

Reactions of 3-Bromo-2,3-dihydro- and 2,3-Dibromo-4*H*-1-benzothiopyran-4-one 1,1-Dioxides with Various Amines

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Reactions of 2,3-dibromo-4*H*-1-benzothiopyran-4-one 1,1-dioxide (1) and 3-bromo-2,3-dihydro-4*H*-1-benzothiopyran-4-one 1,1-dioxide (4) with various amines have been studied. Novel 2-alkylamino and arylamino derivatives (2a–g) were obtained from the reactions of (1) with alkylamines and primary aromatic amines, respectively. The reaction of (1) with secondary aromatic amines gave 2-aryl derivatives (3) together with 2-arylamino derivatives. Tertiary aromatic amines under the same conditions gave only 2-aryl derivatives (3d–i). The reactions of (4) with aromatic amines gave directly the 3-substituted thiochromone 1-oxides (5a–c), which were oxidized with hydrogen peroxide to the corresponding sulphones (6a–c). The ring-closure product (8) was obtained from the reaction of (4) with *o*-aminobenzenethiol.

Compounds related to 2-phenyl-4*H*-1-benzothiopyran-4-ones (thioflavones) are interesting in that they are biologically active and contain a sulphur atom.^{1–3} We have studied the relationship between structure and antimicrobial activity of thioflavones and thioflavone 1,1-dioxides, some of which showed significant activity *in vitro* against *Trichophyton mentagrophytes*.^{4–9}

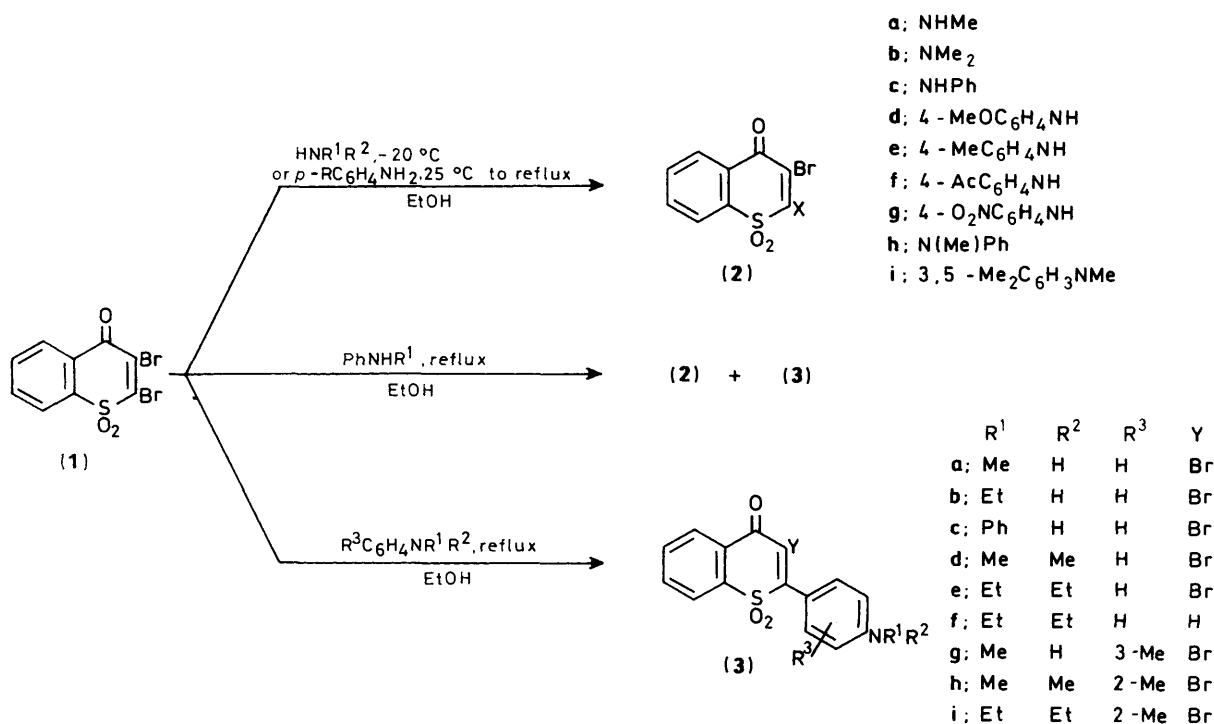
The *S,S*-dioxides of 4*H*-1-benzothiopyran-4-one (thiochromone) are of particular interest; they can be regarded as the sulphone analogues of 1,4-naphthoquinone dyes, used in optical recording media and guest–host liquid crystal displays.^{10,11} Some thiopyran 1,1-dioxides, have already been prepared.¹² However, little is known of the chemistry of thiochromone 1,1-dioxides.¹³

This paper describes the reactions of 2,3-dibromo-4*H*-1-

benzopyran-4-one (2,3-dibromothiochromone) 1,1-dioxide (1) and 3-bromo-2,3-dihydro-4*H*-1-benzothiopyran-4-one 1,1-dioxide (4) with various amines to give 2-alkylamino- and 3-arylamino-thiochromone 1,1-dioxides, which can be viewed as examples of a simple donor–acceptor system.

Results and Discussion

Reactions of 2,3-Dibromothiochromone 1,1-Dioxide (1) with Amines.—It is well known that both 2,3-dichloro- and 2,3-dibromo-thiochromone 1,1-dioxide (1) react smoothly with nucleophiles to give mono- and di-substituted derivatives.¹³ Of the primary amines, only aniline has been reported to react with (1). We have now found that the reaction is general, at least for



Scheme 1.

Table 1. Reactions of 2,3-dibromothiochromone 1,1-dioxide (**1**) with amines

Amine	Product (Formula)	Temp.	Yield (%)	M.p. (°C) (recryst. sol.)	Found (%) (Required)		
					C	H	N
MeNH ₂	(2a) (C ₁₀ H ₈ BrNO ₃ S)	-20 °C	37	157 ^b <i>c</i>	39.9 (39.75)	2.75 (2.7)	4.9 (4.6)
Me ₂ NH	(2b) (C ₁₁ H ₁₀ BrNO ₃ S)	-20 °C	22	163 ^b <i>c</i>	41.7 (41.8)	3.25 (3.2)	4.6 (4.4)
<i>p</i> -MeOC ₆ H ₄ NH ₂	(2d) (C ₁₆ H ₁₂ BrNO ₄ S)	Room	92	188—190 (EtOH)	48.5 (48.75)	3.1 (3.1)	3.8 (3.55)
<i>p</i> -MeC ₆ H ₄ NH ₂	(2e) (C ₁₆ H ₁₂ BrNO ₃ S)	Room	63	194—195 (C ₆ H ₆)	50.7 (50.8)	3.0 (3.2)	3.6 (3.7)
<i>p</i> -AcC ₆ H ₄ NH ₂	(2f) (C ₁₇ H ₁₂ BrNO ₄ S)	Room	8	174 ^b (EtOH)	50.1 (50.3)	2.8 (3.0)	3.65 (3.45)
<i>p</i> -O ₂ NC ₆ H ₄ NH ₂	(2g) (C ₁₅ H ₉ BrN ₂ O ₅ S)	Reflux	48	250—252 (CHCl ₃)	44.3 (44.0)	2.15 (2.2)	6.7 (6.85)
PhNHMe	(2h) (C ₁₆ H ₁₂ BrNO ₃ S)	Reflux	13	146—148 (C ₆ H ₁₂)	50.5 (50.8)	3.3 (3.2)	3.5 (3.7)
PhNHEt	(3a) (C ₁₆ H ₁₂ BrNO ₃ S)	Reflux	15	213—215 (C ₆ H ₆ -C ₆ H ₁₂)	50.8 (50.8)	3.2 (3.2)	3.5 (3.7)
PhNHEt	(3b) (C ₁₇ H ₁₄ BrNO ₃ S)	Reflux	39	224—225 (C ₆ H ₆)	52.2 (52.05)	3.7 (3.6)	3.3 (3.6)
Ph ₂ NH	(3c) (C ₂₁ H ₁₄ BrNO ₃ S)	Reflux	1.2	234—235 (C ₆ H ₆)	57.45 (57.3)	3.4 (3.2)	3.4 (3.2)
PhNMe ₂	(3d) (C ₁₇ H ₁₄ BrNO ₃ S)	Reflux	36	243 ^b (CHCl ₃)	52.1 (52.05)	3.8 (3.6)	3.45 (3.6)
PhNEt ₂	(3e) (C ₁₉ H ₁₈ BrNO ₃ S)	Reflux	35	228—229 (C ₆ H ₆)	54.3 (54.3)	4.1 (4.3)	3.2 (3.3)
<i>o</i> -MeC ₆ H ₄ NMe ₂	(3f) (C ₁₉ H ₁₉ NO ₃ S)	Reflux	15	183—184 (C ₆ H ₆)	66.6 (66.8)	5.4 (5.6)	4.0 (4.1)
<i>o</i> -MeC ₆ H ₄ NMe ₂	(3g) (C ₁₇ H ₁₄ BrNO ₃ S)	Reflux	0.3	238 ^b (C ₆ H ₆)	51.0 (52.05)	3.8 (3.6)	3.7 (3.6)
<i>m</i> -MeC ₆ H ₄ NMe ₂	(3h) (C ₁₈ H ₁₆ BrNO ₃ S)	Reflux	2.3	228—229 (C ₆ H ₆)	53.4 (53.2)	3.8 (4.0)	3.5 (3.45)
<i>m</i> -MeC ₆ H ₄ NEt ₂	(3i) (C ₂₀ H ₂₀ BrNO ₃ S)	Reflux	7.1	218—219 (C ₆ H ₆)	55.3 (55.3)	4.7 (4.6)	3.4 (3.2)
3,5-Me ₂ C ₆ H ₃ NMe ₂	(2j) (C ₁₈ H ₁₆ BrNO ₃ S)	Reflux	1.3	157—158 (C ₆ H ₆)	53.1 (53.2)	3.8 (4.0)	3.3 (3.45)

^a Compound (**2e**) is known (ref. 12). ^b Decomposed. ^c As (**2a**) and (**2b**) were unstable, recrystallization was not possible.

primary aromatic and aliphatic amines, as shown in Table 1. The reaction of (**1**) with *p*-substituted anilines in ethanol gave the 2-arylamino compounds (**2**) in 48—92% yield. The reaction of (**1**) with *p*-nitroaniline, in which the nucleophilicity of the amino group is significantly decreased, also gave a 2-arylamino derivative (**2g**), although 2,3-dichloro-1,4-naphthoquinone (**10**) is unreactive under the same conditions.¹⁴ It is suggested that the electrophilicity of C-2 in (**1**) is enhanced by the strongly electron-withdrawing sulphone group.

The reaction of (**1**) with alkylamines (methylamine and dimethylamine) at -20 °C gave the 2-alkylamino compounds (**2a** and **b**) in good yield (Scheme 1). The products were unstable and gradually decomposed to give brown material at room temperature.

The amination products were identified as the 2-alkylamino or 2-arylamino derivatives, on the basis of their ¹³C n.m.r. spectra: C-2 of the 2-anilino compound (**2c**) suffers a considerable upfield shift (δ 128 p.p.m.) as compared with that of (**1**) (δ 142 p.p.m.), although C-3 is little affected (136 and 134 p.p.m., respectively).

Compound (**1**) with primary amines afforded only monosubstituted products, like 2,3-dichloro-1,4-naphthoquinone (**10**).¹⁵ In 2-amino-3-chloro-1,4-naphthoquinone a second amino group could be introduced after *N*-acylation or *N*-nitrosation.¹⁶ However, the *N*-acetyl compound (**2j**), prepared by acylation of (**2c**) with acetic anhydride was unreactive to alkylamines. It is

suggested that a reaction of the Michael addition type can occur at the 2-position of (**1**), but not at the 3-position.

The reaction of (**1**) with *N*-methylaniline gave the *C*-substituted 2-aryl derivative (**3a**), together with the 2-arylamino derivative (**2h**). The reactions of (**1**) with the more bulky amines *N*-ethylaniline and diphenylamine afforded only aryl derivatives (**3b** and **c**). The arylated compounds were identified as the 2-aryl derivatives on the basis of their ¹H and ¹³C n.m.r. spectra: two different doublet proton signals (at *ca.* 6.60 and 7.50 p.p.m.) were observed, typical of a *p*-substituted *N,N*-dialkylaniline, and the chemical shifts of C-2 and C-3 of (**3**) (150 and 130 p.p.m.) are typical of a 3-bromothioflavone 1,1-dioxide.

The reactions of (**1**) with tertiary aromatic amines afforded the 2-aryl derivatives (**3d—i**) (Table 1). In the reaction with *N,N*-diethylaniline, the 2-aryl derivative (**3e**) and debrominated product (**3f**) were also obtained.

The reaction with substituted *N,N*-dialkylanilines gave the 2-aryl compounds (**3g—i**) in very low yields (less than 10%); this can probably be attributed to steric hindrance by the substituent. The reaction with *N,N,N',N'*-tetramethylaniline did not afford a 2-aryl derivative, but gave the 2-arylamino derivative (**2i**) via *N*-demethylation of the substituted aniline.

Cyclic Voltammograms.—As shown in the Figure, the cyclic voltammogram of (**1**) is markedly different from that of 2,3-dichloro-1,4-naphthoquinone (**10**). The curve of (**1**) shows an

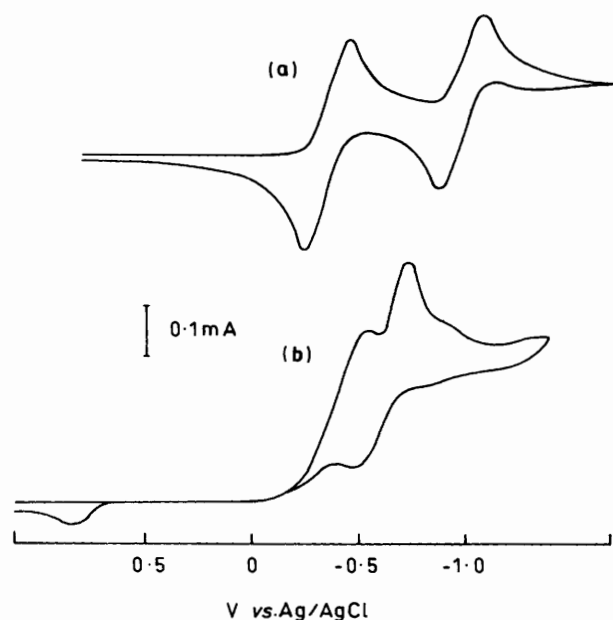


Figure. Cyclic voltammograms: (a) 2,3-dichloro-1,4-naphthoquinone (10); (b) 2,3-dibromothiochromone 1,1-dioxide (1)

Table 2. Reduction potentials of 2,3-dibromothiochromone 1,1-dioxide (1) and 2,3-dichloro-1,4-naphthoquinone (10) measured by cyclic voltammetry^a

Compound	E_{pc}^1/V	E_{pc}^2/V
(1)	-0.55	-0.73
(10)	-0.47	-1.09

^a Glassy carbon cathode, MeCN-Bu₄NClO₄ (0.1M), substrate ca. 0.5 mM, V vs. Ag/AgCl, scan rate 100 mV s⁻¹. ^b First reduction potential. ^c Second reduction potential.

Table 3. Spectroscopic data for 2-alkylamino- and 2-anilino-thiochromone 1,1-dioxide (2)

Compd.	ν_{max}/cm^{-1} ^a	¹ H N.m.r. (270 MHz; CDCl ₃) ^{c,d} δ (J/Hz)	<i>m/z</i> (rel. int.)
(2a)	3 300 (NH) 1 630 (C=O)	3.53 (3 H, s), 5.56–6.00 (1 H, br), 7.60–8.36 (4 H, m)	303 (53%, $M^+ + 2$), 301 (53, M^+), 237 (62, $M^+ - SO_2$), 223 (34), 158 (80, $M^+ - SO_2 - Br$)
(2b)	1 630 (C=O)	3.00 (3 H, s), 3.48 (3 H, s), 7.34–8.30 (4 H, m)	317 (19%, $M^+ + 2$), 315 (19, M^+), 251 (4, $M^+ - SO_2$), 236 (31, $M^+ - Br$), 172 (100, $M^+ - Br - SO_2$)
(2c)	3 055 (NH) ^b 1 630 (C=O) ^b	7.17 (1 H, br s), 7.34–7.46 (5 H, m), 7.76–7.83 (2 H, m), 7.94 (1 H, dd, <i>J</i> 2 and 9), 8.31 (1 H, dd, <i>J</i> 2 and 9)	365 (1.7%, $M^+ + 2$), 363 (1.8, M^+), 299 (13, $M^+ - SO_2$), 284 (0.7, $M^+ - Br$), 220 (100, $M^+ - SO_2 - Br$)
(2d)	3 270 (NH) 1 630 (C=O)	3.82 (3 H, s), 6.94 (2 H, d, <i>J</i> 9), 7.17 (1 H, br s), 7.37 (2 H, d, <i>J</i> 8), 7.74–7.81 (2 H, m), 7.88 (1 H, dd, <i>J</i> 2 and 7), 8.31 (1 H, dd, <i>J</i> 2 and 9)	395 (13%, $M^+ + 2$), 393 (13, M^+), 329 (12, $M^+ - SO_2$), 315 (32), 250 (27, $M^+ - SO_2 - Br$)
(2e)	3 270 (NH) 1 635 (C=O)	2.39 (3 H, s), 7.17 (1 H, br s), 7.23 (2 H, d, <i>J</i> 8), 7.29 (2 H, d, <i>J</i> 9), 7.75–7.79 (2 H, m), 7.90 (1 H, dd, <i>J</i> 2 and 9), 8.31 (1 H, dd, <i>J</i> 2 and 9)	379 (21%, $M^+ + 2$), 377 (20, M^+), 313 (20, $M^+ - SO_2$), 299 (34), 234 (94, $M^+ - SO_2 - Br$)
(2f)	3 300 (NH) 1 660 (C=O)	2.62 (3 H, s), 7.10 (1 H, br s), 7.27 (2 H, d, <i>J</i> 9), 7.81 ^c (1 H, dt, <i>J</i> 1 and 7), 7.86 ^c (1 H, dt, <i>J</i> 1 and 7), 8.03 ^c (2 H, d, <i>J</i> 9), 8.03 ^c (1 H, dd, <i>J</i> 1 and 7), 8.33 (1 H, dd, <i>J</i> 1 and 9)	407 (2%, $M^+ + 2$), 405 (2, M^+), 341 (3, $M^+ - SO_2$), 326 (3, $M^+ - Br$), 263 (32), 262 (4, $M^+ - SO_2 - Br$)
(2g)	3 130 (NH) 1 650 (C=O)	7.18 (2 H, d, <i>J</i> 9), 7.87 (1 H, dt, <i>J</i> 1 and 8), 7.94 (1 H, dt, <i>J</i> 1 and 8), 8.10 (1 H, dd, <i>J</i> 1 and 8), 8.18 (2 H, d, <i>J</i> 9), 8.33 (1 H, dd, <i>J</i> 1 and 8), 10.33 (1 H, br s)	410 (0.3%, $M^+ + 2$), 408 (0.3, M^+), 344 (0.9, $M^+ - SO_2$), 266 (16)
(2h)	1 650 (C=O)	3.67 (3 H, s), 7.08 (1 H, br s), 7.12 (3 H, dd, <i>J</i> 1 and 8), 7.34 (1 H, dt, <i>J</i> 2 and 7), 7.78 (1 H, dt, <i>J</i> 1 and 7), 7.87 (1 H, dt, <i>J</i> 1 and 8), 8.06 (1 H, dd, <i>J</i> 1 and 8), 7.29 (1 H, dd, <i>J</i> 1 and 8)	379 (33%, $M^+ + 2$), 377 (33, M^+), 298 (30, $M^+ - Br$), 234 (100, $M^+ - SO_2 - Br$)
(2i)	1 665 (C=O)	2.29 (6 H, s), 3.65 (3 H, s), 6.74 (2 H, s), 6.76 (1 H, s), 7.77 (1 H, dt, <i>J</i> 1 and 8), 7.85 (1 H, dt, <i>J</i> 1 and 8), 8.05 (1 H, dd, <i>J</i> 1 and 8), 8.28 (1 H, dd, <i>J</i> 1 and 8)	407 (49%, $M^+ + 2$), 405 (47, M^+), 326 (31, $M^+ - Br$), 262 (59, $M^+ - SO_2 - Br$), 247 (100, $M^+ - SO_2 - Br - Me$)

^a For KBr discs. ^b Lit.¹² ν_{max} . 3 255 (NH) and 1 623 cm⁻¹ (C=O). ^c In the case of (2g), solvent CDCl₃-(CD₃)₂SO. ^d In the cases of (2a and b), at 100 MHz. ^e Overlapping signal.

irreversible oxidation–reduction wave, whereas that of (10) shows two reversible oxidation–reduction waves. The first reduction potential of (1) is approximately equal to that of (10) but the second is higher than that of (10); thus the oxidising ability of (1) is less than that of (10) (Table 2).

The difference in oxidising abilities of these compounds was reflected in their reactivity towards triethylamine. Thus the 1,4-naphthoquinone (10) reacted with triethylamine to give *N,N*-diethylvinylamine, which then reacted as expected with (10) to give the 2-diethylaminovinyl compound (11).¹⁵ However, the reaction of (1) with triethylamine did not give the corresponding 2-diethylaminovinyl compound under the same conditions.

Synthesis of 3-Substituted Thiochromone 1,1-Dioxides.—As already mentioned, 3-substituted thiochromone 1,1-dioxides could not be obtained from the reactions of (1) with amines. We therefore sought a synthetic approach to 3-substituted derivatives. 3-Bromothiochromone 1,1-dioxide (4) was selected as starting material, in the expectation that it would be substituted only at the 3-position by nucleophiles. We found that the reaction of (4) with primary aromatic amines afforded the 3-substituted thiochromone 1-oxide (5a–c) oxidation of which by 30% hydrogen peroxide gave the desired 3-arylaminothiochromone 1,1-dioxides (6a–c). These sulphoxides might result from dehydration and oxidation of the 3-arylaminothiochromone 1,1-dioxides, obtained by substitution of bromine in (4). 3-Aminothiochromone 1,1-dioxide (6d) was obtained directly by treating (1) with sodium azide, in low yield. The reaction of (4) with *N,N*-dimethylaniline caused only substitution at the 3-position, to give 3-(4-dimethylaminophenyl)-thiochromone 1,1-dioxide (7).

The reaction of (4) with 2-aminobenzenethiol gave a new heterocycle (8), subsequently oxidized with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) to give the imino compound (9) (Scheme 3). However, the reaction of (4) with 2-aminophenol gave 3-(2-hydroxyanilino)thiochromone 1-oxide (6e). The reaction of (1) with 1,2-diaminobenzene gave many unidentified products.

Table 4. Spectroscopic data for 3-arylthiochromone 1,1-dioxides (3)

Compd.	$\nu_{\max}/\text{cm}^{-1}$ ^a	¹ H N.m.r. (270 MHz; CDCl ₃) ^b δ (J/Hz)	<i>m/z</i> (rel. int.)
(3a)	3 400 (NH) 1 670 (C=O)	2.91 (3 H, s), 4.15—4.35 (1 H, br), 6.70 (2 H, d, <i>J</i> 9), 7.50 (2 H, d, <i>J</i> 9), 7.78 (1 H, dt, <i>J</i> 1 and 8), 7.89 (1 H, dt, <i>J</i> 1 and 8), 8.10 (1 H, dd, <i>J</i> 1 and 8), 8.31 (1 H, dd, <i>J</i> 1 and 8)	379 (100%, <i>M</i> ⁺ + 2), 377 (93, <i>M</i> ⁺), 313 (73, <i>M</i> ⁺ - SO ₂), 298 (12, <i>M</i> ⁺ - Br), 234 (15, <i>M</i> ⁺ - SO ₂ - Br)
(3b)	1 670 (C=O)	1.30 (3 H, t, <i>J</i> 7), 3.23 (2 H, q, <i>J</i> 7), 4.00 (1 H, br s), 6.68 (2 H, d, <i>J</i> 9), 7.48 (2 H, d, <i>J</i> 9), 7.75 (1 H, dt, <i>J</i> 1 and 8), 7.88 (1 H, dt, <i>J</i> 1 and 8), 8.10 (1 H, dd, <i>J</i> 1 and 8), 8.30 (1 H, dd, <i>J</i> 1 and 8)	393 (51%, <i>M</i> ⁺ + 2), 391 (52, <i>M</i> ⁺), 376 (20, <i>M</i> ⁺ - Me), 312 (100, <i>M</i> ⁺ - Me - SO ₂), 234 (15)
(3c)	3 380 (NH) 1 680 (C=O)	6.04 (1 H, br s), 7.04—7.15 ^c (1 H, m), 7.12 ^c (2 H, d, <i>J</i> 8), 7.21 (2 H, dd, <i>J</i> 1 and 8), 7.35 (2 H, tt, <i>J</i> 2 and 8), 7.51 (2 H, d, <i>J</i> 9), 7.79 (1 H, dt, <i>J</i> 1 and 8), 7.89 (1 H, dt, <i>J</i> 1 and 8), 8.11 (1 H, dd, <i>J</i> 1 and 8), 8.31 (1 H, dd, <i>J</i> 1 and 8)	441 (79%, <i>M</i> ⁺ + 2), 439 (77, <i>M</i> ⁺), 375 (58, <i>M</i> ⁺ - SO ₂), 360 (17, <i>M</i> ⁺ - Br), 296 (20, <i>M</i> ⁺ - SO ₂ - Br)
(3d)	1 665 (C=O)	3.07 (6 H, s), 6.80 (2 H, d, <i>J</i> 9), 7.57 (2 H, d, <i>J</i> 9), 7.78 (1 H, dt, <i>J</i> 1 and 9), 7.88 (1 H, d, <i>J</i> 1 and 9), 8.10 (1 H, dd, <i>J</i> 1 and 8), 8.31 (1 H, dd, <i>J</i> 1 and 8)	393 (99%, <i>M</i> ⁺ + 2), 391 (99, <i>M</i> ⁺), 326 (100), 312 (13, <i>M</i> ⁺ - Br), 248 (35, <i>M</i> ⁺ - SO ₂ - Br)
(3e)	1 665 (C=O)	1.23 (6 H, t, <i>J</i> 7), 3.43 (4 H, q, <i>J</i> 7), 4.74 (2 H, dd, <i>J</i> 2 and 9), 7.56 (2 H, dd, <i>J</i> 2 and 9), 7.78 (1 H, dt, <i>J</i> 1 and 8), 7.87 (1 H, dt, <i>J</i> 1 and 8), 8.10 (1 H, dd, <i>J</i> 1 and 8), 8.30 (1 H, dd, <i>J</i> 1 and 7)	421 (51%, <i>M</i> ⁺ + 2), 419 (50, <i>M</i> ⁺), 404 (100, <i>M</i> ⁺ - Me), 376 (8, <i>M</i> ⁺ - Me - CO), 340 (44, <i>M</i> ⁺ - Me - SO ₂), 326 (21), 262 (22)
(3f)	1 640 (C=O)	1.23 (6 H, t, <i>J</i> 7), 3.45 (4 H, q, <i>J</i> 7), 6.73 (2 H, dd, <i>J</i> 2 and 7), 6.82 (1 H, s), 7.73 (1 H, dt, <i>J</i> 1 and 8), 7.84 ^c (1 H, dt, <i>J</i> 1 and 7), 7.87 ^c (2 H, dd, <i>J</i> 2 and 7), 8.10 (1 H, dd, <i>J</i> 1 and 8), 8.20 (1 H, dd, <i>J</i> 1 and 8)	341 (57%, <i>M</i> ⁺), 326 (100, <i>M</i> ⁺ - Me), 262 (76, <i>M</i> ⁺ - Me - SO ₂)
(3g)	3 420 (NH) 1 670 (C=O)	2.19 (3 H, s), 2.97 (3 H, s), 6.71 (1 H, d, <i>J</i> 2 and 8), 7.35 (1 H, s), 7.48 (1 H, dd, <i>J</i> 2 and 8), 7.78 (1 H, dt, <i>J</i> 1 and 8), 7.87 (1 H, dt, <i>J</i> 1 and 8), 8.10 (1 H, dd, <i>J</i> 1 and 8), 8.30 (1 H, dd, <i>J</i> 1 and 8)	393 (100%, <i>M</i> ⁺ + 2), 391 (100, <i>M</i> ⁺), 327 (70, <i>M</i> ⁺ - SO ₂), 312 (48, <i>M</i> ⁺ - Br), 248 (8, <i>M</i> ⁺ - SO ₂ - Br)
(3h)	1 667 (C=O)	2.35 (3 H, s), 3.03 (6 H, s), 6.64 ^c (1 H, s), 6.65 ^c (1 H, dd, <i>J</i> 2 and 9), 7.26 (1 H, dd, <i>J</i> 2 and 8), 7.78 (1 H, dt, <i>J</i> 1 and 8), 7.89 (1 H, dt, <i>J</i> 1 and 8), 8.12 (1 H, dd, <i>J</i> 1, 8), 8.33 (1 H, dd, <i>J</i> 1 and 8)	407 (80%, <i>M</i> ⁺ + 2), 405 (77, <i>M</i> ⁺), 341 (17, <i>M</i> ⁺ - SO ₂), 326 (12, <i>M</i> ⁺ - Br), 262 (82, <i>M</i> ⁺ - SO ₂ - Br), 234 (100, <i>M</i> ⁺ - SO ₂ - Br - CO)
(3i)	1 665 (C=O)	1.21 (6 H, t, <i>J</i> 7), 2.33 (3 H, s), 3.40 (4 H, q, <i>J</i> 7), 6.58 ^c (1 H, s), 6.60 ^c (1 H, d, <i>J</i> 9), 7.21 (1 H, d, <i>J</i> 9), 7.79 (1 H, dt, <i>J</i> 1 and 8), 7.88 (1 H, dt, <i>J</i> 1 and 8), 8.12 (1 H, dd, <i>J</i> 1 and 8), 8.33 (1 H, dd, <i>J</i> 1 and 8)	435 (67%, <i>M</i> ⁺ + 2), 433 (61, <i>M</i> ⁺), 418 (94, <i>M</i> ⁺ - Me), 354 (78, <i>M</i> ⁺ - SO ₂ - Me), 340 (48), 276 (26)

^a For KBr discs. ^b No amino proton signal was observed for compound (3g). ^c Overlapping signal.

Table 5. 3-Substituted thiochromone 1-oxides (5) and 1,1-dioxides (6)

Compd.	Yield (%)	Recryst. solvent	M.p. (°C)	Formula	Found (%) (Required)		
					C	H	N
(5a)	41	EtOH	225 ^a	C ₁₅ H ₁₁ NO ₂ S	66.8 (66.9)	4.0 (4.1)	5.0 (5.2)
(5b)	50	C ₆ H ₆	194 ^a	C ₁₆ H ₁₃ NO ₂ S	67.7 (67.8)	4.4 (4.6)	5.0 (4.9)
(5c)	5	CHCl ₃	> 300	C ₁₅ H ₁₀ N ₂ O ₄ S	57.0 (57.3)	2.35 (3.2)	8.85 (8.9)
(6a)	46	EtOH	218—219	C ₁₅ H ₁₁ NO ₃ S	63.0 (63.15)	3.7 (3.9)	5.0 (5.9)
(6b)	75	EtOH	239—240	C ₁₆ H ₁₃ NO ₃ S	64.1 (64.2)	4.15 (4.4)	4.5 (4.7)
(6c)	75	EtOH	> 300	C ₁₅ H ₁₀ N ₂ O ₅ S	54.3 (54.5)	2.8 (3.05)	8.4 (8.5)
(6d)	2	C ₆ H ₆	199—200	C ₉ H ₇ NO ₃ S	51.6 (51.7)	3.2 (3.4)	6.7 (6.7)

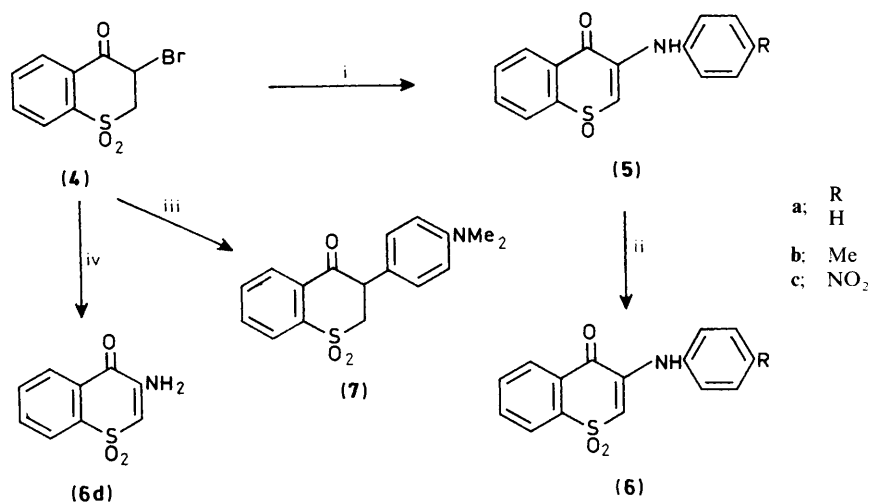
^a Decomposed.

Experimental

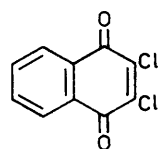
M.p.s were determined for samples in open capillary tubes with a Yamato MD-21 apparatus. ¹H N.m.r. spectra were recorded with a JEOL JNM-MH-100 (100 MHz) spectrometer and a JEOL JNM-GX270 FT (270 MHz) spectrometer, with Me₄Si as internal standard. ¹³C N.m.r. spectra were recorded with a JEOL JNM-GX270 FT (67 MHz) spectrometer, with CDCl₃

as solvent and reference (77.0 p.p.m.). Mass spectra were obtained with a Shimadzu LKB-9000 spectrometer operating at 70-eV. I.r. spectra were recorded with a Shimadzu IR-420 spectrometer for KBr discs. Elemental analyses were recorded with a Yanaco CHN CORDER MT-3.

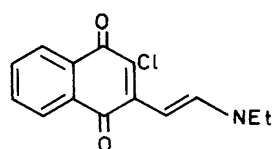
Materials.—2,3-Dibromothiochromone 1,1-dioxide (1),¹³ 3-



Scheme 2. Reagents and conditions: i, *p*-RC₆H₄NH₂, EtOH, reflux; ii, 30% H₂O₂, AcOH, 55 °C; iii, PhNMe₂, EtOH, reflux; iv, NaN₃, MeOH-H₂O, 65 °C



(10)

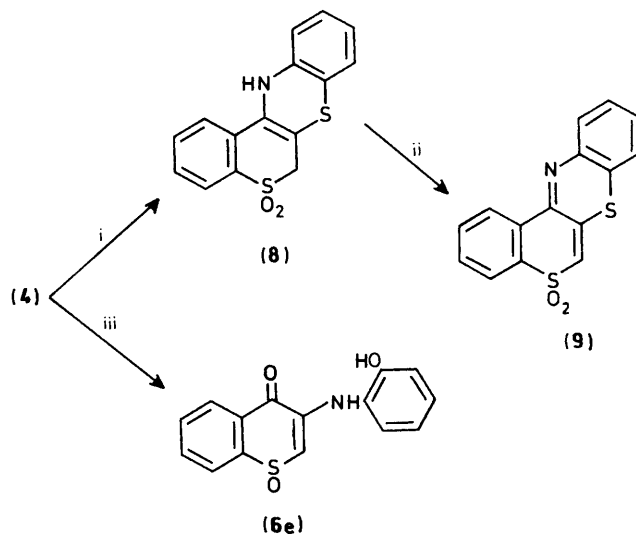


(11)

Bromothiochromanone 1,1-dioxide (4),¹⁷ and 2-anilino-3-bromothiochromone 1,1-dioxide (2c)¹³ were prepared by the methods reported.

Alkylamination of 2,3-Dibromothiochromone 1,1-Dioxide (1).—The alkylamine (1.8 mmol) was added to a stirred suspension of 2,3-dibromothiochromone 1,1-dioxide (1) (300 mg, 0.9 mmol) in ethanol (10 ml) at -20 °C. The mixture was stirred for 8 h and allowed to warm from -20 to 25 °C. It was then filtered to remove starting material (1). The filtrate was concentrated to one-third of its original volume under reduced pressure. The resulting precipitate was filtered off and immediately dried at room temperature *in vacuo* to give the 2-alkylamino product (2). As the product was unstable, all analytical and spectral data were measured without recrystallization (Tables 1 and 2).

Reactions of 2,3-Dibromothiochromone 1,1-Dioxide (1) with Aromatic Amines.—A mixture of 2,3-dibromothiochromone 1,1-dioxide (1) (300 mg, 0.9 mmol), a primary aromatic amine (2 mmol), and ethanol (15 ml) was stirred at the temperature given in Table 1 for 0.5–9 h. After cooling at 0 °C, the resulting precipitate was filtered off and recrystallized to give the 2-arylamino compound (2) or (3). In the reactions of (1) with secondary or tertiary aromatic amines, the reaction mixture was first filtered to remove starting material (1). The filtrate was poured into cold water and acidified with hydrochloric acid. The crude precipitate was chromatographed on silica gel (benzene-acetone as eluant) to give the purified 2-arylamino or 2-aryl compounds (2) or (3). Many by-products were observed on t.l.c. but they could not be isolated. Further details are given in Table 1. Tables 1, 3, and 4 contain analytical and spectroscopic data for compounds (2c–i) and (3a–i). ¹³C N.m.r. spectral data are as follows.



Scheme 3. Reagents and conditions: i, *o*-H₂NC₆H₄SH, EtOH, reflux; ii, DDQ, dry dioxane, reflux; iii, *o*-H₂NC₆H₄OH, EtOH, reflux

2,3-Dibromothiochromone 1,1-dioxide (1): δ_C 124.8, 130.4, 133.8, 134.7, 135.1, 139.6, 141.7, and 170.8.

2-Anilino-3-bromothiochromone 1,1-dioxide (2c): δ_C 104.5, 122.9, 125.8, 125.9, 127.6, 127.8, 129.0, 129.3, 133.6, 133.7, 136.3, 138.7, 151.3, and 172.3.

2-(4-Dimethylaminophenyl)-3-bromothiochromone 1,1-dioxide (3d): δ_C 40.1, 111.5, 115.3, 124.0, 127.2, 128.9, 129.6, 131.3, 133.2, 134.7, 140.8, 152.0, 153.9, and 173.4.

Acylation of 2-Anilino-3-bromothiochromone 1,1-Dioxide (2c).—To a stirred suspension of 2-anilino-3-bromothiochromone 1,1-dioxide (2c) (206 mg, 0.6 mmol) in acetic anhydride (20 ml), concentrated sulphuric acid was added at 0–5 °C until (2c) had dissolved. The mixture was stirred for 1 h at 0–5 °C and carefully poured into ice-water. The precipitate was filtered off and recrystallized to give 2-(*N*-acetylamino)-3-bromothiochromone 1,1-dioxide (2j) as yellow crystals (172 mg, 75%), m.p. 139–141 °C (from ethanol) (Found: C, 50.15; H, 3.1; N, 3.6. C₁₇H₁₂BrNO₄S requires C, 50.3; H, 3.0; N, 3.45%); ν_{max} (KBr)

Table 6. Spectroscopic data for 3-substituted thiochromone 1-oxides (**5**) and 1,1-dioxides (**6**)

Compd.	$\nu_{\max.}/\text{cm}^{-1}$ ^a	¹ H N.m.r. (270 MHz; CDCl ₃) ^b δ (J/Hz)	<i>m/z</i> (rel. int.)
(5a)	1 645 (C=O)	7.22—7.26 (3 H, m), 7.44 (2 H, t, <i>J</i> 8), 7.71 (1 H, dt, <i>J</i> 1 and 8), 7.79 (1 H, dd, <i>J</i> 1 and 8), 7.95 (1 H, dd, <i>J</i> 1 and 7), 8.02 (1 H, dd, <i>J</i> 1 and 7), 8.24 (1 H, d, <i>J</i> 13), 11.57 (1 H, br d)	269 (52%, <i>M</i> ⁺), 253 (100, <i>M</i> ⁺ - O)
(5b)	1 670 (C=O)	2.37 (3 H, s), 7.12 (2 H, d, <i>J</i> 8), 7.24 ^d (2 H, d, <i>J</i> 9), 7.26 ^d (1 H, br s), 7.69 (1 H, dt, <i>J</i> 1 and 7), 7.77 (1 H, dt, <i>J</i> 1 and 7), 7.93 (1 H, dd, <i>J</i> 1 and 8), 8.00 (1 H, dd, <i>J</i> 1 and 8), 8.19 (1 H, d, <i>J</i> 13)	283 (37%, <i>M</i> ⁺), 267 (100, <i>M</i> ⁺ - O)
(5c)	1 640 (C=O)	7.76 (1 H, d, <i>J</i> 9), 7.84 (2 H, d, <i>J</i> 9), 7.93 (1 H, t, <i>J</i> 6), 8.16 (1 H, t, <i>J</i> 6), 8.28 (2 H, dd, <i>J</i> 3 and 9), 8.53 (1 H, d, <i>J</i> 14), 8.98 (1 H, d, <i>J</i> 13), 11.60 (1 H, br d, <i>J</i> 12)	314 (11%, <i>M</i> ⁺), 298 (100, <i>M</i> ⁺ - O)
(6a)	3 225 (NH) 1 655 (3=O)	7.23—7.31 (3 H, m), 7.46 (3 H, dt, <i>J</i> 2 and 7), 7.75 ^c (1 H, dt, <i>J</i> 2 and 7), 7.82 ^c (1 H, dt, <i>J</i> 2 and 8), 7.92 (1 H, dd, <i>J</i> 1 and 8), 7.98 (1 H, dd, <i>J</i> 1 and 8), 8.20 (1 H, d, <i>J</i> 13)	285 (100%, <i>M</i> ⁺), 220 (76, <i>M</i> ⁺ - SO ₂ H)
(6b)	3 225 (NH) 1 650 (C=O)	2.38 (3 H, s), 7.13 (2 H, <i>J</i> 8), 7.25 (2 H, d, <i>J</i> 8), 7.26 (1 H, br s), 7.74 ^c (1 H, dt, <i>J</i> 1 and 8), 7.80 ^c (1 H, dt, <i>J</i> 1 and 8), 7.91 (1 H, dd, <i>J</i> 1 and 8), 7.97 (1 H, dd, <i>J</i> 1 and 8), 8.16 (1 H, d, <i>J</i> 14)	299 (100%, <i>M</i> ⁺), 234 (44, <i>M</i> ⁺ - SO ₂ H)
(6c)	3 225 (NH) 1 660 (C=O)	7.83—8.11 (5 H, m), 8.29 (3 H, dd, <i>J</i> 2 and 8), 8.94 (1 H, d, <i>J</i> 13), 11.56 (1 H, br s, <i>J</i> 13)	330 (41%, <i>M</i> ⁺), 300 (100), 219 (39)
(6d)	3 450 (NH) 3 340 (NH) 1 680 (C=O)	4.90 (2 H, br s), 6.20 (1 H, s), 7.72 (1 H, dt, <i>J</i> 1 and 8), 7.86 (1 H, dt, <i>J</i> 1 and 8), 8.05 (1 H, dd, <i>J</i> 1 and 8), 8.24 (1 H, td, <i>J</i> 2 and 8)	209 (81%, <i>M</i> ⁺), 180 (100), 145 (27, <i>M</i> ⁺ - SO ₂)

^a For KBr discs. ^b Compounds (**5c**) and (**6c**) in (CD₃)₂SO. ^c Overlapping signal.

1 705 (C=O) and 1 670 (C=O); δ_{H} (270 MHz; CDCl₃) 2.15 (3 H, s), 7.28—7.70 (5 H, m), 7.72—7.94 (2 H, m), 8.00 (1 H, dd, *J* 1 and 8 Hz), and 8.28 (1 H, dd, *J* 1 and 8 Hz); *m/z* 407 (0.6%, *M*⁺ + 2), 405 (0.6, *M*⁺), 363 (22), 326 (2, *M*⁺ - Br), 262 (2, *M*⁺ - Br - SO₂), and 220 (100).

General Procedure for the Preparation of 3-Arylaminothiochromone 1-Oxides (5).—A mixture of 3-bromothiochromanone 1,1-dioxide (**4**) (300 mg, 1.1 mmol), aromatic amine (2.2 mmol), and ethanol (7 ml) was refluxed for 2—24 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (benzene–acetone as eluant) to give the purified product (**5**). Analytical and spectroscopic data for the compounds (**5a–c**) are given in Tables 5 and 6.

Oxidation of 3-Arylaminothiochromone 1-Oxides (5).—To a stirred suspension of 3-arylaminothiochromone 1-oxide (**5**) (0.2 mmol) in acetic acid (2 ml), 30% hydrogen peroxide (0.1 ml) was added dropwise at room temperature. The mixture was stirred for 2 h at 55 °C, cooled, and poured into water. The precipitate was filtered off and recrystallized to give the *sulphone* (**6**) (Tables 5 and 6).

3-Aminothiochromone 1,1-Dioxide (6d).—A solution of sodium azide (183 mg, 2.8 mmol) in methanol–water (50%; 2 ml) was added to a solution of 3-bromothiochromanone 1,1-dioxide (**4**) (193 mg, 0.7 mmol) in methanol (3 ml). The mixture was heated at 65 °C for 3.5 h and concentrated under reduced pressure. The precipitate was filtered off and extracted with chloroform. Recrystallization gave *compound* (**6d**) as yellow crystals (3 mg, 2%) (Tables 5 and 6).

3-(2-Hydroxyanilino)thiochromone 1-Oxide (6e).—A mixture of 3-bromothiochromanone 1,1-dioxide (**4**) (200 mg, 0.7 mmol), *o*-aminophenol (80 mg, 0.7 mmol), and ethanol (6 ml) was refluxed for 2 h and filtered to remove starting material (**4**). The filtrate was poured into water and the resulting precipitate was chromatographed on silica gel [benzene–acetone (5:1)] and recrystallized to give *compound* (**6e**) as yellow crystals (33 mg, 21%); m.p. 247 °C (decomp.) (from ethanol) (Found: C, 62.8; H, 3.8; N, 4.8. C₁₅H₁₁NO₃S requires C, 63.15; H, 3.9; N, 4.9%); $\nu_{\max.}$ (KBr) 3 356 (OH) and 1 640 cm⁻¹ (C=O); δ_{H} 6.87—6.94 (1 H, m), 7.00—7.04 (2 H, m), 7.30 (1 H, d, *J* 10 Hz), 7.70 (1 H, dt,

J 1 and 7 Hz), 7.77 (1 H, dt, *J* 1 and 8 Hz), 7.91 (1 H, dd, *J* 1 and 7 Hz), 7.99 (1 H, dd, *J* 1 and 7 Hz), 8.37 (1 H, d, *J* 13 Hz), 9.90 (1 H, br s), and 11.87 (1 H, br d, *J* 13 Hz); *m/z* 285 (13%, *M*⁺) and 269 (100, *M*⁺ - O).

3-(4-Dimethylaminophenyl)thiochromanone 1,1-Dioxide (7).—A mixture of 3-bromothiochromanone 1,1-dioxide (**4**) (299 mg, 1.1 mmol), *N,N*-dimethylaniline (273 mg, 2.3 mmol), and ethanol (5 ml) was refluxed for 8 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel [benzene–acetone (5:1)] and recrystallized to give *compound* (**7**) as a mixture of stereoisomers which could not be separated (90 mg, 26%), m.p. 198—200 °C (from benzene) (Found: C, 64.6; H, 5.4; N, 4.1. C₁₇H₁₇NO₃S requires C, 64.7; H, 5.4; N, 4.4%); $\nu_{\max.}$ (KBr) 1 685 cm⁻¹ (C=O); δ_{H} (270 MHz; CDCl₃) 2.99 (6 H, s), 3.40 (1 H, dd, *J* 3 and 18 Hz), 3.36—3.99 (1 H, m), 4.79 (1 H, dd, *J* 3 and 12 Hz), 6.76 (2 H, dd, *J* 2 and 7 Hz), 7.32 (2 H, dd, *J* 2 and 7 Hz), 7.75 (1 H, dt, *J* 1 and 8 Hz), 7.83 (1 H, dt, *J* 1 and 8 Hz), 8.09 (1 H, dt, *J* 1 and 8 Hz), and 8.18 (1 H, dt, *J* 1 and 8 Hz); *m/z* 315 (23%, *M*⁺) and 251 (100, *M*⁺ - SO₂).

2H,8H-[1]Benzothiopyrano[3,4-b][4,1]benzothiazine 7,7-Dioxide (8).—A mixture of 3-bromothiochromanone 1,1-dioxide (**4**) (202 mg, 0.7 mmol), *o*-aminobenzenethiol (184 mg, 1.5 mmol), and ethanol (5 ml) was refluxed for 2 h and poured into water. The precipitate was filtered off and recrystallized to give the *ring-closure product* (**8**) as orange crystals (158 mg, 71%), m.p. 222 °C (decomp.) (from ethanol) (Found: C, 59.9; H, 3.35; N, 4.6. C₁₅H₁₁NO₂S₂ requires C, 59.8; H, 3.7; N, 4.65%); $\nu_{\max.}$ (KBr) 3 360 cm⁻¹ (NH); δ_{H} (270 MHz; CD₃COCD₃) 2.82 (1 H, d, *J* 9 Hz), 4.07 (2 H, s), 6.90—7.11 (4 H, m), 7.65 (1 H, dt, *J* 1 and 8 Hz), 7.80 (1 H, dt, *J* 1 and 8 Hz), 7.90 (1 H, dd, *J* 1 and 8 Hz), and 7.96 (1 H, dd, *J* 1 and 8 Hz); *m/z* 301 (19%, *M*⁺), 267 (10), and 236 (100).

[1]Benzothiopyrano[3,4-b][4,1]benzothiazine 7,7-Dioxide (9).—To a stirred solution of 2H,8H-[1]benzothiopyrano[3,4-b][4,1]benzothiazine 7,7-dioxide (**8**) (103 mg, 0.3 mmol) in dry dioxane (3 ml) at 50—60 °C, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (95 mg, 0.4 mmol) was added. After the reaction mixture had been refluxed for 1 h, the solvent was removed

under reduced pressure and the residue was chromatographed on silica gel [benzene–acetone (3:1)]. Recrystallization gave compound (9) as orange crystals (63 mg, 61%), m.p. 238–239 °C (from benzene) (Found: C, 60.2; H, 2.85; N, 4.5. $C_{15}H_9NO_2S_2$ requires C, 60.2; H, 3.0; N, 4.7%; ν_{\max} . 1 620 cm^{-1} (C=N); δ_H (270 MHz; $CDCl_3$) 6.83 (1 H, s), 7.29–7.44 (3 H, m), 7.72–7.82 (3 H, m), 8.10 (1 H, dd, *J* 1 and 7 Hz), and 8.75 (1 H, dd, *J* 2 and 7 Hz); *m/z* 299 (100%, M^+), 254 (33), 242 (16), and 236 (20).

Reduction Potential Measurements.—The reduction potentials were obtained by cyclic voltammetry with a Yanagimoto VMA-010 potentiostat analyser and a model WX-1000 X-Y recorder. The cyclic voltammetric measurements were carried out in acetonitrile at room temperature by use of a platinum wire auxiliary electrode, a glassy carbon working electrode, an Ag/AgCl reference electrode, and tetrabutylammonium perchlorate as supporting electrolyte. The scan rate was 100 mV s^{-1} . The concentrations of samples were 5×10^{-4} mol l^{-1} .

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