BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 2600—2602 (1973)

Rearrangement of 2-Aryloxybenzazoles

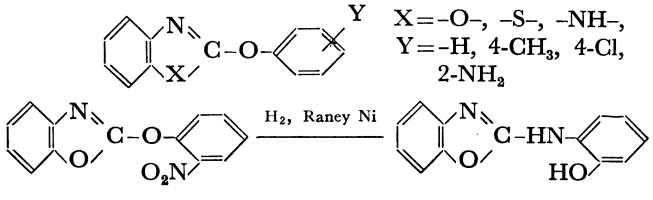
Takeshi NAGAI, Yoshiaki FUKUSHIMA, Toshio KURODA, Hiroshi SHIMIZU, Shizen SEKIGUCHI, and Kohji MATSUI

Department of Synthetic Chemistry, Gunma University, Tenjincho, Kiryu, Gunma 376

(Received January 22, 1973)

O-Acylphenols are known to undergo rearrangement in the presence of Lewis acid[1] or photochemically[2] to give *o*- and/or *p*-acylphenols. Similarly, aryloxy-*s*-triazines give *o*- and/or *p*-hydroxyaryl-*s*-triazines on irradiation.[3] However, aryloxy-*s*-triazines containing 2-amino groups undergo rearrangement to give o-hydroxyarylamino-*s*-triazines in protic solvents in the dark[4] or on irradiation with ultraviolet light in aprotic solvents.[5] This paper reports on the rearrangement of 2-aryloxybenzazoles (benzoxazole, benzothiazole, and benzimidazole).

Preparation of 2-Aryloxybenzazoles. 2-Aryloxybenzazoles having the following general formula were synthesized by the condensation of 2-chlorobenzazoles with the corresponding phenolates. 2-(2-Aminophenoxy)benzothiazole was obtained by the hydrogenation of the corresponding nitro compound. In the hydrogenation of 2-(2-nitrophenoxy)benzoxazole, however, 2-(2-hydroxyanilino)benzoxazole was obtained as the main product instead of 2-(2-aminophenoxy)benzoxazole. 2-Aryloxybenzazoles thus obtained are listed in Table 1.



1) For example, A. H. Blatt, "The Fries Reaction," Organic Reactions, Vol. 1, John Wiley and Sons, Inc., New York, N. Y. (1942), p. 342.

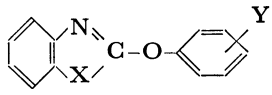
2) a) J. C. Anderson and C. B. Reese, *Proc. Chem. Soc.*, **1960**, 217; *J. Chem. Soc.*, **1963**, 1781; b) H. Kobsa, *J. Org. Chem.*, **27**, 2293 (1962).

3) H. Shizuka, T. Kanai, T. Morita, Y. Ohto, and K. Matsui, *Tetrahedron*, **27**, 4021 (1971).

4) T. Harayama, K. Okada, S. Sekiguchi, and K. Matsui, *J. Heterocycl. Chem.*, **7**, 981 (1970); N. Maeno, T. Itagaki, S. Uno, and K. Matsui, This Bulletin, **45**, 3133 (1972).

5) a) K. Matsui, N. Maeno, S. Suzuki, H. Shizuka, and T. Morita, *Tetrahedron. Lett.*, **17**, 1467 (1970); (b) H. Shizuka, N. Maeno, and K. Matsui, *Mol. Photochem.*, **4**, 335 (1972).

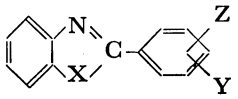
TABLE 1. 2-ARYLOXYBENZAZOLES



X	Y	Mp (°C)	Recrystn. Solvent
O	H	57— 57.5 (56)[a]	Ethanol
O	4-CH_3	62— 63	Ligroin
O	2-NO_2	142—143.5	Acetone-water
O	4-Cl	101—101.5	Ligroin
S	H	51— 52	Petroleum ether
S	4-CH_3	40	Petroleum ether
S	4-Cl	81	Ethanol
S	2-NO_2	108	Ethanol
S	2-NH_2	86— 87	Benzene-ligroin
NH	H	228—229 (222—223)[b]	Ethanol
NH	4-CH_3	259—260	Dioxane

a) P. Seidel, *J. Prakt. Chem.*, **42**, 455 (1890); b) T. Seki, M. Sasajima, and Y. Watanabe, *Yakugaku Zasshi*, **85**, 962 (1965).

TABLE 2. 2-(HYDROXYARYL)BENZAZOLES



X	Y	Z	Yield (%)	Mp (°C)	Recrystn. Solvent
O	H	2-OH	14	125—126 (122—123)[a]	Acetone
		4-OH	31	252—253 (250)[b]	Ethanol
O	5-CH_3	2-OH	30	134—135	Ligroin
O	H	2-NH_2	20	106—107	Acetone
		4-NH_2	25	172—174 (169—170)[c]	Acetone-water
S	H	2-OH	28.5	123—124 (129)[d]	Ethanol
		4-OH	28.5	220—222 (228—229)[e]	Ethanol
S	5-CH_3	2-OH	53	123—124	Ethanol
S	5-Cl	2-OH	19	157—158	Ethanol
NH	H	2-OH	15	243—244 (238—239)[f]	Ethanol
		4-OH	21	278—279 (277—278)[g]	Acetone
NH	5-CH_3	2-OH	11	259—260	Benzene

a) S. Skrap and M. Moser, *Ber.* **55**, 1089 (1922); b) R. Passerini, *J. Chem. Soc.*, **1954**, 2260; c) F. F. Stephens and J. D. Bower, *ibid.*, **1949**, 2971; d) A. W. Hofmannn, *Ber.*, **13**, 1237 (1880); e) M. T. Bogert and H. B. Corbitt, *J. Amer. Chem. Soc.*, **48**, 783 (1926); f) H. Hüber, *Ann.*, **210**, 345 (1881); g) J. Sawlewicz and Z. Sznigir, *Acta Pol. Pharm.*, **18**, 1 (1961); *Chem. Abstr.*, **55**, 27277h (1961).

Rearrangement in the Dark. 2-Aryloxybenzazoles (*ca.* 5.0 g) were heated at 150 °C for 24 hr in nitrobenzene (300 ml) with aluminum chloride in a 1 : 1 molar ratio, but no 2-(hydroxyaryl)benzazoles, Fries rearranged products, were producd. Failure of rearrangement in these cases is attributed to the preferential coordination of aluminium chloride to the ring nitrogen atom instead of the aryloxy oxygen. By heating at 200 °C for 5 hr, no reaction took place in 2-aryloxy-benzoxazoles or -benzthiazoles, 2-aryloxybenzimidazoles being decomposed with cleavage of phenol. However, 2-(2-aminophenoxy)benzthiazole underwent rearrangement slowly in methanol or ethanol to give 2-(2-hydroxyanilino)benzthiazole, a Smiles rearranged product, although it did not react in such aprotic solvents as benzene, cyclohexane, carbon tetrachloride, and butyl ether. The Smiles rearrangement of 2-(2-aminophenoxy)benzthiazole took place readily in the presence of a small amount of hydrochloric acid to give a rearranged product quantitatively; the catalytic effect by acid is attributable to the lowering of electron-density of the ring carbon atoms by the protonation at the ring nitrogen atom. Thus, the formation of 2-(2-hydroxyanilino)benzoxazole by hydrogenation of 2-(2-nitrophenoxy)benzoxazole indicates the ready O→N migration of the 2-benzoxazolyl group of preformed 2-(2-aminophenoxy)benzoxazole.

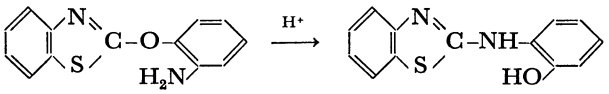
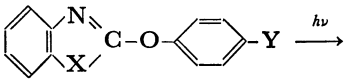
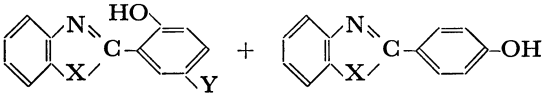


Photo-rearrangement of 2-Aryloxybenzazoles. Irradiation of 2-aryloxybenzazoles (*ca.* 5.0 g) in cyclohexane or ethanol (300 ml) with low pressure mercury lamp gave 2-(2- and/or 4-hydroxyphenyl)benzazoles.[6] The photo-rearranged products thus obtained are listed in Table 2. However, under similar conditions



Y=-H, -CH_3, -Cl



Y=-H, -CH_3, -Cl Y=-H

2-anilinobenzazoles gave no rearranged 2-(2- or 4-aminophenyl)benzazoles. On the other hand, when 2-(2-aminophenoxy)benzthiazole was irradiated in cyclohexane, no 2-(2-aminohydroxyphenyl)benzthiazole, a photo-Fries rearranged product, was obtained, but 2-(2-hydroxyanilino)benzthiazole, a photo-Smiles rearranged product, was obtained in a good yield.

Quantum Yields for the Product Formation from 2-Aryloxybenzazoles. The quantum yields of the product for

6) In the photo-rearrangement of 2-aryloxybenzazoles, several by-products other than rearranged ones were produced (see Experimental). For example, 12 hr's irradiation of 5 g of 2-(4-chlorophenoxy)benzoxazole in 300 ml of ethanol gave 2-(5-chloro-2-hydroxyphenyl)benzoxazole (11%), benzoxazole (1%), *p*-chlorophenol (27%), benzoxazolone (30%), and 2-ethoxybenzoxazole (<1%). In this paper discussion is restricted to rearranged products.

mation from 2-aryloxybenzazoles were measured. The values obtained in ethanol are as follows: 0.084 for 2-(4-methylphenoxy)benzoxazole, 0.025 for 2-(4-methylphenoxy)benzthiazole, and 0.15 for 2-(4-methylphenoxy)benzimidazole. The quantum yields of the product formation from 2-(4-methylphenoxy)benzoxazole at 2537 Å did not change with concentration ($<\sim 7\times10^{-3}$ mol/l) and irradiation time (2~9 min) in the presence of piperylene as a triplet quencher ($10^{-4}\sim 2\times10^{-2}$ mol/l). Similar results were also obtained with 2-(4-methylphenoxy)benzthiazole and -benzimidazole. The results are in line with the general photo-Fries-rearrangement involving the intramolecular process *via* the lowest excited singlet state.

Experimental

Preparation of 2-Aryloxybenzazoles. 2-Aryloxybenzazoles were prepared by the condensation of 2-chlorobenzazoles with the equimolar corresponding phenolates. Typical procedures are described in the case of 2-(4-methylphenoxy)-, 2-phenoxy-benzthiazoles and 2-phenoxybenzoxazole.

2-(4-Methylphenoxy)benzthiazole. After 17 g (0.100 mol) of 2-chlorobenzthiazole and 17.4 g (0.133 mol) of sodium *p*-methylphenoxide in 50 ml of *p*-methylphenol had been heated at 130 °C for 24 hr, the mixture was poured into a large amount of aqueous sodium hydroxide solution. After the mixture had been extracted with benzene, the benzene solution was concentrated and the residue was distilled under reduced pressure (bp 178—178.5 °C/3 mmHg) and recrystallized from ethanol. 2-Phenoxybenzthiazole (bp 178—180 °C/8 mmHg) was prepared by a similar method.

2-Phenoxybenzoxazole. After 15.3 g (0.100 mol) of 2-chlorobenzoxazole and 17.4 g (0.15 mol) of sodium phenoxide in 50 ml of phenol had been heated at 120 °C for 20 hr, the mixture was poured into a large amount of aqueous sodium hydroxide solution and filtered out. The precipitate was recrystallized from ethanol. Other aryloxybenzazoles except for the above-mentioned three aryloxybenzazoles were prepared by similar methods.

Hydrogenation of 2-(2-Nitrophenoxy)benzoxazole: A mixture containing 50 ml of dioxane, 5 g (0.020 mol) of 2-(2-nitrophenoxy)benzoxazole, and 3 g of Raney Nickel was stirred for 12 hr under a pressure of 120 kg/cm² of hydrogen at room temperature. After the catalyst had been removed by filtration and the solvent evaporated, the residue was dissolved in 200 ml of 3% aqueous sodium hydroxide. After filtration the filtrate was neutralized with dilute hydrochloric acid, filtered, and dried to give 3.5 g (80%) of crude 2-(2-hydroxyanilino)benzoxazole. Recrystallzation from ethanol-water gave an analytical sample, mp 176—177 °C. Found: C, 68.72; H, 4.28%. Calcd for $C_{13}H_{10}O_2N_2$: C, 69.01; H, 4.46%.

Smiles and Photo-Smiles Rearrangements of 2-(2-Aminophenoxy)-benzthiazole (2APB): To a solution of 0.5 g (0.002 mol) of 2APB in 10 ml of acetone or ethanol was added a small amount of concd hydrochloric acid (*ca.* 0.08 g). After the mixture had been allowed to stand at room temperature for 2 days (for Smiles rearrangement) or 21 days (for photo-Smiles rearrangement), it was poured into 50 ml of ice-water, filtered, and dried. Recrystallization from benzene gave 2-(2-hydroxyanilino)benzthiazole quantitatively, mp 178.5—179 °C; NMR (DMSO-d_6) τ 0.2(s, OH), 1.7(s, NH). Found: C, 64.70; H, 4.46%. Calcd for $C_{13}H_{10}ON_2S$: C, 64.66; H, 4.16%.

After a solution of 5 g (0.02 mol) of 2APB in 300 ml of ethanol had been irradiated at room temperature with a low pressure mercury lamp (30W) for 7 days, the solvent was distilled off, and the residue was dissolved in 300 ml of benzene. The benzene solution was extracted with 200 ml of 4% sodium hydroxide solution. The aqueous solution was neutralized with hydrochloric acid and extracted with 200 ml of benzene. Column chromatography and recrystallization of the former benzene solution afforded 3.6 g of 2APB and 0.4 g (28.9%, based on the reacted 2APB) of benzthiazolone, and 0.7 g (50%, based on the reacted 2APB) of 2-(2-hydroxyanilino)benzthiazole from the latter benzene solution.

Photo-rearrangement and Actinometry: A low pressure mercury lamp was used as the 2537 Å radiation source with a Vycor glass filter. Irradiation was continued for 7 to 10 days. Actinometry was carried out with a ferric oxalate solution,[7] throughly degassed on a high vacuum line by the freeze-pump-thaw method.

Structural assignments of all products were performed by means of NMR, IR, UV, MS and elemental analyses. The results of the elemental analysis of all new products were within the experimental error.

7) C. G. Hatchard and C. A. Parker, *Proc. Roy. Soc. Ser. A*, **235**, 518 (1956).