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Formation of Directly Mutagenic α-Hydroxy-*N*-Nitrosopiperidine Phosphate Ester by Near-Ultraviolet Irradiation of *N*-Nitrosopiperidine in Phosphate Buffer*

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N-Nitrosodialkylamines are usually promutagens, becoming mutagenic only after metabolic activation. Previously we found that direct-acting mutagens can be formed from *N*-nitrosodialkylamines on exposure to near-ultraviolet light in the presence of phosphate. Since these phosphate compounds are abundantly present in the physiological environment, it was suspected that this non-enzymatic activation may have relevance in the carcinogenic activity of these *N*-nitroso compounds. In the present study, we have isolated the active product formed from *N*-nitrosopiperidine (NPIP) under the irradiation, and have established the structure as the phosphate ester of α-hydroxy-*N*-nitrosopiperidine (NPIP α-phosphate).

A solution of NPIP in sodium-phosphate buffer was irradiated by 313—400 nm wavelength under stirring. The reaction mixture was freeze-dried, and the residue was extracted with methanol. The methanol extract was evaporated and fractionated by preparative HPLC. After the HPLC was repeated three times, active fraction was prepared to a sample for studying the chemical structure. The UV spectrum has maxima at 231 nm and 344 nm and identical with that of authentic NPIP α-phosphate. The mutagenic activity of this sample in *Salmonella* TA 1535 was estimated to be 700 His^+ revertants/A_{231} unit from the dose-dependent response. When treated with alkaline phosphatase, both the photoproduct and NPIP α-phosphate lost their direct-acting mutagenicity. The ^1H-NMR spectrum of the photoproduct was also identical with the spectrum of authentic NPIP α-phosphate. Thus, the isolated photoproduct was identified as the phosphate ester of α-hydroxy-*N*-nitrosopiperidine.

This reaction represents a new, non-enzymatic activation of promutagenic *N*-nitrosodialkylamines.

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