CCCCXX.—*Trypanocidal Activity and Chemical Constitution. Part III. New Sulphur Derivatives of Aromatic Organic Arsenicals* (contd.). *Gold Derivatives of 2-Thiolbenziminazole-5-arsonic Acid.*

By JOHN GARWOOD EVERETT.

IT has already been shown that replacement of the hydrogen of the thiol group of 2-thiolbenziminazole-5-arsonic acid (I) by certain organic groups causes adverse modification of therapeutic activity

(I.) HS·C<N—NH>C$_6$H$_3$·AsO$_3$H$_2$ AuS·C<N—NH>C$_6$H$_3$·CO$_2$H (A.)

(Part II; J., 1930, 2402). The corresponding auromercaptides have now been studied.

Numeration.

R = general. R_1 = −C<N—NH>C$_6$H$_4$

R_2 = −C<N—NH>C$_6$H$_3$·AsO$_3$H$_2$ R_3 = −C<N—NH>C$_6$H$_3$·AsS$_2$

Non-arsenated compounds.	Arylarsonic acids.	Arylarsenic sulphides.
R_1·SAu (IV)	R_2·SAu (II)	R_3·SAu (IX)
R_1·SAu . . . R_1·SH (VII)	R_2H (III)	R_3·SAu . . . R_3·SH (X)
R_1·S·CH$_2$·CO$_2$H (VIII)	R_2·SAu . . . R_2·SH (V)	
	R_2·S·CH$_2$·CO$_2$H (VI)	

The compound (A), known as "triphal," has a certain vogue in the treatment of tuberculosis. The quantities taken in its preparation correspond to equimolecular proportions of 2-thiolbenziminazolecarboxylic acid and gold tribromide (E.P. 225,875/1924).

Equimolecular proportions of (I) and gold trichloride have now been shown to give 2-*aurothiolbenziminazole-5-arsonic acid* (II) and the *sulphate* of benziminazole-5-arsonic acid (III), the formation of the latter being due to oxidation of (I) by the liberated chlorine. This oxidation must proceed in two stages according to the following scheme, hydrolysis occurring at the intermediate sulphinic acid stage,

$$RSH \xrightarrow{Cl + H_2O} R{\cdot}SO_2H \xrightarrow{H_2O} RH + H_2SO_3 \xrightarrow{Cl + H_2O} RH,H_2SO_4$$

since 2-sulphobenziminazole-5-arsonic acid (R_2·SO$_3$H) is extremely resistant to hydrolysis (Part II, *loc. cit.*). When gold trichloride in excess of an equimolecular proportion was used, the excess was recovered unchanged, the arsonic acid (I) not forming a chloroaurate. 2-Aurothiolbenziminazole-5-arsonic acid (II) is *rapidly* soluble in sodium bicarbonate solution: the solution absorbs iodine extremely slowly [distinction from (V)].

The analogy with the non-arsenated compound was established by the production of 2-*aurothiolbenziminazole* (IV) and benziminazole sulphate from equimolecular proportions of 2-thiolbenziminazole and gold trichloride. In this case, when gold trichloride in excess of the equimolecular proportion was used, the benziminazole was recovered as chloroaurate, the sulphuric acid formed remaining in solution.

Zeise (*Ann. Physik*, 1834. **31**, 369) found the optimum conditions for formation of the auromercaptide to be represented by equation (1), as also did Hermann (*Ber.*, 1905, **38**, 2813), using benzyl and

$$(1)\ 3RSH + AuCl_3 = RS{\cdot}Au + RS{\cdot}SR + 3HCl$$

*iso*amyl mercaptans. The auromercaptides were amorphous, and Hermann identified the disulphide in the case of *iso*amyl mercaptan. Balaban and King (J., 1927, 1859), using derivatives of 2-thiolglyoxaline, found the optimum conditions to be represented by the same equation. They obtained amorphous auromercaptides of the type RS·Au, but were unable to isolate any disulphide, recovering instead the original mercaptan. In the present instance, three molecules of (I) and one molecule of gold trichloride yielded 5-*arsono*-2-*aurothiolbenziminazole*-5-*arsono*-2-*thiolbenziminazole* (V), the mother-liquors giving unchanged 2-thiolbenziminazole-5-arsonic acid (I) and a small amount of the *sulphate* of benziminazole-5-arsonic acid (III). The constitution of (V) was shown as follows :—

(a) On treatment with excess of chloroacetic acid it gave (II), together with 2-carboxymethylthiolbenziminazole-5-arsonic acid (VI). Only one molecule of chloroacetic acid could be made to react.

$$(2)\ RSAu \ldots RSH + CH_2Cl{\cdot}CO_2H = RS{\cdot}Au + RS{\cdot}CH_2{\cdot}CO_2H + HCl$$

(b) On treatment with iodine in presence of excess of sodium bicarbonate solution, one molecule of (V) rapidly absorbed four atoms of iodine, with formation of (II) and (III). Beyond this point absorption of iodine was exceedingly slow. Four atoms of iodine are necessary to oxidise one 2-thiolbenziminazole residue to benziminazole (Part I; J., 1929, 678). These two reactions show clearly that one free thiol group is present.

$$(3)\ RSAu \ldots RSH + 4I \longrightarrow RS{\cdot}Au + RH$$

(c) Further, equimolecular proportions of (I) and (II) combined readily to give (V) when a solution of them in aqueous sodium bicarbonate was acidified and boiled. Since (V) so obtained was a white homogeneous crystalline solid, whereas the auromercaptide (II) is deep olive-green and amorphous, the possibility of a mechanical mixture is precluded. The auromercaptide (II) breaks down when

boiled with moderately concentrated hydrochloric acid, half the gold being liberated as metal, with formation of (V).

$$(4)\ 2RS{\cdot}Au \xrightarrow{HCl} RS{\cdot}Au\ .\ .\ .\ RSH + Au$$

In (c) above, no gold was liberated, the yield of (V) agreeing with equation (5), hence the formation of (V) is due to co-ordination of

$$(5)\ 2RS{\cdot}Au + 2RSH = 2(RSAu\ .\ .\ .\ RSH)$$

(I) and (II), and not to decomposition of the auromercaptide (II) according to equation (4).

Both the arsenated and the non-arsenated auromercaptide (II) and (IV) readily break down with hydrochloric acid according to equation (4), a small amount of the *sulphate* of the corresponding cyclic amidine (RH,H_2SO_4) being also produced in each case. In sharp contrast to this is the extreme stability of both the arsenated and the non-arsenated co-ordination compound (V) and (VII), both of which recrystallise unchanged after prolonged boiling with 1 : 1 hydrochloric acid. This difference in stability makes it probable that the initial stage in equation (4) is complete breakdown of two molecules of auromercaptide to disulphide and gold. This is probably

$$(6)\ 2RS{\cdot}Au = RS{\cdot}SR + 2Au$$

followed by hydrolysis of the disulphide according to equation (7) (compare Balaban and King, *loc. cit.*; Otto and Schiller, *Ber.*, 1876,

$$(7)\ 2RS{\cdot}SR + 2H_2O = 3RSH + RH + SO_2$$

9, 1589), the sulphur dioxide reducing a further portion of disulphide to mercaptan. Co-ordination of the mercaptan and unchanged auromercaptide then takes place, with formation of (V) or (VII). The formation of the co-ordination compound (V) from three molecules of (I) and one molecule of gold trichloride is similarly explained. The auromercaptide and disulphide are formed by the initial reaction represented by equation (1). The concentration of acid being insufficient to decompose the auromercaptide, no metallic gold is formed in this case.

5-Arsono-2-aurothiolbenziminazole-5-arsono-2-thiolbenziminazole (V) is *slowly* soluble in sodium bicarbonate solution; this solution rapidly absorbs iodine [distinction from (II)].

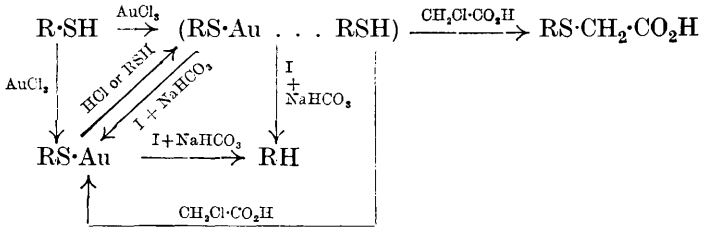
The analogy with the non-arsenated compound was established by the preparation of 2-*aurothiolbenziminazole*-2-*thiolbenziminazole* (VII) in a similar manner. Its constitution was shown in the same way, excess of chloroacetic acid giving 2-aurothiolbenziminazole (IV) and 2-carboxymethylthiolbenziminazole (VIII), and iodine and excess of sodium bicarbonate giving (IV) and benziminazole.

A molecular-weight determination by Barger's microscopical

method (J., 1904, **85**, 286) showed that a solution containing 25 g. per litre in ethyl alcohol (maximum solubility) is isotonic with a 0·105*M*-solution of azobenzene in the same solvent. The molecular weight is therefore 25/0·105 = 238. Half the calculated molecular weight is 248, so that the compound appears to be completely dissociated under these conditions. This result was unexpected, but fits in well with the modern theory of co-ordination compounds, the solid substance most likely consisting of a close-packed arrangement of RSH and RSAu *ions* (compare *Ann. Reports*, 1927, p. 282). As a check on the method a similar determination was carried out with 2-thiolbenziminazole, the result giving 143 as the molecular weight of this substance (calc., 150).

Co-ordination compounds of the type (RSAu . . . RSH) do not appear to be formed in the glyoxaline series (compare Balaban and King, *loc. cit.*).

The foregoing reactions are summarised as follows :—



Gold Derivatives of Arylarsenic Sulphides.—*2-Aurothiolbenziminazole-5-arsenic disulphide* (IX) was prepared by passing hydrogen sulphide into a suspension of 2-aurothiolbenziminazole-5-arsonic acid (II) in cold water. The co-ordinated *2-aurothiolbenziminazole-5-arsenic disulphide-2-thiolbenziminazole-5-arsenic disulphide* (X) was obtained by dissolving the co-ordinated arsonic acid (V) in boiling hydrochloric acid (1 : 1), passing hydrogen sulphide into the nearly boiling solution, and treating the precipitate with sodium bicarbonate. It was an amorphous yellow powder which on treatment with iodine and water regenerated the co-ordinated arsonic acid (V).

Therapeutic Results.—The above-mentioned compounds have been tested against an experimental infection of *T. equiperdum* in mice with the following results : *T* = maximum tolerated dose in mg./g. of mouse; *C* = minimum curative dose in mg./g. of mouse, and is the smallest single dose which will cause the disappearance of all trypanosomes from the peripheral blood stream of all eight mice within 72 hours; *r* = average number of days elapsing between disappearance and reappearance of trypanosomes in the peripheral blood-stream; *i* = intravenous; *o* = oral.

			C		
Arylarsenic Sulphides.		T.	(8 mice).	T/C.	r.
2-Thiolbenziminazole-5-arsenic disulphide, R_3·SH	*i*	0·05	0·006	8·0	>30
	o	10·0	0·2	50·0	14
2-Aurothiolbenziminazole-5-arsenic disulphide (IX), R_3·SAu	*i*	0·05	0·005	10·0	5
	o	>5·0	0·4	>12·0	12
2-Aurothiolbenziminazole-5-arsenic disulphide-2-thiolbenziminazole-5-arsenic disulphide (X), (R_3·SAu . . . R_3·SH)	*i*	0·025	0·005	5·0	6
	o	>5·0	0·025	>200·0	11
Arylarsonic Acids.					
2-Thiolbenziminazole-5-arsonic acid (I), R_2·SH	*i*	0·5	0·5	1·0	>30
	o	10·0	0·1	100·0	15
2-Aurothiolbenziminazole-5-arsonic acid (II), R_2·SAu	*i*	0·125	0·1	1·25	5
	o	>5·0	0·1	>50·0	7
5-Arsono-2-aurothiolbenziminazole-5-arsono-2-thiolbenziminazole (V), R_2·SAu . . . R_2·SH	*i*	0·25	0·05	5·0	>30
	o	10·0	0·1	100·0	6
Non-arsenated Compounds.					
2-Thiolbenziminazole, R_1·SH	*i*	0·1	>0·1(0)	<1·0	—
	o	1·0	>1·0(0)	<1·0	—
2-Aurothiolbenziminazole (IV), R_1·SAu	*i*		insoluble		
	o	0·25	>0·25(0)	<1·0	—
2-Aurothiolbenziminazole-2-thiolbenziminazole (VII), R_1·SAu . . . R_1·SH	*i*	0·01	>0·01(0)	<1·0	—
	o	0·5	>0·5 (0)	<1·0	—

Conclusions.—The very marked therapeutic activity of the co-ordinated arylarsenic disulphide (X), when administered orally, is the only outstanding feature. The introduction of gold causes increased toxicity when administered intravenously, which is compensated by increased therapeutic activity. The toxicity remains practically unaltered in oral administration, as does therapeutic activity, with the one exception mentioned above. The non-arsenated gold compounds were all inactive.

The author is indebted to Dr. Levaditi, of the Pasteur Institute, for kindly testing the gold arsenical (V) against *B. Tuberculosis*. It was quite inactive.

Experimental.

2-Aurothiolbenziminazole-5-arsonic Acid (II).—(1) 2-Thiolbenziminazole-5-arsonic acid (2·74 g.) was boiled with water (600 c.c.) till dissolved, and gold trichloride (3 g.) in water (25 c.c.) added gradually to the hot solution. The precipitated acid (II), which was at first brown, then white, and finally green, was removed by filtration, the filtrate being retained (A). It was washed well with water, and dried in a vacuum over sulphuric acid, forming a shining black cake, which was olive-green when powdered. Traces of metallic gold were removed by dissolution in sodium bicarbonate solution, filtration, reacidification, and drying as before (yield, 3·5 g.) (Found : As, 15·0; N, 5·6; S, 6·3; Au, 40·3; loss at 120°, 4·7. $C_7H_6O_3N_2SAsAu,1\frac{1}{4}H_2O$

requires As, 15·2; N, 5·7; S, 6·5; Au, 40·0; H_2O, 4·6%). The dried acid may be heated to 120° without decomposition. The damp, freshly prepared acid liberates gold when heated.

The filtrate (A) after concentration gave a syrupy residue, which crystallised on being scratched and was then stirred with cold alcohol, dried at 100°, and proved to be the sulphate of benziminazole 5-arsonic acid (III), m. p. and mixed m. p. 210°, with preliminary softening at 190° (yield, 0·6 g.; calc. 0·885 g.) (Found: As, 22·0; N, 8·2; S, 9·5%).

(2) 5-Arsono-2-aurothiolbenziminazole-5-arsono-2-thiolbenziminazole (V) (1·86 g.) was dissolved in water (10 c.c.) and 2*N*-sodium hydroxide (6·4 c.c.). Chloroacetic acid (0·5 g.) in water (5 c.c.) containing sufficient sodium hydroxide to neutralise it was added, and the solution boiled gently for 2 hours, water being added as required. The development of acidity could not be followed owing to the excess of sodium hydroxide necessary for solution. The solution was cooled, filtered (charcoal), and made distinctly acid (Congo-red) with hydrochloric acid. 2-Aurothiolbenziminazole-5-arsonic acid (II) was precipitated as a yellow mass, which changed slowly to olive-green. It was removed by filtration, the filtrate being retained (A), and treated as in (1) above (yield, 1 g.) (Found: As, 15·1; N, 5·6; S, 6·5; Au, 40·2; loss at 120°, 4·3%).

The filtrate (A) was filtered (charcoal) and made just acid (Congo-red) by addition of sodium hydroxide solution; 2-carboxymethylthiolbenziminazole-5-arsonic acid (VI) crystallised slowly (yield, 0·63 g.) (Found: As, 22·5; N, 8·4; S, 9·8. Calc.: As, 22·6; N, 8·5; S, 9·7%. Compare Part II, *loc. cit.*).

(3) 5-Arsono-2-aurothiolbenziminazole-5-arsono-2-thiolbenziminazole (V) (3·71 g.) was dissolved in water (25 c.c.) containing an excess of sodium bicarbonate (20 g.), and *N*/2-iodine (40 c.c.) was added, which was absorbed rapidly. The solution was made just acid (Congo-red) with hydrochloric acid, the precipitated 2-aurothiolbenziminazole-5-arsonic acid (II) being removed and the filtrate retained (A). The precipitate (II) was treated with sodium bicarbonate solution, filtered from the deposited gold (0·2 g.), reacidified, and dried as in (1) above (yield, 1·5 g.) (Found: As, 15·0; N, 5·7; S, 6·4; Au, 40·5; loss at 120°, 4·8%).

The filtrate (A), after removal of deposited gold (0·115 g.), was evaporated to low bulk and filtered (charcoal), benziminazole-5-arsonic acid (III) crystallising slowly (yield, 0·6 g.) (Found in acid dried at 80°: As, 31·0; N, 11·4. Calc.: As, 31·0; N, 11·5%).

The total amount of metallic gold obtained was 0·315 g. This is formed owing to the relatively very slow reaction between iodine and the auromercaptide (II) (see below). The yield of (II) obtained

(1·5 g.) leaves 0·85 g. unaccounted for. This would react with iodine to give 0·3563 g. of gold, agreeing fairly closely with that actually obtained.

2-Aurothiolbenziminazole-5-arsonic acid (II) prepared by the above three methods was an olive-green amorphous powder insoluble in water or organic solvents.

Treatment of (II) *with Hydrochloric Acid.*—2·82 G. were boiled with hydrochloric acid (1 : 6; 200 c.c.) for 10 minutes, the deposited gold removed, and the filtrate retained (A). The precipitated gold was boiled with dilute sodium hydroxide solution, collected on a Gooch crucible, washed, ignited, and weighed (yield, 0·58 g.; calc., 0·591 g.). The filtrate was acidified with hydrochloric acid and added to (A); 5-arsono-2-aurothiolbenziminazole-5-arsono-2-thiolbenziminazole (V) was deposited on cooling (yield, 1·9 g.) (Found in acid dried at 80° : As, 19·6; N, 7·4; S, 8·6; Au, 26·0; loss at 120°, 2·3%). In a separate experiment the filtrate (A) was worked up without the gold washings. After removal of (V), the mother-liquors were evaporated to dryness and the residue was treated with alcohol. The sulphate of benziminazole-5-arsonic acid (III) remained (0·08 g.; m. p. 210° with preliminary softening at 190°).

Treatment of (II) *with Sodium Hydroxide Solution.*—1 G. was boiled under reflux with sodium hydroxide solution (25%, 50 c.c.) for 5 hours, the deposited gold removed, and the filtrate retained (A). The precipitated gold was treated [illegible]
0·19 g.; calc., 0·2096 g.). The filtrate (A) was [illegible] hydrochloric acid, 5-arsono-2-aurothiolbenziminazole-5-arsono-2-thiolbenziminazole (V) being deposited (yield, 0·65 g.) (Found in acid dried at 80° : As, 19·6; S, 8·5; Au, 26·1; loss at 120°, 2·2%).

Treatment of (II) *with Iodine.*—1·2 G. were dissolved in water (5 c.c.) containing excess of sodium bicarbonate (10 g.) and *N*/2-iodine (20 c.c.) was added gradually in portions of 1 c.c. The first 3 c.c. were absorbed in about 1 hour, absorption of the whole 20 c.c. occupying about 24 hours. The liquor was decanted (A), and the residue of gold and sodium bicarbonate treated with a large volume of water. The residue of gold was boiled with dilute sodium hydroxide solution, collected on a Gooch crucible, washed, ignited, and weighed (yield, 0·475 g.; calc. for $RSAu + 4I \longrightarrow RH + Au$, 0·4925 g.). The liquor (A) was concentrated and made just acid (Congo-red) with hydrochloric acid; benziminazole-5-arsonic acid (0·2 g.) was slowly precipitated (m. p. of sulphate, 209° with preliminary softening at 190°).

The Sulphate of Benziminazole-5-arsonic Acid.—A solution of benziminazole-5-arsonic acid (1·2 g.) in water (10 c.c.) containing sulphuric acid (0·5 g.) was filtered and evaporated to dryness; the

residual thick syrup crystallised on being scratched. It was treated with alcohol, recrystallised from water, and dried at 100°; m. p. 210° with preliminary softening at 190° (Found: As, 22·0; N, 8·1; S, 9·5. $C_7H_7O_3N_2As,H_2SO_4$ requires As, 22·1; N, 8·2; S, 9·4%).

2-*Aurothiolbenziminazole* (IV).—(1) 2-Thiolbenziminazole (1·5 g.) was boiled with water (300 c.c.) till dissolved, and gold trichloride (3 g.) in water (25 c.c.) added gradually to the hot solution. The precipitated 2-aurothiolbenziminazole (IV) was removed, the filtrate retained (A), and the precipitate treated with dilute sodium hydroxide solution, re-washed, and dried in a vacuum over sulphuric acid. Decomp. 235° (yield, 2·5 g.) (Found: N, 8·0; S, 9·3; Au, 57·2. $C_7H_5N_2SAu$ requires N, 8·1; S, 9·2; Au, 56·9%). The filtrate (A), after removal of further traces of (IV), was evaporated to dryness; the residue consisted of benziminazole sulphate, m. p. 165° (alone or mixed with an authentic specimen) (yield, 0·5 g.; calc., 0·6 g.).

In a second experiment excess of gold trichloride (4 g.) was used. The yield of (IV) was again 2·5 g. The filtrate (A) was evaporated to dryness, traces of gold which separated being removed during the concentration. The yellow residue was extracted with ether, giving gold trichloride (0·3 g.). The still yellow residue was extracted with alcohol, giving yellow prisms of benziminazole chloroaurate (0·6 g.), m. p. 204° (alone or mixed with an authentic specimen). The final residue was white and soluble in water; the solution gave a strong reaction for sulphate.

(2) A solution of 2-aurothiolbenziminazole-2-thiolbenziminazole (VII) (2·5 g.) in water (25 c.c.) and 2*N*-sodium hydroxide (30 c.c.) was treated with chloroacetic acid (0·94 g.) in water (12 c.c.) and sodium hydroxide as in the case of the non-arsenated analogue. The precipitated 2-aurothiolbenziminazole (IV) was treated as in (1) above (yield, 1·6 g.); decomp. 234° (Found: N, 8·2; S, 9·3; Au, 57·1%). The filtrate was filtered (charcoal) and made just acid (Congo-red) by addition of sodium hydroxide solution. 2-Carboxymethylthiolbenziminazole (VIII), which crystallised at once (1·0 g.), was recrystallised from 50% alcohol; m. p. 190° with preliminary softening at 140° (alone or mixed with an authentic specimen) (Found in acid dried at 80°: N, 12·3; S, 14·2; loss at 110°, 7·8%).

(3) 2-Aurothiolbenziminazole-2-thiolbenziminazole (VII) (2·48 g.) was dissolved in cold ethyl alcohol (400 c.c.) and water (250 c.c.). Sodium bicarbonate (40 g.) was added, followed by *N*/2-iodine (40 c.c.), added gradually with shaking, and more water at intervals to hasten absorption, which was complete after several hours. The slow absorption was due to presence of alcohol. After filtration, the filtrate was retained (A), and the precipitate treated with much

water to remove sodium bicarbonate. The residue was 2-aurothiolbenziminazole (IV), which was treated as in (1) above (yield, 1·1 g.); decomp. 235° (Found: N, 8·0; S, 9·4; Au, 57·2%).

The filtrate (A) was evaporated to dryness, unchanged initial material (VII) and metallic gold being removed during the concentration. The white residue was treated with just enough water to dissolve the salts, benziminazole (0·4 g.) remaining undissolved. It was recrystallised from dilute alcohol; m. p. 170°. M. p. of chloroaurate, 204°. (Owing to its insolubility, 2-aurothiolbenziminazole does not react with iodine in presence of sodium bicarbonate.)

2-*Aurothiolbenziminazole* (IV) prepared by the above three methods was a brown amorphous powder insoluble in water, organic solvents or sodium hydroxide solution.

Treatment of 2-*Aurothiolbenziminazole* (IV) *with Hydrochloric Acid.*—2·1 G. were boiled with hydrochloric acid (200 c.c.; 1 : 6) for 10 minutes, the deposited gold was removed, and the filtrate retained (A). The gold was boiled with dilute sodium hydroxide solution, washed, ignited, and weighed (yield, 0·572 g.; calc., 0·591 g.). The filtrate was acidified and added to (A), the precipitate which formed on cooling was removed, and the filtrate retained (B). The precipitate was treated with cold dilute sodium hydroxide solution; 0·1 g. of 2-aurothiolbenziminazole, decomp. 230°, remained undissolved (Found: Au, 56·2%). The filtrate was acidified, giving 2-aurothiolbenziminazole-2-thiolbenziminazole (VII) (1·1 g.) (Found: S, 12·8; Au, 39·6%). The filtrate (B) was filtered (charcoal) and evaporated to dryness, the residue dissolved in a little water, and the filtered solution neutralised with sodium bicarbonate; benziminazole (0·05 g.) slowly crystallised, m. p. 170° (alone or mixed with an authentic specimen).

Treatment of (IV) *with Sodium Hydroxide Solution.*—1 G. was boiled under reflux with sodium hydroxide solution (25%, 50 c.c.) for 5 hours. No reaction occurred, (IV) being recovered unchanged.

5-*Arsono*-2-*aurothiolbenziminazole*-5-*arsono*-2-*thiolbenziminazole* (V).—(1) 2-Thiolbenziminazole-5-arsonic acid (4·93 g.) was dissolved in boiling water (1500 c.c.), and gold trichloride (1·82 g.) in water (30 c.c.) added gradually. An immediate white precipitate formed, which was removed from the hot solution, the filtrate being retained (A). It was purified by solution in sodium bicarbonate and reprecipitation (yield, 4·4 g.) (Found in acid dried at 80°: As, 19·5; N, 7·4; S, 8·3; Au, 26·0; loss at 120°, 2·4. $C_{14}H_{13}O_6N_4S_2As_2Au,H_2O$ requires As, 19·7; N, 7·3; S, 8·4; Au, 25·8; H_2O, 2·4%).

The filtrate (A) was evaporated to dryness, the residue (B) extracted with water, and the extract evaporated to dryness. This gave a sticky material, which was treated with cold alcohol; the

sulphate of benziminazole-5-arsonic acid (III) (0·1 g.) remained undissolved, m. p. 210°, softening at 190°. The combined filtrates gave with barium chloride 0·25 g. of barium sulphate. The remainder of the residue (B) (insoluble in water) was extracted with dilute hydrochloric acid; benziminazole-5-arsonic acid crystallised slowly from the neutralised extract (0·2 g.; m. p. of sulphate, 210°, softening at 190°). The ultimate remainder of residue (B) was dissolved in sodium bicarbonate solution, filtered (charcoal), and reacidified, yielding 2-thiolbenziminazole-5-arsonic acid (I) (1 g.) (Found in acid dried at 80°: As, 27·3; N, 10·2; S, 11·9. Calc.: As, 27·4; N, 10·2; S, 11·7%).

(2) By treatment of 2-aurothiolbenziminazole-5-arsonic acid with hydrochloric acid. See under (II).

(3) By treatment of 2-aurothiolbenziminazole-5-arsonic acid with sodium hydroxide solution. See under (II).

(4) *By direct co-ordination.* 2-Aurothiolbenziminazole-5-arsonic acid (1·18 g.) and 2-thiolbenziminazole-5-arsonic acid (0·69 g.) were dissolved together in water (100 c.c.) and sufficient sodium bicarbonate. The solution was filtered (charcoal), acidified (Congo-red) with hydrochloric acid, and boiled, the precipitated acid (V) coagulating to form masses of long white threads. Water (50 c.c.) and hydrochloric acid (25 c.c.) were immediately added and the whole was boiled, solution occurring. On cooling, (V) crystallised in long white prisms (1·7 g.) (Found in acid dried at 80°: As, 19·6; N, 7·4; S, 8·5; Au, 25·9: loss at 120°, 2·4%).

5-Arsono-2-aurothiolbenziminazole-5-arsono-2-thiolbenziminazole (V) obtained by the above four methods consisted of long white prisms (or matted white threads) insoluble in water or alcohol. It was *slowly* soluble in sodium bicarbonate solution, the solution rapidly absorbing iodine (distinction from II). It was readily soluble in cold dilute sodium hydroxide solution, and moderately easily soluble in boiling hydrochloric acid (1 : 1), crystallising unchanged on cooling. It was stable towards mineral acids and alkalis, but was decomposed by chloroacetic acid and by oxidising agents, which attack the thiol half of the molecule.

2-Aurothiolbenziminazole-2-thiolbenziminazole (VII).—(1) 2-Thiolbenziminazole (2·7 g.) in boiling water (500 c.c.) was treated with gold trichloride (1·82 g.) in water (30 c.c.). The precipitate was removed, dissolved in cold dilute sodium hydroxide solution, reprecipitated, dried at 80°, and crystallised twice from alcohol, forming slender white prisms (2·4 g.), softening and shrinking at 193° (Found: N, 11·2, 11·4; S, 12·9, 12·8; Au, 39·9, 39·8. $C_{14}H_{11}N_4S_2Au$ requires N, 11·3; S, 12·9; Au, 39·7%).

The original filtrate was evaporated to dryness, the residue

extracted with water, and the extract evaporated to dryness. This gave benziminazole sulphate (0·2 g.), m. p. 165°. The remainder of the residue (insoluble in water) was extracted with dilute hydrochloric acid; benziminazole (0·03 g.), m. p. 170°, crystallised from the neutralised extract. The ultimate remainder of residue was dissolved in sodium hydroxide solution, filtered (charcoal) and reacidified, giving 2-thiolbenziminazole (0·5 g.), m. p. 296° (Found : N, 18·6; S, 21·4. Calc. : N, 18·7; S, 21·3%).

(2) By treatment of 2-aurothiolbenziminazole with hydrochloric acid. See under (IV).

(Direct co-ordination experiments were unsuccessful, owing to the insolubility of 2-aurothiolbenziminazole.)

2-*Aurothiolbenziminazole-2-thiolbenziminazole* (VII) obtained by the above two methods consisted of long white prisms (or matted white threads), softening and shrinking at 193°. It was readily soluble in cold dilute sodium hydroxide solution and sparingly soluble in boiling 1 : 1 hydrochloric acid, recrystallising unchanged on cooling. It was moderately easily soluble (2·5%) in alcohol but insoluble in benzene. It resembled (V) in its behaviour towards mineral acids, alkalis, chloroacetic acid, and oxidising agents.

2-*Carboxymethylthiolbenziminazole* (VIII) (compare Stephen and Wilson, J., 1926, 2531; 1928, 1420).—A solution of 2-thiolbenziminazole (1·5 g.) and chloroacetic acid (0·94 g.) in water (4 c.c.) and sufficient 2*N*-sodium hydroxide was boiled gently for 1 hour, filtered (charcoal), and made just acid (Congo-red) with hydrochloric acid. The precipitated acid, recrystallised from 50% alcohol and dried at 80°, formed bunches of white prisms (1·8 g.), m. p. 190° with preliminary softening at 140° (Found : N, 12·3; S, 14·3; loss at 110°, 8·1. Calc. : N, 12·4; S, 14·2; $1H_2O$, 8·0%). It was moderately easily soluble in hot water or alcohol and readily soluble in 50% alcohol and in sodium bicarbonate solution. The last solution did not absorb iodine, showing that the $CH_2 \cdot CO_2H$ group is attached to sulphur and not to nitrogen. The acid was readily soluble in dilute mineral acids. After being dried to constant weight at 110°, it melted at 190° without preliminary softening, this being due to sudden loss of water at 140°.

2-*Aurothiolbenziminazole-5-arsenic Disulphide* (IX).—2-Aurothiolbenziminazole-5-arsonic acid (II) (2·35 g.) was suspended in water (200 c.c.), and hydrochloric acid (25 c.c.) added. Hydrogen sulphide was passed for 30 minutes into the cold suspension, which was then kept for 12 hours. The precipitate was washed, pressed on a porous plate, and air-dried, 2-*aurothiolbenziminazole-5-arsenic disulphide* thus being obtained as a brown amorphous powder, readily soluble in dilute sodium hydroxide solution (yield, 2·4 g.) (Found : As, 14·7;

N, 5·5; S, 19·3; Au, 39·4; loss at 120°, 4·0. $C_7H_4N_2S_3AsAu,H_2O$ requires As, 14·9; N, 5·6; S, 19·1; Au, 39·2; H_2O, 3·6%).

2-*Aurothiolbenziminazole*-5-*arsenic Disulphide*-2-*thiolbenziminazole*-5-*arsenic Disulphide* (X).—5-Arsono-2-aurothiolbenziminazole-5-arsono-2-thiolbenziminazole (V) (2·5 g.) was dissolved in boiling hydrochloric acid (1 : 1; 700 c.c.), and hydrogen sulphide passed in for 10 minutes. The yellow precipitate was washed with water and dried at 60°. Several repetitions always gave a product containing 4·0—5·0% of hydrochloric acid. This monohydrochloride was treated with sodium bicarbonate solution and dried at 60° (yield, 2·5 g.) (Found : As, 19·3; N, 7·0; S, 25·0; Au, 26·0. $C_{14}H_9N_4S_6As_2Au$ requires As, 19·4; N, 7·2; S, 24·9; Au, 25·5%). 2-*Aurothiolbenziminazole*-5-*arsenic disulphide*-2-*thiolbenziminazole*-5-*arsenic disulphide* (X) so obtained was a yellow, amorphous powder, readily soluble in dilute sodium hydroxide solution. On treatment with iodine and water the mercaptan sulphur was not removed (Part I; J., 1929, 672), the product being the co-ordinated arylarsonic acid (V).

Treatment of (X) *with Iodine and Water.*—The disulphide (X) (2·6 g.) was stirred with water, *N*/2-iodine being added till no more was absorbed (35 c.c.). A solution of the precipitate in aqueous sodium bicarbonate was filtered (charcoal) and acidified (Congo-red) with hydrochloric acid. 5-Arsono-2-aurothiolbenziminazole-5-arsono-2-thiolbenziminazole (V) crystallised at once in long white threads (1·8 g.) (Found in acid dried at 80° : As, 19·5; N, 7·3; S, 8·5; Au, 25·6; H_2O, 2·2%).

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