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(54) Title: METHODS OF CHEMICAL SYNTHESIS AND PURIFICATION OF DIAMINOPHENOTHIAZINIUM COMPOUNDS INCLUDING METHYLTHIONINIUM CHLORIDE (MTC)

(57) Abstract: This invention pertains generally to the field of chemical synthesis and purification, and more specifically to methods of synthesizing and purifying certain 3,7 diamino-phenothiazin-5-ium compounds (referred to herein as "diaminophenothiazinium compounds") including Methythioninium Chloride (MTC) (also known as Methylene Blue). In one embodiment, the method comprises the steps of, in order: nitrosylation (NOS); nitrosyl reduction (NR); thiosulfonic acid formation (TSAF); oxidative coupling (OC); Cr(VI) reduction (CR); isolation and purification of zwitterionic intermediate (IAPOZI); ring closure (RC); chloride salt formation (CSF); one of: sulphide treatment (ST); dimethyldithiocarbamate treatment (DT); carbonate treatment (CT); ethylenediaminetetraacetic acid treatment (EDTAT); organic extraction (OE); and recrystallisation (RX). The present invention also pertains to the resulting (high purity) compounds, compositions comprising them (*e.g.*, tablets, capsules), and their use in methods of inactivating pathogens, and methods of medical treatment and diagnosis, etc., for example, for tauopathies, Alzheimer's disease (AD), skin cancer, melanoma, viral diseases, bacterial diseases, or protozoal diseases. Wherein: each of $R^1$ and $R^9$ is independently selected from:-H; $C_{1-4}$ alkenyl; and halogenated $C_{1-4}$akyl; each of $R^{3NA}$ and $R^{3NB}$ is independently selected from: $C_{1-4}$ alkyl; $C_{2-4}$alkenyl; and halogenated $C_{4-1}$ alkyl; each of $R^{7NA}$ and $R^{7NB}$ is independently selected from: $C_{1-4}$ alkyl; $C_{2-4}$alkenyl; and halogenated $C_{1-4}$ alkyl; and X is one or more anionic counter ions to achieve electrical neutrality.

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