

Photoreaction of 2'-Halobenzanilide: Synthesis of 2-Phenylbenzoxazole

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Irradiation of 2'-bromobenzanilide in acetonitrile containing sodium hydroxide under nitrogen leads to the formation of the intramolecular photosubstituted product, 2-phenylbenzoxazole (45%) along the minor photoreduced and photo-Fries type product. The photoreaction of 2'-chlorobenzanilide under the same condition as above gives the photo-Fries type reaction product, 2-amino-3-chlorobenzophenone (22%) with minor product, 2-phenylbenzoxazole. The photoreaction of 2'-chlorobenzanilide in acetonitrile produces a photocyclized product, phenanthridone (19%) along with minor products, 2-phenylbenzoxazole, benzanilide, 2-amino-3-chlorobenzophenone, and 4-amino-3-chlorobenzophenone, while that of 2'-bromobenzanilide produces photosubstituted product, 2- phenylbenzoxazole.

key words: 2'-Halobenzanilide, 2-phenylbenzoxazole, Photosubstitution, Photoreduction, Photo-Fries type reaction, Photocyclization

INTRODUCTION

The photochemistry of haloarene, especially 2-haloarene tethered to arene, is of special interest in connection with photochemical ring formation method and photochemical degradation method of pollutant haloarene [1-4]. The photochemistry of 2-halobenzanilides is quite well known: the photoreaction of 2-chlorobenzanilide gives a cyclized product, phenanthridone, while that of 2-bromobenzanilide gives a reduced product, benzanilide [5]. However, the photochemistry of 2'-halobenzanilide is not much known and is diverse depending upon the reaction condition: the photoreaction of 2'-chlorobenzanilide gives intractable mixture in cyclohexane [6]; in benzene, the reaction yields 2'-phenylbenzanilide [6] and phenanthridone [7]. Furthermore, we recently found that intramolecular photosubstitution of N-(2-halophenyl)pyridinecarboxamide in a basic and neutral media produced 2-pyridinylbenzoxazole [8].

Thus, we decided to reinvestigate the photochemical behavior of 2'-halobenzanilide in a basic and neutral media.

Results

2'-halobenzanilide (**1a** and **1b**) were prepared by acylation of 2-haloaniline with benzoyl chloride in pyridine. The

detail of the preparation method is described in the experimental section.

The uv/vis absorption spectral change of 2'-chlorobenzanilide (**1a**) on irradiation time was measured and is shown in Figure 1. An increase around 320 nm and clear isosbestic points indicates that formation of phenanthridone is a major one. The uv/vis absorption spectral change of 2'-bromobenzanilide (**1b**) in basic aqueous acetonitrile solution (H₂O/ acetonitrile 1/ 9, [NaOH]= 0.05 M.) on irradiation time was measured and is shown in Figure 2. An increasing peak around 290 nm with a little scattering isosbestic points shows that the intramolecular photosubstitution is the major one, even though there are the minor reactions. Thus, a preparative photoreaction was carried out in basic and neutral media in order to identify the products.

When a 0.7 mmolar solution of 2'-bromobenzanilide (0.2

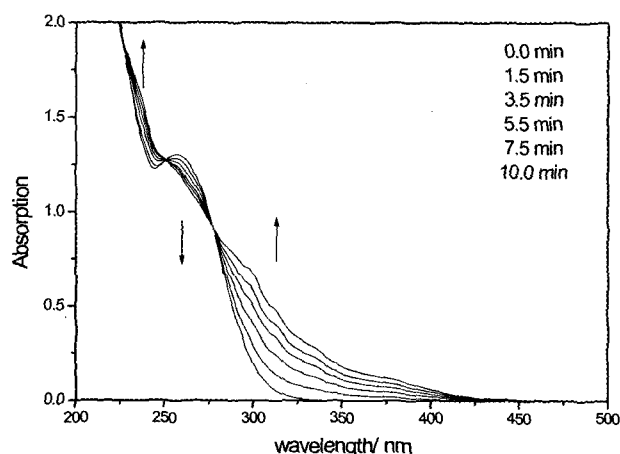


Figure 1. Uv/vis absorption spectra change of 2'-chlorobenzanilide in neutral acetonitrile on irradiation time.

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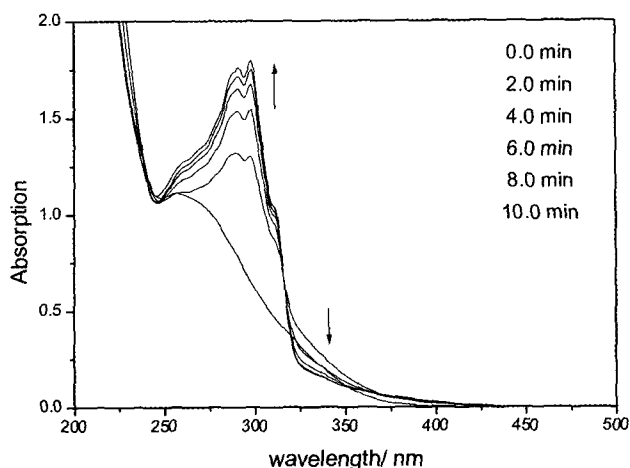
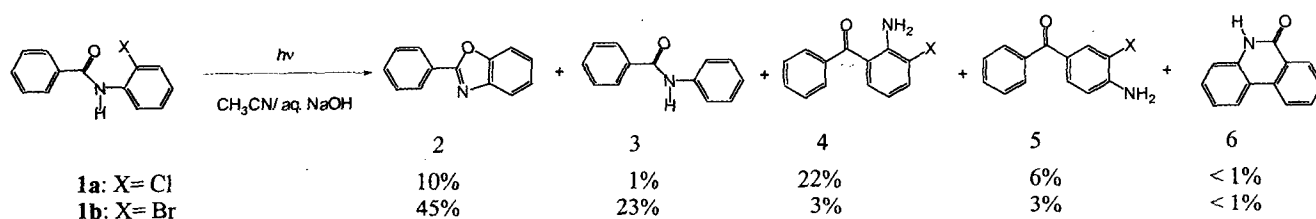


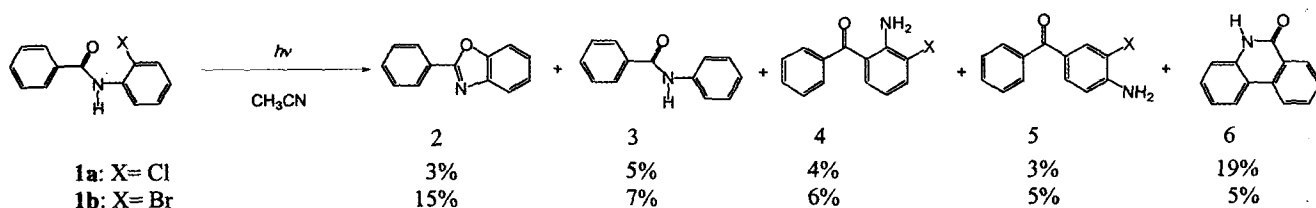
Figure 2. Uv/vis absorption spectra change of 2'-bromobenzanilide in a basic medium ($H_2O/$ acetonitrile = 1/9, $[NaOH]=$ 0.05 M) on irradiation time.

g) in acetonitrile (400 mL) containing 100 mL aqueous NaOH (0.05 M) was irradiated in a pyrex immersion well photolysis apparatus with circulating nitrogen, an intramolecular photosubstituted product, 2-phenyl-1,3-benzoxazole (45%), was obtained along with minor products, benzanilide (23%), 2-amino-3-bromobenzophenone (3%), and 4-amino-3-bromobenzophenone (3%) (scheme 1). These results indicate that 2-phenyl-1,3-benzoxazole can be readily prepared by the intramolecular photosubstitution of 2'-bromobenzanilide in a basic medium as has been reported in the previous paper.⁹ This reaction is simple and valuable for the preparation of 2-arylbenzoxazole.

Scheme 1



Scheme 2



When the basic aqueous acetonitrile solution of **1a** was irradiated as above, the photo-Fries type product, 2-amino-

3-chlorobenzophenone, was obtained in 22% yield along with minor products, 2-phenyl-1,3-benzoxazole (10% yield), benzanilide (1%), and phenanthridone (trace). These results indicate that for bromo anilide (**1b**) intramolecular photo-substitution is major, while for chloro analog (**1a**) photo-Fries type reaction is major.

In order to know the effect of the medium we studied the photoreaction of **1a** and **1b** in neutral acetonitrile. When a 1.3 molar solution of 2'-chlorobenzanilide (**1a**, 0.24 g) in acetonitrile (500 mL) was irradiated in a pyrex immersion well photolysis apparatus with circulating nitrogen, a photocyclization product, phenanthridone (19%) was obtained along with minor products, 2-phenyl-1,3-benzoxazole (3%), benzanilide (5%), 2-amino-3-chlorobenzophenone (4%), and 4-amino-3-chlorobenzophenone (3%) (scheme 2). The reaction is similar to the results reported [5,7]. The photochemical behavior of 2-bromobenzanilide (**1b**) is similar to that of **1a** (scheme 2). However, intramolecular photosubstitution reaction is major in the reaction of **1b** in neutral acetonitrile.

Experimental Section:

General procedure for the synthesis of 2'-halobenzanilide

The desired 2-haloaniline (for 2-chloroaniline, 2.55 g, 0.02 mole) is stirred in 20 mL of pyridine and one equivalent of benzoyl chloride (2.8 g, 0.02 mole) is added dropwise at ice bath temperature. The mixture is stirred in ice bath for 2 hrs and in room temperature for 3 hrs. When 250 mL of water is added, a white solid is precipitated. The resulting solid is isolated typically in 66% yield.

2'-chlorobenzanilide:

Yield 66 %; mp (crystallized from n-hexane) 100-102 °C

(lit. value 103.5 °C)⁸; UV (λ_{\max} in acetonitrile) 260 nm ($\epsilon_{260}=1.2 \times 10^4$ L/mol.cm); IR (KBr) 3225, 3059, 1653 cm^{-1} ; ¹H-NMR (400 MHz, DMSO-D₆) δ 10.06 (s, 1H), 8.01 (dt, J=6.9, 1.5 Hz, 2H), 7.60-7.54 (m, 5H), 7.40 (td, J=6.0, 1.6 Hz, 1H), 7.33 (td, J=6.0, 1.5 Hz, 1H); MS m/z (rel. intensity) 233 (25, M⁺+2) 231 (93, M⁺), 196 (15, M⁺-Cl). Analytical Cal. for C₁₃H₁₀ONCl: C, 67.40; H, 4.35; N, 6.05. Found: C, 67.40; H, 4.37; and N, 5.97.

2'-bromobenzanilide:

Yield 97 %; mp (crystallized from cyclohexane) 115-117 °C (lit. value 112.5 °C) [9]; UV (λ_{\max} in acetonitrile) 259 nm ($\epsilon_{259}=8.4 \times 10^3$ L/mol.cm); IR (KBr) 3275, 3055, and 1651 cm^{-1} ; ¹H-NMR (400 MHz, DMSO-D₆) δ 10.05 (s, 1H), 8.01 (dt, J=6.9, 1.8 Hz, 2H), 7.72 (dd, J= 6.9, 1.2 Hz, 1H), 7.63-7.51 (m, 4H), 7.43 (td, J=6.6, 1.5 Hz, 1H), 7.20 (td, J=6.3, 1.5 Hz, 1H); MS m/z (rel. intensity) 277 (4, M⁺+2), 275 (3, M⁺), 196 (26, M⁺-Br). Analytical Cal. for C₁₃H₁₀ONBr: C, 56.55; H, 3.65; N, 5.07. Found: C, 56.61; H, 3.64; N, 4.99.

UV absorption spectra change measurements

An acetonitrile solution of 2'-chlorobenzanilide in uv cuvette ([**1a**] = 1.2×10^{-4} M) was irradiated with Xe-lamp light (filtered by ethyl alcohol). The spectral change is shown in Figure 1. A basic aqueous acetonitrile solution of 2'-bromobenzanilide in uv cuvette (concentration of **1b** = 1.4×10^{-4} M, H₂O/ acetonitrile 1/9, concentration of NaOH = 0.05 M) was irradiated as above and the spectral change is shown in Figure 2.

Preparative Photoreaction. Photoreaction of 2'-bromobenzanilide (**1b**) in a basic medium. General Procedure.

To a large (500 mL) quartz immersion well photolysis unit with provision for circulation of nitrogen were added 400 mL of acetonitrile, 100 mL aqueous NaOH (1 M) and 0.7 mmole (0.20 g) of 2'-bromobenzanilide (**1b**). With nitrogen circulation, the solution was irradiated with a 450 W mercury lamp (medium pressure) at 110 V at 4 °C for 1.5 hr. After evaporation of the solvent, preparative TLC gave R_f values in n-hexane/ ethylacetate (4:1) of 0.11, 0.24, 0.64, 0.73, and 0.78. They were identified as benzanilide, 4-amino-3-bromobenzophenone (yellow color), 2'-bromobenzanilide (recovered), 2-phenyl-1,3-benzoxazole, and 2-amino-3-bromobenzophenone (yellow color), respectively.

Benzanilide (R_f 0.11):

Yield 23%; mp (crystallized from ethanol) 165-166 °C (lit. value 161 °C) [9].

4-Amino-3-bromobenzophenone (R_f 0.24):

Yield 3%; UV (λ_{\max} in acetonitrile) $\lambda = 318$ nm ($\epsilon_{318}=4.5 \times 10^3$ L/mol.cm), 239 nm ($\epsilon_{239} = 4.8 \times 10^3$ L/mol.cm); ¹H-NMR (400 MHz, DMSO-D₆) δ 7.75 (d, J=1.8, 1H), 7.60 (t, J= 6.6, 1.2 Hz, 3H), 7.54- 7.49 (m, 3H), 6.82 (d, J= 8.4, 1H), 6.29 (s, 2H); MS m/z (relative intensity) 277 (39, M⁺+2), 276 (100, M⁺+1), 275(58, M⁺), 195 (10), 105 (18), 77 (63).

2-phenyl-1, 3-benzoxazole (R_f 0.73):

Yield 45%; mp 101-103 °C (lit. value 102 °C)¹¹; UV (λ_{\max} in Cyclohexane) 299 nm ($\epsilon_{299} = 2.7 \times 10^4$ L/mol.cm); IR (KBr) 3056, and 1615 cm^{-1} ; ¹H-NMR(400 MHz, DMSO-D₆) δ 8.25 (d, J= 5.1 Hz, 2H), 7.78 (t, J=5.4 Hz, 2H), 7.52 (m, 3H), and 7.35 (m, 2H); MS m/z (rel. intensity) 196 (13, M⁺+1), 195 (100, M⁺), 167 (20), 92 (15), 77 (48).

2-Amino-3-bromobenzophenone (R_f 0.78):

Yield 3%; mp (crystallized from n-hexane) 86 °C; UV (λ_{\max} in acetonitrile) 375 nm ($\epsilon_{375} = 5.7 \times 10^3$ L/mol.cm), and 326 nm ($\epsilon_{326} = 6.1 \times 10^3$ L/mol.cm); ¹H-NMR (400 MHz, DMSO-D₆) δ 7.66 (d, J=7.5, 1H), 7.52 (m, 5H), 7.29 (d, J= 8.0 Hz, 1H), 6.93 (s, b, 2H), 6.49 (t, J= 7.5, 8.0 Hz, 1H); MS m/z (rel. intensity) 277 (6, M⁺+2), 275 (5, M⁺), 196 (17), 105 (49), 91 (10), 77 (100).

Photoreaction of 2'-chlorobenzanilide (**1a**) in a basic medium:

The procedure is the same as above. The reaction time was 4 hrs. The products are benzanilide (R_f=0.11, 1%), 4-amino-3-chlorobenzophenone (R_f 0.30, 6%), 2'-chlorobenzanilide (R_f 0.67, 16 %), 2-phenyl-1, 3-benzoxazole (R_f 0.73, 10%), and 2-amino-3-chlorobenzophenone (R_f 0.76, 22%).

4-Amino-3-chlorobenzophenone:

Yield 6 %; mp (crystallized from cyclohexane) 132 °C (lit. value 134-135 °C) [9]; UV (λ_{\max} in cyclohexane) 318 nm ($\epsilon_{318}=4.8 \times 10^3$ L/mol.cm), 242 nm ($\epsilon_{242} = 4.1 \times 10^3$ L/mol.cm), and 206 nm ($\epsilon_{206} = 8.6 \times 10^3$ L/mol.cm); ¹H-NMR (400 Hz, DMSO-D₆) δ 7.64 - 7.61 (m, 5H), 7.53 (d, J= 7.4 Hz, 1H), 7.48 (dd, J= 7.1, 1.9 Hz, 1H), 6.86 (d, J= 7.1, 1H), and 6.4 (s, 2H); MS m/z (relative intensity) 233 (19, M⁺+2) 231 (57, M⁺), 196 (16), 154 (29), 128 (2, M⁺-C₆H₅CO), 126 (7, M⁺-C₆H₅CO), 105 (22), 91 (29), 77 (100).

2-Amino-3-chlorobenzophenone:

Yield 22 %; mp (crystallized from n-hexane) 103- 104 °C (lit. 102-105) [11,12] ; UV(λ_{\max} in acetonitrile) 375 ($\epsilon_{375} = 5.3 \times 10^3$ L/mol.cm), and 318 ($\epsilon_{318} = 5.8 \times 10^3$ L/mol.cm); ¹H-NMR

(400 MHz, DMSO- D_6) 7.64-7.61 (m, 4H), 7.56-7.48 (m, 3H); 6.86, 6.83 (d, $J=8.7$ Hz, 1H), and 6.41 (s, br., 2H); MS m/z (relative intensity): 233 (13, $M^+ + 2$), 232 (28, $M^+ + 1$), 231 (37, M^+), 196 (13), 154 (26), 105 (27), 77 (61).

General Procedure for Photoreaction of 2'-bromobenzanilide (1b) in a neutral medium.

A solution of 0.9 mmole (0.25 g) of 2'-bromobenzanilide (**1b**) in 500 mL of acetonitrile was photolysed with a medium pressure mercury lamp (450 W, 110 V) at 4 °C for 1.5 hr in a large quartz immersion well photolysis unit that has an arrangement for circulation of nitrogen. After irradiation, the solution was dried in rotary vacuum, redissolved in 30 ml mixture of *n*-hexane/ethylacetate (4:1 by volume), and then developed on preparative TLC plates (silica gel) with *n*-hexane/ethylacetate (4/1). Six components appeared on preparative TLC plate: their R_f values were 0.06, 0.11, 0.24, 0.64, 0.73, and 0.78. These components were identified as phenanthridone (5%), benzanilide (7%), 4-amino-3-bromobenzophenone (5%, yellow color), 2'-bromobenzanilide (40%, recovered), 2-phenyl-1,3-benzoxazole (15%), and 2-amino-3-bromobenzophenone (6%, yellow color), respectively. The upper three components were redeveloped again with benzene/dichloromethane (2: 1).

Phenanthridone:

Yield 5%; mp 292 °C (lit. value 292- 294) [5]; 1H -NMR (400 MHz, DMSO- D_6) δ 11.68 (s, 1H), 8.52 (d, $J= 8.5$ Hz, 1H), 8.40 (d, $J= 8.0$ Hz, 1H), 8.34 (d, $J= 7.5$ Hz, 1H), 7.86 (t, $J= 7.5$ Hz, 1H), 7.65 (t, $J= 7.5$ Hz, 1H), 7.49 (t, $J= 7.5$ Hz, 1H), 7.38 (d, $J= 8.0$ Hz, 1H), and 7.27 (t, $J= 7.5$ Hz, 1H); MS m/z (relative intensity) 195 (M^+ , 52), 167 ($M^+ - CO$, 25), 87 (34), 77 (28), 75 (40), and 51 (100).

Photoreaction of 2'-chlorobenzanilide (1a) in acetonitrile:

When the solution of 2'-chlorobenzanilide (**1a**, 1.3 mmole, 0.24 g) in acetonitrile (500 mL) was treated as above, identical products were observed.

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