

hydroxide was poured into a large beaker, heated almost to the boiling point and stirred vigorously with a mechanical stirrer. 4-Toluenesulfonechloride was then added in small portions. A vigorous reaction ensued with each addition of the chloride. After all of the material had been added the clear solution was cooled, whereupon the amide precipitated. The latter was separated, dissolved in boiling water and treated with charcoal. After filtration the sulfonamide separated from the cold, concentrated solution in the form of colorless crystals.

Summary

Eight analogs of novocaine and several compounds analogous to stovaine and β -eucaine have been prepared and tested for local anesthetic action by application to the tip of the tongue. It was found, at least as far as the compounds discussed in this paper are concerned, that the local anesthetic action of a compound can be retained by the substitution of 2-pyrrolyl for the benzoyl and the 4-aminobenzoyl group and by the replacement of dimethyl- and diethylamino by the 1-pyrrolyl and 1-pyrrolidyl nuclei.

ANN ARBOR, MICHIGAN

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

DISTIBYLS. I. TETRAPHENYLDISTIBYL. ATTEMPTS TO OBTAIN TETRAPHENYLDIBISMUTHYL¹

BY F. F. BLICKE, U. O. OAKDALE AND F. D. SMITH

RECEIVED OCTOBER 2, 1930

PUBLISHED MARCH 6, 1931

We began our present study in the hope that we might obtain tetraphenyldistibyl, $(C_6H_5)_2Sb-Sb(C_6H_5)_2$, and tetraphenyldibismuthyl, $(C_6H_5)_2Bi-Bi(C_6H_5)_2$, compounds analogous to the diarsyls² which have been investigated recently in this Laboratory. It was found that the first mentioned compound could be prepared from the interaction of diphenylstibyl iodide and sodium hypophosphite.³

Tetraphenyldistibyl, in solution, proved to be extremely reactive toward oxygen and the gas was absorbed with the same rapidity which is so characteristic of a solution of a tetra-aryldiarsyl or a triarylmethyl; hence the preparation of the distibyl was carried out in a free radical apparatus and the product isolated in an atmosphere of nitrogen or carbon dioxide.

¹ This paper represents the first part of a dissertation to be submitted to the Graduate School by U. O. Oakdale in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

This investigation was made possible by the aid of the Parke, Davis and Company Fellowship and by a grant from the Faculty Research Fund of the University of Michigan.

² Blicke and Smith, *THIS JOURNAL*, **51**, 2272 (1929); Blicke, Weinkauff and Hargreaves, *ibid.*, **52**, 780 (1930); Blicke and Smith, *ibid.*, **52**, 2937 (1930).

³ Schmidt [*Ann.*, **421**, 235 (1920)] stated that tetraphenylstibyl oxide, $(C_6H_5)_2Sb-O-Sb(C_6H_5)_2$, when treated with hypophosphorous acid, yields a yellow compound which he thought might be tetraphenyldistibyl. However, no analysis or further description of the material was recorded.

The amount of oxygen absorbed corresponded to that required for the formation of tetraphenylstibyl peroxide, $(C_6H_5)_2Sb-O-O-Sb(C_6H_5)_2$. The colorless, crystalline distibyl possessed a sharp melting point and dissolved in organic solvents with the formation of colorless solutions.

Diphenylbismuthyl iodide, dissolved in bromobenzene, was shaken with molecular silver, mercury, zinc powder and copper bronze, respectively. In the case of the first two metals black precipitates were formed. However, none of the solutions obtained absorbed oxygen. Sodium hypophosphite, at ordinary temperature, did not seem to react with an alcoholic solution of diphenylbismuthyl iodide. When the mixture was warmed a black product was produced. A mixture of diphenylbismuthyl iodide, bromobenzene and copper was placed in an absorption flask, connected with an oxygen reservoir, and shaken vigorously for eight hours. The absorption of oxygen, based on peroxide formation, was approximately 50% of the calculated amount. Similar results were obtained with molecular silver.

Experimental Part

Diphenylstibyl Iodide.—Two hundred grams of crude, dry phenylstibinic acid⁴ was dissolved in 500 cc. of hydrochloric acid and 250 cc. of water added to precipitate colored impurities. After filtration the solution of phenylstibinic acid was cooled with ice and treated with sulfur dioxide for three hours. The mixture was then allowed to remain in an ice-bath for six hours. The phenyldichlorostibine,⁵ which had separated in crystalline form, was filtered with suction. To prepare phenylstibine oxide a cold acetone solution of phenyldichlorostibine was added, dropwise, to cold dilute ammonia water. The mixture was stirred vigorously during this process and kept cold by the addition of ice. The precipitated phenylstibine oxide was filtered with suction, washed with acetone and dried.

Twenty-gram portions of finely powdered, crude phenylstibine oxide were placed in 250-cc. Erlenmeyer flasks fitted with two-holed stoppers through which inlet and outlet tubes were inserted. A stream of dry nitrogen was passed through the flasks and the latter were heated at 90° in an oil-bath for two hours. The viscous reaction products, which contained tetraphenylstibyl oxide, were extracted several times with hot alcohol, the alcoholic extracts filtered and the alcohol removed.⁶ The oily residue obtained from each twenty-gram portion of phenylstibine oxide was treated with 10 cc. of acetic acid and stirred, whereupon the material crystallized almost immediately. This substance, diphenylstibyl acetate, was filtered with suction and recrystallized from acetic acid; 1 cc. of acetic acid was used for each gram of the acetate; m. p. 133–135°.⁷

In order to convert the acetate into the corresponding chloride or bromide, or the chloride into the iodide, it is essential that all products should be in a very pure state before the conversion is attempted.

For the preparation of diphenylstibyl chloride 20 g. of pure diphenylstibyl acetate was dissolved in 60 cc. of hot acetic acid. The solution was cooled quickly to room

⁴ Schmidt, *Ann.*, **421**, 189 (1920).

⁵ Solutions of this material are powerful skin irritants.

⁶ This process represents a slight modification of that used by Schmidt [*Ann.*, **421**, 234 (1920)] for the conversion of phenylstibine oxide into tetraphenylstibyl oxide.

⁷ Schmidt [*Ann.*, **429**, 140 (1922)] recorded the melting point as 132°.

temperature and 80 cc. of hydrochloric acid was added immediately in small portions. The mixture was cooled during the addition of the hydrochloric acid. The chloride precipitated at once in crystalline form and was recrystallized from an equal weight of acetic acid; m. p. 68°.⁸

When diphenylstibyl acetate was dissolved in hot acetic acid, the solution cooled to room temperature and an excess of 48% hydrobromic acid added an oil precipitated. When cooled the latter became solid. After three recrystallizations from acetic acid the compound, undoubtedly diphenylstibyl bromide, melted at 86°.

Diphenylstibyl iodide was prepared as follows. Twenty grams of the chloride, dissolved in 25 cc. of pure acetone, was added to three times the calculated amount of sodium iodide dissolved in the same solvent. After twelve hours the sodium chloride was removed and the acetone allowed to evaporate spontaneously. The crystalline iodide, obtained after the addition of water to the residue, was recrystallized twice from acetic acid and twice from absolute alcohol; m. p. 68–70°. The iodide is not affected by cold water and is hydrolyzed only very slowly by boiling water.

*Anal.*⁹ Calcd. for $C_{12}H_{10}SbI$: Sb, 30.23; I, 31.51. Found: Sb, 30.20; I, 31.42.

Neither diphenylstibyl iodide nor triphenylmethyl bromide, dissolved in bromobenzene, absorbs oxygen. When diphenylstibyl iodide (0.003 mole) and triphenylmethyl bromide (0.003 mole) were put into a test-tube, the latter constricted and then filled quickly with bromobenzene which had been saturated with nitrogen a deep red solution was formed immediately. When the tube was broken in an oxygen absorption apparatus¹⁰ 51 cc. of oxygen was absorbed very rapidly. This quantity of oxygen is more than that required for the formation of triphenylmethyl peroxide (34.2 cc.) and is less than that necessary for the formation of both triphenylmethyl peroxide and tetraphenylstibyl peroxide. A phenomenon entirely analogous to that described above is observed when diphenylarsyl iodide and triphenylmethyl bromide are mixed.¹¹

Action of Metals on Diphenylstibyl Iodide.—Two tubes were prepared each of which contained diphenylstibyl iodide, bromobenzene¹² and copper bronze.¹³ After the tubes had been shaken for a definite period of time the one tube was broken in an oxygen absorption apparatus while the contents of the other tube were analyzed for copper halide. Several series of such tubes were shaken for different periods of time. The data obtained showed that the percentage of iodine removed, which should serve as a measure of the amount of tetraphenylstibyl formed, did not correspond to the percentage of oxygen absorbed. The latter was calculated based on the assumption that tetraphenylstibyl peroxide, $(C_6H_5)_2Sb-O-O-Sb(C_6H_5)_2$, is the primary product of the oxidation. These results indicate that the distibyl undergoes decomposition or that it is rendered inactive toward oxygen by combination with unchanged diphenylstibyl iodide or the copper halide. However, we have shown that the isolated distibyl, dissolved in bromobenzene, retains its activity toward oxygen for a period of several days at least.

In one instance the distibyl was allowed to absorb oxygen as fast as it was formed. One and six-tenths grams of diphenylstibyl iodide, 15 cc. of bromobenzene and 2 g. of copper were placed in an absorption flask attached to a reservoir filled with oxygen and

⁸ Michaelis and Günther, *Ber.*, **44**, 2318 (1911).

⁹ Method of Thompson and Oakdale, *THIS JOURNAL*, **52**, 1195 (1930).

¹⁰ Gomberg and Schoepfle, *ibid.*, **39**, 1661 (1917).

¹¹ Blicke and Smith, *ibid.*, **51**, 2275 (1929).

¹² This solvent was used because of its comparatively low vapor pressure. Gomberg and Schoepfle, *ibid.*, **39**, 1661 (1917).

¹³ Magnesium powder, molecular silver, mercury and zinc dust were tried but only copper and zinc seemed to remove the halogen rapidly.

the absorption flask was shaken vigorously and continuously. After five minutes 20 cc., after one hour 32 cc. and after nine hours 44.8 cc., the amount of the gas calculated for peroxide formation, had been absorbed. An analysis of the copper halide formed showed that practically all of the iodine had been removed from the diphenylstibyl iodide at the end of nine hours.

Tetraphenylstibyl.—Three and two-tenths grams of diphenylstibyl iodide, dissolved in 25 cc. of absolute alcohol, was poured into a free radical apparatus¹⁴ of 125-cc. capacity. One and three-tenths grams of sodium hypophosphite was dissolved in 5 cc. of water and 20 cc. of alcohol added. This solution was then poured into the radical apparatus. The reaction mixture was protected from light and allowed to remain at ordinary temperature for twelve hours. The distibyl separated from the mixture in the form of pale yellow-green needles. The liquid was decanted through the stopcock with the aid of suction and the product was washed several times with small amounts of alcohol, whereupon it became practically colorless. The compound was dried by allowing the apparatus to remain attached to the suction pump for six hours. The material was then removed from the radical apparatus in the manner described previously in the case of diarsyls.¹⁵ The amount of distibyl isolated was usually somewhat in excess of one gram.

The product when pure was practically colorless and the copper wire test proved it to be halogen free. In a sealed tube filled with nitrogen it melted at 121–122°. In order to prevent oxidation during the weighing of the material it was found advantageous to compress the distibyl in the form of tablets in a tablet machine. Each tablet was then weighed in a closed tube, filled with nitrogen, just large enough to contain it.

*Anal.*⁹ Calcd. for $C_{24}H_{20}Sb_2$: Sb, 43.93. Found: Sb, 44.13.

The diarsyl reacts instantly with iodine. In an apparatus filled with nitrogen there was placed 0.4320 g. of the distibyl. The latter was then dissolved in 15 cc. of benzene and a *N*/10 solution of iodine in carbon tetrachloride was added. The iodine color disappeared instantly but after 15.8 cc. of the solution had been added a permanent color was produced. The calculated amount of iodine solution necessary for the formation of diphenylstibyl iodide is 15.7 cc. The solution was poured into a dish and the carbon tetrachloride evaporated. The yellow, crystalline residue was washed with a very small amount of acetic acid; m. p. 64–65°. Mixed with diphenylstibyl iodide it melted at the same temperature.

Potassium permanganate, dissolved in acetone, is decolorized instantly by the distibyl.

A portion of the isolated tetraphenylstibyl, which weighed 0.7609 g., was dissolved in bromobenzene and the solution preserved in a sealed tube, protected from light for four days. The tube was then broken in an oxygen absorption apparatus. Twenty-nine cc. of oxygen was absorbed almost instantly; the calculated amount is 29.4 cc.

Triphenylbismuthine.—Phenylmagnesium bromide was prepared from 80 g. of bromobenzene (0.5 mole), 12 g. of magnesium and 300 cc. of ether. After the addition of 200 cc. of dry benzene the solution was stirred vigorously and 41 g. of finely-divided, freshly distilled bismuth trichloride (0.13 mole)¹⁶ was added in five portions during the

¹⁴ Gomberg and Schoepfle, *THIS JOURNAL*, 39, 1659 (1917). The lower stopcock on the apparatus was removed.

¹⁵ Blicke, Weinkauff and Hargreaves, *ibid.*, 52, 782 (1930).

¹⁶ The best quality of bismuth trichloride which we could obtain contained considerable liquid. The material was drained thoroughly, placed on a porous plate and the latter put into a desiccator. After several days the chloride was distilled from a retort with a very short side arm.

course of one-half hour. The mixture was then heated on a steam-bath and stirred for four hours. The mixture was decomposed with ice and ammonium chloride, the ether layer separated and dried with fused sodium sulfate. After removal of the solvent the oily residue soon solidified. The material was washed with petroleum ether (30–60°); m. p. 76–77°; yield, 48 g., or 84% of the calculated amount.¹⁷

Diphenylbismuthyl Iodide.—Twenty three grams of diphenylbismuthyl chloride¹⁸ was dissolved in 200 cc. of absolute alcohol, 9 g. of solid sodium iodide added and the mixture shaken for twelve hours. It was then poured into 600 cc. of boiling water. Diphenylbismuthyl iodide separated in the form of yellow flakes. The latter were filtered, washed with water and dried in a vacuum desiccator. The product was treated with hot ethyl acetate in order to dissolve the diphenylbismuthyl iodide, the mixture cooled to room temperature and filtered to remove the red by-product. The solvent was distilled from the filtrate under diminished pressure in a stream of nitrogen. The iodide was powdered, triturated with 20 cc. of petroleum ether (30–60°) in order to remove triphenylbismuthine, the petroleum ether decanted and the process repeated several times; m. p. 132–134°.¹⁹

Diphenylbismuthyl iodide, dissolved in acetone, instantly decolorizes potassium permanganate dissolved in the same solvent. If a carbon tetrachloride solution of iodine is added to the bismuthyl iodide, dissolved in benzene, the first portion of the iodine solution is decolorized immediately. Upon further addition of iodine a brick-red and then a brown precipitate is formed.

Summary

Tetraphenyldistibyl, $(C_6H_5)_2Sb-Sb(C_6H_5)_2$, has been prepared from diphenylstibyl iodide and sodium hypophosphite. The distibyl, in solution, is just as reactive toward oxygen as solutions of tetra-aryldiarsyls or triarylmethyls.

We have not been able to obtain tetraphenyldibismuthyl by the methods used for the preparation of the analogous arsenic and antimony compounds.

ANN ARBOR, MICHIGAN

¹⁷ From phenylmagnesium bromide and bismuth trichloride Pfeiffer [*Ber.*, **37**, 4622 (1904)] obtained a 25% yield of triphenylbismuthine.

¹⁸ Challenger and Allpress, *J. Chem. Soc.*, 107, 19 (1915).

¹⁹ Gillmeister [*Ber.*, **30**, 2843 (1897)] obtained the iodide from triphenylbismuthine dichloride and sodium iodide.