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1,5-Dichloro-9H-thioxanthen-9-one (**2**) was prepared by cyclization of 2-chloro-6-[(2-chlorophenyl)thio]benzoic acid (**10**) obtained from 2-chloro-6-iodobenzoic acid (**9**) and 2-chlorobenzenethiol. Similarly, 1,7-dichloro-9H-thioxanthen-9-one (**6**) was prepared from **9** via 2-chloro-6-[(4-chlorophenyl)thio]benzoic acid (**11**). Compound **6** was also obtained by condensation of 2-chloro-6-mercaptobenzoic acid (**12**) with chlorobenzene in the presence of sulfuric acid.

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In order to synthesize a variety of 9H-thioxanthen derivatives in search of various biologically active agents such as schistosomicidal, antitumor, neurotropic and psychotropic agents, several dichloro derivatives of 9H-thioxanthen-9-one have been prepared [1-5]. However, of these dichloro-9H-thioxanthen-9-ones in which a chlorine is substituted at the 1-position of the 9H-thioxanthen ring, 1,5- (**2**) and 1,7-dichloro-9H-thioxanthen-9-ones (**6**) are yet unknown.

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Nargund *et al.* [6] prepared dichloro-9H-thioxanthen-9-one **A** (mp 185°) by cyclization of 3-chloro-2-[(3-chlorophenyl)thio]benzoic acid (**1**) with sulfuric acid, and believed the product to be 1,5-dichloro-9H-thioxanthen-9-one (**2**), because dichloro-9H-thioxanthen-9-one **A** could not be separated into **2** and 3,5-dichloro-9H-thioxanthen-9-one (**3**) by recrystallization and was not identical with **3** (mp 255°) prepared by cyclization of 4-chloro-2-[(2-chlorophenyl)thio]benzoic acid (**4**).

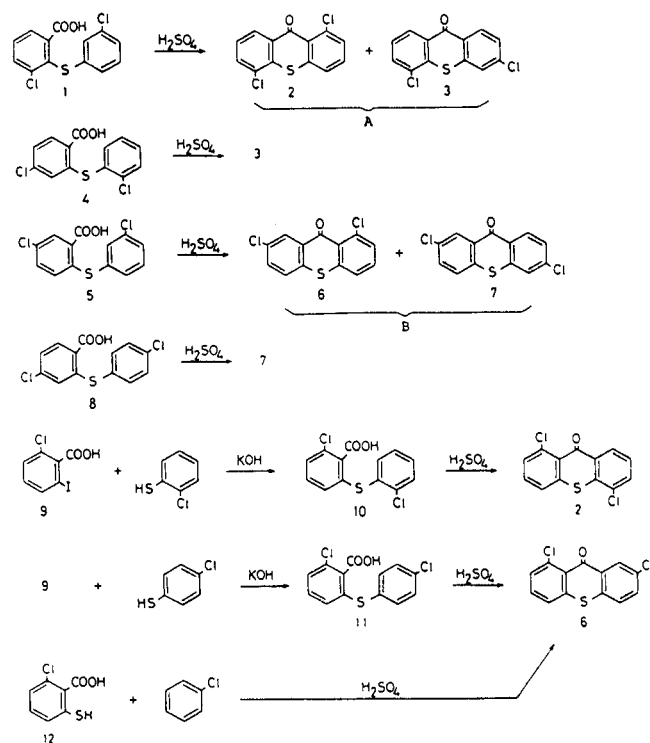
Furthermore, dichloro-9H-thioxanthen-9-one **B** (mp 228-229°) obtained by cyclization of 5-chloro-2-[(3-chlorophenyl)thio]benzoic acid (**5**) was believed to be 1,7-dichloro-9H-thioxanthen-9-one (**6**) by Nargund *et al.* [7], because dichloro-9H-thioxanthen-9-one **B** could not be separated into **6** and 2,6-dichloro-9H-thioxanthen-9-one (**7**) by recrystallization and was different from **7** (mp 273-275°) prepared by cyclizing 4-chloro-2-[(4-chlorophenyl)thio]benzoic acid (**8**).

In the previous paper [8], however, we synthesized 1-chloro-9H-thioxanthen-9-one by cyclization of 2-chloro-6-(phenylthio)benzoic acid or by condensation of 2-chloro-6-mercaptobenzoic acid (**12**) with benzene, and proved that chloro-9H-thioxanthen-9-one obtained by cyclization of 2-

[(3-chlorophenyl)thio]benzoic acid and reported by Mahishi *et al.* [9] as 1-chloro-9H-thioxanthen-9-one was a mixture of 1- and 3-chloro-9H-thioxanthen-9-ones, although the product could not be separated into two isomeric chloro-9H-thioxanthen-9-ones by recrystallization.

Moreover, in our previous report [10], 1,7-dichloro-9H-thioxanthen-9-one was prepared by cyclizing 2-chloro-6-(4-chlorophenoxy)benzoic acid, and dichloro-9H-thioxanthen-9-one obtained by cyclization of 5-chloro-2-(3-chlorophenoxy)benzoic acid and reported by Nargund *et al.* [11] as 1,7-dichloro-9H-thioxanthen-9-one was proved to be a mixture of 1,7- and 2,6-dichloro-9H-thioxanthen-9-ones, although the product could not be separated into two isomers by recrystallization, column chromatography or thin-layer chromatography.

Based on the above facts, dichloro-9H-thioxanthen-9-one **A** obtained by cyclization of **1** is expected to be a mix-



ture of **2** and **3** whose mutual separation should be difficult, and dichloro-9*H*-thioxanthen-9-one **B** prepared by cyclization of **5** also must be a troublesome mixture of **6** and **7**. Actually, recently Wiley *et al.* [4] have obtained 1-benzenesulfonamido-7-chloro-9*H*-thioxanthen-9-one and unreacted **7** by the reaction of the cyclization product of **5** with benzenesulfonamide.

Therefore, in this paper **2** was prepared by cyclization of 2-chloro-6-[(2-chlorophenyl)thio]benzoic acid (**10**) obtained by the reaction of 2-chloro-6-iodobenzoic acid (**9**) [12] with 2-chlorobenzenethiol, and **6** was prepared by cyclization of 2-chloro-6-[(4-chlorophenyl)thio]benzoic acid (**11**) obtained similarly from **9** and 4-chlorobenzenethiol. Each of these benzoic acids **10** and **11** gives a sole dichloro-9*H*-thioxanthen-9-one **2** and **6**, respectively, on cyclization. The resulting 1,5-dichloro-9*H*-thioxanthen-9-one (**2**) had a melting point of 225–226° and 1,7-dichloro-9*H*-thioxanthen-9-one (**6**) revealed mp 234–235°. These melting points are different from those (185° and 228–229°, respectively) reported by Nargund *et al.* [6,7], as expected.

Condensation of 2-chloro-6-mercaptobenzoic acid (**12**) [8] with chlorobenzene in the presence of sulfuric acid gave only one kind of dichloro-9*H*-thioxanthen-9-one in 63% yield, which was identical with 1,7-dichloro isomer **6**. As both crude **9** and **12** were prepared from 2-amino-6-chlorobenzoic acid in 70% and 30% yields, respectively, each of overall yields of **6** from 2-amino-6-chlorobenzoic acid *via* **9** or **12** was 41% and 19%, respectively.

## EXPERIMENTAL

Melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. The ir spectra were recorded with a Hitachi 260-10 spectrophotometer. The <sup>1</sup>H nmr spectra were obtained on a JEOL JNM-FX 200 spectrometer in deuteriochloroform using tetramethylsilane as an internal standard. The mass spectra were measured with Hitachi RMU-7M double focusing spectrometer.

### 2-Chloro-6-[(2-chlorophenyl)thio]benzoic Acid (**10**).

Compound **9** (2.82 g, 10 mmoles) and copper powder (0.07 g) were added to a solution of 2-chlorobenzenethiol (1.45 g, 10 mmoles) and potassium hydroxide (1.90 g, 34 mmoles) in water (20 ml). The solution was heated under reflux for 6 hours, cooled and filtered. The filtrate was acidified with hydrochloric acid. The resulting oily precipitate was solidified by rubbing with a glass rod. The solid (2.15 g, 72%) was collected and recrystallized from aqueous acetic acid to give colorless needles, mp 133–135°; ir (potassium bromide): 1700 cm<sup>-1</sup> (C=O); <sup>1</sup>H nmr: δ 7.04–7.40 (7H, m, ArH); ms: m/z 298 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>13</sub>H<sub>8</sub>Cl<sub>2</sub>O<sub>2</sub>S: C, 52.19; H, 2.70. Found: C, 52.07; H, 2.71.

### 1,5-Dichloro-9*H*-thioxanthen-9-one (**2**).

A mixture of **10** (10.5 g, 3.5 mmoles) and concentrated sulfuric acid (8 ml) was heated at 100° for 30 minutes. After cooling, the solution was poured into ice-water (200 ml). The resulting precipi-

tate was collected, washed with water, and treated with 5% aqueous sodium bicarbonate. The insoluble product was recrystallized from acetone to give **2** (0.71 g, 72%) as pale yellow needles, mp 225–226°; ir (potassium bromide): 1640 cm<sup>-1</sup> (C=O); <sup>1</sup>H nmr: δ 7.33–7.57 (4H, m, 2,3,4,7-H), 7.64 (1H, dd, J = 8.0, 1.4 Hz, 6-H), 8.35 (1H, dd, J = 8.0, 1.4 Hz, 8-H); ms: m/z 280 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>13</sub>H<sub>6</sub>Cl<sub>2</sub>OS: C, 55.54; H, 2.15. Found: C, 55.42; H, 2.18.

### 2-Chloro-6-[(4-chlorophenyl)thio]benzoic Acid (**11**).

This compound was prepared from **9** (2.82 g, 10 mmoles) and 4-chlorobenzenethiol (1.45 g, 10 mmoles) in a manner similar to that described for the preparation of **10**. The product (2.38 g, 80%) was recrystallized from aqueous acetic acid to give colorless needles, mp 116°; ir (potassium bromide): 1700 cm<sup>-1</sup> (C=O); <sup>1</sup>H nmr: δ 7.00–7.44 (7H, m, ArH); ms: m/z 298 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>13</sub>H<sub>8</sub>Cl<sub>2</sub>O<sub>2</sub>S: C, 52.19; H, 2.70. Found: C, 52.31; H, 2.71.

### 1,7-Dichloro-9*H*-thioxanthen-9-one (**6**).

a) This compound was prepared from **11** (10.5 g, 3.5 mmoles) in a manner similar to that described for the preparation of **2**. The product was recrystallized from acetone to give **6** (0.73 g, 74%) as yellow needles, mp 234–235°; ir (potassium bromide): 1640 cm<sup>-1</sup> (C=O); <sup>1</sup>H nmr: δ 7.30–7.49 (4H, m, 2,3,4,5-H), 7.55 (1H, dd, J = 8.5, 2.3 Hz, 6-H), 8.39 (1H, d, J = 2.3 Hz, 8-H); ms: m/z 280 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>13</sub>H<sub>6</sub>Cl<sub>2</sub>OS: C, 55.54; H, 2.15. Found: C, 55.72; H, 2.13.

b) A mixture of **12** (0.47 g, 2.5 mmoles), chlorobenzene (3 ml) and concentrated sulfuric acid (8 ml) was stirred for 8 hours at room temperature, allowed to stand overnight, and finally heated at 100° for 1 hour. After cooling, water was added to the reaction mixture. The precipitate was collected, washed with water, and treated with 5% aqueous sodium bicarbonate. The insoluble product (0.51 g, 73%) was recrystallized from acetone to give yellow needles, mp 233–235°, both alone and admixed with a sample obtained by method a). The ir and <sup>1</sup>H nmr spectra were identical with those of a sample obtained by method a).

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