

Title	Formation of directly mutagenic $\alpha$ -hydroxy-N-nitrosopiperidine phosphate ester by near-ultraviolet irradiation of N-nitrosopiperidine in phosphate buffer
Sub Title	
Author	有元, 佐賀恵(Arimoto, Sakae) 島田, 浩美(Shimada, Hiromi) 鵜川, さと子(Ukawa, Satoko) 望月, 正隆(Mochizuki, Masataka) 早津, 彦哉(Hayatsu, Hikoya)
Publisher	共立薬科大学
Publication year	1989
Jtitle	共立薬科大学研究年報 (The annual report of the Kyoritsu College of Pharmacy). No.34 (1989. ) ,p.81- 81
JaLC DOI	
Abstract	
Notes	抄録
Genre	Technical Report
URL	<a href="https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=AN00062898-00000034-0081">https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=AN00062898-00000034-0081</a>

慶應義塾大学学術情報リポジトリ(KOARA)に掲載されているコンテンツの著作権は、それぞれの著作者、学会または出版社/発行者に帰属し、その権利は著作権法によって保護されています。引用にあたっては、著作権法を遵守してご利用ください。

The copyrights of content available on the Keio Associated Repository of Academic resources (KOARA) belong to the respective authors, academic societies, or publishers/issuers, and these rights are protected by the Japanese Copyright Act. When quoting the content, please follow the Japanese copyright act.

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

Sakae ARIMOTO\*\*, Hiromi SHIMADA\*\*, Satoko UKAWA,  
Masataka MOCHIZUKI and Hikoya HAYATSU\*\*

有元佐賀恵\*\*, 島田浩美\*\*, 鶴川さと子, 望月正隆, 早津彦哉\*\*

*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  $\alpha$ -hydroxy-*N*-nitrosopiperidine (NPIP  $\alpha$ -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  $\alpha$ -phosphate. The mutagenic activity of this sample in *Salmonella* TA 1535 was estimated to be 700 His<sup>+</sup> revertants/A<sub>231</sub> unit from the dose-dependent response. When treated with alkaline phosphatase, both the photoproduct and NPIP  $\alpha$ -phosphate lost their direct-acting mutagenicity. The <sup>1</sup>H-NMR spectrum of the photoproduct was also identical with the spectrum of authentic NPIP  $\alpha$ -phosphate. Thus, the isolated photoproduct was identified as the phosphate ester of  $\alpha$ -hydroxy-*N*-nitrosopiperidine.

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

---

\* 本報告は *Biochem. Biophys. Res. Commun.*, 162 (3), 1140—1146 (1989) に発表.

\*\* 岡山大学薬学部