NEW ORGANO-METALLIC COMPOUNDS*

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Inorganic and organic compounds of mercury and arsenic have long been used in the treatment of disease, due to pathological conditions of the blood. Most of these diseases are caused by the existence of bacteria in the blood stream, chiefly of the family known as the Protozoa. To this type of maladies belong sleeping sickness, syphilis, and malaria; in animals, surra, dourine, tsetse fly disease, etc.

Of the several diseases mentioned above, there is no doubt but that syphilis has been the most dangerous, and far-reaching in its effect on mankind, and the one giving the chief incentive to the study of compounds useful in the treatment of diseases of this type.

It must be remembered, however, that the compounds to be spoken of in this paper, were not always tried out on animals and human subjects infected with syphilis, but in many cases other members of the Protozoa group were the parasites, notably those causing sleeping sickness. The pharmacology of these drugs is, therefore, not in an altogether satisfactory condition to make any great generalizations with accuracy as yet.

One of the earliest derivatives of arsenic or organic nature to be used was Atoxyl, para-aminophenyl arsenic acid (sodium salt):

$$NH_2\text{–}C_6H_4\text{–}AsO(ONa)_2$$

This compound was used with some success in the treatment of sleeping sickness and syphilis, but was found very toxic to the host, and often led to blindness, so that it is very little used at present.

Salvarsan, 606, or chemically *p,p'*-dihydroxy-*m,m'*-diamino-arseno benzene hydrochloride, a derivative of Atoxyl, has been the most successful in the treatment of syphilis, of the many organic derivatives of arsenic prepared to date:

$$HCl\text{–}NH_2\text{–}OH\text{–}C_6H_3\text{–}As = As\text{–}C_6H_3\text{–}OH\text{–}NH_2\text{–}HCl$$

As to the results obtained by the use of this compound, and the method of administration, all are familiar, as well as with its newer derivative, Neosalvarsan; the sodium formaldehyde sulphoxylate salt of Salvarsan, mixed with some sodium sulphite:

$$HO\text{–}NH_2C_6H_3\text{–}As = As\text{–}C_6H_3\text{–}OH\text{–}NH\text{–}CH_2SO_2Na$$

It is of interest to know of some of the compounds probably investigated by Ehrlich in his search which resulted in the discovery of Salvarsan:

Para-amino-phenyl arsenic acid
Para-hydroxy-phenyl arsenic acid
Ortho, meta, and *para* toluidine arsenic acids
Ortho, meta, and *para* cresol arsenic acids
Naphthyl arsenic acids

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* Presented before the Cincinnati Branch of the American Pharmaceutical Association.

Naphthol arsenic acids
Naphthylamine arsenic acids
Amino phenyl arsenoxids
Hydroxy phenyl arsenoxids
Para-hydroxy-*meta*-aminophenyl arsenic acid
Meta-dihydroxy arsenic acids
Meta-para-dihydroxy arsenic acid
Meta-para-diamino arsenic acid
Meta-para-diamino arsenoxids
Meta-para-dihydroxy arsenoxides
p,p'-dihydroxy-arseno benzol
p,p'-diamino-arseno benzol
Di-acetyl *p,p'*-diamino phenol

Besides the above mentioned compounds, many of their gold mercury, platinum and other metallic salts have been made.

Furthermore, it should be remembered, that in the arrangement of the elements according to Mendelejeff, in what is known as the periodic system, the following elements occur in the same column as arsenic: Nitrogen, Phosphorus, Vanadium, Columbium, Antimony, Tantalum, and Bismuth. Compounds of these elements would, therefore, be expected to have many of the general chemical and physiological properties of those of arsenic. Compounds of these elements have been made of analogous structure to those of arsenic, also mixed compounds of them with arsenic:

C_6H_5–Sb = As–C_6H_3–NH_2–OH
C_6H_5–Bi = As–C_6H_3–NH_2–OH
C_6H_5–P = As–C_6H_3–NH_2–OH
C_6H_5–N = As–C_6H_3–NH_2–OH
Nitro-phenyl stibinic acid
Amino-phenyl stibinic acid
Hydroxy-phenyl stibinic acid
Hydroxy-phenyl stibinoxide
Amino-phenyl stibinoxide
Nitro-phenyl stibinoxide

Compounds of the sulphur group and arsenic have also been prepared:

S = As–C_6H_3–OH–NH_2
Se = As–C_6H_3–OH–NH_2
Te = As–C_6H_3–OH–NH_2

Many of these compounds have been found useful, but as they do not excel Salvarsan, and are often very difficult to make, there is very little probability of them ever being used to any great extent.

As might be expected, the commercial success of Salvarsan and Neosalvarsan has greatly stimulated the study of the organic mercury compounds. The organic compounds of mercury may be placed in two classes,

Type R–Hg–R Type R–Hg–X

where R is an organic radical, either aliphatic or aromatic, and X is a negative radical or atom as the halogens, nitric acid or sulphate radical, the acetyl radical, etc.

It has been found that, as a general rule, the compounds of the second type are five times as toxic as those of the first class, and it may be said that the toxicity of the compounds of mercury increases with the solubility in the body fluids, and

the ease with which ionic mercury can be split off, and is lowered by the ease in which it can be eliminated. The organic compounds of mercury have not come up to expectations, as they are slow of action, and have been found in most cases to be more poisonous to the host than to the bacteria they are meant to kill. The following are a few of the two classes of compounds prepared:

Type R–Hg–R	Type R–Hg–X
Mercury diphenyl C_6H_5–Hg–C_6H_5	Phenyl mercuric chloride C_6H_5–Hg–Cl
Mercury diphenol HO–C_6H_4–Hg–C_6H_4–OH	Phenol mercuric chloride HO–C_6H_4–Hg–Cl
Mercury dibenzoyl COOH–C_6H_4–Hg–C_6H_4COOH	Benzoyl mercuric chloride COOH–C_6H_4–Hg–Cl
Mercury dinaphthyl $C_{10}H_7$Hg–$C_{10}H_7$	Naphthyl mercuric chloride $C_{10}H_7$–Hg–Cl
Mercury dinaphthol OH–$C_{10}H_6$Hg–$C_{10}H_6$OH	Naphthol mercuric chloride OH–$C_{10}H_6$–Hg–Cl
Diamino-dibenzoyl mercury NH_2–COOH–C_6H_3–Hg–C_6H_3–COOH–NH_2	Aminobenzoyl mercuric chloride NH_2–COOH–C_6H_3–Hg–Cl
Dibenzyl mercury C_6H_5–CH_2–Hg–CH_2–C_6H_5	Benzyl mercuric chloride C_6H_5–CH_2–Hg–Cl
Diamino-dihydroxy-diphenyl mercury OH–NH_2–C_6H_3–Hg–C_6H_3–NH_2–OH	Amino-hydroxy-phenyl mercury OH–NH_2–C_6H_3–HgCl

It should be noted that this last compound of mercury is the analogue of Salvarsan.

Besides the typical compounds listed above, there are a myriad of others; derivatives of the aliphatic hydrocarbons, of the dyes, of the alkaloids, quinoline, the pyrazolones, etc. The ones, however, that apparently are the most effective are aromatic derivatives, but even these are too poisonous to be of value in the treatment of syphilis, so that there is very little probability of them ever becoming of equal importance, in this field, to the arsenic compounds.

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CHANGE OF COLOR IN GREEN EXTRACTS.

Green extracts from the leaves of plants very rapidly lose their color when exposed to light and air, the chlorophyll being converted into chlorophyllan. Yet in living plants exposure to light and air has no effect on the green tint. The author assumes that there is a special enzyme in the plant—an "anti-oxidase"—which protects chlorophyll from the action of light and oxygen, and also from the peroxidase of the tissues, which readily destroys it. In the living plant anti-oxidase accumulates in the plastids in sufficient quantity to counteract the peroxidase. In extracts the equilibrium between the enzymes is disturbed and the pigments are quickly destroyed. During the period of assimilation of the plastids in the living plant the chlorophyll is constantly used up and constantly replaced. The function of the anti-oxidase is to regulate this process, and thus prevent too rapid oxidation.—V. Lyubimenko, *Bull. Acad. Sci. Petrog.*; *Chem. Abstr.*, 1916, 10, 2467; through *Pharmaceutical Journal.*