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论文

α-羟基化吡咯烷亚硝胺代谢及形成DNA加合物反应机理的理论研究

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摘要:

采用密度泛函理论, 在B3LYP/6-31G**水平上, 研究了气相和水溶剂中, *α*-羟基化吡咯烷亚硝胺(α-hydroxylation-NPYR, A)代谢为终致癌物重氮氢氧化物(B)、重氮烷阳离子(C)和氧离子(D), 以及C与鸟嘌呤碱基相互作用的反应机理. 化合物A代谢为终致癌物, 涉及异构化和质子化过程, 是相对容易进行的放热反应. 终致癌物C与鸟嘌呤在N7位形成DNA加合物F和G的反应, 遵循S_N2机理. 加合物G由F异构形成, 且有相对高的异构化能(气相: 244.77 kJ/mol; 水溶剂中: 234.83 kJ/mol), 这与实验上得到加合物G是主要癌变物的结果一致.

关键词: *α*-羟基化吡咯烷亚硝胺; 密度泛函理论; DNA加合物; 致癌

Theoretical Study of the Reaction Mechanism for the Formation of DNA Adducts by *α*-Hydroxy-nitrosopyrrolidine

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Abstract:

The reaction mechanism for the formation of ultimate carcinogens diazohydroxide(B), diazonium(C) and oxoniumions(D) by α-hydroxylation-NPYR and the alkylation process of C and guanine were investigated including solvent effects at the B3LYP/6-31G** level. The formation of ultimate carcinogens involves isomerization and protonation. And the process is relatively easy to occur. The alkylation reaction by ultimate carcinogen C and N7 site of guanine is an S_N2 process, and forms DNA adduct F and G. Adduct G is isomerized by F. The isomerization energies are relatively high(in the gas phase: 244.77 kJ/mol; in solvent of water: 234.83 kJ/mol), which is consistent with the experiment that adduct F is the primary alkylation product.

Keywords: *α*-Hydroxy-nitrosopyrrolidine; Density functional theory; DNA adduct; Carcinogen

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