müller, *Annalen*, 1894, **284**, 25-35.
5. Biltz and Krebs, *ibid.*, 1912, **391**, 194-95.

STUDIES IN ANTIMALARIALS SOME N¹-(8-CHLORO-5-QUINOLYL)-N⁵- SUBSTITUTED BIGUANIDES

In continuation of our work on quinoline substituted biguanides as possible antimalarials,¹

a number of N¹-(8-chloro-5-quinolyl)-N⁵-substituted biguanides of type (I) have now been synthesised. May, et al² have prepared a few methoxy-8-quinolyl biguanides but found them inactive against blood inoculated *P. gallinaceum* infection. In the present



series of compounds, the similarity to paludrine³ is kept up in that the biguanide chain is at 5-position and the chlorine atom at the 8-position of the quinoline nucleus. It may also be interpreted that a pyridine ring is fused to the *p*-chlorobenzene nucleus, present in paludrine and it is hoped that they will be active against malaria parasites.

The compounds (*vide* Table I), were prepared by condensing 8-chloro-5-amino-quinoline hydrochloride with the appropriate cyanoguanidines in alcoholic solution. The base was liberated from the reaction mixture by treating it with dilute alkali solution and purified by recrystallising from organic solvents. The acetates prepared in the usual manner, were purified by recrystallisation from absolute alcohol and dry acetone.

While both the base and the salt (No. 1 in Table I) from the reaction with cyanoguanidine contain one molecule of water of crystallisation