Formation of Chloroamines from Styrene under Conditions Mimicking Those of Water "Chlorination" Treatment

Kazuhiro NOJIMA,* Chiho ISOGAMI, Yukinari ITOH, Yasuhiro TAKAHASHI, and Minako KOBASHI

Faculty of Pharmaceutical Sciences, Josai University, 1–1 Keyakidai, Sakado, Saitama 350–02, Japan.
Received December 10, 1993; accepted January 27, 1994

The reaction of styrene with sodium hypochlorite in the presence of ammonium ion in 0.3 M phosphate buffer (pH 6.0) at room temperature afforded *N*-chloro-1-phenyl-2-chloroethylamine and *N,N*-dichloro-1-phenyl-2-chloroethylamine. 1-Phenyl-2-chloroethylamine hydrochloride, obtained as the reduction product of the two *N*-chloroamines, was shown to be mutagenic in the *Salmonella typhimurium* test.

Keywords *N*-chloro-1-phenyl-2-chloroethylamine; *N,N*-dichloro-1-phenyl-2-chloroethylamine; 1-phenyl-2-chloroethylamine hydrochloride; 2-phenylaziridine; mutagenicity; water treatment

Many kinds of pollutants are released into river and lakes and are subsequently exposed to a so-called "chlorination" treatment to make the water suitable for drinking. Rook[1] has shown that various halo-derivatives can be formed during the chlorination of natural waters.

Styrene monomer is used in large quantities as the starting material for the manufacture of styrene resin and is known to be released into the environment.[2] Also, it is well known that residual styrene monomer, in styrene resin used for packing foods, can be eluted from the packaging.[3] Hence, the metabolism, mutagenicity and carcinogenicity of styrene have been examined in detail by many researchers.[4] Watabe *et al.*[4d,5] established that styrene is metabolized to styrene 3,4-oxide, which exhibits stronger mutagenicity than benzo[*a*]pyrene 4,5-oxide. As far as synthetic reactions are concerned, Schmitz *et al.*[6] have reported that styrene reacts with dichloramine in ether to give *N*-chloro-2-phenylaziridine.

However, the behavior of styrene under the conditions used for water treatment, *i.e.* exposure to sodium hypochlorite in the presence of ammonium ion (a common water pollutant), has not yet been described. We wish to report here that chlorinated derivatives of styrene are formed under such conditions.

MATERIALS AND METHODS

Melting points are determined on a Yamato melting-point apparatus using capillary tubes and are uncorrected. Infrared (IR) spectra were recorded on a Jasco FT/IR-5300 infrared spectrophotometer using KBr disks for solids. Electron-impact mass spectra (EI-MS) were recorded using a JEOL DX-300 spectrometer. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on a JEOL GX 270 FT spectrometer. Chemical shifts were measured as ppm downfield from an internal standard (tetramethylsilane). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broad. Gas liquid chromatography (GLC) were performed using a Shimadzu GC-9A instrument equipped with a column packed with 1.5% SE-30 on Chromosorb WAW DMCS (the column temperature was maintained at 60 °C for styrene). High-performance liquid chromatography (HPLC) was carried out using a Waters LC Module 1 equipped with a UV (254 nm) detector and a Nova-Pak C8 (3.9 × 150 mm) column; the mobile phase was a mixture of methanol and acetic acid (95 : 5, v/v) at a flow rate of 1 ml/min. Column chromatography was performed on Kieselgel 60 (Merck, 70—230 mesh) or silanized Kieselgel 60 (Merck, 70—230 mesh). Thin-layer chromatography (TLC) was carried out using pre-coated silanized Kieselgel 60 plates (Merck) and spots were detected using aqueous potassium iodide solution or iodine.

The chemicals used in the experiments were supplied by Aldrich Chemical Co., Ltd., Tokyo Kasei Chemical Co., Ltd., and Wako Chemical Co., Ltd., and were purified before use, if necessary. Since commercial dichloromethane contains methanol to inhibit decomposition, the following treatment was carried out to remove it prior to use. Commercial dichloromethane was maintained in contact with anhydrous calcium chloride overnight at room temperature, and then filtered. The filtrate was washed three times with distilled water and then dried over anhydrous sodium sulfate.

Synthesis of 1-Phenyl-2-chloroethylamine Hydrochloride (1) A solution of di-*tert*-butyldicarbonate (2.5 g, 11.5 mmol) in dioxane (2 ml) was added dropwise to a stirred solution of phenylglycinol (1.37 g, 10 mmol) in dioxane (30 ml) and distilled water (15 ml) at room temperature. The mixture was stirred for 20 h at room temperature, followed by concentration under reduced pressure and then distilled water was added to afford a crystalline residue, which was recrystallized from a mixture of benzene and *n*-hexane to give *N-tert*-butoxycarbonyl-1-phenyl-2-hydroxyethylamine as colorless needles (2.0 g, 84%), mp 142—143 °C. *Anal.* Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.57; H, 7.96; N, 5.66.

Triphenylphosphine (524 mg, 2.0 mmol) and carbon tetrachloride (3.9 ml) were added to a stirred solution of *N-tert*-butoxycarbonyl-1-phenyl-2-hydroxyethylamine (540 mg, 2.3 mmol) in anhydrous acetonitrile (20 ml) at room temperature. The mixture was stirred for 2 d at room temperature, followed by concentration under reduced pressure and purification by column chromatography (silanized Kieselgel 60, 90 g; benzene : *n*-hexane = 1 : 2)

to afford a crystalline residue, which was recrystallized from *n*-hexane to give *N-tert*-butoxycarbonyl-1-phenyl-2-chloroethylamine as colorless needles (164 mg, 28%), mp 110—111 °C. *Anal.* Calcd for $C_{13}H_{18}ClNO_2$: C, 61.05; H, 7.09; N, 5.48. Found: C, 60.77; H, 7.04; N, 5.31.

N-tert-Butoxycarbonyl-1-phenyl-2-chloroethylamine (110 mg, 0.43 mmol) was dissolved in 20% HCl (5 ml) and ethanol (10 ml) and the mixture allowed to stand for 2 d at room temperature. The resulting solution was evaporated to dryness under reduced pressure to give a crystalline residue, which was recrystallized from a mixture of ethanol and *n*-hexane to afford 1-phenyl-2-chloroethylamine hydrochloride (**1**) as colorless needles (68 mg, 82%), mp 184—186 °C (dec.). IR (KBr): 2950, 1600, 1520, 1490, 1455, 1420, 770, 720, 700 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 4.01 (2H, d), 4.67 (1H, t), 7.50 (5H, m). *Anal.* Calcd for $C_8H_{11}Cl_2N$: C, 50.02; H, 5.77; N, 7.29. Found; C, 49.74; H, 5.71; N, 7.17.

Synthesis of 2-Phenyl-2-chloroethylamine Hydrochloride (2) Following the procedure described above, treatment of 2-amino-1-phenylethanol (1.37 g, 10 mmol) with di-*tert*-butyldicarbonate (2.5 g, 11.5 mmol) gave *N-tert*-butoxycarbonyl-2-hydroxy-2-phenylethylamine as colorless needles (2.0 g, 85%), mp 123—124 °C. *Anal.* Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.62; H, 8.04; N, 5.76.

Treatment of *N-tert*-butoxycarbonyl-2-hydroxy-2-phenylethylamine (540 mg, 2.3 mmol) with triphenylphosphine (524 mg, 2.0 mmol) and carbon tetrachloride (3.9 ml) afforded *N-tert*-butoxycarbonyl-2-chloro-2-phenylethylamine as a colorless oil (182 mg, 31%), which was treated with 20% HCl (5 ml) and ethanol (10 ml) to give 2-phenyl-2-chloroethylamine hydrochloride (**2**) as colorless needles (114 mg, 83%), mp 148—149 °C. IR (KBr): 3000, 2880, 1595, 1550, 1140, 890, 755, 695 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 3.52 (2H, d), 5.24 (1H, t), 7.44 (5H, m). *Anal.* Calcd for $C_8H_{11}Cl_2N$: C, 50.02; H, 5.77; N, 7.29. Found: C, 49.78; H, 5.69; N, 7.17.

Synthesis of *N*-Tosyl-1-phenyl-2-chloroethylamine (A) Tosyl chloride (480 mg, 2.5 mmol) was added to a solution of 1-phenyl-2-chloroethyalmine hydrochloride (**1**) (96 mg, 0.5 mmol) in pyridine (10 ml). The mixture was allowed to stand at 80 °C for 2 h, then poured into ice-water (30 ml) to give a crystalline residue, which was filtered and washed with distilled water. The resulting residue was dried under reduced pressure and recrystallized from benzene to give *N*-tosyl-1-phenyl-2-chloroethylamine (A) as colorless needles (129 mg, 95%), mp 172—173 °C. IR (KBr): 3260, 1600, 1500, 1460, 1430, 1320, 1310, 1170 cm^{-1}. EI-MS *m/z* (%): 273 (M^+ − HCl, 6.8). *Anal.* Calcd for $C_{15}H_{16}ClNO_2S$: C, 58.15; H, 5.21; N, 4.52. Found: C, 57.95; H, 5.31; N, 4.49.

Synthesis of *N*-Tosyl-2-phenylaziridine (B) Potassium hydroxide (25 mg, 0.45 mmol) was added to a solution of *N*-tosyl-1-phenyl-2-chloroethylamine (93 mg, 0.3 mmol) in methanol (100 ml), and the mixture heated under reflux for 2 h. The resulting solution was concentrated under reduced pressure, followed by the addition of distilled water (50 ml) saturated with NaCl, and then extracted with benzene (50 ml). The benzene phase was washed with distilled water (50 ml) saturated with NaCl, dried over anhydrous sodium sulfate and filtered. The resulting benzene solution was evaporated to dryness under reduced pressure to give an oily residue, which was crystallized from benzene and *n*-hexane to afford *N*-tosyl-2-phenylaziridine (B) as colorless plates (56 mg, 67%), mp 91—92 °C. EI-MS *m/z* (%): 273 (M^+, 24), 118 (M^+ − 155, 100). IR (KBr): 3040, 3000, 1595, 1495, 1460, 1310, 1230, 1190, 1160, 1095, 910, 820, 800 cm^{-1}. ^{1}H-NMR (CD_3OD) δ:2.42 (3H, s), 2.46 (1H, d), 2.94 (1H, d), 3.75 (1H, dd), 7.20—7.32 (5H, m), 7.41 (2H, d), 7.85 (2H, d). *Anal.* Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12. Found: C, 65.86; H, 5.78; N, 4.94.

Reaction of Styrene with Sodium Hypochlorite in the Presence of Ammonium Ion Ammonium chloride (2.4 g, 45 mmol) was added to a suspension of styrene (428 μl, 3.75 mmol) in 0.3 M phosphate buffer (pH 6.0) solution (500 ml). After the salt dissolved, 15% sodium hypochlorite solution (5.0 ml) was added, the mixture was stirred for 1 h at room temperature, and then extracted with dichloromethane (50 ml × 2). The resulting dichloromethane phase was washed with distilled water (50 ml), dried over anhydrous sodium sulfate, and then filtered. Identification of the reaction products was carried out as described in Results and Discussion.

Mutagenicity Assay The mutagenicity of 1-phenyl-2-chloroethylamine hydrochloride (**1**) was determined using the pre-incubation method of Yahagi,[7] which is a modification of the Ames method,[8] using strains TA98 and TA100 of *Salmonella typhimurium*, with or without S9 mix. The S9 fraction was prepared from the liver of rats treated with polychlorinated biphenyl.

RESULTS AND DISCUSSION

In order to investigate whether any products were formed by the reaction of styrene with sodium hypochlorite in the presence of ammonium ion in 0.3 M phosphate buffer (pH 6.0), TLC of the extract after 1 h of chlorination was performed on pre-coated silanized Kieselgel 60 plates. Spots were detected using aqueous potassium iodide solution to identify compounds with active chlorine atoms. Two spots with *Rf* values of 0.49 and 0.26 were clearly present on the thin-layer plate. They might be *N*-chloroamines, because of their reaction with potassium iodide.

Schmitz *et al.*[6] have already reported that styrene reacts with dichloramine in ether to give *N*-chloro-2-phenylaziridine and it is also well known that ammonium ion reacts with sodium hypochlorite at pH 6.0 to form a mixture of chloramine and dichloramine.[9] Therefore, it is possible that our products might include *N*-chloro-2-phenylaziridine.

In order to perform a direct comparison, we decided to synthesize *N*-chloro-2-phenylaziridine from 2-phenylaziridine. Brois,[10] Hassner *et al.*,[11] Kotera and Kitahonoki[12] and Zwierzak and Osowska[13] have all reported different routes to 2-phenylaziridine. Based on the yield and our confirmation of the structure of the product, we adopted one of these methods: the formation of 2-phenylaziridine[10] by the thermal elimination of sulfuric acid from 1-phenyl-2-aminoethanol sulfate ester in the pres-

ence of alkali. When the TLC behavior of the extract was compared with that of *N*-chloro-2-phenylaziridine, with *Rf* values of 0.34 and 0.14, obtained from the reaction of 2-phenylaziridine with *tert*-butyl hypochlorite, we found that the products in the extract differed from *N*-chloro-2-phenylaziridine, which had been synthesized by Kostyanovskii *et al.*[14] Also, Kostyanovskii *et al.* reported that their 2-substituted *N*-chloroaziridine contained *trans*- and *cis*-isomers.[15]

For further investigation, the two putative *N*- chloroamines in the extract were isolated by column chromatography on silanized Kieselgel 60 using *n*-hexane as an eluent. Since one of the isolated *N*-chloroamines, corresponding to spot **a** with an *Rf* value of 0.26 on the thin-layer plate, was unstable owing to the disproportionation described later, and the other isolated *N*-chroroamine, corresponding to spot **b** with an *Rf* value of 0.49, coexisted with a substantial amount of unreacted styrene, the products were reduced with benzylmercaptan in the presence of HCl. Briefly, each fraction was treated with 10% HCl and benzylmercaptan under vigorous stirring. Stirring was continued for 1 h, then the aqueous layer was separated and washed three times with dichloromethane. The resulting aqueous solution was evaporated to dryness under reduced pressure to give a crystalline residue, which was recrystallized from a mixture of ethanol and *n*-hexane. Each fraction afforded the same product, colorless needles, mp 184—186 °C (dec.). IR (KBr): 2950, 1600, 1520, 1490, 1455, 1420, 770, 720, 700 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 4.01 (2H, d), 4.67 (1H, t), 7.50 (5H, m). *Anal.* Calcd for $C_8H_{11}Cl_2N$: C, 50.22; H, 5.77; N, 7.29. Found: C, 50.05; H, 5.74; N, 7.29. The IR spectrum of the colorless needles derived from spot **a** was identical with that from spot **b**. From the ^{1}H-NMR spectrum, it was found that the reduction product contained one methylene, one methine and one phenyl proton. On the basis of these results and the elemental analysis, the structure of the reduction product was considered to be **1** or **2** (Chart 1).

We then set out to synthesize **1** and **2** according to the route described in the experimental section. The amino group in the starting material was protected by using di-*tert*-butyldicarbonate. The resultant *N*-*tert*-butoxycarbonyl derivatives were chlorinated with carbon tetrachloride in the presence of tripheylphosphine to afford *N*-*tert*-butoxycarbonyl-*β*-chloroamines, which were treated with aqueous hydrochloric acid to give the corresponding *β*-chloroamine hydrochlorides (**1** and **2**). By comparison of IR spectra, melting points and ^{1}H-NMR spectra, the reduction product described above was identified as compound **1**, 1-phenyl-2-chloroethylamine hydrochloride. Next, 1-phenyl-2-chloroethylamine hydrochloride (**1**) was subjected to chlorination using an excess of *tert*-butyl hypochlorite in *n*-hexane, after being treated with an excess of NaOH in methanol. The resulting *n*-hexane solution was spotted onto pre-coated silanized Kieselgel 60 plates and developed with *n*-hexane. The thin-layer chromatogram showed that the chlorination product corresponds to spot **b**. Moreover, when the *N*-chloroamine corresponding to spot **a** was treated with *tert*-butyl hypochlorite, spot **a** vanished and spot **b** appeared. Thus the *N*-chloroamines corresponding to spots **a** and **b** were shown to be *N*,*N*-dichloro-1-phenyl-2-chloroethylamine (**4**) and *N*-chloro-1-phenyl-2-chloroethylamine (**3**), respectively. The reaction found by us can be interpreted as shown in Chart 2. After addition of $NHCl_2$, produced by the reaction of ammonium hydrochloride with sodium hypochlorite in 0.3 M phosphate buffer (pH 6.0), to styrene, the resulting *N*-chloro-1-phenyl-2-chloroethylamine (**3**) might disproportionate to give *N*,*N*-dichloro-1-phenyl-2-chloroethylamine (**4**). From the product distribution, the chloro-cation appears predominantly to attack the methylene carbon in styrene but not the methine carbon.

Kovacic *et al.*[16] have reported that dialkyl-*N*-chloroamines react with some olefins in the presence of Fe^{2+} or Cu^+ to give chloroamination products, and proposed that a chloro-radical participates in the addition reaction. Minisci *et al.*[17] have reported that the reaction of *N*-chloropiperidine with styrene in the presence of Fe^{2+} gives C_6H_5–CHCl–CH_2–NC_5H_{10}.

However, neither Fe^{2+} nor Cu^+, which might generate a chloro-radical, was used in our experiments. The attack of a chloro-cation on the methylene carbon in styrene would be consistent with the reaction of styrene with bromine.[18] The total yield of the products (**3** and **4**) is shown in Table I. The residual styrene in the extract was analyzed by GLC. As the *N*-chloroamines (**3** and **4**) were unstable, the following procedure was employed for their determination. The extract was treated with a mixture of benzylmercaptan and 10% hydrochloric acid, and the resultant aqueous solution was evaporated to dryness under reduced pressure to give a residue which was dissolved in methanol. This methanol solution was

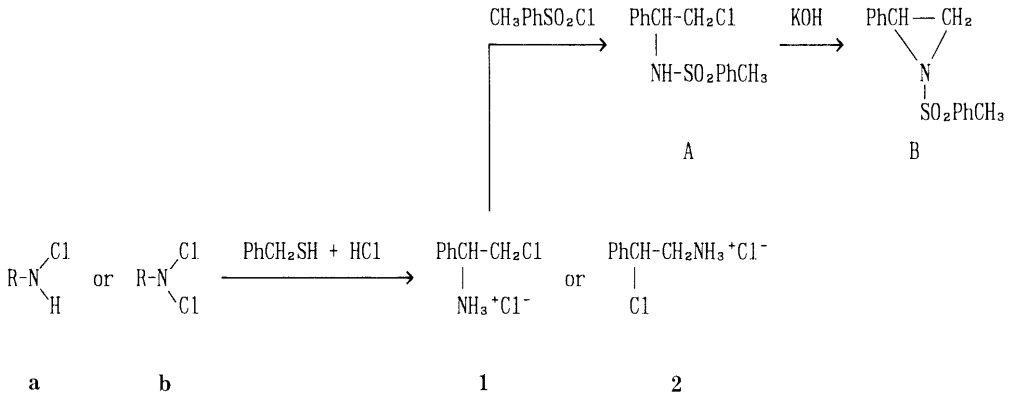
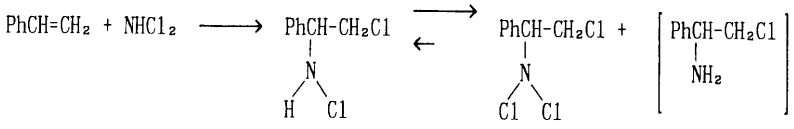


Chart 1



3 4

Chart 2

TABLE I.[a] Total Yield of *N*-Chloroamines (**3** and **4**) from Styrene

Run	Ratio of styrene conversion	Product (yield)[b]
1	46%	**3** and **4** (17%)
2	50%	**3** and **4** (14%)
3	34%	**3** and **4** (15%)

a) Styrene, 3.75 mmol. *b*) Yields are based on the quantity of styrene reacted.

TABLE II. Mutagenicity of 1-Phenyl-2-chloroethylamine Hydrochloride Tested Using *Salmonella typhimurium* TA 98 and TA 100

Substance	μg/plate	TA 98		TA 100	
		−S9 mix	+S9 mix	−S9 mix	+S9 mix
Control		30	45	132	135
1-Phenyl-2-chloroethyl-	25	33	41	388	326
amine hydrochloride	50	42	45	684	554
	100	40	50	1068	924
	250	64	59	2688	2096
	500	63	93	3820	3738
Benzo[*a*]pyrene	5	29	253	127	1340
AF-2[a]	0.2	423	131		
	0.02			430	310

a) 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide.

analyzed by HPLC.

β-Haloamines are key materials in the synthesis of aziridines.[13] The ability of aziridinium salts to undergo facile ring opening[10b] by nucleophiles may account for the carcinostatic action of aziridines and related β-haloamines, possibly by alkylating enzyme sites.[19]

When we tried to convert compound **1**, obtained by the reduction of the *N*-chloroamines (**3** and **4**) with benzylmercaptan in the presence of hydrochloric acid, to a stable crystalline solid soluble in organic solvents, by the use of tosyl chloride in pyridine, we obtained *N*-tosyl-1-phenyl-2-chloroethylamine (A). Treatment of this with potassium hydroxide in methanol gave *N*-tosyl-2-phenylaziridine (B), as shown in Chart 1. This result casts doubt on the report by Schmitz *et al.*[6] that styrene reacted with dichloramine in ether to give *N*-chloro-2-phenylaziridine, since they treated the product (*N*-chloroamine) derived from styrene and dichloramine with potassium iodide (reduction) and then converted it to a stable derivative (derivatization and dehydrochlorination?) using ammonium thiocyanate. In other words, cyclization leading to the aziridine may have occurred during the work-up.

If *N*-chloro-1-phenyl-2-chloroethylamine (**3**) and *N*,*N*-dichloro-1-phenyl-2-chloroethylamine (**4**) are ingested *via* drinking water treated by "chlorination," they might readily be reduced *in vivo* to 1-phenyl-2-chloroethylamine hydrochloride (**1**) by L-ascorbic acid or tocopherol found in foods and by sodium erythrobate or *dl*-α-tocopherol added as antioxidants to foods. We therefore examined the mutagenicity of compound **1** using Yahagi's method,[7] which is a modification of the Ames procedure.[8] The mutagenic activity of compound **1** tested with strains TA98 and TA100 of *Salmonella typhimuriumin*, with or without S9 mix, is presented in Table II. Generally, the tested chemical is considered mutagenic if it induces more than twice the number of revertants as the control. It was observed that compound **1** was mutagenic for both strains and that addition of S9 mix did not affect its mutagenic activity in these strains.

Acknowledgement The authors wish to thank Y. Hirose, Saitama Prefectural Institute of Public Health, for conducting the mutagenicity test.

REFERENCES

1) *a*) J. J. Rook, *J. Water Treat. Exam.*, **23**, 234 (1974); *b*) *Idem*, *Environ. Sci. Technol.*, **11**, 478 (1977).
2) *a*) A. Tossavainen, *Scand. J. Work Environ. Health*, **4**, Suppl. 2, 7 (1978); *b*) R. Tokunaga, S. Takahata, M. Onoda, T. Ishi-i, K. Sato, M. Hayashi, M. Ikeda, *Int. Arch. Arbeitsmed.*, **33**, 257 (1974).
3) T. Kawamura *et al.*, "Standard Methods of Analysis for Hygienic Chemists with Commentary," ed. by Y. Yamane, Kimbara Inc., Tokyo, 1990, p. 795.
4) *a*) O. M. Bakke, R. R. Scheline, *Toxicol. Appl. Pharmacol.*, **16**, 691 (1970); *b*) T. Watabe, M. Isobe, T. Sawahara, K. Yoshikawa, E. Takabatake, *Scand. J. Work Environ. Health*, **4**, Suppl. 2, 142 (1978); *c*) Pantarotto, R. Fanelli, F. Bidoli, P. Morazzoni, M. Salmona, K. Szczawinska, *ibid.*, **4** (Suppl. 2), 67 (1978); *d*) T. Watabe, A. Hiratsuka, T. Aizawa, T. Sawahata, N. Ozawa, M. Isobe, E. Takabatake, *Mutat. Res.*, **93**, 45 (1982).
5) T. Watabe, A. Hiratsuka, T. Aizawa, T. Sawahata, *Tetrahedron Lett.*, **23**, 1185 (1982).
6) E. Schmitz, U. Bicker, S. Schramm, K.-P. Diets, *J. Prakt. Chemie*, **320**, 413 (1978).
7) T. Yahagi, *Tampakushitsu Kakusan Koso*, **20**, 1178 (1975).
8) B. N. Ames, J. McCann, E. Yamasaki, *Mutat. Res.*, **31**, 347 (1975).
9) R. Sawamura *et al.*, "Standard Methods of Analysis for Hygienic Chemists. with Commentary," ed. by Y. Yamane, Kimbara Inc., Tokyo, 1990, p. 951.
10) S. J. Brois, *J. Org. Chem.*, **27**, 3532 (1962).
11) *a*) A. Hassner, M. E. Lorber, C. Heathcock, *J. Org. Chem.*, **32**, 540 (1970); *b*) A. Hassner, G. J. Matthews, F. W. Fowler, *J. Am. Chem. Soc.*, **91**, 5046 (1969).
12) K. Kotera, K. Kitahonoki, *Org. Syn.*, **48**, 75 (1968).
13) A. Zwierzak, K. Osowska, *Angew. Chem., Int. Ed. Engl.*, **15**, 302 (1976).
14) R. G. Kostyanovskii, A. A. Fomichev, V. M. Novikov, *Zh. Strukt. Khim.*, **12**, 722 (1971).
15) R. G. Kostyanovskii, Z. E. Samojlova, I. I. Tchervin, *Tetrahedron Lett.*, **1969**, 719.
16) P. Kovacic, M. K. Lowry, K. W. Field, *Chem. Rev.*, **70**, 639 (1970).
17) F. Minisci, R. Galli, M. Cecere, *Tetrahedron Lett.*, **1966**, 3163.
18) K. Yates, W. V. Wright, *Tetrahedron Lett.*, **1965**, 1927.
19) S. A. Dyogteva, *Angew. Chem., Int. Ed. Engl.*, **1**, 600 (1962).