# Synthesis of Some 2-Substituted-thioxanthones



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This paper presents the synthesis of 2-amino-, 2-acetamido- and 2-benzamidothioxanthones and their 10,10-dioxides.

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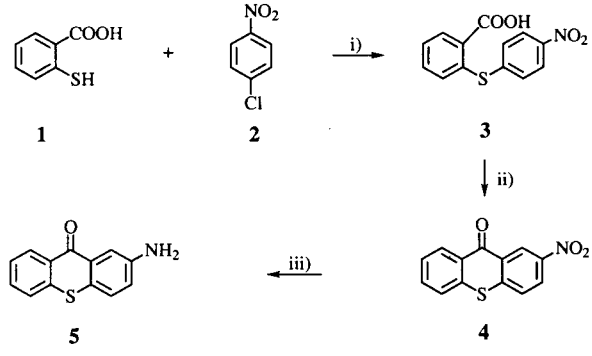
Thioxanthone derivatives have been shown to possess two useful properties such as the medicinal and the photoinitiation activities [1-9]. As a part of a basic study on novel photoinitiators and drugs from thioxanthone derivatives, the synthesis of 2-alkylamino- and 2-acet (or benz)amidothioxanthones was investigated. The most useful method for the formation of the thioxanthone ring is a [6+0] cyclization of phenylthiobenzoic acids with concentrated sulfuric acid [10, 11]. Phenylthiobenzoic acids are prepared from the corresponding arylmercaptans and aryl halides by the Ullmann reaction [10].

2-Aminothioxanthone (**5**) prepared from 2-nitrothioxanthone (**4**) is a useful starting material for the synthesis of 2-alkylamino, 2-alkanamido- and 2-benzamidothioxanthones. Arur *et al.* [5] and Minzhao *et al.* [12] prepared 2-nitrothioxanthone from 2-chloro-5-nitrobenzoic acid and thiophenol in two steps. Because the two raw materials are expensive, we chose thiosalicylic acid and *p*-nitrochlorobenzene as the starting materials for the synthesis of 2-nitrothioxanthone.

In this paper, we report the results of the synthesis of some 2-alkylamino- and 2-acetamido- (or benzamido)-thioxanthones and their 10,10-dioxides.

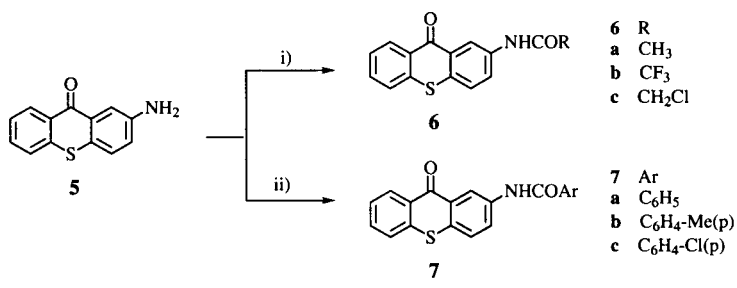
Scheme I




i) NaOEt, dimethylformamide, reflux. ii) Polyphosphoric acid/acetic acid, 140°C. iii) Fe/$NH_4Cl$/EtOH/$H_2O$, reflux.

In the first preparation of **3** from **1** and **2** under Ullmann conditions, we found by-products on the tlc plate. Thus, after reacting thiosalicylic acid with ethanolic sodium ethoxide, the resulting salt of **1** was then condensed with **2** to give **3** in 83% yield. First, when the synthesis of **4** was cyclized with concentrated sulfuric acid, we obtained **4** in low yield along with several impurities. Therefore, we chose more mild acids such as polyphosphoric acid or acetic acid as the cyclization solvent. Cyclization of **3** in

Scheme II




i) Alkanoic anhydride, acetic acid (except for **6b**), room temperature.
ii) Benzoyl chloride, chloroform, triethylamine, room temperature.

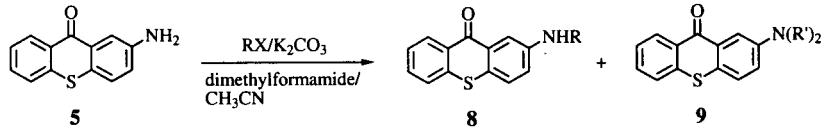
polyphosphoric acid/acetic acid (3:1, w/v) under reflux condition (140°) afforded 2-nitrothioxanthone (**4**) in 80% yield. Treatment of **3** with only polyphosphoric acid or with acetic acid, however, did not give compound **4**. The structures of **3** and **4** were established by ir, nmr and elemental analysis. The infrared spectrum of **4** showed the absorption bands of a carbonyl group (1650 $cm^{-1}$) and a nitro group (1520, 1340 $cm^{-1}$), but the bands for a carboxylic acid group of **3** were not detected.

Reduction [13] of **4** with iron/ammonium chloride in ethanol/water under reflux conditions gave only the corresponding 2-amino derivative **5** in 90% yield. The structure of **5** was established by ir, nmr and elemental analysis. The infrared spectrum of **5** revealed the absorption bands of a carbonyl group (1640 $cm^{-1}$) and an amino group (3400, 3250 $cm^{-1}$). The proton magnetic resonance spectrum of **5** showed the proton signal of the amino group at δ 5.71 ppm.

Acylation of **5** with alkanoic acid anhydrides gave the corresponding 2-acetamido derivatives **6** in 74-96% yield. Reaction of **5** with benzoic acid halides also yielded the corresponding 2-benzamido derivatives **7** in 76-91% yield. Alkylation of **5** with methyl iodide or benzyl bromide in the presence of potassium carbonate afforded the corresponding *N*-alkyl derivatives **8a** or **8b** in low yield. Whereas, treatment of **5** with *p*-bromobenzyl bromide in the presence of potassium carbonate gave **8c** in 37% yield and **9** in 25% yield. The structures of **6-9** were established by ir, nmr and elemental analysis.

On the other hand, we attempted the synthesis of 2-substituted-thioxanthone 10,10-dioxides. Compound **11** was prepared from **4** *via* **5** (Method A) or **10** (Method B), respectively. Compound **4** was oxidized by *m*-chloroperoxybenzoic acid in chloroform to **10** in 70% yield. Reduction of **10** with iron/ammonium chloride in ethanol/water gave **11** in 75% yield. Oxidation of **5** with *m*-chloroperoxybenzoic acid in chloroform yielded **11** in 75% yield. Treatment of **6** or **7** with *m*-chloroperoxybenzoic acid in chloroform furnished the corresponding dioxides **12** in 56-89% yield. The structures of **10-12** were established by ir, nmr and elemental analysis.

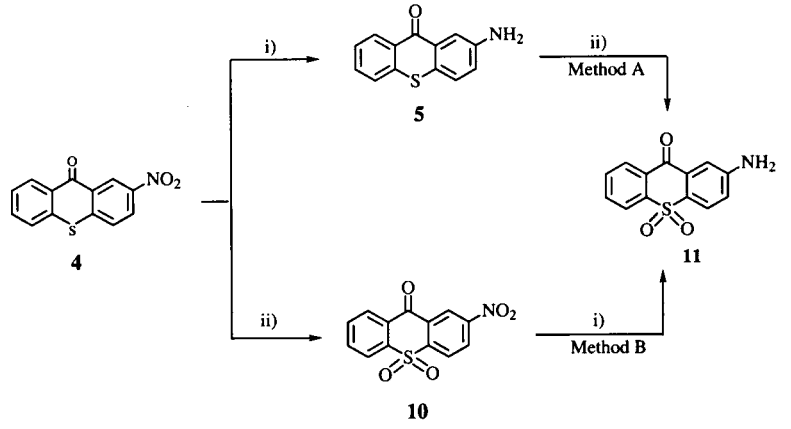
Scheme III




| 8 | a | b | c |
|---|---|---|---|
| R | $CH_3$ | $-CH_2C_6H_5$ | $-CH_2C_6H_4$-Br(p) |

R' = $-CH_2C_6H_4$-Br(p)

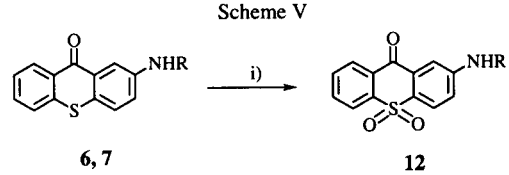
Scheme IV




i) Fe, $NH_4Cl$, ethanol, water, reflux. ii) *m*-Chloroperoxybenzoic acid, chloroform, room temperature.

Further work including the biological activity, the electrochemical properties and the photoinitiation activity are under way in our laboratory.

Scheme V




i) *m*-Chloroperoxybenzoic acid, chloroform, room temperature.

| 12 | a | b | c | d | e | f |
|---|---|---|---|---|---|---|
| R | $-COCH_3$ | $-COCF_3$ | $-COCH_2Cl$ | $-COC_6H_5$ | $-COC_6H_4-CH_3$(p) | $-COC_6H_4$-Cl(p) |

Table 1

Yields, Melting Points and Infrared Spectral Data of **3–12**

| Compound No. | Yield (%) | mp (°C) (lit mp) | IR (potassium bromide) ($cm^{-1}$) |
|---|---|---|---|
| **3** | 83 | 232-234 | 3300-2500 (m), 1680, 1600, 1530, 1350, 1260, 860, 750 |
| **4** | 80 | 226-228 (227) [5] | 1650, 1600, 1520, 1340, 750 |
| **5** | 90 | 231-233 (227) [5] | 3400, 3250, 1640, 1600, 1500, 1460, 1360, 1340, 750 |
| **6a** | 74 | 247-248 (242-244) [14] | 3340, 1690, 1630, 1600, 1530, 1320, 760 |
| **6b** | 96 | 218-220 | 3300, 3120, 1740, 1640, 1600, 1500, 1340, 1300, 1220, 1170, 760 |
| **6c** | 86 | 220-223 | 3310, 1730, 1630, 1580, 1530, 1410, 740 |
| **7a** | 76 | 225-228 | 3250, 1660, 1640, 1600, 1530, 1420, 1340, 1280, 780, 710 |
| **7b** | 89 | 220-222 | 3310, 1670, 1630, 1600, 1520, 1480, 1320, 760 |
| **7c** | 91 | 295-297 | 3350, 1690, 1640, 1600, 1540, 1490, 1330, 760 |
| **8a** | 28 | 150-152 | 3300, 1640, 1600, 1590, 1500, 1350, 1280, 740 |
| **8b** | 36 | 164-166 | 3380, 1640, 1600, 1590, 1340, 800, 750 |
| **8c** | 37 | 204-206 | 3380, 3000, 2900, 1640, 1600, 1350, 750 |
| **9** | 25 | 200-203 | 3000, 2900, 1640, 1600, 1480, 1440, 1390, 1000, 740 |
| **10** | 90 | 268-270 | 3100, 1690, 1600, 1550, 1330, 1310, 1180, 780 |
| **11** | 75 | 230-233 | 3510, 3400, 1680, 1630, 1600, 1500, 1450, 1350, 1300, 1170, 1130, 760 |
| **12a** | 87 | 242-244 | 3380, 1720, 1680, 1600, 1540, 1300, 1240, 1170, 1120, 760 |
| **12b** | 80 | 220-221 | 3380, 2980, 1720, 1680, 1600, 1540, 1300, 1240, 1170, 1120, 760 |
| **12c** | 56 | 250-252 | 3350, 1720, 1680, 1600, 1530, 1300, 1150, 1120, 760 |
| **12d** | 76 | 221-223 | 3360, 1680, 1600, 1540, 1300, 1150, 1120, 760, 720 |
| **12e** | 72 | 250-253 | 3390, 1690, 1680, 1590, 1540, 1510, 1410, 1300, 1150, 1120, 760 |
| **12f** | 89 | 275-277 | 3400, 1700, 1680, 1590, 1540, 1500, 1420, 1340, 1160, 1260, 1130, 760 |

## EXPERIMENTAL

Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. Magnetic resonance spectra were obtained on a Varian Unity Plus 300 or a Bruker FTNMR-DRX 500 spectrometer with chemical shift values reported in δ units (part per million) relative to an internal standard (tetramethylsilane). Infrared spectral data were obtained on a Hitachi 270-50 spectrophotometer. Elemental analyses were performed with a Perkin Elmer 240C. Open-bed chromatography was carried out silica gel 60 (70-230 mesh, Merck) using gravity flow. The column was packed as slurries with the elution solvent.

2-Carboxy-4'-nitrodiphenyl Sulfide (**3**).

Thiosalicylic acid (**1**, 1.54 g, 10 mmoles) was dissolved in ethanol (30 ml). After adding ethanolic sodium ethoxide (25 ml, 2%) with stirring, the solvent was evaporated under reduced pressure. The resulting residue was dissolved in dimethylformamide (30 ml). *p*-Chloronitrobenzene (**2**, 1.8 g, 11.4 mmoles) was added to the solution. The reaction mixture was refluxed for 3 hours. After cooling to room temperature, water (60 ml) was added with stirring. The resulting precipitate was filtered and dissolved in aqueous potassium carbonate solution (50 ml, 5%). The solution was washed with chloroform (30 ml) to remove excess *p*-chloronitrobenzene. The water solution was neutralized with aqueous hydrochloric acid (15 ml, 15%). The resulting precipitate was filtered, washed with methanol (5 ml) and dried in air to give **3** in 83% (2.3 g) yield.

2-Nitrothioxanthone (**4**).

A mixture of polyphosphoric acid (90 g, phosphorus pentoxide 85%/phosphoric acid 115%) and acetic acid (30 ml) was heated. Compound **3** (3 g, 10.9 mmoles) was added slowly to the acid solution. The mixture was allowed to react for 1 hour at 140° with stirring. After cooling to room temperature, the mixture was poured into ice water (50 ml) with stirring. The product was extracted with chloroform (300 ml). The chloroform solution was dried over anhydrous magnesium sulfate and evaporated under reduced pressure. The resulting residue was dissolved in chloroform (200 ml). After adding an aqueous potassium carbonate solution (50 ml, 5%), the solution was stirred for 0.5 hours at room temperature. The organic layer was separated using a separatory funnel and concentrated until the formation of crystals. The resulting crystals were filtered and dried in air to give **4** in 80% yield (2.24 g).

Table 2

$^1$H NMR Spectral Data for **3-12**

| Compound No. | Solvent [a] | $^1$H NMR (δ, ppm) [b] |
|---|---|---|
| **3** | D | 7.20 (t, 1H, J = 7.5), 7.47 (m, 2H), 7.59 (d, 2H, J = 8.9), 7.94 (dd, 1H, J = 1.5), 8.23 (dd, 2H, J = 1.8), 13.50 (bs, OH) |
| **4** | D | 7.69 (m, 1H), 7.87 (m, 1H), 7.96 (t, 1H, J = 7.5, 1.0), 8.17 (d, 1H, J = 8.9), 8.51 (m, 2H), 9.12 (d, 1H, J = 2.6) |
| **5** | D | 5.71 (s, $NH_2$), 7.12 (t, 1H, J = 6.6, 1.9), 7.53 (t, 2H, J = 5.7, 8.2), 7.74 (m, 3H), 8.46 (d, 1H, J = 8.0) |
| **6a** | D | 2.09 (s, 3H), 7.58 (t, 1H, J = 7.0, 7.8), 7.81 (m, 3H), 8.04 (dd, 1H, J = 2.3), 8.47 (d, 1H, J = 8.0), 8.72 (d, 1H, J = 2.1), 10.36 (bs, NH) |
| **6b** | D | 7.61 (t, 1H, J = 7.5, 7.1), 7.85 (m, 3H), 8.09 (dd, 1H, J = 2.0), 8.48 (d, 1H, J = 7.9), 8.84 (d, 1H, J = 1.7), 11.64 (bs, NH) |
| **6c** | D | 4.23 (s, 2H), 7.59 (s, 1H), 7.82 (t, 3H, J = 6.5, 15.7), 8.04 (d, 1H, J = 8.0), 8.48 (d, 1H, J = 7.3), 8.73 (s, 1H), 10.72 (bs, NH) |
| **7a** | D | 7.61 (m, 4H), 7.81 (m, 3H), 8.04 (t, 2H, J = 6.8, 1.3), 8.26 (dd, 1H, J = 2.3), 8.50 (d, 1H, J = 7.7), 8.97 (d, 1H, J = 2.3), 10.67 (bs, NH) |
| **7b** | D | 2.40 (s, 3H), 7.37 (d, 2H, J = 7.9), 7.59 (t, 1H, J = 7.5), 7.81 (m, 3H), 7.95 (d, 2H, J = 7.9), 8.28 (dd, 1H, J = 2.3), 8.50 (d, 1H, J = 8.0), 8.95 (s, 1H), 10.57 (bs, NH) |

Table 2 (continued)

$^1$H NMR Spectral Data for **3-12**

| Compound No. | Solvent [a] | $^1$H NMR (δ, ppm) [b] |
|---|---|---|
| **7c** | D | 7.62 (dd, 3H, J = 8.4, 7.5), 7.79 (t, 1H, J = 7.0, 7.9), 7.87 (d, 2H, J = 10.1), 8.06(d, 2H, J = 8.2), 8.26 (d, 1H, J = 8.9), 8.50 (d, 1H, J = 8.1), 8.93 (s, 1H), 10.71 (bs, NH) |
| **8a** | D | 2.78 (d, 3H, J = 4.7), 6.29 (d, NH, J = 4.9), 7.13 (dd, 1H, J = 2.7), 7.54 (m, 3H), 7.71 (m, 1H), 7.79 (d, 1H, J = 8.0), 8.46 (t, 1H, J = 7.1, 1.1) |
| **8b** | D | 4.39 (s, 2H), 6.90 (bs, NH), 7.22 (dd, 2H, J = 6.3, 8.8), 7.37 (t, 4H, J = 7.8, 7.3), 7.55 (d, J = 8.8), 7.74 (dd, 2H, J = 7.5, 6.4), 8.42 (d, 1H, J = 7.7) |
| **8c** | D | 4.37 (s, 2H), 6.94 (bs, NH), 7.17 (dd, 1H, J = 2.2), 7.36 (d, 2H, J = 8.1), 7.53 (m, 5H), 7.70 (t, 1H, J = 7.0, 7.7), 7.77 (d, 1H, J = 8.0), 8.42 (d, 1H, J = 8.0) |
| **9** | D | 4.82 (s, 4H), 7.26 (d, 5H, J = 8.3), 7.54 (d, 5H, J = 7.8), 7.62 (t, 2H, J = 3.4, 4.9), 7.71 (t, 1H, J = 6.9, 8.2), 7.78 (d, 1H, J = 8.0), 7.78 (d, 1H, J = 8.0), 8.39 (d, 1H, J = 8.0) |
| **10** | D | 8.03 (t, 1H, J = 7.4, 7.2), 8.13 (t, 1H, J = 5.9, 7.2), 8.30 (d, 1H, J = 7.5), 8.37 (d, 1H, J = 7.4), 8.53 (d, 1H, J = 8.6), 8.78 (t, 1H, J = 2.0, 6.5), 8.86 (s, 1H) |
| **11** | D | 6.57 (s, $NH_2$), 7.03 (d, 1H, J = 8.3), 7.35 (s, 1H), 7.82 (d, 1H, J = 8.5), 7.90 (t, 1H, J = 7.5, 7.3), 8.01 (t, 1H, J = 7.1, 7.5), 8.14 (d, 1H, J = 7.6), 8.22 (d, 1H, J = 7.6) |
| **12a** | D | 2.15 (s, 3H), 7.96 (t, 1H, 7.6, 7.5), 8.05 (t, 1H, J = 6.1, 7.6), 8.19 (m, 3H), 8.29 (d, 1H, J = 7.5), 8.51 (d, 1H, J = 1.3), 10.69 (bs, NH) |
| **12b** | D | 7.95 (t, 1H, J = 7.6), 8.04 (t, 1H, J = 7.6), 8.19 (m, 3H), 8.30 (d, 1H, J = 7.5), 8.50 (d, 1H, J = 1.3), 10.93 (bs, NH) |
| **12c** | D | 4.38 (s, 2H), 7.96 (t, 1H, J = 7.7, 7.5), 8.06 (t, 1H, J = 6.7, 7.6), 8.21 (d, 3H, J = 4.4), 8.30 (d, 1H, J = 7.4), 8.52 (s, 1H), 11.06 (bs, NH) |
| **12d** | D | 7.61 (m, 3H), 8.03 (m, 4H), 8.24 (m, 2H), 8.31 (dd, 1H, J = 0.7, 1.0), 8.49 (dd, 1H, J = 2.1, 2.2), 8.77 (d, 1H, J = 2.1), 10.94 (bs, NH) |
| **12e** | D | 2.41 (s, 3H), 7.39 (d, 2H, J = 8.1), 7.97 (m, 3H), 8.07 (m, 1H), 8.24 (m, 2H), 8.31 (dd, 1H, J = 1.0), 8.49 (dd, 1H, J = 2.2), 8.77 (dd, 1H, J = 2.3, 2.1), 10.84 (bs, NH) |
| **12f** | D | 7.60 (d, 2H, J = 8.4), 7.97 (t, 1H, J = 7.6, 7.4), 8.07 (t, 3H, J = 4.5, 8.4), 8.28 (m, 3H), 8.47 (d, 1H, J = 8.7), 8.75 (d, 1H, J = 1.5), 10.98 (bs, NH) |

[a] Solvent; D = Dimethyl-$d_6$ sulfoxide. [b] Abbriviations used; s = singlet, d = doublet, dd = double doublet, t = triplet, bs = broad singlet, m = multiplet, J = in Herz unit. All NH and OH proton signals were exchangeable with deuterium oxide.

Table 3

Elemental Analytical Data of **3-12**

| Compound No. | Molecular Formula | Elemental Analyses (%) (Calcd./Found) C | H | N | S |
|---|---|---|---|---|---|
| **3** | $C_{13}H_9NO_4S$ | 56.72 | 3.30 | 5.09 | 11.65 |
| | | 56.78 | 3.28 | 5.20 | 11.74 |
| **4** | $C_{13}H_7NO_3S$ | 60.69 | 2.74 | 5.44 | 12.46 |
| | | 60.75 | 2.55 | 5.43 | 12.44 |
| **5** | $C_{13}H_9NOS$ | 68.70 | 3.99 | 6.16 | 14.11 |
| | | 68.92 | 3.90 | 6.17 | 14.31 |
| **6a** | $C_{15}H_{11}NO_2S$ | 66.90 | 4.12 | 5.20 | 11.90 |
| | | 67.12 | 3.99 | 5.15 | 12.04 |
| **6b** | $C_{15}H_8NO_2SF_3$ | 55.73 | 2.49 | 4.33 | 9.92 |
| | | 55.86 | 2.56 | 4.64 | 9.93 |
| **6c** | $C_{15}H_{10}NO_2SCl$ | 59.31 | 3.32 | 4.61 | 10.55 |
| | | 59.48 | 3.43 | 4.69 | 10.65 |
| **7a** | $C_{20}H_{13}NO_2S$ | 72.49 | 3.95 | 4.23 | 9.67 |
| | | 72.68 | 3.96 | 4.38 | 9.55 |
| **7b** | $C_{21}H_{15}NO_2S$ | 73.02 | 4.38 | 4.06 | 9.28 |
| | | 73.30 | 4.55 | 4.16 | 9.34 |
| **7c** | $C_{20}H_{12}NO_2SCl$ | 65.66 | 3.31 | 3.83 | 8.76 |
| | | 65.56 | 3.32 | 3.83 | 8.92 |
| **8a** | $C_{14}H_{11}NOS$ | 69.68 | 4.59 | 5.80 | 13.29 |
| | | 69.85 | 4.57 | 5.63 | 13.11 |
| **8b** | $C_{20}H_{15}NOS$ | 75.68 | 4.76 | 4.41 | 10.10 |
| | | 75.69 | 4.98 | 4.25 | 10.40 |
| **8c** | $C_{20}H_{14}NOSBr$ | 60.62 | 3.56 | 3.53 | 8.09 |
| | | 60.75 | 3.74 | 3.60 | 7.89 |

Table 3 (continued)

| Compound No. | Molecular Formula | Elemental Analyses (%) (Calcd./Found) C | H | N | S |
|---|---|---|---|---|---|
| **9** | $C_{27}H_{19}NOSBr_2$ | 57.37 | 3.39 | 2.48 | 5.67 |
| | | 57.10 | 3.31 | 2.51 | 5.65 |
| **10** | $C_{13}H_7NO_5S$ | 53.98 | 2.44 | 4.84 | 11.08 |
| | | 54.10 | 2.65 | 4.89 | 11.30 |
| **11** | $C_{13}H_9NO_3S$ | 60.22 | 3.50 | 5.40 | 12.37 |
| | | 59.98 | 3.48 | 5.50 | 12.50 |
| **12a** | $C_{15}H_{11}NO_4S$ | 59.79 | 3.68 | 4.65 | 10.64 |
| | | 59.69 | 3.57 | 4.44 | 10.42 |
| **12b** | $C_{15}H_8NO_4SF_3$ | 50.71 | 2.27 | 3.94 | 9.02 |
| | | 50.98 | 2.34 | 3.97 | 9.06 |
| **12c** | $C_{15}H_{10}NO_4SCl$ | 53.66 | 3.00 | 4.17 | 9.55 |
| | | 53.88 | 2.96 | 4.15 | 9.52 |
| **12d** | $C_{20}H_{13}NO_4S$ | 66.11 | 3.61 | 3.85 | 8.82 |
| | | 66.35 | 3.69 | 3.87 | 8.95 |
| **12e** | $C_{21}H_{15}NO_4S$ | 66.83 | 4.01 | 3.71 | 8.49 |
| | | 66.80 | 3.98 | 3.75 | 8.68 |
| **12f** | $C_{20}H_{12}NO_4SCl$ | 60.38 | 3.04 | 3.52 | 8.06 |
| | | 60.56 | 3.25 | 3.55 | 8.19 |

2-Aminothioxanthone (**5**).

A mixture was **4** (1.3 g, 5.05 mmoles), ethanol (200 ml), water (60 ml), ammonium chloride (1.64 g, 30.65 mmoles) and iron (0.9 g, 16.12 mmoles) was refluxed for 3 hours. After removal of the inorganic substances by filtration using silica gel,

the residue was washed with ethanol (30 ml). The combined filtrate was concentrated under reduced pressure. The product was extracted with chloroform (150 ml). The chloroform solution was dried over anhydrous magnesium sulfate and evaporated to give **5** in 90% (1.03 g) yield.

2-Acetamidothioxanthone (**6a**).

A mixture of acetic acid (30 ml), acetic anhydride (3.25 g, 31.8 mmoles) and **5** (0.21 g, 0.92 mmole) was stirred for 1 hour at room temperature. After adding water (50 ml) with stirring, the precipitate was filtered and washed with water (50 ml x 4) and methanol (3 ml). The resulting precipitate was recrystallized from chloroform to give **6a** in 74% yield (0.17 g).

2-Trifluoroacetamidothioxanthone (**6b**).

A solution of trifluoroacetic anhydride (20 ml) and **5** (0.23 g, 0.88 mmole) was stirred for 2 hours. After evaporating the solvent under reduced pressure, the residue was dissolved in chloroform (70 ml). Ethanol (20 ml) was added to the solution. The mixture was concentrated to about 20 ml. After adding *n*-hexane (30 ml) to the residue with stirring, the resulting precipitate was filtered and dried in air to give **6b** in 96% yield (0.31 g).

2-Chloroacetamidothioxanthone (**6c**).

A solution of acetic acid (40 ml), **5** (0.21 g, 0.92 mmole) and chloroacetic anhydride (1 g, 5.88 mmoles) was stirred for 1 hour. After adding water (40 ml) with stirring, the resulting precipitate was filtered and washed with ethanol (3 ml) to give **6c** as yellow powder in 86% yield (0.23 g).

2-Benzamidothioxanthone (**7a**).

A mixture of **5** (0.23 g, 1 mmoles), chloroform (30 ml), triethylamine (0.14 g, 1 mmole) and benzoyl chloride (0.242 g, 1.72 mmoles) was stirred for 2 hours at room temperature. After adding water (20 ml) with stirring, the organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure. The resulting crystals were washed with methanol (10 ml) and then with *n*-hexane to give **7a** in 76% yield (0.26 g).

2-(*p*-Methylbenzamido)thioxanthone (**7b**).

A mixture of *p*-toluoyl chloride (0.386 g, 2.5 mmoles), **5** (0.23 g, 1 mmole), triethylamine (0.14 ml, 1 mmole) and chloroform (40 ml) was allowed to react for 1.5 hours at room temperature with stirring. After adding chloroform (30 ml) and water (20 ml) with stirring for 0.5 hours, the organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure. The resulting residue was washed with methanol (30 ml) and dried in air to give **7b** in 89% yield (0.31 g).

2-(*p*-Chlorobenzamido)thioxanthone (**7c**).

A solution of **5** (0.2 g, 0.88 mmole), *p*-chlorobenzoyl chloride (0.275 g, 1.57 mmoles), triethyl amine (0.15 g, 1.43 mmoles) and chloroform (40 ml) was stirred for 2 hours at room temperature. After adding water (40 ml) with stirring for 0.5 hours, the organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure. The resulting residue was washed with ethanol (20 ml) and dried in air to afford **7c** in 91% yield (0.288 g).

2-Methylaminothioxanthone (**8a**).

A solution of **5** (0.21 g, 0.92 mmole), potassium carbonate (0.13 g, 0.94 mmole), methyl iodide (0.23 g, 1.62 mmoles) and dimethylformamide (10 ml) was stirred for 7 hours at room temperature. After adding water (50 ml) with stirring, the product was extracted with chloroform (50 ml). The organic layer was dried over anhydrous magnesium sulfate and evaporated under reduced pressure. The residue was triturated in *n*-hexane. The resulting precipitate was filtered and dissolved in chloroform (20 ml). The chloroform solution was applied to the top of an open-bed silica gel column (3 x 15 cm). The column was eluted with chloroform. Fractions containing the product (Rf = 0.55, chloroform/methanol = 5:0.1, v/v) were combined and evaporated under reduced pressure to give **8a** in 28% yield (0.06 g).

2-Benzylaminothioxanthone (**8b**).

A mixture of **5** (0.2, 0.88 mmole), potassium carbonate (0.13 g, 0.94 mmole), benzyl chloride (0.55 g, 4.34 mmoles), acetonitrile (15 ml) and dimethylformamide (10 ml) was stirred for 8 hours at 100°. After evaporating the solvent, water (30 ml) was added to the residue with stirring. The resulting precipitate was filtered and dissolved in chloroform (20 ml). The chloroform solution was then applied to the top of an open-bed silica gel column (3 x 15 cm). The column was eluted with chloroform. Fractions containing the product (Rf = 0.78, chloroform) were combined and evaporated under reduced pressure to give **8b** in 36% yield (0.1 g).

2-(*p*-Bromobenzylamino)thioxanthone (**8c**) and 2-Di(*p*-bromobenzylamino)thioxanthone (**9**).

A mixture of **5** (0.2 g, 0.88 mmole), *p*-bromobenzyl bromide (0.49 g, 1.96 mmoles), potassium carbonate (0.13 g, 0.94 mmole) acetonitrile (15 ml) and dimethylformamide (15 ml) was allowed to react for 1.5 hours at 100°. After evaporating the solvent, water (50 ml) was added to the residue with stirring. The product was extracted with chloroform (80 ml). The solution was dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure. The residue was triturated in ethanol (20 ml) and filtered. The resulting precipitate was dissolved in chloroform (10 ml). The chloroform solution was applied to the top of an open-bed silica gel column (3 x 15 cm). The column was eluted with chloroform. Fractions containing **9** (Rf = 0.66, chloroform) were combined and evaporated under reduced pressure to give **9** in 25% yield (0.125 g). Fractions containing **8c** (Rf = 0.29, chloroform) were combined and evaporated under reduced pressure to give **8c** in 37% yield (0.13 g).

2-Nitrothioxanthone 10,10-Dioxide (**10**).

A mixture of **4** (0.26 g, 1 mmole), *m*-chloroperoxybenzoic acid (0.63 g, 2 mmoles, 50-56%) and chloroform (30 ml) was refluxed for 1.5 hours. After cooling to room temperature, the solvent was evaporated under reduced pressure. To the residue was added chloroform (200 ml) and aqueous potassium carbonate (5%, 30 ml). After stirring for 0.5 hours at room temperature, the organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to give **5** in 70% yield (0.2 g).

2-Aminothioxanthone 10,10-Dioxide (**11**).

Method A.

A mixure of **5** (0.2 g, 0.88 mmole), *m*-chloroperoxybenzoic acid (0.6 g, 1.76 mmoles, 50-60%) and chloroform (30 ml) was stirred for 1.5 hours at room temperature. After evaporating the solvent under reduced pressure, ethanol (30 ml) was added to

the residue with stirring. The resulting precipitate was filtered and dried in air to give **11** in 75% yield (0.1 g).

Method B.

A solution of **10** (0.15 g, 0.52 mmole), ethanol (40 ml), ammonium chloride (0.17 g, 3.18 mmoles), water (10 ml) and iron powder (0.09 g, 1.6 mmoles) was refluxed for 3 hours. After removal of the inorganic substances by filtration using silica gel, the residue was washed with ethanol (20 ml). The combined filtrate was evaporated under reduced pressure. The resulting residue was washed with water (100 ml) and then with ethanol (5 ml) to give **11** in 75% yield (0.1 g).

2-Acetamidothioxanthone 10,10-Dioxide (**12a**).

A mixture of **6a** (0.117 g, 0.43 mmole), *m*-chloroperoxybenzoic acid (0.32 g, 1.02 mmoles, 50-60%) and chloroform (40 ml) was stirred for 1 hour at room temperature. After evaporating the solvent under reduced pressure, the residue was dissolved in methanol (20 ml). To the solution was added *n*-hexane (20 ml) with stirring. The resulting precipitate was filtered and dried in air to give **12a** in 87% yield (0.12 g).

2-Trifluoroacetamidothioxanthone 10,10-dioxide (**12b**).

A mixture of **6b** (0.16 g, 0.5 mmole), *m*-chloroperoxybenzoic acid (0.5 g, 1.45 mmoles, 50-60%) and chloroform (40 ml) was stirred for 1 hour at room temperature. After concentrating the solution to 10 ml, methanol (20 ml) was added to the residue with stirring. The resulting precipitate was filtered and dried in air to give **12b** in 74% yield (0.131 g).

2-Chloroacetamidothioxanthone 10,10-Dioxide (**12c**).

A mixture of **6c** (0.1 g, 0.33 mmole), *m*-chloroperoxybenzoic acid (0.25 g, 0.78 mmole, 50-60%) and chloroform (20 ml) was stirred for 1 hour at room temperature. After evaporating the solvent under reduced pressure, the residue was triturated in methanol (20 ml). The resulting precipitate was filtered and dried in air to give **12c** in 56% yield (0.06 g).

2-Benzamidothioxanthone 10,10-Dioxide (**12d**).

A mixture of **7a** (0.17 g, 0.51 mmole), *m*-chloroperoxybenzoic acid (0.35 g, 1.12 mmoles, 50-60%) and chloroform (40 ml) was stirred for 1 hour at room temperature. After evaporating the solvent under reduced pressure, the residue was dissolved in ethanol (15 ml). To the solution was added *n*-hexane (20 ml) with stirring. The resulting precipitate was filtered and dried in air to give **12d** in 76% yield (0.14 g).

2-(*p*-Methylbenzamido)thioxanthone 10,10-Dioxide (**12e**).

A mixture of **7b** (0.17 g, 0.49 mmole), *m*-chloroperoxybenzoic acid (0.35 g, 1.12 mmoles, 50-60%) and chloroform (40 ml) was stirred for 1 hour at room temperature. After evaporating the solvent under reduced pressure, the residue was dissolved in ethanol (20 ml). To the solution was added *n*-hexane (10 ml) with stirring. The resulting precipitate was filtered and dried in air to give **12e** in 72% yield (0.13 g).

2-(*p*-Chlorobenzamido)thioxanthone 10,10-Dioxide (**12f**).

A mixture of **7c** (0.18 g, 0.49 mmole), *m*-chloroperoxybenzoic acid (0.34 g, 1.08 mmoles, 50-60%) and chloroform (40 ml) was stirred for 1 hour at room temperature. After evaporating the solvent under reduced pressure, the residue was triturated in ethanol (20 ml). The resulting precipitate was filtered and dried in air to give **12f** in 89% yield (0.17 g).

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## REFERENCES AND NOTES

[1] S. Archer and C. M. Suter, *J. Am. Chem. Soc.*, **74**, 4296 (1952).

[2] K. Sindelar, B. Kakac, E. Svatek, J. Holubek, J. Metysova, M. Hrubantova and M. Protiva, *Collect. Czech. Chem. Commun.*, **38**, 3321 (1973); *Chem. Abstr.*, **80**, 82876d (1974).

[3] B. S. Ross and R. A. Wiely, *J. Med. Chem.*, **28**, 870 (1985).

[4] H. D. H. Showalter, M. M. Angelo, E. M. Berman, G. D. Kanter, D. F. Ortwine, S. G. Ross-Kesten, A. D. Sercel, W. R. Turner, L. M. Werbel, D. F. Worth, E. F. Elslager, W. R. Leopold and J. L. Shillis, *J. Med. Chem.*, **31**, 1527 (1988).

[5] P. V. Arur and S. N. Kulkarni, *Indian J. Chem.*, **20B**, 50 (1981).

[6] G. Amirzadeh and W. Schnabel, *Makromol. Chem.*, **182**, 2821 (1981).

[7] E. W. Tsai, L. Throckmorton, R. Mckellar, M. Baar, M. Kluba, D. S. Marynick, K. Rajeshwar and A. L. Ternay, Jr., *J. Electroanal. Chem.*, **210**, 45 (1986).

[8] J. P. Fouassier and D. J. Lougnot, *J. Appl. Polym. Sci.*, **34**, 477 (1987).

[9] B. M. Monroe and G. C. Weed, *Chem. Rev.*, **93**, 435 (1993).

[10] I. Okabayashi, N. Murakami and K. Sekiya, *J. Heterocyclic Chem.*, **26**, 635 (1989).

[11] A. R. Katritzky, C. W. Rees, and E. F. V. Scriven, Comprehensive Heterocyclic Chemistry II, A. McKillop, ed, Vol **5**, Pergamon, 1996, p 612.

[12] X. Minzhao, W. Jindi and Q. Guozhen, *J. East China Inst. Chem. Technol.*, **19**, 310 (1993).

[13] S. D. Cho, W. Y. Choi, S. G. Lee, Y. J. Yoon and S. C. Shin, *Tetrahedron Letters*, **37**, 7059 (1996).

[14] N. Raseanu, *Rev. Chim.* (Bucharest), **20**, 659 (1969).