Analysis of mutagenicity of nitrobenzanthrones by molecular orbital calculations

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3-Nitrobenzanthrone (3-NBA) detected in diesel exhaust was found to be a very strong mutagen by the Ames test. On the other hand, 9-NBA is less potent as a mutagen than 3-NBA and 11-NBA is devoid of mutagenicity. To explain the difference in mutagenicity among the three isomers theoretically, we proposed the metabolic activation pathway of NBAs and performed molecular orbital calculations by the PM5 and HF/6-31G(d) methods.

The metabolic pathway was as follows: NBA taken into living things is subjected to nitroreduction and *N*-hydroxy-3-aminobenzanthrone (*N*-OH-ABA) is formed via nitrosobenzanthrone. Subsequently, the *N*-OH-ABA is converted to 3-aminobenzanthrone or to *N*-acetoxy-3-aminobenzanthrone (*N*-Aco-ABA). While the former is smoothly excreted from the body, the latter becomes an ultimate carcinogen, nitrenium ion. Finally, this electrophilic reagent binds to the DNA bases and forms NBA-DNA adduct, leading to mutagenicity. We calculated the heat of formation, HOMO energy, LUMO energy for parent molecules and their activated intermediates described above. The activation energy (*E*a) was also calculated for the binding reaction between the NBAs and DNA bases.

No correlations were found between the heats of formation and mutagenic activities. The LUMO energies, however, of parent molecules, nitrosobenzanthrones and *N*-Aco-ABAsbecome larger in the order of 3-, 9-, and 11-NBA; the HOMO energies of 3-NBA and its two intermediates are smallest. These findings indicate that the mutagenicity of NBAs increases as the electrophilicity of parent molecules and the two intermediates. But the correlation between *E*a and mutagenicity was poor, suggesting that once nitrenium ions are produced, they bound to the DNA base immediately. Thus the mutagenicity of NBAs strongly depends on the rate nitrenium-ion formation.