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Received May 25, 1995

Revised September 6, 1995

A *N*-heterocyclic compound containing two hetero atoms, imidazo[5,1-*a*]isoindole, was synthesized in 40% yield by the intramolecular photocyclization of *N,N'*-bis(*o*-chlorobenzyl)imidazolium salts **1** in water (neutral or pH ~4) or of *N*-(*o*-chlorobenzyl)imidazole **2**, in aqueous acid (pH ~4). However, the photocyclized compound **3** was not formed effectively in basic aqueous solution (3 equivalents of sodium hydroxide or pyridine) or in acetonitrile by the photochemical reaction of *N,N'*-bis(*o*-chlorobenzyl)imidazolium salts **1** or *N*-(*o*-chlorobenzyl)imidazole (**2**).

J. Heterocyclic Chem., **32**, 1835 (1995).

In view of the development of *N*-heterocyclic compound synthesis, intramolecular photocyclization of *N*-(2-halophenyl)alkylpyridinium salts have been studied [1-3]. The concepts of the study were extended to the heterocyclic ring system containing two hetero atoms. Thus, the *N,N'*-bis(*o*-chlorobenzyl)imidazolium salt and *N*-(*o*-chlorobenzyl)imidazole were prepared and their photocyclization reactions were studied. Here, we report that a *N*-heterocyclic system containing two nitrogen atoms is synthesized simply by the intramolecular photocyclizations of *N,N'*-bis(*o*-chlorobenzyl)imidazolium salt (**1**) and *N*-(*o*-chlorobenzyl)imidazole (**2**).

N,N'-Bis(*o*-chlorobenzyl)imidazolium chloride (**1**) was prepared by refluxing *o*-chlorobenzyl chloride (0.07 mole, 9.0 ml) with imidazole (0.035 mole, 2.0 g) in acetonitrile (50 ml) in the presence of sodium carbonate for 2 days. The ¹H nmr spectrum of *N,N'*-bis(*o*-chlorobenzyl)imidazolium chloride (**1**) obtained has signals corresponding to the imidazole protons at 9.67 (s, 1H), and 7.87 (s, 2H). The phenyl protons are at 7.40-7.60 (m, 8H), and the benzyl protons at 5.64 (s, 4H).

N-(*o*-Chlorobenzyl)imidazole (**2**) was also prepared by refluxing imidazole (0.06 mole, 4.3 g), sodium hydride (0.1 mole, 2.5 ml) and *o*-chlorobenzyl chloride (0.06 mole, 0.7 ml) in dimethoxyethane (50 ml) for 2 days.

First of all, the ultraviolet absorption spectra changes vs irradiation time (time interval 5 minutes) were measured upon irradiation of the imidazolium salt **1** in water with monochromatic light of wavelength 267 nm (Figure 1). Three new bands on 420, 370 and 293 nm were observed. The spectrum changes show that the imidazolium salt is photolabile and a kinetic study for the product is possible. The product absorbed around 293 nm was identified as 5*H*-imidazo[5,1-*a*]isoindole (*vide infra*). The products absorbed around 420 and 370 nm (small amounts) and have not yet been identified.

When the aqueous solution of *N,N'*-bis(*o*-chlorobenzyl)imidazolium chloride (**1**, 500 mg, water 500 ml) in

a water-cooled quartz photo-vessel was irradiated for 15 minutes with a Hg-lamp (Hanovia, 200 W, high pressure) under Ar, a *N*-heterocyclic compound, 5*H*-imidazo[5,1-*a*]isoindole (**3**, 40% yield), was obtained along with minor products, *N*-(*o*-chlorobenzyl)imidazole (10%), *N*-benzylimidazole (3%), *o*-chlorobenzyl alcohol (10%), and *o*-chlorobenzyl chloride (3%) (Scheme 1). This indicates that photofragmentation and photoreduction reactions also occurred during the photocyclization of **1** in water.

The ¹H nmr spectrum of 5*H*-imidazo[5,1-*a*]isoindole has phenyl proton 7 at 7.68 (d, 1H), proton 4 at 7.58 (d, 1H), proton 6 at 7.38 (t, 1H) and proton 5 at 7.36 (t, 1H) and the signals assignable to the benzyl protons (3) and

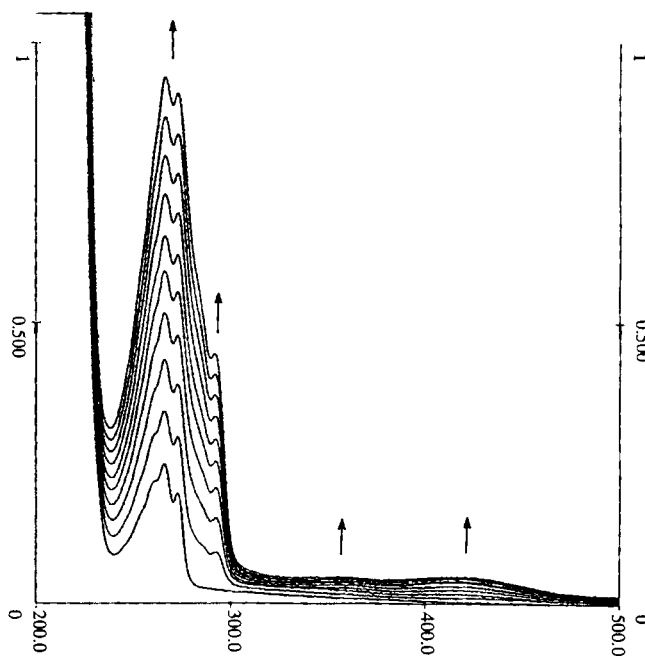


Figure 1. Ultraviolet absorption spectra changes of imidazolium salt **1** vs irradiation time upon irradiation of **1** in water with monochromatic light (267 nm).

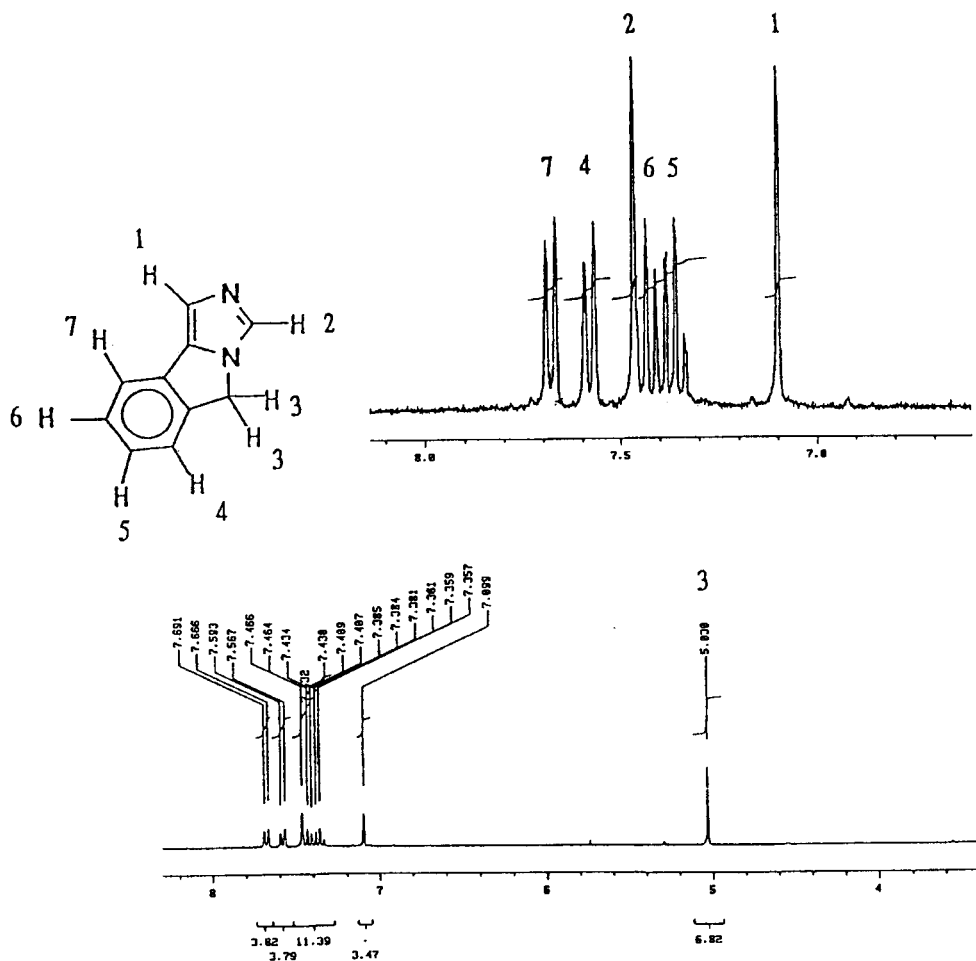
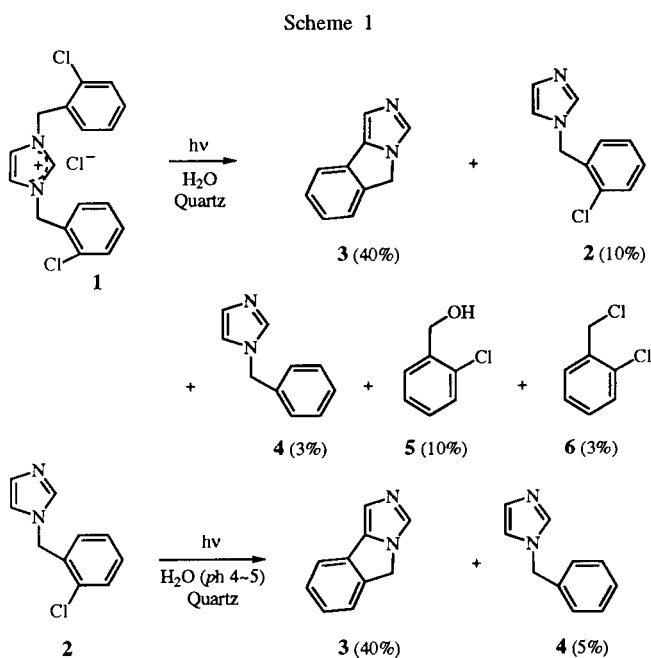


Figure 2. ^1H nmr (300 MHz) spectrum of $5H$ -imidazo[5,1- a]isoindole in DMSO-d_6 .



imidazole protons (1 and 2) at 5.03 (s, 2H), 7.46 (s, 1H) and 7.10 (s, 1H), respectively (see Figure 2). The ir spectrum shows the characteristic absorption at 1732 and 1616 cm^{-1} for the cyclic imine structure. The mass spectra shows the molecular ion peaks of 156 and an interesting fragment of 129 formed by expelling $\text{HC}=\text{N}$. The ultraviolet absorption spectra shows the λ_{max} in methanol is 276.0 nm ($\epsilon = 4300$).

When the acidic aqueous solution of **2** (250 mg, 1.4×10^{-3} mole, pH 4-5) was irradiated as above, the photocyclized product, $5H$ -imidazo[5,1- a]isoindole was obtained in 40% yield. This suggests that the N -(o -chlorobenzyl)-imidazole generated from the bisbenzylimidazolium salt produces the $5H$ -imidazo[5,1- a]isoindole as a secondary photoproduct.

The relative rate of the formation of photocyclized product, **3** (λ_{max} 293) from **1** and **2** in acetonitrile was identical. This indicates that N -(o -chlorobenzyl)imidazole formed rapidly from the fragmentation reaction of the imidazolium salt **1**, and undergoes photocyclized reaction to give **3**. The reaction mechanism is not clear at this

time. We could not get a better yield from the reaction in methyl alcohol or acetonitrile solvents. We believe that the photocyclization of the *N,N'*-bis(*o*-chlorobenzyl)imidazolium salt and *N*-(*o*-chlorobenzyl)imidazole open up synthetic methods for 5 or 6-membered polyhetero-atom heterocyclic compounds.

EXPERIMENTAL

All melting and boiling points were determined on an Electrothermal Melting Point Apparatus and are uncorrected. Nuclear magnetic resonance (¹H nmr) spectra were measured in deuteriochloroform on a Bruker AM-300, 300 MHz spectrometer. The gc-ms were determined on Hewlett Packard 5890 Series II. The photochemical reaction products were analyzed by a FID detector in the gas chromatography with HP-1 capillary column (cross-linked 5% methyl silicon, 25 m). Ultraviolet absorption spectra were measured on Shimadzu, UV-265.

Synthesis of *N,N'*-Bis(*o*-chlorobenzyl)imidazolium Chloride (1).

Imidazole (2.04 g, 0.03 mole) and *o*-chlorobenzylchloride (9.02 ml, 0.07 mole) were dissolved in 50 ml of acetonitrile. Sodium carbonate (3.18 g, 0.03 mole) was added to the acetonitrile solution and the resulting heterogeneous solution was refluxed for two days. The solution was cooled to room temperature and the solid obtained was removed by filtration. The filtrate was concentrated to a few ml by rotatory evaporator. Acetone (100 ml) was added to the concentrated solution and the solution was stirred overnight to give a white solid. This solid was washed with acetone three times and diethyl ether twice. After drying at reduced pressure, 9.926 g of pure solid was obtained in 94% yield, mp 163-164°; ¹H nmr (300 MHz, DMSO-*d*₆): δ ppm 9.67 (s, 1H, imidazole HC=N), 7.87 (d, 2H, J = 2.4 Hz, imidazole N-HC=CH-N), 7.4-7.6 (m, 8H, phenyl H), 5.64 (s, 4H, benzyl H); ir (potassium bromide): 3127, 3059, 2851, 1636, 1552, 1476, 1443 cm⁻¹; uv (water): λ_{max} (ε) 267 (570).

Anal. Calcd. for C₁₇H₁₅N₂Cl₃ (353.68): C, 57.73; H, 4.27; N, 7.92. Found: C, 57.60; H, 4.25; N, 7.82.

Synthesis of *N*-(*o*-Chlorobenzyl)imidazole (2).

Imidazole (4.3 g, 0.06 mole), sodium hydride (2.5 ml, 0.1 mole) and *o*-chlorobenzyl chloride (0.7 ml, 0.06 mole) were dissolved in dimethoxyethane (50 ml) and refluxed for 2 days. The solid (sodium chloride) formed was removed by filtration. The solvent was removed from the filtrate by distillation at reduced pressure. The resulting liquid was purified by vacuum distillation to give 6.9 g of a sticky liquid in 60% yield, bp 98-104°/1 Torr; ¹H nmr (300 MHz, DMSO-*d*₆): δ 7.77 (s, 1H, N=CH-N), 7.48 (m, 1H, Ph H), 7.35 (m, 2H, Ph H), 7.20 (s, 1H, imidazole C=CH-N), 7.08 (m, 1H, Ph H), 6.95 (s, 1H, imidazole N-CH=C), 5.32 (s, 2H, benzyl H); ir (neat): 3111, 1595, 1507, 1445, cm⁻¹; uv (methanol): λ_{max} (ε) 267.0 (215).

Anal. Calcd. for C₁₀H₉N₂Cl (192.65): C, 62.35; H, 4.71; N, 14.54. Found: C, 62.40; H, 4.81; N, 14.30.

Synthesis of 5*H*-Imidazo[5,1-*a*]isoindole (3).

Into a water-cooled quartz photoreactor were introduced 500 mg of 1 and 500 ml of triple distilled water (degassed and Argon purged). The homogeneous solution was irradiated for 15 minutes with an Hg-lamp (Hanovia 200 W, high pressure) under

argon. The solution turned to light yellow after the irradiation and the pH of the solution was about 4. After adjusting the pH of the solution to about 9 by adding sodium bicarbonate, the organic products from the yellow solution were extracted by chloroform (2 x 20 ml) and ethyl acetate (2 x 20 ml). The solvent was removed by rotatory evaporator and the resulting products were purified by using tlc (silica gel IB-F, 250 μ) eluting with a solvent mixture of chloroform and methanol (4:1 by volume). The photocyclized product 3 was obtained in 40% yield [88 mg, Rf = 0.8 silica gel IB-F, 250 μ, chloroform/methanol (4/1)]; ¹H nmr (300 MHz, DMSO-*d*₆): δ ppm 7.68 (d, 1H, J = 7.5 Hz, phenyl H), 7.58 (d, 1H, J = 7.8 Hz, phenyl H), 7.46 (s, 1H, imidazole N=CH-N), 7.38 (t, 1H, J = 7.5 Hz, phenyl H), 7.36 (t, 1H, J = 7.5 Hz, phenyl H), 7.10 (s, 1H, imidazole N=CH-N), 5.03 (s, 2H, benzyl H) (Figure 2); ms: m/z (relative intensity) 156 (100%, M+), 129 (17%, M-N=CH), 103 (4%, M-C₃H₃N); uv (methanol): λ_{max} (ε) 276.0 (4300), 293 (2900).

Anal. Calcd. for C₁₀H₈N₂ (156.19): C, 76.90; H, 5.16; N, 17.94. Found: C, 77.05; H, 5.27; N, 17.80.

When the preparative photoreaction mixture was eluted with GC column (sample injection 1 μl, injection temperature 220°, detector temperature 250°, Att. 10), five product peaks (retention time 5.03, 5.28, 9.38, 11.24, and 11.77) appeared. They were identified as *o*-chlorobenzyl chloride (5.03), *o*-chlorobenzyl alcohol (5.28), *N*-benzylimidazole (9.38), 5*H*-imidazo[5,1-*a*]isoindole (11.24) and *N*-(*o*-chlorobenzyl)imidazole (11.77) by comparing them with those of the authentic samples.

The preparative photoreaction of 2 is the same as that of 1 above.

Kinetic Study.

To the distilled water in a uv quartz cell was added imidazole salt 1, the amount of which was optimized to give the absorption of the solution about 0.4 at 267 nm in uv-vis spectrum. The quartz cell was then stopped with a silicon septum and the solution in the quartz cell was purged with Ar for 20 minutes. The ultraviolet spectra were taken upon irradiating the above solution every 5 minutes with monochromatic light of wavelength 267 nm (Figure 1). The first spectrum of the solution of 1 was taken without irradiation. The new peak at about 293 nm which originated from the photocyclized product appeared and the intensities of both peaks at about 293 nm and 267 nm were increased upon irradiation of 1 with monochromatic light (267 nm). The relative rate of the formation of 3 by irradiating the 1 or 2 in acetonitrile was determined by measuring the change of the absorption peak at 293 nm (ε₂₉₃ of 3 = 2900). Acetonitrile was chosen because both reactants are soluble, although the photocyclization is effective in water.

Acknowledgements.

The present studies were supported by the Basic Science Research Program, Ministry of Educations, 1995 (project No. BSR1-95-3402) and the Korea Science and Engineering Foundation (project No. 93-0500-09-01-3), Korea.

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