A number of $9:10$-thiopela $2:10$-diene-$4$-ones with various substitutions (Table I - V) have been synthesised by a novel and general route for testing their physiological activities. This involves the condensation of an anthranilic acid with an \( \alpha \)-thiocyanoketone in presence of a protonic reagent (65); a mechanism for the reaction has been postulated (70).

Certain reactions involving thiocyanooacetone as the thiocyanate component yielded two products viz., $9:10$ and $10:11$-thiopegas or angular and linear thiopegas respectively. The linear structures, in such cases, which record lower melting points than their angular counterparts, have been confirmed by unequivocal syntheses (70, 110, 111).

Two possible mechanisms for the formation of the linear products, which explain the unusual behaviour of thiocyanooacetone, have been put forth. The first mechanism visualises a dipolar structure for thiocyanooacetone. Eventually, it points to a new field of research viz., a study of the factors influencing a thiocyanae-isothiocyanate transformation. The second one presumes a carbonium ion formation.
The failure of the reaction involving \( \alpha \)-thiocyanoketones containing more than one phenolic hydroxy groups and the inability of 5-chloro-anthranilic acid to react with any hydroxy thiocyanoketone to yield thiopegans has been explained. The failure in case of 3-methyl anthranilic acid is believed to be due to the steric hinderance on account of the methyl group.

9:10-Thiopegan derivatives containing phenolic hydroxy groups have shown encouraging antibacterial properties especially against S. typhi, S. para typhi and Streptococcus haemolyticus (Appendix I page 147).

4-Keto-2-thio-tetrahydroquinazolines have been prepared by two new different methods and the mechanisms of the reactions explained. These have been condensed (as sodium salts) with various \( \alpha \)-haloketones to give 4-keto-3:4-dihydroquinazolyl-2-mercaptoacetophenones with a view to effect their cyclisation for obtaining 9:10 or 10:11-thiopegan derivatives. However, attempts at the ring closure have not succeeded so far.

Section B

1. 4-Imino-9:10-thiopega-2:10-diene hydrochloride and their 7-chloro derivatives have been synthesised for testing their antibacterial properties. This involves reacting of an ortho-amino-benzo-nitrile with \( \alpha \)-thiocyanoketones. Only angular products were obtained as confirmed by hydrolysis to the corresponding known 4-keto-9:10-thiopegans (Section A-1).
Some of the imino thiopegans tested have shown promising antibacterial results in vitro tests (Appendix I page 151).

ii. 4-Imino-2-thio-tetrahydroquinazoline has been synthesised by a new method of preparative value which also promises general applicability. It involves interaction of an ortho-amino benzo-nitrile with ammonium thiocyanate at 170-80°.

The imino tetrahydroquinazoline has been condensed with various α-haloketones to give 4-imino-3:4-dihydroquinazolyl-2-mercapto acetophenones. Attempts at their cyclisation would be made in due course.

iii. A novel method for securing an amino residue in position 4 of the 9:10-thiopegan structure has been discovered which enables a facile introduction of basic chains important for antimalarial and other biological properties. The reaction involves interaction between an ortho-amino Schiff base and an α-thiocyanoketone. These compounds are being tested for their physiological properties.

Section C.

i. A number of 10:11-thiopega 2:9-diene-4-ones have been synthesised by condensation of 2-chloro-thiazoles with anthranilic acids for therapeutic elaboration (70,81,82,110 and 111).

ii. Reaction between anthranilic acid and allyl isothiocyanate has been carried out which yields 3-allyl-4-keto-2-
thio-tetrahydroquinazoline which on treatment with HCl gives 2-methyl-10:11-thiopega-9-ene-4-one (cf. 119, 120, 121).

Further, 2-methylene-10:11-thiopega 9-ene-4-one has been synthesised which undergoes isomerisation to 2-methyl 10:11-thiopega-2:9-diene-4-one on mild treatment with sulphuric acid or alkalis, which is also obtained by reductive debromination of the bromo base obtained by bromination of the methylene thiopegan.

2-Bromo-methyl-10:11-thiopega-2:9-diene-4-one and its 6-methyl and 6-chloro derivatives have been condensed with various bases with a view to introduce the physiologically important basic moieties.

Superior pathways for certain intermediates mentioned above have also been discovered.

The various sets of the above reactions have been sequentially carried out starting with 5-chloro, 5-methyl and 4-methyl anthranilic acids with a view to obtain a number of compounds for biological testing.

PART II.

Section A

A convenient method, which leads to the facile production of 2-hydroxy thiazoles, has been developed (71-73). It entails heating of an \( \lambda \)-thiocyanoketone in acetic acid solution containing a little water and catalytic amounts of sulphuric acid. A mechanism for the reaction has been postulated.

These thiazoles have been used as authentic samples for comparison with some of these obtained as side reaction
products in few cases (Part I, Section A,1).

One compound, 2-hydroxy-4-(2'4'-dihydroxyphenyl)thiazole has shown encouraging antibacterial properties in in vitro tests. The other hydroxy thiazoles await testing.

Section B.

2-Chlorothiazoles have been synthesised by treatment of \( \alpha \)-thiocyanoketones with dry HCl at 5-10\(^\circ\) in a neutral solvent like ether.

A mechanism for the above reaction has been postulated which also explains the diminished tendency of \( \omega \)-thiocyanono-2:4-dimethyl aceto phenone and \( \omega \)-thiocyanono-2:5-dimethyl aceto phenone to yield the corresponding 2-chloro-thiazoles. The abnormal reaction products obtained in these cases are considered to be simple addition products of the thiocyanoketones with HCl which give rise to the corresponding amides on hydrolytic treatment. These are under further investigation.

These chlorothiazoles have been utilised as important intermediates for the synthesis of 10:11-thiopegan derivatives (Tables XI - XIV).

Part III.

2-Aryl-amino \( \Delta^2 \)-thiazolines have been synthesised through the cyclisation of the thiourea derivatives obtained by reacting various aromatic amines with allyl isothiocyanate.

One of these compounds, 2-(p-phenetidino)-5-methyl \( \Delta^2 \)-thiazoline has shown a high antitubercular activity (p.152) against Mycobacterium tuberculosis; it completely inhibits the growth of the strain H 37 RV at 1:800000 and partially at 1:6250000 in serum broth dilution. The other compounds of the series await testing.

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