Reduction Property and Mutagenicity of Newly Synthesized Nitroarenes as Environmental Mutagens

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Introduction

Although nitroarenes cause acute concern because of their toxicity and their presence in automobile and diesel exhaust fumes, their study has been limited to nitropyrenes and a few other nitroarenes. Mononitrated benzo[α]pyrenes (1-, 3- and 6-nitroBaPs) are formed by nitrification of BaP with NOx. The present study deals with 1) synthesis of 1,6- and 3,6-dinitroBaPs and 6-aza analogues of 1- and 3-nitroBaPs, 2) their detection in urban air, and 3) the relationship between mutagenicity and nitro reduction property which is critical for metabolic activation to a mutagen.

Methods

DinitroBaPs (1,6- and 3,6-) were synthesized by nitrification of BaP with HNO3,1) 6-AzaBaP N-oxide prepared from perinaphthenone was nitrated with HNO3 to form 1- and 3-nitro-6-azaBaP N-oxides, and then 1- and 3-nitro-6-azaBaPs were obtained by deoxygenation of these N-oxides with PBr3.2) 6-Cyanated 1- and 3-nitroBaPs and 3-, 6- and 8-cyanated 1-nitropyrenes were synthesized by nitration of 6-cyanoBaP and 1-cyanopyrene, respectively. Reduction potentials were determined by cyclic voltammetry in dimethylformamide containing 0.1M tetraethylammonium perchlorate. Mutagenic activities were tested on Salmonella typhimurium TA98 and TA98NR, which lacks classical nitroreductase, in the absence of S9 mixture.

Results and Discussion

Mutagenicity of newly synthesized dinitroBaPs and 1- and 3-nitro-6-azaBaPs and their N-oxides was quite strong in Salmonella typhimurium TA98 and even in TA98NR. 3-Nitro-6-azaBaP N-oxide showed particularly high mutagenicity in TA98 (396000 rev/nmol) and in TA98NR (427000 rev/nmol). 3,6-DinitroBaP and nitrated azabBaPs were detected at concentrations of 0.3—1.8 ng per gram of particulates in urban air. These compounds are classified as direct-acting mutagens in environmental pollutants as 1,6- and 1,8-dinitropyrenes.

Half-wave reduction potentials (El/2) of these compounds indicated that their first and second electron-reductions occurred much more easily than those of 1- and 3-nitroBaPs. 6-Cyano derivatives of 1- and 3-nitroBaPs also showed strong mutagenicity nearly equal to that of dinitroBaPs in both strains. The ease of these electrochemical reductions suggests facile reduction of nitroso derivatives in metabolic processes. Similar results were obtained in the nitropyrene series (mono and dinitropyrenes and 3-, 6- and 8-cyanated 1-nitropyrenes) and the ease of first and second electron reduction is correlated to mutagenic activity of TA98 and TA98NR, respectively. This chemical property is one of the fundamental factors responsible for the highly mutagenic potency in both TA98 and TA98NR.

References