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Activation of N-Nitrosodialkylamines by Near-Ultraviolet Irradiation: Formation of Directly-acting Mutagens and DNA-Damaging Products*

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On near-ultraviolet (UVA) irradiation in a phosphate buffer, N-nitrosomorpholine (NMOR) and N-nitrosopyrrolidine (NPYR) were converted into directly-acting mutagens. The activated NPYR was fractionated, and the active product was isolated. The compound was shown to be identical to α -phosphonooxy NPYR on the basis of several properties: retention times in high-performance liquid chromatograms, mutagenic specificity and potency, ultraviolet spectrum, and inactivation by phosphatase treatment. Photoactivation was inhibited by superoxide dismutase, and therefore superoxide is implicated as playing a key role in mutagen formation. N-Nitrosoproline (NPRO) and eighteen other N-nitrosodialkylamines were irradiated with UVA in the presence of ϕ X 174 RFIDNA. The DNA underwent single-strand breaks to give RFII DNA, indicating that N-nitrosodialkylamines in general have this property. DNA chain cleavage was inhibited both by superoxide dismutase and hydroxyl-radical scavengers. These results provide new information on the genotoxic mechanism of action of N-nitrosodialkylamines.

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