99. *Arsonic and Stibonic Acids derived from Quinoline and Acridine. Part I.*

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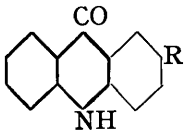
FOR the preparation of 3-aminoacridone (I, R = NH_2) in moderately large quantities the following two methods were found suitable: (1) 4'-Nitrodiphenylamine-2-carboxylic acid (Goldberg, *Ber.*, 1906, **39**, 1691) is reduced by ferrous sulphate and ammonia, and the resulting 4'-aminodiphenylamine-2-carboxylic acid heated with 96% sulphuric acid at 100° (Ullmann and Bader, *Annalen*, 1907, **355**, 335). (2) Condensation of *o*-bromobenzoic acid and *p*-aminoacetanilide in amyl-alcoholic solution in presence of potassium carbonate and copper powder yields *4'-acetamidodiphenylamine-2-carboxylic acid*, from which 3-aminoacridone is readily obtained by treatment with 96% H_2SO_4 at 100°.

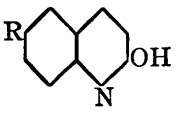
3-Aminoacridone is converted into *acridone-3-arsonic acid* (I, R = AsO_3H_2) by the Bart reaction under appropriate conditions, and into *acridone-3-stibonic acid* (I, R = SbO_3H_2) under the conditions described by Morgan and Cook (J., 1930, 743).

* Wieland and Wiedersheim do not record a m. p. for this acid; our product did not depress the m. p. of a specimen, m. p. 186°, very kindly supplied by Professor Wieland.

By similar methods, 6-amino-2-hydroxyquinoline (II, R = NH_2) yields *2-hydroxyquinoline-6-arsonic acid* (II, R = AsO_3H_2) (compare Balaban, J., 1930, 2350) and *2-hydroxyquinoline-6-stibonic acid* (II, R = SbO_3H_2).

The chemotherapeutic action of these organo-metallic compounds is being investigated.

(I.) 



(II.)

Experimental.

4'-Aminodiphenylamine-2-carboxylic Acid (compare Ullmann and Bader, *loc. cit.*).—To a hot solution of 4'-nitrodiphenylamine-2-carboxylic acid (38 g.) (Goldberg, *loc. cit.*) in 1 l. of water containing aqueous ammonia (150 c.c.; *d* 0·88), was added ferrous sulphate (252 g.) in 1 l. of water containing 1 c.c. of concentrated sulphuric acid. After 2 hours' heating on the water-bath and 15 minutes' boiling, the liquid was filtered hot, and the residue extracted thrice with dilute aqueous ammonia. 4'-Aminodiphenylamine-2-carboxylic acid was precipitated from the combined pale blue filtrates at its isoelectric point by the addition of dilute hydrochloric acid. The well-washed purplish-white precipitate, which readily oxidised on heating, was dried to constant weight in a vacuum desiccator. It had m. p. 195° (recrystallised from xylene, m. p. 204°) and was pure enough for conversion into 3-aminoacridone by Ullmann and Bader's method (*loc. cit.*). Yield, 26 g.

4'-Acetamidodiphenylamine-2-carboxylic Acid.—*o*-Bromobenzoic acid (40 g.), mixed with *p*-aminoacetanilide (30 g.), potassium carbonate (30 g.), and copper powder (0·2 g.), was heated under reflux in 200 c.c. of amyl alcohol at 155° for 4 hours. The amyl alcohol was then removed in steam, the cooled solution neutralised with dilute hydrochloric acid, and the dark purple precipitate washed acid-free and dried on the water-bath (yield, 49·2 g.). Recrystallised from alcohol and thrice from xylene, the *acid* formed creamy-white needles, m. p. 240° (Found: N, 10·4. $C_{15}H_{14}O_3N_2$ requires N, 10·4%). It was readily soluble in alcohol, acetone, ether, and acetic acid, moderately soluble in hot xylene, and almost insoluble in benzene, water, and ligroin.

3-Aminoacridone.—The preceding acid (40·5 g.) was heated with 200 c.c. of 96% sulphuric acid at 100°. After 3 hours, when an intense blue-green fluorescence had developed, the mixture was poured on ice (400 g.) and the whole was reheated for 2 hours to effect complete hydrolysis of the acetamido-group. On cooling and partial neutralisation, grey-green crystals of 3-aminoacridone sulphate separated. A small quantity of the base was obtained by complete neutralisation of the mother-liquor. Yield of crude aminoacridone, 29·2 g.; m. p. 290°, and 297° after recrystallisation from alcohol.

Acridone-3-arsonic Acid.—A solution of 3-aminoacridone (2·1 g.) in hot hydrochloric acid (4·5 c.c.; *d* 1·19) was cooled below 0° and slowly treated with sodium nitrite (0·8 g. in 4 c.c. of water), the greenish hydrochloride being replaced by bright yellow crystals of the diazo-compound. After 30 minutes, the solution was neutralised at 0° with 5*N*-sodium hydroxide, and 13 c.c. of a solution [containing arsenious oxide (1·5 g.) in 5*N*-sodium hydroxide (3 c.c.) and sodium carbonate (3 g.) in water (9 c.c.), plus 0·3 c.c. of a 10% $CuSO_4,4NH_3,H_2O$ solution (Slater, J., 1930, 1211)] were added, nitrogen being evolved. After remaining over-night at room temperature, the mixture was heated at 40° for a short time, the liquid filtered warm, and the residue extracted thrice with hot 5% sodium hydroxide solution. The combined filtrates, which exhibited an intense purplish-blue fluorescence, were brought to about p_H 3·5; the acid then precipitated was purified by repeated solution in and reprecipitation from cold dilute sodium carbonate solution. Yield, 1·33 g. (Found: As, 22·8. $C_{13}H_{10}O_4NAs$ requires As, 23·5%).

Acridone-3-arsonic acid forms a yellow amorphous powder which remains unmelted at 400°. It is slightly soluble in boiling acetic acid and in cold concentrated hydrochloric acid, but very soluble in concentrated sulphuric acid. The fluorescence in the last two solutions and in concentrated aqueous sodium hydroxide is bluish-green.

Yellow mercury, calcium, lead, barium, and magnesium salts, a greenish-yellow copper salt and a brown ferric salt were prepared from neutral solutions of the ammonium salt. Only the magnesium salt was crystalline.

Acridone-3-stibonic Acid.—3-Aminoacridone (2·1 g.) was diazotised as above, and the

diazo-mixture added slowly together with 6*N*-sodium hydroxide (5 c.c.) to an ice-cold sodium antimonite solution prepared from antimony chloride (3·3 g.), 5*N*-hydrochloric acid (5 c.c.), and glycerol (5 c.c.), 6*N*-sodium hydroxide being added until the precipitated material redissolved. After dilution with water (200 c.c.), the whole was kept over-night and the solid was then collected and the stibonic acid extracted from it with hot 6*N*-sodium hydroxide, reprecipitated with acetic acid, converted into the chloride, and regenerated by solution in dilute sodium hydroxide solution and reprecipitation by acetic acid (Found: Sb, 33·1. $C_{13}H_{10}O_4NSb$ requires Sb, 33·3%). *Acridone-3-stibonic acid* formed a light brown, amorphous powder, unmelted at 400°. Its solutions in aqueous sodium hydroxide and carbonate show a weak purple-blue fluorescence. White gelatinous calcium and magnesium salts, a yellowish-green amorphous copper salt, and a yellow amorphous ferric salt were prepared.

2-Hydroxyquinoline-6-arsonic Acid.—6-Amino-2-hydroxyquinoline (1·6 g.) was diazotised, and the neutralised solution treated with the arsenite–copper mixture as in the preparation of acridone-3-arsonic acid. After standing over-night, the whole was heated on the water-bath, the solution filtered hot, and the residue extracted with hot 5% sodium hydroxide solution. The gelatinous precipitate obtained on neutralising the extracts was removed, and the filtrate evaporated to 50 c.c. The whitish-yellow crystalline precipitate that separated over-night was washed with a little water, dried, and recrystallised from hot water, forming microscopic yellowish crystals, unmelted at 400° (Found: As, 27·8. $C_9H_8O_4NAs$ requires As, 27·9%). Solutions of *2-hydroxyquinoline-6-arsonic acid* in dilute aqueous sodium hydroxide or carbonate exhibit no fluorescence. White crystalline calcium and magnesium salts, a pale green copper salt and a brown ferric salt, both amorphous, were prepared.

2-Hydroxyquinoline-6-stibonic acid was prepared from 6-amino-2-hydroxyquinoline (1·7 g.) and purified as in the case of acridone-3-stibonic acid (yield, 1·25 g.) (Found: Sb, 38·1. $C_9H_8O_4NSb$ requires Sb, 38·6%). The reddish-brown amorphous acid was unmelted at 300°, but charred at 310°. It was relatively insoluble in cold dilute mineral acids. White gelatinous calcium and magnesium salts, a yellowish-green amorphous copper salt, and a brown gelatinous ferric salt were prepared.

We thank the Carnegie Trust for the Universities of Scotland for a Scholarship (to A. H. C. P. G.), and the Department of Scientific and Industrial Research for a grant (to M. M. B.).

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EDINBURGH. [*Received, January 29th*, 1934.]