

SYNTHESIS OF AZIRIDINE DERIVATIVE FROM α -SILYL CARBANION AND THEIR MUTAGENICITY

Takeo Konakahara, Masayuki Matsuki, Kenji Sato, Yoshiharu Hisamatsu†,
and Hidetsuru Matsushita†

Department of Industrial and Engineering Chemistry, Faculty of Science
and Technology, Science University of Tokyo, Noda, Chiba 278, Japan; and

†The Institute of Public Health, Shirokanedai, Minato-ku, Tokyo 108, Japan

Reaction of 2-(trimethylsilylmethyl)pyridine ($1a$) with p-substituted benzaloxime O-methyl ether (2) in LDA/THF medium gave trans-2-aryl-3-(2-pyridyl)-aziridine ($3a$) together with (Z)-1-amino-1-aryl-2-(2-pyridyl)ethene ($4a$) as a by-product. When the THF solution of 2 was added to the α -silyl carbanion of $1a$ (Method A), yield of $3a$ was low, and it varied from 7 to 38% with the reaction conditions. Furthermore, considerable amounts of $4a$ (31 - 11%) was obtained. The reverse addition (Method B), however, gave selectively $3a$ (Ar, yield % of $3a$ and $4a$; C_6H_5 , 80, 6; p-ClC₆H₄, 85, 2; p-CH₃C₆H₄, 60, 9; p-CH₃OC₆H₄, 58, 12; p-(CH₃)₂NC₆H₄, 74, trace, respectively).

At room temperature, the ¹H-NMR spectrum of $3a$ (Ar = C₆H₅) shows singlets at δ 3.2 and 2.99, assignable to the aziridine-ring CH protons, and a broad signal at δ 2.46 assignable to the imino proton. The signals for the aziridine-ring CH protons at first broaden with decreasing temperature and ultimately split into AB quartets. This temperature dependence of the ¹H-NMR spectrum is explained by the inversion of the imino nitrogen, and ΔF^* was estimated to be about 14 kcal/mol at the coalescence temperature ($T_c = 0$ °C).

Three aziridines $3a$ (Ar = C₆H₅, p-CH₃C₆H₄, p-ClC₆H₄) were examined in mutagenicity for *Salmonella typhimurium* TA100 and TA98 by Ames' method. The chloro derivative of $3a$ showed no mutagenicity for TA100 and TA98 while the unsubstituted derivative showed quasi-mutagenicity for TA100 in the presence of S-9_{mix}, which was prepared from S-9, magnesium chloride, potassium chloride, glucose 6-phosphate, NADPH, NADH, and phosphate buffer. The S-9 was isolated from the liver of a male rat given a PCB (KC-500) injection. The methyl derivative of $3a$ showed mutagenicity for TA100 in spite of the presence or the absence of S-9_{mix}. Each of the aziridines $3a$ used, was toxicant for TA100 and TA98. The starting materials $1a$ and 2 showed no mutagenicity for either TA100 or TA98.