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The substituted 6-bromo and 6-chloro-5*H*-benzo[*a*]phenoxazin-5-ones, prepared by condensation of substituted 2-aminophenols with 2,3-dibromo or 2,3-dichloro-1,4-naphthoquinone in methanolic potassium hydroxide solution, have been dehalogenated to substituted 5*H*-benzo[*a*]phenoxazin-5-ones in the presence of sodium hydrosulfite dissolved in aqueous pyridine under nitrogen atmosphere.

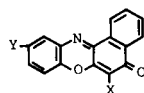
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Although benzophenoxazones are receiving special attention, their synthetic methods described to date are considerably tedious (1-5). We previously reported that 6-alkylthio- and 6-phenylthio-5*H*-benzo[*a*]phenoxazin-5-ones were prepared by the photochemical reaction of 5*H*-benzo[*a*]phenoxazin-5-one with alkylthiols and thiophenol (6). In view of a potential interest for this class of compounds in pharmacology, we report a novel route for the synthesis of some 5*H*-benzo[*a*]phenoxazin-5-one derivatives.

In this work, 5*H*-benzo[*a*]phenoxazin-5-one and its 10-chloro and 10-methyl derivatives (**4a-c**) could be prepared by modified dehalogenation of their 6-bromo or 6-chloro derivatives (**3a-f**), which were prepared by condensation of

substituted 2-aminophenols (**1a-c**) with 2,3-dibromo- or 2,3-dichloro-1,4-naphthoquinone (**2a,b**) in methanolic potassium hydroxide solution at room temperature. It is worthy to note that, by condensation of 2-aminophenol (**1a**) with 2,3-dichloro-1,4-naphthoquinone (**2b**) in pyridine or in refluxing methanolic potassium hydroxide solution, 6-chloro-5*H*-benzo[*a*]phenoxazin-5-one (**3d**) was obtained instead of 5*H*-benzo[*a*]phenoxazin-5-one (**4a**) described by VanAllan (7). We have prepared the compound **3a** by condensation of 2-aminophenol (**1a**) with 2,3-dichloro-1,4-naphthoquinone (**2b**): (a) in the presence of anhydrous potassium acetate in refluxing benzene; and (b) in methanolic potassium hydroxide solution at room temperature.

Table 1  
Physical Properties of 5*H*-Benzo[*a*]phenoxazin-5-one Derivatives



Compound No.	X	Y	Procedure Yield, %	Mp °C	Molecular Formula	Elemental Analysis		
						Analysis	Calcd. (Found)	
						C	H	N
<b>3a</b>	Br	H	42	196-197	C <sub>16</sub> H <sub>8</sub> BrNO <sub>2</sub> (326.1)	58.92 (59.19)	2.47 (2.63)	4.29 (4.09)
<b>3b</b>	Br	Cl	82	240-241	C <sub>16</sub> H <sub>7</sub> BrClNO <sub>2</sub> (360.6)	53.29 (53.19)	1.96 (2.03)	3.88 (3.79)
<b>3c</b>	Br	CH <sub>3</sub>	43	222-223	C <sub>17</sub> H <sub>10</sub> BrNO <sub>2</sub> (340.2)	60.02 (60.20)	2.96 (2.94)	4.12 (4.19)
<b>3d</b>	Cl	H	A, 60 B, 95	209-210	C <sub>16</sub> H <sub>8</sub> ClNO <sub>2</sub> (281.7)	68.22 (68.17)	2.86 (2.68)	4.97 (4.95)
<b>3e</b>	Cl	Cl	64	251-252	C <sub>16</sub> H <sub>7</sub> Cl <sub>2</sub> NO <sub>2</sub> (316.1)	60.79 (60.91)	2.23 (2.16)	4.43 (4.44)
<b>3f</b>	Cl	CH <sub>3</sub>	37	240-241	C <sub>17</sub> H <sub>10</sub> ClNO <sub>2</sub> (295.7)	69.05 (68.70)	3.41 (3.53)	4.74 (4.57)
<b>4a</b>	H	H	70 (a) 97 (b)	201-202	C <sub>16</sub> H <sub>9</sub> NO <sub>2</sub> (247.3)	77.72 (77.55)	3.67 (3.54)	5.67 (5.84)
<b>4b</b>	H	Cl	60 (a) 98 (b)	245-246	C <sub>16</sub> H <sub>8</sub> ClNO <sub>2</sub> (281.7)	68.22 (68.18)	2.86 (2.63)	4.97 (4.99)
<b>4c</b>	H	CH <sub>3</sub>	86 (a) 98 (b)	211-212	C <sub>17</sub> H <sub>11</sub> NO <sub>2</sub> (261.3)	78.15 (78.60)	4.24 (4.11)	5.36 (5.31)

(a) Compound was obtained by dehalogenation of 10-substituted 6-chloro-5*H*-benzo[*a*]phenoxazin-5-ones. (b) Compound was obtained by dehalogenation of 10-substituted 6-bromo-5*H*-benzo[*a*]phenoxazin-5-ones.



The preparation of 6-chloro-5H-benzo[a]phenoxazin-5-one (**3d**).

Method A.

To a refluxing suspension of 2,3-dichloro-1,4-naphthoquinone (**2b**) and anhydrous potassium acetate (5.89 g, 60 mmoles) in 80 ml benzene was added dropwise with stirring an alcoholic solution of 2-aminophenol (**1a**) (5.45 g, 50 mmoles). After refluxing and stirring for an additional 3 hours, the mixture was cooled to room temperature. The precipitate formed was collected, washed well with water and recrystallized from benzene.

Method B.

6-Chloro-5H-benzo[a]phenoxazin-5-one (**3d**) was prepared by condensation of **1a** with **2b** just as was **3a**.

General Procedure for the Preparation of 10-Substituted 5H-Benzo[a]phenoxazin-5-ones (**4a-c**).

A suspension of 6,10-substituted 5H-benzo[a]phenoxazin-5-ones (**3a-f**) (10 mmoles), sodium hydrodisulfite (15.1 g, 100 mmoles), benzene (10 ml) and dioxane (20 ml) in 30 ml of water was bubbled with nitrogen for 20

minutes. After reduction of the starting materials, the suspension was then heated to reflux. At the beginning of the refluxing, 25 ml of pyridine was added to the mixture and the refluxing was continued for 3 hours under nitrogen atmosphere. After removal of the organic solvents under reduced pressure, the precipitate was collected, washed well with water and 5% aqueous acetic acid and recrystallized from benzene.

#### REFERENCES AND NOTES

- (1) F. Kehrmann, J. Markusfeld and B. Mascioni, *Chem. Ber.*, **28**, 353 (1895).
- (2) A. Butenandt, E. Biekert and W. Schäfer, *Ann.*, **632**, 134 (1960).
- (3) T. J. King and C. E. Newall, *J. Chem. Soc.*, 480 (1965).
- (4) O. F. Hepp, *Chem. Ber.*, **36**, 1807 (1903).
- (5) G. B. Afanas'eva, K. I. Pashkevich and I. Ya. Postovskii, *Khim. Geterotsykl. Soedin.*, 742 (1971); *Chem. Abstr.*, **76**, 24279t (1972).
- (6) Y. Ueno, Y. Takeuchi, J. Koshitani and T. Yoshida, *J. Heterocyclic Chem.*, **18**, 259 (1981).
- (7) J. A. VanAllan and G. A. Reynolds, *J. Org. Chem.*, **28**, 527 (1963).