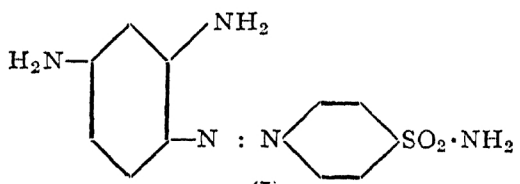
The Chemotherapy of Tuberculosis.

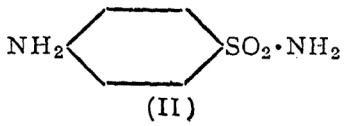
THE recent discovery of the specific action of Prontosil (I), sulphanilamide (II) and the diacetyl derivative of 4 : 4′-diamino-diphenyl sulphone (III) in infections due to the *cocci* and other bacteria[1] led the present author to try some of the derivatives of the above compounds in the case of tuberculosis also. The general procedure adopted is to react the amino-groups of the compounds (I), (II) and (III)—as such and also their derivatives—with allyl mustard oil to yield compounds (with allylthiourea groupings) resembling 'lopion' (the gold salt of IV) which is known to be least toxic and not deranging the kidneys.

Thus *para*-aminobenzene sulphonamide (II), *para*-aminocinnamic acid, *para*-amino mandelic acid and 4 : 4′-diaminodiphenyl-sulphon (III), yielded the corresponding allylthiourea derivatives with allyl mustard oil. Sulphanilic acid, however, did not undergo a similar condensation. It furnished with *p*-acetaminobenzenesulphonic chloride in alkaline solution *p*-acetamino-benzene sulphonamino benzene sulphonic acid (V) which was hydrolysed to the corresponding amine and the latter with allyl mustard oil yielded the allylthiourea derivative.

Prontosil (I) condensed with allyl-mustard oil to yield the allylthiourea derivative. Though *meta*- and *para*-phenylenediamines yield only monothioureas with one molecule of potassium thiocyanate, it has now been found that even with one molecule of allyl mustard oil the above diamines furnished almost exclusively phenylene di-allylthioureas. However *m*- and *p*-acetphenylenediamines condensed with allyl mustard oil to the corresponding acetamino-phenyl allylthiourea derivatives (VI) which were hydrolysed with hydrochloric acid (6N) to the corresponding hydrochlorides of aminophenyl allylthioureas (VII). Of these, the *meta*-isomer coupled with diazotised *p*-aminosulphanilamide to yield the dyestuff (VIII) related to prontosil (*vide* preparation from prontosil), while the *para*-isomer did not undergo a similar coupling. *p*-aminocinnamic acid also failed to couple with diazotised *p*-sulphanilamide while 4-aminothiouracil with the same reagent yielded the dyestuff (IX). Similar dyes are being prepared by using the compound (III) in place of (II) in the above reactions.



(I)



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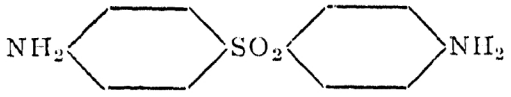
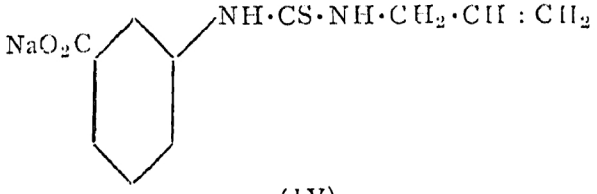
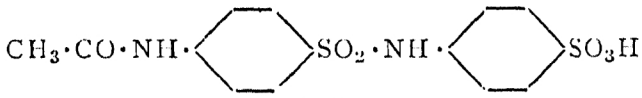


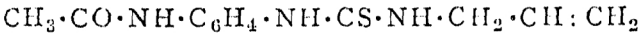
(III)



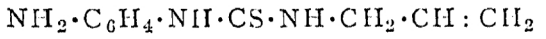
(IV)



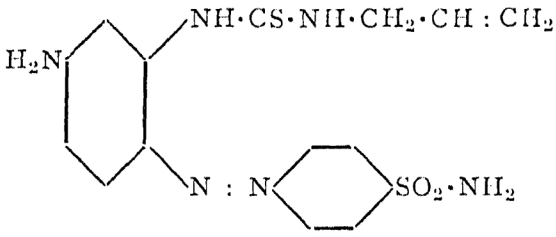
(V)



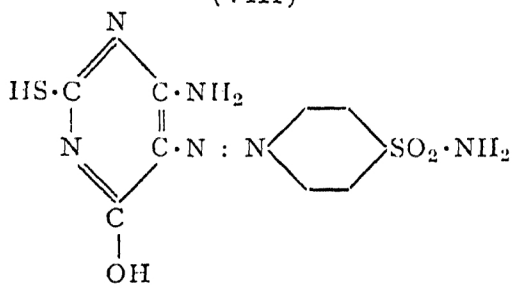
(VI)



(VII)



(VIII)



(IX)

Under the usual conditions, all the above compounds described yield gold salts, the pharmocological examinations of which are being carried out elsewhere.

Full details of the experiments will be published elsewhere.

The author thanks Dr. P. C. Guha for his kind interest in this work.

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April 28, 1938.

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[1] Buttle, *Proc. Roy. Soc. Med.*, 1937, **31**, 154; *cf. Annales Medico-chirurgicales*, 1938, **3**, No. 3.