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A similar order was observed also in the cytotoxicity. Mutagenic and cytotoxic potencies of these α -hydroxy *N*-nitrosamines in V79 cells were well correlated not only with those of model compounds, α -acetoxy and α -hydroperoxy *N*-nitrosamines, but with their alkylating ability measured by alkylation of thiophenol. The mutagenic activity of the α -hydroxy *N*-nitrosamines in V79 cells was shown to be in parallel with that in *Salmonella typhimurium* TA1535 and with that of *N*-nitrosodialkylamines in V79 cells after metabolic activation by rat hepatocytes. The results obtained here supported further that the α -hydroxy *N*-nitrosamine is the active species in the metabolic activation of carcinogenic and mutagenic *N*-nitrosodialkylamines.

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Metabolism of *N*-Nitrodialkylamines

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In vitro and *in vivo* metabolism of *N*-nitramines were investigated to compare their mode of action with that of *N*-nitrosamines. *N*-Nitrodibutylamine and *N*-nitrodiethylamine were incubated with rat liver microsomes and hepatocytes, and the products were analyzed by HPLC and GLC. The *in vitro* metabolic pattern of these *N*-nitramines was quite similar to that of the corresponding *N*-nitrosamines except that *N*-nitromonoalkylamines (produced by α -hydroxylation) were isolated and characterized in the incubation with the *N*-nitrodialkylamines. Seven *N*-nitramines including glucuronides were isolated and identified from urine of rats given *N*-nitrodibutylamine, which were produced by ω , ω -1, and α oxidations of the *N*-nitramine. The *in vivo* metabolic pattern of *N*-nitrodibutylamine was also similar to that of *N*-nitrosodibutylamine, except that *N*-nitromonobutylamine (a product of α -hydroxylation) was isolated and characterized.

N-Nitramines were mutagenic to *E. coli* WP2 *hcr*⁻ but not to *S. typhimurium* TA1535. *N*-Nitrodibutylamine and *N*-nitrodiethylamine were mutagenic only in the presence of hepatic microsomes, while *N*-nitromonobutylamine and *N*-nitromonoethylamine were direct mutagens. Thus, the *N*-nitrodialkylamine is also metabolically activated to a mutagen through α -hydroxylation.

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