The Mechanisms for Thermal and Photochemical Isomerizations of N-Substituted 2-Halopyrroles: Syntheses of N-Substituted 3-Halopyrroles

Sung-Hyun Park, Hong-Joo Ha, Chultaek Lim, Dong-Kwon Lim, Kwang-Hee Lee, and Yong-Tae Park*

*Kyungpook National University, Daegu 702-701, Korea. *E-mail: ytpark@knu.ac.kr*
Received May 23, 2005

Halopyrroles, N-substituted 2-halopyrroles were prepared by halogenation of N-substituted pyrroles with NBS, NCS, or surfuryl chloride. N-Substituted 3-halopyrroles were synthesized by acid-catalyzed thermal and photochemical isomerization reactions of N-substituted 2-halopyrroles. Both the thermal and photochemical reactions were acid-catalyzed. For the acid-catalyzed isomerization, a mechanism of [1,3] bromine shift followed by deprotonation is operated. For the acid-catalyzed photoisomerization, an excited triplet state of 2-protonated N-benzyl-2-halopyrrole produces an intermediate N-substituted pyrrole complex with halonium ion which is equilibrated with N-substituted pyrrole plus halonium ion, and then the halonium ion newly adds to 3-position of N-substituted pyrrole followed by deprotonation to afford N-benzyl-3-halopyrrole.

Key Words : N-Benzyl-2-halopyrrole, N-Benzyl-3-halopyrrole, Photochemical isomerization, Thermal isomerization, Pyrrole ring complex with bromonium ion
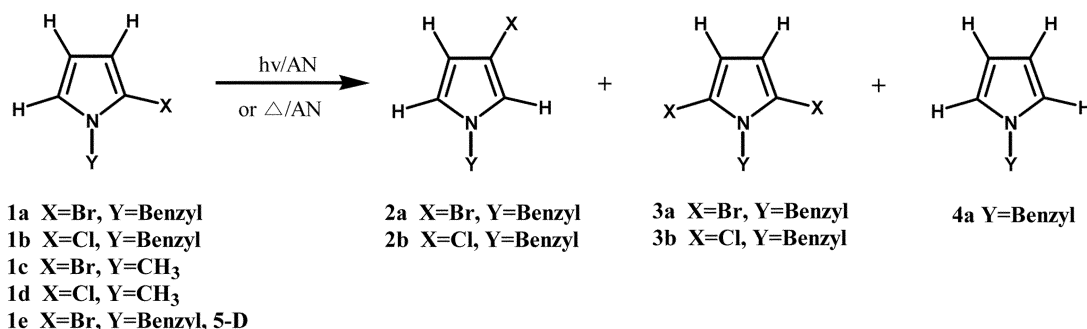
Introduction

Pyrroles are an important class of heterocyclic compounds having many different activities in a variety of biological environments. Therefore, many methods for the syntheses of pyrrole derivatives are described in the literature.[1] Particularly, the isomerization method for the syntheses of pyrrole derivatives is interesting and valuable because of its simplicity. Several isomerization methods for the syntheses of pyrrole derivatives are known. Acid-catalyzed isomerizations of 2-substituted-pyrrole and N-substituted-pyrrole derivatives afford 3-substituted pyrrole derivatives and 2- and 3-substituted pyrrole derivatives, respectively.[2-4] Photoisomerization of pyrrole derivatives are also known.[5,6] Irradiation of 2-cyanopyrrole in methanol yields 3-cyanopyrrole as a major product.[5a] Photoreaction of N-acetylpyrrole in cyclohexane or ethanol affords 2-acetylpyrrole.[5c] For photoisomerization of 2-cyanopyrrole the transposition mechanism involving 2,5-bonding followed by walk of aziridine nitrogen atom is reported.[6] For photoisomerization of N-acetylpyrrole, an intermediate, aziridine valence isomer of 2-H pyrrole is involved in the reaction.[5c]

However, only one report is available for the syntheses of 3-halopyrrole derivatives from corresponding 2-halopyrroles: Gilow and Burton[7] observed that 1-methyl-, 1-benzyl-, and 1-phenyl-2-bromopyrroles undergo isomerization and disproportionation when treated with hydrogen bromide or trifluoroacetic acid in carbon tetrachloride in the study of halogenation of pyrrole and substituted pyrroles. Thus, the diversification of the isomerization for the syntheses of 3-halopyrrole derivatives from the corresponding 2-halopyrrole derivatives and the descriptions of the mechanisms are necessary. In this paper, we describe a photoisomerization method for synthesis N-substituted 3-halopyrrole from N-substituted 2-halopyrrole in addition to the thermal isomerization and two mechanisms for the thermal and photochemical isomerizations of N-substituted 2-halopyrrole.

Results and Discussion

Preparation of N-Benzyl-2-halopyrrole (1a-1e). N-Benzylpyrrole was prepared by addition of potassium hydroxide to DMSO solution of pyrrole followed by benzylation with benzyl chloride. This method is simpler than the literature method.[8] N-Benzyl-2-bromopyrrole (**1a**)

1a X=Br, Y=Benzyl
1b X=Cl, Y=Benzyl
1c X=Br, Y=CH₃
1d X=Cl, Y=CH₃
1e X=Br, Y=Benzyl, 5-D

2a X=Br, Y=Benzyl
2b X=Cl, Y=Benzyl

3a X=Br, Y=Benzyl
3b X=Cl, Y=Benzyl

4a Y=Benzyl

Scheme 1

and *N*-methyl-2-bromopyrrole (**1c**) were prepared by bromination of *N*-benzylpyrrole and *N*-methylpyrrole with *N*-bromosuccinimide (NBS), respectively.[7] *N*-Benzyl-2-chloropyrrole (**1b**) was prepared by chlorination of *N*-benzylpyrrole with *N*-chlorosuccinimide (NCS). *N*-Methyl-2-chloropyrrole (**1d**) was prepared by chlorination of *N*-methylpyrrole with sulfuryl chloride. In order to study NMR kinetics on the thermal and photochemical isomerization reactions, *N*-benzyl-2-bromo-5-deuteriopyrrole (**1e**) was prepared: first of all, *N*-benzyl-2,5-dibromopyrrloe was prepared by the method of Gilow and Burton[7]; one of the bromine groups of *N*-benzyl-2,5-dibromopyrrole was lithiated with butyl lithium and then worked up with D$_2$O.

Preparative Photoisomerization. When an acetonitrile solution of *N*-benzyl-2-bromopyrrole (**1a**, 400 mL, 1.7 × 10^{-3} M) was irradiated with a 100W-medium pressure Hg lamp for 7 min at room temperature under Ar and then the reaction mixture was separated by Al$_2$O$_3$[9] column with an eluent, chloroform and hexane (1 : 3), *N*-benzyl-3-bromo-pyrrole (**2a**, 60%) was obtained as major product with a minor products, *N*-benzylpyrrole (**4a**, 10%) and *N*-benzyl-2,5-dibromopyrrole (**3a**, 10%) (Scheme 1). The ^{1}H NMR spectrum of *N*-benzyl-3-bromopyrrole has methylene protons of benzyl group at 5.00 (s, 2H) ppm, 4-, 5-, and 2-protons of pyrrole ring at 6.16 (m, 1H), 6.59 (m, 1H), and 6.65 (m, 1H) ppm, respectively, and phenyl protons from 7.11 to 7.34 ppm (m, 5H). The lower field absorption of 2-proton on pyrrole ring than that of 5-proton is due to the deshielding effect of bromine group on 3-position of pyrrole ring in addition to ring current effect of phenyl ring. This assignment was confirmed by observing a stronger inter-action of 5-proton of *N*-benzyl-3-bromopyrrole with 4-proton than the interaction of 2-proton with 4-proton in two-dimensional NMR spectrum (not shown).

The isomeric pyrrole product, *N*-benzyl-3-chloropyrrole (**2b**) was also obtained from the photoreactions of *N*-benzyl-

2-chloropyrrole (**1b**). However, *N*-methyl-2-halopyrroles, **1c** and **1d** gave tarry products instead of isomeric products. This implies that the phenyl group of **1a** and **1b** is important for the isomerization and blocking for the polymerization. The synthesis of 3-substituted pyrrole is difficult because generally electrophilic halogenation on pyrrole derivative occur at 2-position of the pyrrole due to high electron density of 2- and 5-positions of pyrrole. Thus, this method is simple and straightforward for the syntheses of *N*-benzyl-3-halopyrrole.

Reactivity and Mechanism. In order to study the reactivities of the reactants and the reaction mechanisms, the relative rates for the photoreaction of *N*-benzyl-2-halopyrrole (**1**) were measured in the several conditions. First of all, an acetonitrile solution of *N*-benzyl-2-halopyrrole (for example **1a**, 1 × 10^{-2} M, 3 mL) in a quartz cell was deaerated with argon or oxygen and irradiated with Xe-lamp (450W) or monochromatic light for a limited time. When a small portion of the irradiated solution was analyzed on GC/MS, four peaks whose retentions times were 6.3, 8.7, 9.9 and 11.1 min appeared. The four peaks are identified as *N*-benzylpyrrole (**4a**), *N*-benzyl-2-bromopyrrole (**1a**), *N*-benzyl-3-bromopyrrole (**2a**), and *N*-benzyl-2,5-dibromo-pyrrole (**3a**). The relative yields were determined by peak areas. The pertinent results are given in Table 1.

Photoreaction of *N*-benzyl-2-bromopyrrole (**1a**) for 10 min gave *N*-benzyl-3-bromopyrrole (**2a**) as a major product (59%) and *N*-benzylpyrrole (**4a**) as a minor product (13%) with trace amount of *N*-benzyl-2,5-dibromopyrrole (**3a**) as observed in preparative photoreaction. The reaction proceeded for 73% of starting material for 10 min (entry 1). *N*-Benzyl-2-chloropyrrole (**1b**) gave the isomerized (20%) and disproportionated (6%) products but not reduced product for 60 min under the same condition as **1a**. The reaction of **1b** proceeded for 26% of starting material for 60 min (entry 2). Thus, bromopyrrole **1a** is more reactive

Table 1. Reactivity Variation on Photoeaction of *N*-Benzyl-2-Halopyrrole with Broad Light

Entry	Reactant	Condition	Irr. Time (min)	Product (%)			
				recover.	2 (2a,2b)	3 (3a,3b)	4 (4a)
1	**1a**	AN*/Ar	10	27	59	tr	13
2	**1b**	AN/Ar	60	74	20	6	0
3	**1a**	AN/O$_2$	10	44	24	15	11
4	**1b**	AN/O$_2$	60	99	tr	0	0
5	**1a**	AN/benzophenone/Ar	30**	59	19	10	12
6	**1a**	AN/aq NaOH/Ar	10	79	5	8	8
7	**1b**	AN/aq NaOH/Ar	60	74	19	7	0
8	**1a**	AN/TEA†/Ar	10	82	4	7	7
9	**1a**	CCl$_4$/TFA††/Ar	10	19	63	7	8
10	**1b**	AN/TFA/Ar	60	72	22	6	0
11	**1a**	benzene/Ar	10	98	1	0	0
12	**1a**	cyclohexane/Ar	10	96	tr	0	tr
13	**1a**	CCl$_4$/Ar	10	91	tr	0	tr
14	**1a**	MeOH/Ar	10	95	tr	0	tr

*AN stands for acetonitrile. **irradiated for 30 min with monochromatic light of 330 ± 5 nm. †TEA stands for trietylamine. ††TFA stands for trifluoroaceticacid.

toward the photoreaction than chloropyrrole **1b**. This result indicates that a cleavage reaction of the bond between carbon and halogen of the pyrrole ring occurs. Observation of the bond cleavage between halogen and carbon of pyrrole ring in the reaction can not be explained by the mechanism involving 2,5 bonding followed by [1,3] nitrogen shift and rearomatization for the photoisomerization of 2-cyano-pyrrole.[5,6]

In the presence of oxygen the reactions were retarded (entry 3, 4). These results imply that triplet states of the pyrroles are involved in the reaction. This conclusion is confirmed by observing that the photoreaction occurs when a triplet sensitizer, benzophenone is irradiated with mono-chromatic light, 330 ± 5 nm which is not absorbed by **1a** (entry 5).

In the basic medium the photoreaction of **1a** was retarded whereas in the acidic medium the reaction was accelerated (entry 6, 8, 9). These results imply the reaction is acid-catalyzed one. However, the photoreaction rate of **1b** in a acidic medium is a little faster than that of **1b** in a basic medium, probably because of the low reactivity of **1b**. It is worth mentioning that isomerization reaction of **1a** was slow at a very early stage and was accelerated at later stage without an acid. In other words, there was an induction period for the isomerization reaction in acetonitrile without an acid. This result can be understood in assumption of hydrogen bromide formation during the induction period, by which the isomerization of **1a** is catalyzed.

In the nonpolar solvents the reaction was slow (entry 11-13). These results can be explained by assuming that in nonpolar medium a charged species involved in the reaction is difficult to form. In line with this assumption is the fact that a hybrid product, *N*-benzyl-2-bromo-5-chloropyrrole along the expected products was detected in the photo-reaction of equal amount of **1a** and **1b** in acetonitrile. In polar solvent, methanol the reaction was also slow (entry 14). Protonation on **1a** or **1b** for the acidic-catalytic reaction

is blocked in methanol because proton is eliminated by tying it up on oxygen of hydroxyl group of methanol.

The thermal reaction of the pyrroles **1a** and **1b** were tested. An acetonitrile solution of **1a** or **1b** was not changed at room temperature for 1 days. However, the acetonitrile solution of bromopyrrole **1a** containing a small amount of trifluoroacetic acid (TFA) at 50 °C for 1 hr produced **2a** (77%), **4a** (7%), and dibromopyrroles[10a] as observed by Gilow and Burton.[7] Chloropyrrole **1b** also produced **2b** (30%) and dichloropyrrole[10b] in the presence of catalytic amount of TFA for 5 hrs at 80 °C. Thus, the thermal reactions are also acid-catalyzed ones and bromopyrrole **1a** is more reactive toward the thermal reaction than chloro-pyrrole **1b**.

To clarify the reaction mechanisms, appearances of proton nuclear magnetic resonances on the initial states (recognizable size in NMR spectra) of the thermal and photochemical reactions of deuterated pyrrole, **1e** were examined. First of all, NMR spectra for deuteriochloroform solution of *N*-benzyl-2-bromo-5-deuteriopyrrole (**1e**) in NMR tube were taken with 300 MHz NMR before the thermal or photo-chemical reaction (a in Figure 1). The singlet peak at 5.08 ppm (2 H) is corresponding to benzyl protons of **1e**, multiplet peaks at 6.20 ppm (1.91 H) to 3- and 4-protons on pyrrole ring, multiplet peaks above 7.00 ppm (4.91 H) for phenyl protons, and small peak at 6.71 ppm (0.2 H, 80% deuteration) for unsubstituted 5-proton of the pyrrole. The solution of **1e** in the NMR tube was placed at 70 °C water bath for 15 min and then NMR spectra of the reacted solution was acquired (b in Figure 1). A big peak at 4.96 ppm (2.00 H) in the NMR spectra of the reacted solution corresponds to benzyl proton of isomeric product, **2a** and small peaks at 5.08 and 5.05 ppm are for benzyl protons of the reactant and reduced product, *N*-benzylpyrrole, respectively. The three small peaks at 4.91, 5.01 and 5.07 ppm are corresponding to benzyl protons of doubly brominated products[10a] but not *N*-benzyl-2,5-dibromopyrrole. The multi-
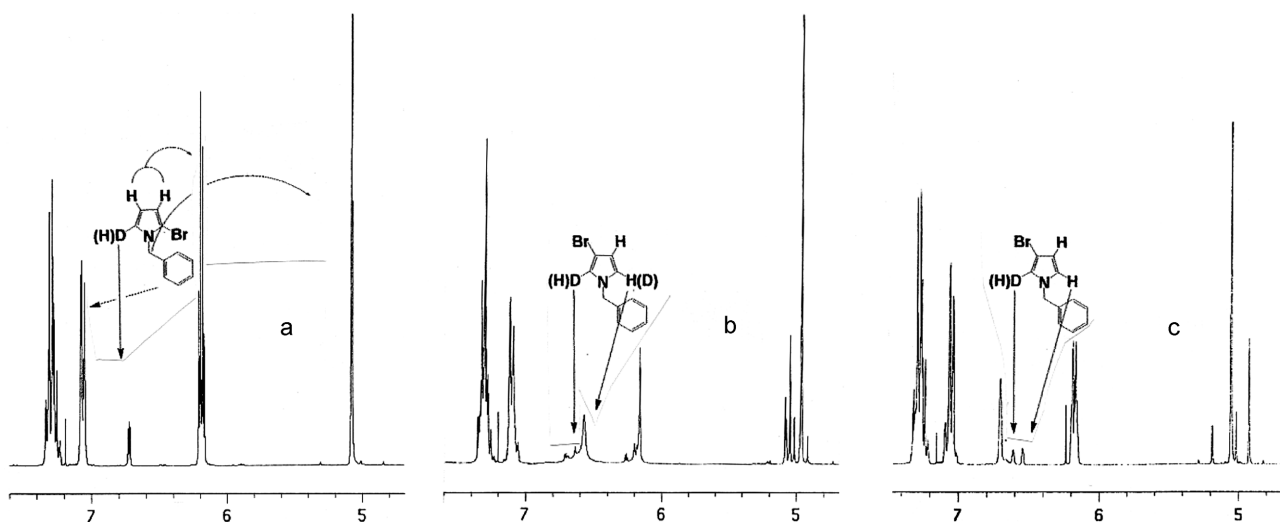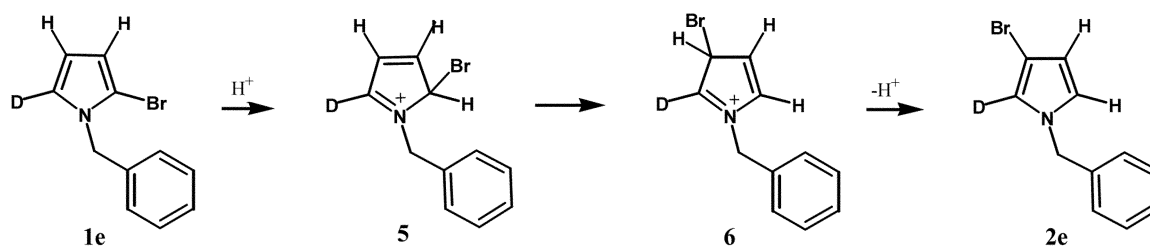

Figure 1. Proton NMR spectrum of *N*-benzyl-2-bromo-5-deuteriopyrrole (**1e**) in deuteriochloroform before reaction (a) and the NMR spectra changes on thermal (b) and photochemical (c) reactions.
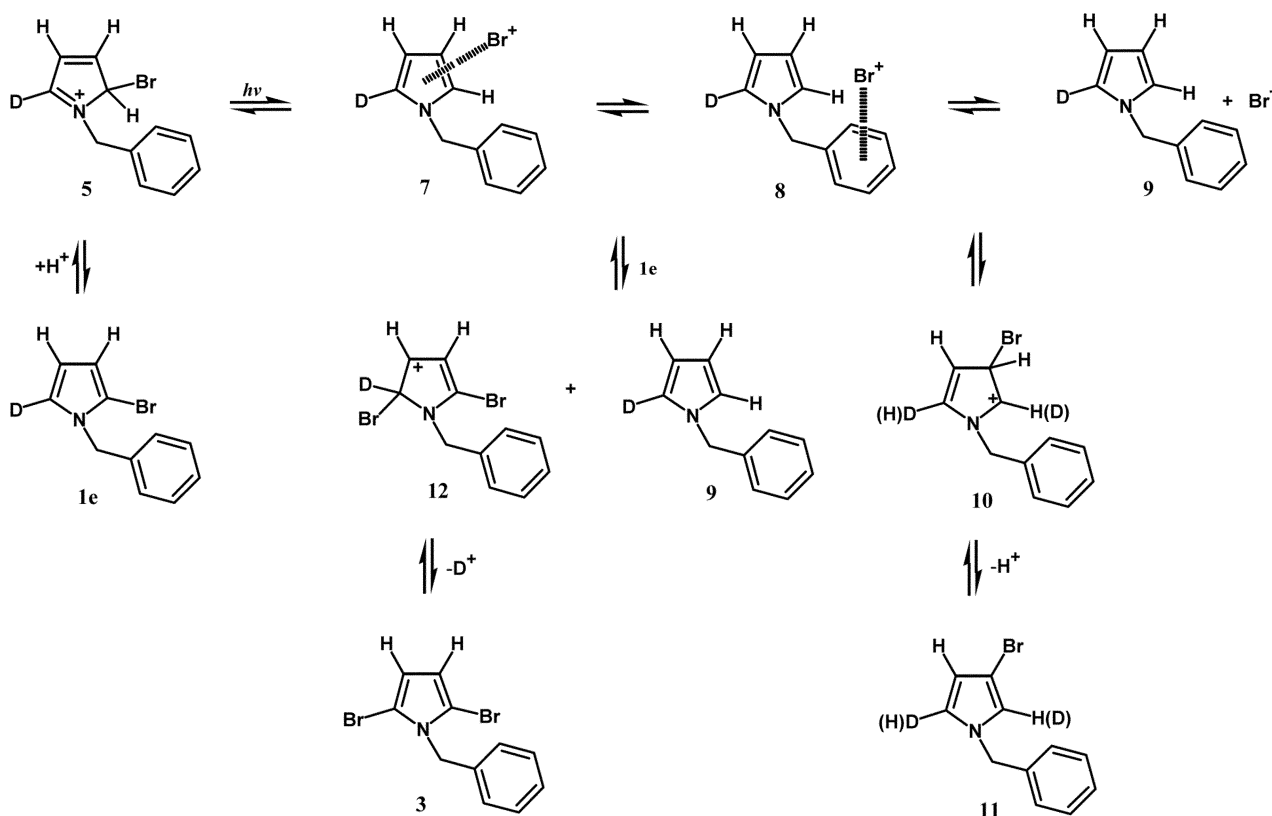
Scheme 2

plet peaks at 6.20 ppm decrease due to the reaction proceeding comparing with that of reactant (from 1.91 H to 0.84 H). The unsubstituted proton at 5-position of pyrrole ring decreases as starting material underwent reaction and a new small peak at 6.68 ppm is due to 2,5-protons of *N*-benzylpyrrole. An important observation is that the peak at 6.64 ppm (0.16 H) corresponding to 2-proton of pyrrole ring of isomeric product, **2a** is smaller than the peak at 6.57 ppm (0.71 H) corresponding to 5-proton of the pyrrole ring of isomeric product **2a**. This means that deuterium resides in the 2-position of pyrrole of isomerized product and thus bromo group at 2-position of pyrrole ring of reactant is shifted to 4-position of reactant to give *N*-benzyl-3-bromo-2-deuteriopyrrole.

It is noteworthy that *N*-benzyl-2,5-dibromopyrrole was not observed in the NMR of this thermal reaction. The following mechanism for the thermal reaction of *N*-substituted 2-bromopyrrole is proposed (Scheme 2).

Protonation on 2-carbon of pyrrole of reactant, **1e** proceeds to form intermediate **5** because electron charge density is higher on 2- and 5-carbons of the pyrrole ring than 3- or 4-carbon and a protonation on 2- or 5-position of reactant also relieves strain between benzyl group and sp² C-hydrogen of resonance form of pyrrole moiety. The 2-protonated *N*-benzyl-2-bromo-5-deuteriopyrrole (2-*H* pyrrole) undergoes 1,3-bromine shift to give intermediate **6**. Deprotonation of intermediate **6** affords the isomeric product, *N*-benzyl-3-bromo-2-deuteriopyrrole. The disproportionated products are formed by reaction of protonated pyrrole **5** or **6** with reactant. *N*-benzyl-2-chloropyrrole (**1b**) is less reactive than *N*-benzyl-2-bromopyrrole (**1a**) because of difficulty of 1,3-chlorine shift in the mechanism. This mechanism is different from that of the rearrangement of 2-acylpyrrole, in which acylium ion and the pyrrole are produced as intermediates.[2]

After the solution of **1e** was irradiated at 0 °C with Xe-lamp (200W) for 3 min, NMR spectra of the solution was

Scheme 3

acquired (c in Figure 1). The peak at 4.96 ppm is for benzyl protons of isomerized product, *N*-benzyl-3-bromo-2-deuteriopyrrole, the peak at 5.05 ppm for benzyl protons of reduced product, *N*-benzyl-2-deuteriopyrrole, the peak at 5.07 ppm for benzyl protons of reactant, and the peak at 5.20 ppm for benzyl protons of disproportionated product, *N*-benzyl-2,5-dibromopyrrole. By integration, reaction totally proceeded in 19% of reactant, isomerized in 13% and disproportinated in 6% yields. The peaks at 6.18 ppm are for 3- and 4-protons of pyrrole ring of isomerization and reduction products and the singlet peak at 6.23 ppm is for 3,4-protons of *N*-benzyl-2,5-dibromopyrrole. The broad and multiplet peaks above 7.00 ppm are for phenyl protons of reactant and products. The most important observations are that the peaks at 6.54 and 6.61 ppm, which are for 5- and 2-protons of pyrrole ring of isomeric product, were equivalent in size at even initial stage of the reaction and the peak at 6.71 ppm corresponding to unsubstituted 5-proton of pyrrole ring of reactant surprisingly increased compared to that of reactant. The results can be explained by involving symmetric intermediate, *N*-benzyl-2-deuteriopyrrole in the reaction, which gave isomeric product or reactant by newly brominating of the intermediate. The very small peak at 6.68 ppm is for 2-protons of pyrrole ring of reduced product, *N*-benzyl-2-deuteriopyrrole. The following reaction mechanism which is consistent to the results of kinetics is proposed (Scheme 3).

Excited triplet state of C-protonated *N*-benzyl-2-bromo-pyrrole (2-*H* pyrrole) populated upon direct irradiation or by photosensitizer reaction under acidic medium yields a symmetric intermediate, pyrrole ring complex of *N*-benzyl-pyrrole with bromonium ion (**7**) in which are equilibrated with phenyl complex of *N*-benzylpyrrole with bromonium ion (**8**) and separated *N*-benzylpyrrole plus bromonium ion (**9**). The electrophilic bromonium ion from **7**, **8**, or **9** adds newly to 3- and 2-position of the intermediate pyrrole ring, to give protonated *N*-benzyl-3-bromopyrrole (**10**) and protonated reactant (**5**), which afford isomeric product (**11**) and reactant (**1**) by deprotonation, respectively. The bromonium ion can also add to 5-positions of reactant (**1**) to give disproportionated products (**9**). When a small amount of anisole was added in the photoreaction of **1a**, detection of the presence of *p*-bromanisole (1% against total products), which is intermolecularly electrophilic substitution product of anisole with bromonium ion, supports the mechanism.

Experimental Section

General. Pyrrole and *N*-methylpyrrole were distilled prior to use. Melting points were uncorrected and determined on an Electrothermal Melting Point Apparatus. GC analyses were performed on a GC Instrument equipped with a flame detector and a 50 m × 0.32 mm (nonpolar) column. GC/MS analyses were carried out on a capillary column (0.25 mm, 30 m) (helium as carrier gas). ^{1}H NMR and 2D NMR spectra were recorded in CDCl$_3$ solution.

Irradiation was carried out with 100-W medium pressure

Hg lamp at room temperature for preparative studies. Light source from Xe-Arc lamp (450 W) was used for kinetic and NMR kinetic studies.

Synthesis of *N*-Benzylpyrrole. To a stirred mixture of DMSO (350 mL), KOH (24 g, 0.43 mol) and pyrrole (30 mL, 0.43 mol) in a 500 mL three-necked round-bottomed flask equipped with a thermometer, dropping funnel, and condenser was added benzyl chloride (50 mL, 0.43 mol) dropwise. The resulting mixture was stirred at 65 °C for 1 hr. After stripping of DMSO *in vacuo*, distillation (58 °C/0.5 mmHg, lit.[11] bp 247 °C) gave colorless oil (57 g, 85%).

Synthesis of *N*-Benzyl-2-bromopyrrole (1a). Fresh distilled *N*-benzylpyrrole (3 g, 0.02 mol) was dissolved in 80 mL of THF and cooled in a dry ice/acetone bath. NBS (3.4 g, 0.02 mol) was added to the THF solution of *N*-benzylpyrrole and the resulting mixture was stirred until all the NBS was in solution. The mixture was allowed to stand in a freezer (−10 °C) for 3 hr. After adding sodium sulfite (3 g) and sodium hydroxide (2 g) to the mixture, the mixture was stripped of solvent and extracted with carbon tetra-chloride. After carbon tetrachloride portion was concentrated by evaporation, performance of column chromatograph for the concentrated mixture gave a colorless oil (Al$_2$O$_3$ column; 32 cm × 3 cm, eluent; hexane/chloroform = 3/1): Yield 2.6 g (60%): UV (λ_{max} in acetonitrile) 255 nm (ε = 1.1 × 10^4 L/mole·cm); ^{1}H NMR (CDCl$_3$) δ5.09 (s, 2H), 6.19 (m, 2H), 6.72 (m, 1H), 7.06-7.34 (m, 5H); MS (EI) m/z (rel intensity) 237 (29, M$^+$+2), 235 (29, M$^+$), 156 (80), 91 (100).

Synthesis of *N*-Benzyl-2-chloropyrrole (1b). *N*-Benzyl-pyrrole (1 g, 0.01 mol) was chlorinated with NCS (1.7 g, 0.013 mol) in THF as described in the case of **1a**. Performance of chromatograph for the reaction mixture gave a colorless crystal (1 g, 40%); mp 123-124 °C; UV (λ_{max} in AN) 251 nm (ε = 1.1 × 10^4 L/mole·cm); ^{1}H NMR (CDCl$_3$) δ 5.08 (s, 2H), 6.08 (m, 1H), 6.14 (m, 1H), 6.63 (m, 1H), 7.08-7.34 (m, 5H); MS (EI) m/z (rel intensity) 193 (3, M$^+$+2), 191 (9, M$^+$) 156 (50), 89 (100).

Synthesis of *N*-Methyl-2-bromopyrrole (1c). *N*-Methyl-pyrrole (1 g, 0.01 mol) was brominated with NBS (2.2 g, 0.01 mol) in THF as described in the case of **1a**. Colorless oil (1 g, 50%). UV (λ_{max} in AN) 240 nm (ε = 1.0 × 10^4 L/mole·cm); ^{1}H NMR (CDCl$_3$) δ3.58 (s, 3H), 6.12 (m, 2H), 6.67 (m, 1H): MS (EI) m/z (rel intensity) 161 (97, M$^+$+2), 159 (100, M$^+$), 79 (52).

Synthesis of *N*-Methyl-2-chloropyrrole (1d). In a 100 mL three-necked flask fitted with a thermometer, a reflux condenser, and a 50 mL dropping funnel was placed 5 g of *N*-methylpyrrole in 20 mL of diethyl ether. After the flask was cooled to 0 °C with ice and an ether solution of sulfuryl chloride (8.5 g of sulfuryl chloride in 20 mL of ether) was added dropwise over a period of 10 min, the mixture was stirred at 10 °C for 10 min. A solution of 10% potassium carbonate was added to the mixture and then the mixture was extracted with diethyl ether. After drying with magnesium sulfate, vacuum distillation (40-42 °C/10 mm Hg) gave colorless oil (5.2 g, 75%). UV (λ_{max} in AN) 240 nm (ε = 1.2 × 10^4 L/mole·cm); ^{1}H NMR (CDCl$_3$) δ3.57 (s,

3H), 6.02 (dd, J = 2.1, J = 1.8 Hz, 1H), 6.08 (t, J = 3.0 Hz, 1H), 6.58 (t, J = 3.0 Hz, 1H); MS (EI) m/z (rel intensity) 117 (3, M^++2), 115 (9, M^+), 101 (100).

Synthesis of *N*-Benzyl-2-bromo-5-deuteriopyrrole (1e). First of all, *N*-benzyl-2,5-dibromopyrrole (**3a**) was prepared as described in literature.[7] In a 100-mL round bottomed three-necked flask fitted with a thermometer, a condenser, and a dropping funnel was placed 8 g of *N*-benzyl-2,5-dibromopyrrole (0.026 mol) and 50 mL of THF. The solution was cooled to −78 °C with dry ice and acetone. To the solution, 10.4 mL of hexane solution of N-BuLi (2.5 M) was added slowly. The mixture was stirred for a period of 7 min and 10 mL of D_2O was added. The mixture was extracted with diethyl ether and the ether portion was concentrated. Performance for the concentrated ether portion gave a colorless oil (3 g, 50%). UV (λ_{max} in AN) 255 nm (ε = 1.1 × 10^4 L/mole·cm); ^{1}H NMR (CDCl$_3$) δ 5.08 (s, 2H), 6.20 (m, 2H), 6.71 (m, 0.2H, unsubstituted H), 7.00-7.34 (m, 5H); MS (EI) m/z (rel intensity) 238 (5, M^++2), 236 (15, M^+).

Preparative Photoreaction of *N*-Benzyl-2-bromopyrrole (1a)- General Procedure. To a large immersion well photolysis unit with provision for circulating nitrogen was added 400 mL of an approximately 4.5 × 10^{-3} M acetonitrile solution of *N*-benzyl-2-bromopyrrole (**1a**). With nitrogen circulation, the solution was irradiated with a 100 W Hg-lamp (medium pressure) 7 min. After evaporation solvent, the mixture was chromatographed (alumina gel 60, 32 × 3 cm) with eluent, hexane/chloroform (3/1) to give 240 mg of *N*-benzyl-3-bromopyrrole (**2a**, 60%), 27 mg of *N*-benzyl-2,5-dibromopyrrole (**3a**, 5%), and 14 mg of *N*-benzylpyrrole (**4a**, 5%). **2a**: colorless crystal (recrystallization from *n*-hexane), mp 75-76 °C; UV (λ_{max} in AN) 260 nm (ε = 1.0 × 10^4 L/mole·cm); ^{1}H MNR (CDCl$_3$) δ 5.00 (s, 2H), 6.16 (m, 1H), 6.59 (m, 1H), 6.65 (m, 1H), 7.11-7.34 (m, 5H); MS (EI) m/z (rel intensity) 237 (66, M^++2), 235 (66, M^+), 91 (100). **3a**: colorless crystal (recrystallization from hexane), mp 65-66 °C; UV (λ_{max} in AN) 260 nm (ε = 1.1 × 10^4 L/mole·cm); ^{1}H NMR (CDCl$_3$) δ 5.24 (s, 2H), 6.26 (s, 2H), 7.04-7.35 (m, 5H); MS (EI) m/z (rel intensity) 317 (35, M^++4), 315 (68, M^++2), 313 (36, M^+), 91 (100). **4a**: colorless oil; UV (λ_{max} in AN) 230 nm (ε = 1.2 × 10^4 L/mole·cm); ^{1}H NMR (CDCl$_3$) δ 5.05 (s, 2H), 6.19 (d, J = 2.1 Hz, 2H), 6.68 (d, J = 2.1 Hz, 2H), 7.09-7.33 (m, 5H); MS (EI) m/z (rel intensity) 157 (20, M^+), 128 (100).

Preparative Photoreaction of *N*-Benzyl-2-chloropyrrole (1b). Photoreaction of **1b** was performed as described for **1a**. Isomerized and disproportionated products (**2b**, 60%, **3b**, 5%) were isolated. **2b**: colorless crystal (recrystallization from hexane); mp 45-46 °C; UV (λ_{max} in AN) 240 nm (ε = 1.2 × 10^4 L/mole·cm); ^{1}H NMR (CDCl$_3$) δ 5.08 (s, 2H), 6.18 (m,1H), 6.60 (m, 1H), 6.66 (m, 1H), 7.11-7.34 (m, 5H). MS (EI) m/z (rel intensity) 193 (13, M^++2), 191 (37, M^+), 156 (50), 91 (100). **3b**: colorless oil; UV (λ_{max} in AN) 244 nm (ε = 1.3 × 10^4 L/mole·cm); ^{1}H NMR (CDCl$_3$) δ 5.17 (s, 2H), 6.09 (s, 2H), 7.07-7.34 (m, 5H); MS (EI) m/z (rel intensity) 229 (1, M^++4), 227 (6, M^++2), 225 (10, M^+), 191 (66), 91 (100).

Kinetics

Photoreaction of *N*-Benzyl-2-bromopyrrole (1a) - General Procedure. An acetonitrile solution of *N*-benzyl-2-bromopyrrole (**1a**, 1.3 × 10^{-2} M, 3 mL) in a quartz vessel was deaerated with argon and irradiated with Xe-lamp (or monochromatic light) for 10 min. When a small portion of the solution was analyzed on GC/MS using a capillary column, four peaks whose retention times were 6.3, 8.7, 9.9, and 11.1 min appeared. These peaks are identified as reduced product **4a**, reactant **1a**, isomerized product **2a**, and *N*-benzyl-2,5-dibromopyrrole (**3a**), respectively. The relative yields for the photoreactions of **1** are shown in Table 1.

Photoreaction of *N*-Benzyl-2-chloropyrrole (1b). Three peaks at retention times 7.6, 8.7, and 9.3 min. are reactant, isomerized product **2b**, and doubly chlorinated product **3b**, respectively.

Thermal Reaction of *N*-Benzyl-2-Bromopyrrole (1a) - General Procedure. After an acetonitile solution of *N*-benzyl-2-bromopyrrole (**1a**, 1.3 × 10^{-2} M, 10 mL) in the presence of trifluoroacetic acid (1 × 10^{-3} M) was stirred at 50 °C for 1 hr, a small amount of the solution was analyzed on GC/MS as above. The products were identified as **2a** (77%), **4a** (7%) and dibromopyrroles.[10a]

Thermal Reaction of *N*-Benzyl-2-chloropyrrole (1b). After an acetonitrile solution of **1b** (1.3 × 10^{-2} M, 10 mL) in the presence of trifluoroacetic acid (1 × 10^{-3} M) was stirred at 80 °C for 5 hr, a small amount of the solution was analyzed on GC/MS as above. The products were identified as **2b** (30%) and dichloropyrrole (7%).[10b]

NMR Study of *N*-Benzyl-2-bromo-5-deuteriopyrrole (1e). Two mL of deuteriochloroform solution of 0.02 M *N*-benzyl-2-bromo-5-deuteriopyrrole (**1e**, stock solution) was placed in NMR tube and proton NMR spectra was taken before reactions (a in Figure 1). For thermal reaction, after two mL of the stock solution in NMR tube was placed in 70 °C bath for 15 min, the proton NMR spectra was taken and shown in Figure 1(b). For photoreaction, after two mL of the stock solution in a qurtz NMR tube was irradiated with Xe-lamp (450 W) at 0 °C for 3 min, proton NMR spectra was taken and shown in Figure 1(c).

Detection of Hybrid Product, *N*-Benzyl-2-bromo-5-chloropyrrole. A acetonitrile solution of **1a** and **1b** (each 7.0 × 10^{-3} M, 3 mL) was irradiated with Xe-lamp for 20 min. In addition to several peaks corresponding photoproducts expected from each reactant, mass spectra for a peak at retention time 9.6 min showed that the relative intensity of M^+ (269), M^++2 (271), and M^++4 (273) was 3 : 4 : 1, indicating an intermolecular substitution product, *N*-benzyl-2-bromo-5-chloropyrrole.

Detection of *p*-Bromoanisole in the Photoreaction of 1a in the Presence of Anisole. When three mL of acetonitrile solution of **1a** (1 × 10^{-2} M) containing small amount of anisole was irradiated, a peak for 4-bromoanisole appeared in GC spectra in addition to the expected photoproducts (1/100 peak ratio is obtained for 4-bromoanisole to total products).

References

1. (a) Cordell, G. A. *J. Org. Chem.* **1975**, *40*, 3161. (b) Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1998**, 615. (c) Gilchrist, T. L. *Heterocyclic Chemistry*, 3rd ed.; Longman: England, 1997; p 192. (c) Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: New York, 1994; Vol. 2, p 119. (e) Jones, R. A. In *the Chemistry of Heterocyclic Compounds*; Taylor, E. C., Ed.; Wiley & Sons: New York, 1990; Vol. 48, Part 1.
2. Carson, J. R.; Davis, N. M. *J. Org. Chem.* **1981**, *46*, 839.
3. De Rosa, M. *J. Org. Chem.* **1982**, *47*, 1008.
4. Carmona, O.; Greenhouse, R.; Landeros, R. Muchowski, J. M. *J. Org. Chem.* **1980**, *45*, 5336.
5. (a) Hiraoka, H. *J. Chem. Soc., Chem. Commun.* **1970**, 1306. (b) Hiraoka, H. *J. Chem. Soc., Chem. Commun.* **1971**, 1610. (c) Shizuka, H.; Okutsu, E.; Mori, Y.; Tanaka, I. *Mol. Photochem.* **1969**, *1*, 135. (d) Patterson, J. M.; Ferry, J. D.; Boyd, M. R. *J. Am. Chem. Soc.* **1973**, *95*, 4356. (e) Patterson, J. M.; Burka, L. T. *Tetrahedron Lett.* **1969**, 2215. (f) Patterson, J. M.; Bruser, D. M. *Tetrahedron Lett.* **1973**, 2959.
6. (a) Barltrop, J.; Day, A. C.; Moxon, P. D.; Ward, R. R. *J. Chem. Soc., Chem. Commun.* **1975**, 786. (b) Barltrop, J.; Day, A. C.; Ward, R. W. *J. Chem. Soc., Chem. Commun.* **1978**, 131.
7. Gilow, H. M.; Burton, D. E. *J. Org. Chem.* **1981**, *46*, 2221.
8. Hobbs, C. F.; McMillin, C. K.; Papadopoulos, E. P.; VanderWerf, C. A. *J. Am. Chem. Soc.* **1962**, *84*, 43.
9. Silica gel can be also used. However, basic aluminum oxide is better than acidic silica gel.
10. (a) GC/MS spectra for the reaction solution showed that in addition to isomeric product, there were three doubly brominated products such as *N*-benzyl-2,3-dibromopyrrole, *N*-benzyl-2,4-dibromopyrrole, and *N*-benzyl-3,4-dibromopyrrole as minor products, although the positions of bromine group are not determined. However, *N*-benzyl-2,5-dibromopyrrole is not observed. (b) GC/MS spectra for the reaction solution of **1b** showed that in addition to **2b** there was one doubly chlorinated product that the position was not determined.
11. CRC, Handbook of Chemistry and Physics, 56th Ed.; CRC Press: 1975; p C-472.