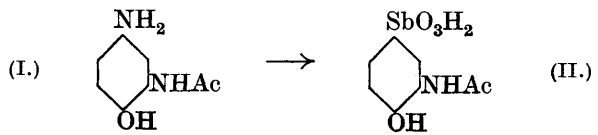
CCXX.—3-*Acetamido*-4-*hydroxyphenylstibinic Acid.*

By ISIDORE ELKANAH BALABAN.

MORGAN and COOK (this vol., p. 737) state that the substance resulting from the action of acetic anhydride on an aqueous suspension of 3-amino-4-hydroxyphenylstibinic acid is probably 3-acetamido-4-hydroxyphenylstibinic acid, although they remark on its extreme solubility in water.

In 1926 the author investigated certain phenylstibinic acids, with a view to preparing the antimony analogues of stovarsol (3-acetamido-4-hydroxyphenylarsinic acid), tryparsamide (sodium *N*-phenylglycineamide-*p*-arsinate), troposan (5-acetamido-2-hydroxyphenylarsinic acid), and cyclosan (3-hydroxy-1 : 4-benz*iso*oxazine-6-arsinic acid). Although a certain measure of success was attained, the investigation was discontinued owing to the very great difficulty of purification and the failure to obtain these acids in a crystalline form. It was soon discovered that the ease with which antimony is eliminated from phenylstibinic acids made it desirable to build up the required amine and introduce the stibinic acid residue in the last stage. In this way *p*-amino-*o*-acetamidophenol (I) furnished 3-*acetamido*-4-*hydroxyphenylstibinic acid* (II).



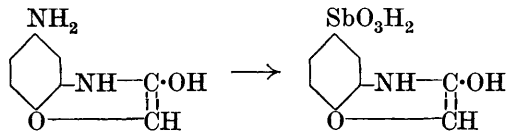
This acid is insoluble in water and all the usual solvents except 98% formic acid, in which it is readily soluble in the cold. It gave the following figures when tested on mice infected with *T. equiperdum*: (administration intravenous), *M.T.D.*, 0·1; *M.C.D.*, 0·03; *C/T*, 1/3; (administration oral), *M.T.D.*, 0·4; *M.C.D.*, 0·1; *C/T*, 1/4.

When 3-nitro-4-hydroxyphenylstibinic acid was reduced with ferrous sulphate and sodium hydroxide at 0°, and the amino-acid acetylated *in situ*, an unsatisfactory product was obtained which was not examined.

Brahmachari (*Indian J. Med. Res.*, 1922, **10**, 510) has reported the preparation of sodium *N*-phenylglycineamide-*p*-stibinate, but all attempts to repeat the preparation proved unsuccessful (compare Morgan and Cook, *loc. cit.*).

p-Nitro-*o*-aminophenol gave by the Bart–Schmidt reaction a product which may have contained 5-nitro-2-hydroxyphenylstibinic acid; the antimony content, however, was 8% low.

6-Amino-3-hydroxy-1 : 4-benz*iso*oxazine (III) gave 3-*hydroxy*-1 : 4-*benz*isoo*xazine*-6-*stibinic acid* (IV) in very poor yield.

(III.)  (IV.)

Brahmachari (*Indian J. Med. Res.*, 1925, **13**, 111) stated that "urea stibamine" was prepared from *p*-aminophenylstibinic acid and urea in water, this compound presumably being a salt. Attempts to prepare the *s*-carbamide of the above acid were, however, unsuccessful.

EXPERIMENTAL.

p-Amino-*o*-acetamidophenol (I) (B.P. 278,789) is conveniently prepared as follows: A concentrated solution of sodium hydrosulphite (50 g.) is added portionwise to *p*-nitro-*o*-acetamidophenol (19·6 g.) in 2*N*-sodium hydroxide until the colour of the solution is pale brown, the temperature being maintained at 30° by the addition of ice. After removal of unchanged material (4·6 g., m. p. 274°), the solution is made neutral to litmus with hydrochloric acid and concentrated in a vacuum until crystallisation begins; on keeping, 7·6 g., m. p. 160°, of the amino-compound are obtained (yield, 59·6%).

3-*Acetamido*-4-*hydroxyphenylstibinic Acid* (II).—The above amine (8·25 g.) and antimony trichloride (11·4 g.) in hydrochloric acid (7·5 c.c.) were added to water (45 c.c.) and hydrochloric acid (7·5 c.c.), the mixture was treated at 0° with sodium nitrite (3·45 g.) in water

(23 c.c.), and after 3 hours the antimony double salt of the diazo-compound (May, J., 1912, **101**, 1037; Schmidt, *Annalen*, 1920, **421**, 188; 1922, **429**, 145; *Ber.*, 1924, **57**, 1143) was collected and added in small quantities to ice-cold 2*N*-sodium hydroxide (150 c.c.). The whole was stirred for 4 hours and kept over-night and the liquid was then filtered and acidified (Congo-red) with hydrochloric acid, the crude *stibinic acid* being obtained as a voluminous precipitate (8·1 g.). It was dissolved (7·0 g.) in 2*N*-ammonia, an excess of hydrochloric acid added, and the solution treated with charcoal, filtered, neutralised to Congo-paper with sodium acetate, and poured into a large volume of water; the acid then separated as a white powder, which became light brown after drying in a vacuum desiccator (yield, 1·8 g.) (Found : Sb, in two different preparations, 38·1, 38·1; N, 4·1. $C_8H_{10}O_5NSb$ requires Sb, 37·9; N, 4·4%). A specimen which had been sealed in an ampoule for 3½ years was readily soluble in 2*N*-ammonia, whereas one kept in an ordinary specimen tube was not now wholly soluble.

3-*Hydroxy*-1 : 4-*benz*isoo*xazine*-6-*stibinic acid* (IV), prepared from 12 g. of 6-amino-3-hydroxy-1 : 4-benz*iso*oxazine hydrochloride by the Bart–Schmidt reaction, was obtained as an almost colourless, amorphous powder (1·25 g.), which became light brown after drying in a vacuum desiccator (Found : Sb, 37·9. $C_8H_8O_5NSb$ requires Sb, 38·1%). It was insoluble in water and the usual solvents, but readily soluble in dilute alkali solution.

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