The Synthesis and Chemistry of 5-Carboxy-8-mercaptoquinoline Hydrochloride Monohydrate: An Intermediate in the Synthesis of Novel H^+,K^+-ATPase Inhibitors

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The title compound **3** was prepared in six steps from 5-nitro-8-hydroxyquinoline in 14% overall yield, using a substituted pyrimidine as a protecting group for sulfur. This offers a simple entry into the synthesis of 5-carboxy-8-substituted thioquinolines, useful intermediates for the synthesis of H^+,K^+-ATPase inhibitors.

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We have had a long-standing interest in gastrointestinal agents, most recently H^+,K^+-ATPase inhibitors [1]. Agents such as omeprazole (**1**) [2,3] are able to significantly reduce stomach acid production by irreversibly inhibiting H^+,K^+-ATPase, the 'proton pump' which is responsible for the terminal step in gastric acid secretion. Although ulcer healing rates with this class of inhibitors are significantly faster than with other therapies, irreversible inhibition leads to prolonged achlorhydria, which may lead to serious side effects. It was our intention, therefore, to develop structurally novel, reversible inhibitors of H^+,K^+-ATPase. A reversible inhibitor would be expected to have a shorter duration of action and thus not promote prolonged achlorhydria upon chronic dosing.

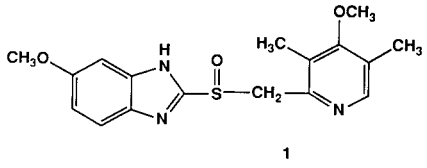

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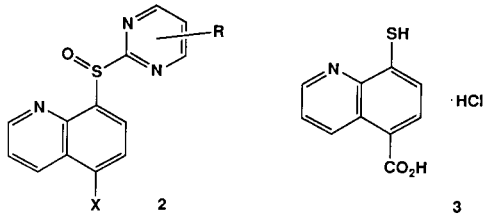
Figure 1

In an attempt to find replacements for the benzimidazole and pyridine moieties of omeprazole, we discovered a series of compounds, pyrimidine-quinoline sulfoxides **2**, which inhibited H^+,K^+-ATPase [4]. Structure activity relationships (SAR) suggested that we pursue quinolines with electron withdrawing groups in the 5-position, including the analogs in which the 5-position contained a carboxylic acid, ester or nitrile. Although the corresponding 8-oxygen substituted quinolines with 5-nitrile [5] or 5-carboxyl [6] had been reported, no published reports of the corresponding 8-sulfur analogs had been found. We wish to report here the synthesis of a number of mercaptoquinoline derivatives, utilizing the previously unknown species 5-carboxy-8-mercaptoquinoline hydrochloride (**3**). We will also present some additional related chemistry of this molecule.

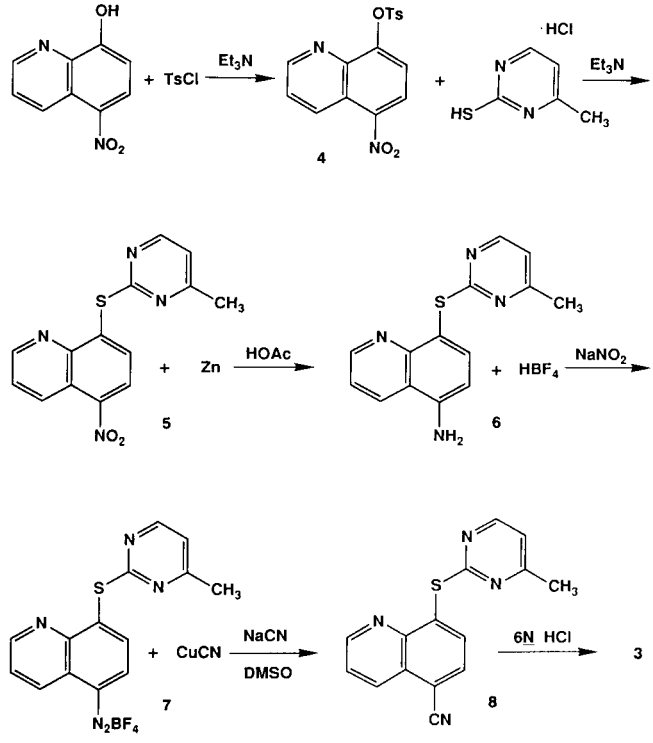


2 3

Figure 2

The route we followed to synthesize **3** is shown in Scheme I. 5-Nitro-8-tosylquinoline (**4**) was prepared from 8-hydroxy-5-nitroquinoline and tosyl chloride in 98% yield. Reaction of **4** with 2-mercapto-4-methylpyrimidine hydrochloride gave compound **5** in 86% yield. Initial attempts to reduce the nitro group with stannous chloride in concentrated hydrochloric acid produced mixtures of the desired amine **6**, unreacted starting material **5** and 5-

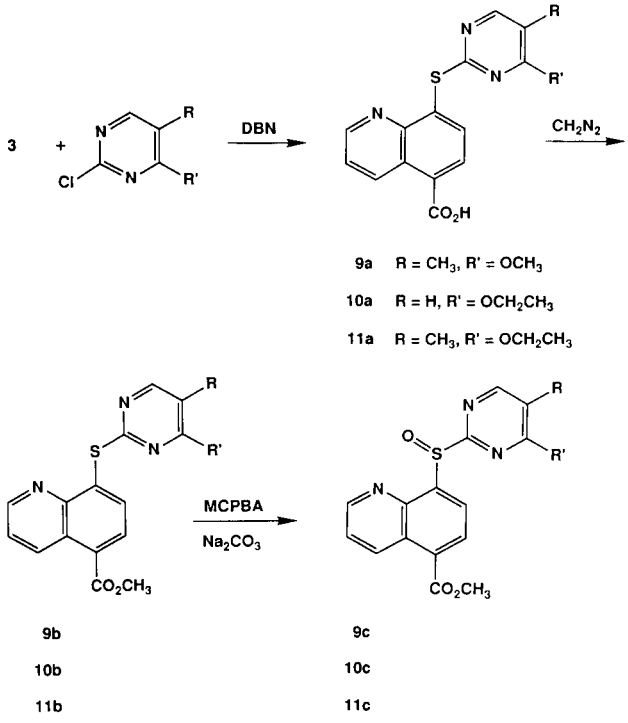
Scheme I



amino-8-mercaptoquinoline, whereas reduction with zinc in acetic acid gave amine **6** in 94% yield. Treatment of the amine with tetrafluoroboric acid and sodium nitrite yielded the stable diazonium salt **7** in 61% yield. The modified Sandmeyer reaction [7] of this diazonium salt **7** with sodium cyanide and copper cyanide in dimethyl sulfoxide gave the nitrile **8** in 52% yield. Hydrolysis of the nitrile and pyrimidine group with 6*N* hydrochloric acid gave **3** which slowly crystallized out of the reaction mixture in 54% yield. Thus, **3** was obtained in six steps in an overall yield of 14%.

We had originally intended to introduce the sulfur and appropriately substituted pyrimidine early in the synthesis of each target inhibitor and then carry out the transformations at the 5-position, as shown. However, in our first example, where the pyrimidine contained a methyl group in the 4-position, hydrolysis of **8** with 6*N* hydrochloric acid gave compound **3**, where the carboxylic acid was obtained at the 5-position, and the 4-methylpyrimidine was removed at the 8-position to give SH. In effect, the 4-methylpyrimidine moiety acted as a protecting group for sulfur while the transformations at the 5-position were carried through to the carboxylic acid. For our purposes this proved useful in that **3** was a common intermediate that could be coupled with substituted 2-chloropyrimidines to easily give the desired pyrimidine-quinoline sulfides (and ultimately the sulfoxides), thus eliminating the need to carry the different pyrimidines through each step from compound **4**. We are currently investigating the utility of 4-methylpyrimidine as a general protecting group for sulfur.

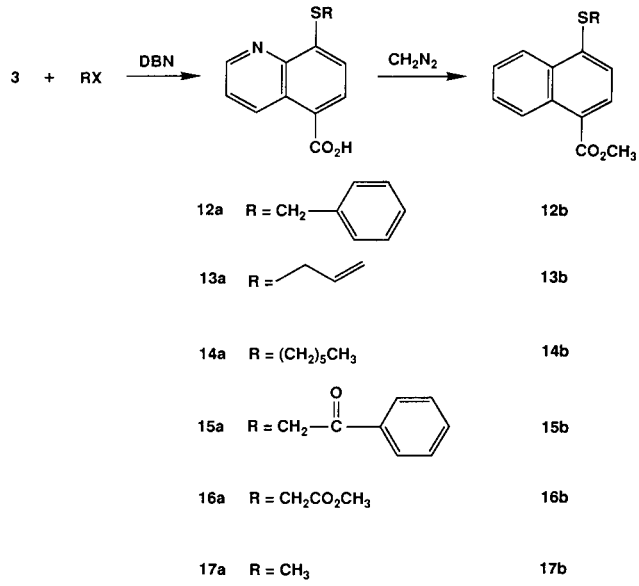
Scheme II



To complete the syntheses of the desired H^+,K^+-ATPase inhibitors, **3** was reacted with a number of substituted 2-chloropyrimidines in the presence of 1,5-diazabicyclo-[4.3.0]non-5-ene to give the sulfide analogs **9a-11a** (Scheme II). However, these carboxylic acid products could not easily be obtained in a pure form since they were associated with excess amounts of base. Therefore, the pure methyl esters **9b-11b** were prepared by reaction of the carboxylic acids with diazomethane. Small amounts of concentrated hydrochloric acid were added to the reaction mixtures to liberate the free carboxylic acids before the addition of the diazomethane, and large excesses of diazomethane were used to ensure complete esterification in the presence of any excess hydrochloric acid. Oxidation with *m*-chloroperbenzoic acid gave the targets **9c-11c**.

In an investigation separate from our H^+,K^+-ATPase inhibitor work, the reaction of **3** with a number of more common electrophiles in the presence of 1,5-diazabicyclo-[4.3.0]non-5-ene all gave the expected sulfides **12a-17a** in good to excellent yields (Scheme III). As in the above cases, the pure methyl esters **12b-17b** were prepared with diazomethane.

Scheme III



In conclusion, several novel H^+,K^+-ATPase inhibitors were prepared, which featured a unique quinoline substitution pattern. These compounds exhibited activity that was comparable to that of omeprazole [4]. In the course of their syntheses, 4-methylpyrimidine was employed as a protecting group for sulfur, which when removed, gave the intermediate **3**, from which the sulfoxides of interest could be easily prepared.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary

melting point apparatus and are uncorrected. The ^1H nmr and ^{13}C nmr spectra were recorded on either a Varian XL-300 or a Bruker WM-250 instrument. Chemical shifts are expressed in ppm relative to internal deuteriodimethyl sulfoxide or deuteriochloroform. Infrared spectra were taken in potassium bromide pellets with a Perkin-Elmer 283B infrared spectrometer. Low resolution mass spectra were recorded on a Finnigan 4510 GC mass spectrometer. Elemental analyses were determined by Pfizer's Central Research Analytical Department.

The solvents and reagents used were commercially available and used directly without further purification. All reactions were monitored by thin-layer chromatography on 0.25 mm x 5 cm x 10 cm silica gel 60 GF-254 (Merck) plates using uv light for visualization. Flash chromatography was performed using 32-63μm silica gel (Woelm) according to the method of Still *et al.* [8].

5-Nitro-8-tosylquinoline (**4**).

This was prepared from 5-nitro-8-hydroxyquinoline and tosyl chloride according to the procedure of Debat, *et al.* [9], mp 130-131°; ^1H nmr (deuteriodimethyl sulfoxide): δ 8.95 (dd, J = 5 Hz, J = 1 Hz, 1H, quinoline H_2), 8.82 (dd, J = 8 Hz, J = 1 Hz, 1H, quinoline H_4), 8.47 (d, J = 9 Hz, 1H, quinoline H_6), 7.82 (d, J = 9 Hz, 2H, phenyl H_2, H_6), 7.81 (dd, J = 8 Hz, J = 5 Hz, 1H, quinoline H_3), 7.70 (d, J = 9 Hz, 1H, quinoline H_7), 7.41 (d, J = 9 Hz, 2H, phenyl H_3, H_5), 2.37 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 161.6 (quinoline C_8), 152.2 (quinoline C_2), 148.8 (quinoline C_5), 146.0 (phenyl C_4), 143.6 (phenyl C_1), 140.5 (quinoline C_9), 131.9 (quinoline C_4), 130.1 (phenyl C_3, C_5), 128.4 (phenyl C_2, C_6), 125.2 (quinoline C_6), 125.0 (quinoline C_3), 121.9 (quinoline C_{10}), 120.8 (quinoline C_7), 21.2 (CH_3); ir (potassium bromide): 1530 (NO_2 asymmetric stretch), 1375 (SO_2 asymmetric stretch), 1340 (NO_2 symmetric stretch), 1180 (SO_2 symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 280 (M^+-SO_2, 18), 233 (5), 155 (41), 115 (7), 91 (100), 65 (18); high resolution ms: Calcd. for $C_{16}H_{12}N_2O_3$ (M^+-SO_2) m/e 280.0848. Found: m/e 280.0880.

Anal. Calcd. for $C_{16}H_{12}N_2O_5S$: C, 55.81; H, 3.51; N, 8.14. Found: C, 55.87; H, 3.45; N, 8.06.

4-Methyl-2-[(5-nitro-8-quinolyl)thio]pyrimidine (**5**).

Triethylamine (17.6 g, 174 mmoles) was added to a suspension of **4** (30.0 g, 87.1 mmoles) and 2-mercapto-4-methylpyrimidine hydrochloride (14.2 g, 87.2 mmoles) in dimethylformamide (400 ml) at room temperature under nitrogen. The resulting solution was stirred at room temperature for 23 hours, then diluted with water (600 ml). The solid that separated was collected, washed with water (50 ml) and dried to give 48.35 g of crude material. This was dissolved in chloroform (1200 ml), and the organic solution was washed first with 1 *M* aqueous sodium hydroxide solution (1200 ml), then water (1200 ml), dried over anhydrous magnesium sulfate, and evaporated *in vacuo* to give 26.99 g of crude yellow solid. Repeated purification by flash chromatography, eluting with chloroform gave 22.46 g (86% yield) of yellow solid. A portion (0.500 g) was recrystallized from carbon tetrachloride (100 ml) to give 0.284 g (57% recovery) of yellow solid, mp 169-170°; ^1H nmr (deuteriochloroform): δ 9.04 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.97 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.43 (d, J = 8 Hz, 1H, quinoline H_6), 8.35 (d, J = 6 Hz, 1H, pyrimidine H_6), 8.34 (d, J = 8 Hz, 1H, quinoline H_7), 7.65 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 6.94 (d, J = 6 Hz, 1H, pyrimidine H_5), 2.45 (s, 3H, CH_3); ^{13}C nmr (deuteriochloroform): δ 169.5 (pyrimidine C_2), 168.6 (pyrimidine C_4), 157.0 (pyrimidine C_6), 150.7 (quinoline C_2), 145.9 (quinoline C_5), 144.5 (quinoline C_8), 141.7 (quinoline C_9), 132.9 (quinoline C_4), 130.6 (quinoline C_6), 124.6 (quinoline C_7), 124.5 (quinoline C_3), 121.4 (quinoline C_{10}), 118.1 (pyrimidine C_5), 24.1 (CH_3); ir (potassium bromide): 1560 (NO_2 asymmetric stretch), 1325 (NO_2 symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 298 (M^+, 100), 283 (3), 265 (16), 252 (23), 251 (23), 240 (9), 206 (11), 174 (69), 159 (11), 128 (40), 126 (18), 114 (10), 66 (12); high resolution ms: Calcd. for $C_{14}H_{10}N_4SO_2$ m/e 298.0524. Found: m/e 298.0507.

Anal. Calcd. for $C_{14}H_{10}N_4SO_2$: C, 56.36; H, 3.38; N, 18.78. Found: C, 56.08; H, 3.23; N, 18.61.

4-Methyl-2-[(5-amino-8-quinolyl)thio]pyrimidine (**6**).

Zinc dust (21.00 g, 321.2 mmoles) was added in portions to a suspension of **5** (21.1 g, 70.8 mmoles) in glacial acetic acid (850 ml) at room temperature. The brown suspension was stirred at room temperature for 1 hour, then poured slowly with stirring into an ice-cold solution of 5 *M* aqueous potassium hydroxide (3400 ml). The solid that separated was collected then triturated with methylene chloride (3 x 3000 ml). All of the organic extracts were combined and evaporated *in vacuo* to give 17.87 g (94% yield) of brown solid. A portion (0.71 g) was purified by flash chromatography, eluting with ethyl acetate to give 0.50 g (70% recovery) of orange solid which was then recrystallized from carbon tetrachloride (2200 ml) to give 0.149 g (30% recovery) of orange solid, mp 172-175°; ^1H nmr (deuteriodimethyl sulfoxide): δ 8.75 (dd, J = 4 Hz, J = 1 Hz, 1H, quinoline H_2), 8.57 (dd, J = 4 Hz, J = 1 Hz, 1H, quinoline H_4), 8.17 (d, J = 5 Hz, 1H, pyrimidine H_6), 7.75 (d, J = 8 Hz, 1H, quinoline H_7), 7.38 (dd, J = 8 Hz, J = 4 Hz, 1H, quinoline H_3), 6.93 (d, J = 5 Hz, 1H, pyrimidine H_5), 6.73 (d, J = 8 Hz, 1H, quinoline H_6), 6.45 (s, 2H, NH_2), 2.28 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 171.4 (pyrimidine C_2), 167.3 (pyrimidine C_4), 157.1 (pyrimidine C_6), 148.8 (quinoline C_5), 148.4 (quinoline C_2), 145.4 (quinoline C_8), 141.6 (quinoline C_7), 141.6 (quinoline C_9), 136.1 (quinoline C_4), 118.9 (quinoline C_3), 118.7 (quinoline C_{10}), 116.8 (pyrimidine C_5), 108.2 (quinoline C_6), 23.4 (CH_3); ir (potassium bromide): 3410-3250 (asymmetric NH stretch), 3250-3050 (symmetric NH stretch), 1560 (NH bend) cm^{-1}; ms: m/e (relative intensity) 268 (M^+, 100), 253 (4), 235 (45), 210 (17), 175 (11), 144 (89), 131 (36), 117 (9); high resolution ms: Calcd. for $C_{14}H_{12}N_4S$ m/e 268.0783. Found: m/e 268.0752.

Anal. Calcd. for $C_{14}H_{12}N_4S$: C, 62.66; H, 4.51; N, 20.88. Found: C, 62.96; H, 4.50; N, 20.83.

4-Methyl-2-[(5-diazoniumtetrafluoroboro-8-quinolyl)thio]pyrimidine (**7**).

A solution of sodium nitrite (4.53 g, 65.7 mmoles) in water (100 ml) was added dropwise with stirring to a solution of **6** (17.4 g, 64.9 mmoles) in water (100 ml) and 48% tetrafluoroboric acid (142 ml) at 0°. After stirring at 0° for 30 minutes, the solid that separated was collected, washed with water (200 ml), then ether (200 ml) and dried to give 14.46 g (61% yield) of brown solid, mp 129°; ^1H nmr (deuteriodimethyl sulfoxide): δ 9.25 (dd, J = 5 Hz, J = 2 Hz, 1H, quinoline H_2), 9.10 (d, J = 9 Hz, 1H, quinoline H_6), 8.98 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.81 (d, J = 9 Hz, 1H, quinoline H_7), 8.73 (d, J = 5 Hz, 1H, pyrimidine H_6), 8.15 (dd, J = 9 Hz, J = 5 Hz, 1H, quinoline H_3), 7.47 (d, J = 5 Hz, 1H, pyrimidine H_5), 2.53 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 169.4 (pyrimidine C_2), 165.6 (pyrimidine C_4), 158.4

(pyrimidine C_6), 154.7 (quinoline C_5), 153.2 (quinoline C_2), 142.6 (quinoline C_9), 136.3 (quinoline C_6), 132.3 (quinoline C_4), 127.6 (quinoline C_7), 126.8 (quinoline C_3), 123.3 (quinoline C_8), 120.3 (pyrimidine C_5), 106.9 (quinoline C_{10}), 23.6 (CH_3); ir (potassium bromide): 2220 (N=N stretch) cm^{-1}; ms: m/e (relative intensity) 271 (M^+-N_2,BF_3,54), 238 (20), 213 (14), 179 (12), 147 (100), 134 (32), 120 (17), 107 (14), 67 (24), 61 (61); high resolution ms: Calcd. for $C_{14}H_{10}FN_3S$ (M^+-N_2,BF_3) m/e 271.0580. Found: m/e 271.0586.

4-Methyl-2-[(5-cyano-8-quinolyl)thio]pyrimidine (**8**).

Cuprous cyanide (17.69 g, 197.5 mmoles) and sodium cyanide (12.61 g, 257.2 mmoles) were mixed with dimethyl sulfoxide (175 ml), and the resulting viscous resin gradually dissolved after stirring overnight. Powdered **7** (14.5 g, 39.5 mmoles) was added in small portions with stirring, keeping the temperature of the reaction mixture at 20°. After 10 minutes the reaction mixture was diluted with water (220 ml), and the resulting suspension was extracted with ethyl acetate (7 x 300 ml). The combined organic extracts were dried over anhydrous magnesium sulfate, then evaporated *in vacuo* to give 26.06 g of crude brown solid. Repeated purification by flash chromatography, eluting with ethyl acetate gave 5.71 g (52% yield) of yellow solid. A portion (0.300 g) was recrystallized from hexane (300 ml) to give 0.250 g (83% recovery) of yellow solid, mp 127-128°; ^1H nmr (deuteriodimethyl sulfoxide): δ 9.04 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.51 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.45 (d, J = 8 Hz, 1H, quinoline H_6), 8.44 (d, J = 5 Hz, 1H, pyrimidine H_6), 8.23 (d, J = 8 Hz, 1H, quinoline H_7), 7.82 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 7.19 (d, J = 5 Hz, 1H, pyrimidine H_5), 2.39 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 168.7 (pyrimidine C_2), 168.1 (pyrimidine C_4), 157.5 (pyrimidine C_6), 151.6 (quinoline C_2), 144.8 (quinoline C_9), 139.3 (quinoline C_8), 133.5 (quinoline C_4), 133.1 (quinoline C_7), 131.6 (quinoline C_6), 127.1 (quinoline C_{10}), 124.4 (quinoline C_3), 118.2 (pyrimidine C_5), 116.4 (CN), 108.5 (quinoline C_5), 23.5 (CH_3); ir (potassium bromide): 2300 (C≡N stretch) cm^{-1}; ms: m/e (relative intensity) 278 (M^+, 68), 263 (4), 245 (16), 220 (13), 186 (14), 185 (14), 154 (100), 141 (17), 127 (11), 123 (10), 114 (18), 66 (13); high resolution ms: Calcd. for $C_{15}H_{10}N_4S$ m/e 278.0626. Found: m/e 278.0594.

Anal. Calcd. for $C_{15}H_{10}N_4S$: C, 64.73; H, 3.62; N, 20.13. Found: C, 64.60; H, 3.42; N, 20.16.

5-Carboxy-8-mercaptoquinoline Hydrochloride Monohydrate (**3**).

A solution of **8** (1.3 g, 4.7 mmoles) in 6*N* hydrochloric acid (150 ml) was refluxed for 6 hours, then cooled. After standing at room temperature for 2 days, the solid that separated was collected and dried to give 0.61 g (54% yield) of yellow solid, mp 188-189°; ^1H nmr (deuteriodimethyl sulfoxide): δ 9.40 (dd, J = 9 Hz, J = 3 Hz, 1H, quinoline H_4), 9.06 (dd, J = 4 Hz, J = 3 Hz, 1H, quinoline H_2), 8.18 (d, J = 8 Hz, 1H, quinoline H_6), 7.81 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 7.78 (d, J = 8 Hz, 1H, quinoline H_7); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 167.2 (CO_2), 149.8 (quinoline C_2), 144.9 (quinoline C_9), 140.6 (quinoline C_8), 134.8 (quinoline C_4), 130.9 (quinoline C_6), 126.3 (quinoline C_{10}), 124.9 (quinoline C_5), 123.6 (quinoline C_3), 122.7 (quinoline C_7); ir (potassium bromide) 3100-2500 (OH stretch), 1685 (C=O stretch) cm^{-1}; ms: m/e (relative intensity) 205 (M^+, 100), 188 (12), 161 (38), 117 (14), 91 (12); high resolution ms: Calcd. for $C_{10}H_7NO_2S$ m/e 205.0198. Found: m/e 205.0186.

Anal. Calcd. for $C_{10}H_7NO_2S{\cdot}HCL{\cdot}H_2O$: C, 46.24; H, 3.88; N, 5.39. Found: C, 46.26; H, 3.73; N, 5.45.

General Procedure For The Addition of Halides To **3** To Give Sulfides **9a-18a**.

1,5-Diazabicyclo[4.3.0]non-5-ene was added dropwise to a solution of **3** and the halide in methanol. The reaction mixture was stirred at room temperature under nitrogen for 2 hours, then concentrated *in vacuo* to give the crude product, which was purified by flash chromatography.

General Procedure For The Preparation of Methyl Esters **9b-17b** With Diazomethane.

Concentrated hydrochloric was added to a solution of the acid in methanol and ethyl acetate and this solution was cooled at 0°. About 1/3 of a dry ether solution of diazomethane prepared from *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine [10] was added with stirring. After 5 minutes, additional concentrated hydrochloric acid was added and an additional 1/3 of the ether solution of diazomethane was added with stirring. After 5 minutes, additional concentrated hydrochloric acid was added and the final 1/3 of the ether solution of diazomethane was added with stirring. After stirring for 5 minutes, the reaction mixture was quenched by the addition of 7*M* aqueous acetic acid then evaporated *in vacuo* to give the crude product, which was purified by flash chromatography and recrystallization.

General Procedure For The Preparation of Sulfoxides **9c-11c** With *m*-Chloroperbenzoic Acid.

m-Chloroperbenzoic acid was added to a suspension of sodium bicarbonate and the sulfide in anhydrous tetrahydrofuran at 0° under nitrogen. The reaction was stirred at 0° for 15 minutes, then warmed to room temperature and stirred for 1 hour, then concentrated *in vacuo* to give the crude product, which was purified by flash chromatography.

4-Methoxy-5-methyl-2-[(5-carboxy-8-quinolyl)thio]pyrimidine (**9a**).

1,5-Diazabicyclo[4.3.0]non-5-ene (0.62 g, 5.0 mmoles), **3** (0.30 g, 1.2 mmoles) and 2-chloro-4-methoxy-5-methylpyrimidine (0.21 g, 1.3 mmoles) were reacted in methanol (75 ml) to give 1.115 g of yellow oil which was purified by flash chromatography, eluting with 3:7 methanol:ethyl acetate to give 0.459 g (100% yield) of yellow solid, mp 210-212°; ^1H nmr (deuteriodimethyl sulfoxide): δ 9.37 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.91 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.33 (d, J = 8 Hz, 1H, quinoline H_6), 8.19 (d, J = 8 Hz, 1H, quinoline H_7), 8.16 (s, 1H, pyrimidine H_6), 7.66 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 3.66 (s, 3H, OCH_3), 2.01 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 170.0 (pyrimidine C_2), 167.1 (CO_2), 166.4 (pyrimidine C_4), 156.9 (pyrimidine C_6), 150.0 (quinoline C_2), 146.0 (quinoline C_9), 138.6 (quinoline C_8), 135.0 (quinoline C_6), 132.1 (quinoline C_4), 129.5 (quinoline C_7), 127.4 (quinoline C_{10}), 126.6 (quinoline C_5), 122.8 (quinoline C_3), 114.4 (pyrimidine C_5), 53.8 (OCH_3), 11.9 (CH_3); ir (potassium bromide): 3250-2500 (OH stretch), 1660 (C=O stretch) cm^{-1}; ms: m/e (relative intensity) 327 (M^+, 77), 326 (100), 312 (24), 294 (30), 253 (52), 219 (21), 205 (29), 186 (16), 173 (71), 132 (20), 128 (20), 83 (27), 55 (19); high resolution ms: Calcd. for $C_{16}H_{13}N_3O_3S$ m/e 327.0680. Found: m/e 327.0662.

4-Methoxy-5-methyl-2-[(5-methoxycarbonyl-8-quinolyl)thio]pyrimidine (**9b**).

Concentrated hydrochloric acid (8 drops) was added to a solution of **9a** (0.41 g, 1.2 mmoles) in methanol (70 ml) and ethyl acetate (70 ml). The dry ether solution of diazomethane (total 31

mmoles) was added in thirds as described above. The reaction was quenched by the addition of 7*M* aqueous acetic acid (20 ml), then evaporated *in vacuo* to give 1.017 g of yellow solid which was purified by flash chromatography, eluting with ether to give 0.246 g (58% yield) of yellow solid, mp 173-174°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.24 (d, J = 9 Hz, 1H, quinoline H_4), 8.97 (d, J = 4 Hz, 1H, quinoline H_2), 8.41 (d, J = 8 Hz, 1H, quinoline H_6), 8.24 (d, J = 8 Hz, 1H, quinoline H_7), 8.21 (s, 1H, pyrimidine H_6), 7.73 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 3.95 (s, 3H, ester CH_3), 3.70 (s, 3H, OCH_3), 2.03 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 167.2 (pyrimidine C_2), 166.2 (pyrimidine C_4), 165.9 (CO_2), 157.0 (pyrimidine C_6), 150.3 (quinoline C_2), 145.6 (quinoline C_9), 138.6 (quinoline C_8), 134.4 (quinoline C_6), 131.3 (quinoline C_4), 130.1 (quinoline C_7), 126.1 (quinoline C_{10}), 126.0 (quinoline C_5), 123.4 (quinoline C_3), 114.7 (pyrimidine C_5), 53.8 (OCH_3), 52.5 (ester CH_3), 11.9 (CH_3); ir (potassium bromide): 1690 (C=O stretch), 1255 (C-O-C asymmetric stretch), 1180 (C-O-C symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 341 (M^+, 73), 340 (100), 326 (27), 308 (28), 267 (49), 240 (15), 213 (13), 187 (61), 170 (16), 159 (27), 141 (19), 128 (19); high resolution ms: Calcd. for $C_{17}H_{15}N_3O_3S$ m/e. Found: m/e 341.0855.

Anal. Calcd. for $C_{17}H_{15}N_3O_3S$: C, 59.81; H, 4.43; N, 12.31. Found: C, 59.77; H, 4.39; N, 12.17.

4-Methoxy-5-methyl-2-(5-methoxycarbonyl-8-quinolylsulfinyl)pyrimidine (**9c**).

m-Chloroperbenzoic acid (70% purity) (0.14 g, 0.6 mmole), sodium bicarbonate (0.22 g, 2.6 mmoles) and **9b** (0.18 g, 0.5 mmole) were reacted in tetrahydrofuran (25 ml) to give 0.570 g of white solid which was purified by flash chromatography, eluting with 49:1 ethyl acetate:triethylamine to give 0.123 g (65% yield) of yellow solid, mp 176-177°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.17 (d, J = 8 Hz, 1H, quinoline H_4), 8.81 (d, J = 4 Hz, 1H, quinoline H_2), 8.50 (d, J = 8 Hz, 1H, quinoline H_6), 8.35 (s, 1H, pyrimidine H_6), 8.34 (d, J = 8 Hz, 1H, quinoline H_7), 7.69 (dd, J = 8 Hz, J = 4 Hz, 1H, quinoline H_3), 3.98 (s, 3H, ester CH_3), 3.65 (s, 3H, OCH_3), 2.02 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 168.0 (pyrimidine C_2), 166.5 (pyrimidine C_4), 166.0 (CO_2), 157.2 (pyrimidine C_6), 150.8 (quinoline C_2), 144.2 (quinoline C_9), 140.0 (quinoline C_8), 134.4 (quinoline C_6), 130.2 (quinoline C_4), 129.2 (quinoline C_{10}), 126.1 (quinoline C_7), 125.6 (quinoline C_5), 123.7 (quinoline C_3), 119.7 (pyrimidine C_5), 54.1 (OCH_3), 52.8 (ester CH_3), 12.2 (CH_3); ir (potassium bromide): 1705 (C=O stretch), 1260 (C-O-C asymmetric stretch), 1130 (symmetric stretch), 1050 (S=O stretch) cm^{-1}; ms: m/e (relative intensity) 357 (M^+, 49), 309 (54), 294 (73), 219 (100), 188 (15), 175 (10), 159 (10), 123 (17); high resolution ms: Calcd. for $C_{17}H_{15}N_3O_4S$ m/e 357.0784. Found: m/e 357.0759.

Anal. Calcd. for $C_{17}H_{15}N_3O_4S$: C, 57.13; H, 4.23; N, 11.76. Found: C, 57.00; H, 3.99; N, 11.42.

4-Ethoxy-2-[(5-carboxy-8-quinolyl)thio]pyrimidine (**10a**).

1,5-Diazabicyclo[4.3.0]non-5-ene (0.62 g, 5.0 mmoles), **3** (0.30 g, 1.2 mmoles) and 2-chloro-4-ethoxypyrimidine (0.21 g, 1.3 mmoles) were reacted in methanol (60 ml) to give 1.126 g of orange oil which was purified by flash chromatography, eluting with 1:1 methanol:ethyl acetate to give 0.546 g (100% yield) of yellow solid, mp 100° (foams); ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.46 (dd, J = 9 Hz, J = 1 Hz, 1H, quinoline H_4), 8.87 (dd, J = 4 Hz, J = 1 Hz, 1H, quinoline H_2), 8.24 (d, J = 6 Hz, 1H, pyrimidine H_6), 8.22 (d, J = 8 Hz, 1H, quinoline H_6), 8.07 (d, J = 8 Hz, 1H, quinoline H_7), 7.58 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 6.57 (d, J = 6 Hz, 1H, pyrimidine H_5), 3.95 (q, J = 7 Hz, 2H, CH_2), 0.99 (t, J = 7 Hz, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 170.3 (pyrimidine C_2), 168.1 (CO_2), 168.1 (pyrimidine C_4), 158.0 (pyrimidine C_6), 149.9 (quinoline C_2), 145.9 (quinoline C_9), 145.4 (quinoline C_8), 135.9 (quinoline C_6), 134.4 (quinoline C_4), 128.0 (quinoline C_7), 127.9 (quinoline C_{10}), 126.8 (quinoline C_5), 121.9 (quinoline C_3), 104.5 (pyrimidine C_5), 62.1 (CH_2), 13.9 (CH_3); ir (potassium bromide): 3500-2700 (OH stretch), 1660 (C=O stretch) cm^{-1}; ms: m/e (relative intensity) 327 (M^+, 55), 326 (49), 298 (59), 239 (50), 212 (19), 205 (16), 173 (42), 166 (100), 149 (20), 138 (28), 128 (31), 85 (33); high resolution ms: Calcd. for $C_{16}H_{13}N_3O_3S$ m/e 327.0678. Found: m/e 327.0688.

4-Ethoxy-2-[(5-methoxycarbonyl-8-quinolyl)thio]pyrimidine (**10b**).

Concentrated hydrochloric acid (10 drops) was added to a solution of **10a** (0.46 g, 1.4 mmoles) in methanol (60 ml) and ethyl acetate (60 ml). The dry ether solution of diazomethane (total 35.5 mmoles) was added as described above. The reaction was quenched by the addition of 7*M* aqueous acetic acid (20 ml), then evaporated *in vacuo* to give 0.536 g of tan solid which was purified by flash chromatography, eluting with ether to give 0.276 g (57% yield) of white solid, mp 117-118°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.22 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.97 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.41 (d, J = 8 Hz, 1H, quinoline H_6), 8.31 (d, J = 6 Hz, 1H, pyrimidine H_6), 8.24 (d, J = 8 Hz, 1H, quinoline H_7), 7.73 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 6.65 (d, J = 6 Hz, 1H, pyrimidine H_5), 4.01 (q, J = 7 Hz, 2H, CH_2), 3.96 (s, 3H, ester CH_3), 1.04 (t, J = 7 Hz, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 169.6 (pyrimidine C_2), 168.2 (CO_2), 166.2 (pyrimidine C_4), 158.2 (pyrimidine C_6), 150.6 (quinoline C_2), 146.0 (quinoline C_9), 137.4 (quinoline C_8), 134.4 (quinoline C_6), 132.8 (quinoline C_4), 130.0 (quinoline C_7), 126.9 (quinoline C_{10}), 126.4 (quinoline C_5), 123.3 (quinoline C_3), 105.1 (pyrimidine C_5), 62.3 (CH_2), 52.6 (ester CH_3), 13.9 (CH_3); ir (potassium bromide): 1695 (C=O stretch), 1245 (C-O-C asymmetric stretch), 1170 (symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 341 (M^+, 83), 312 (77), 308 (33), 280 (11), 253 (100), 226 (31), 218 (19), 187 (83), 159 (30), 141 (13), 95 (12); high resolution ms: Calcd. for $C_{17}H_{15}N_3O_3S$ m/e 341.0834. Found: m/e 341.0824.

Anal. Calcd. for $C_{17}H_{15}N_3O_3S$: C, 59.81; H, 4.43; N, 12.31. Found: C, 59.82; H, 4.30; N, 12.12.

4-Ethoxy-2-(5-methoxycarbonyl-8-quinolylsulfinyl)pyrimidine (**10c**).

m-Chloroperbenzoic acid (70% purity) (0.18 g, 0.7 mmole), sodium bicarbonate (0.28 g, 3.3 mmoles) and **10b** (0.22 g, 0.7 mmole) were reacted in tetrahydrofuran (30 ml) to give 0.696 g of yellow solid which was purified by flash chromatography, eluting with 49:1 ethyl acetate:triethylamine to give 0.131 g (56% yield) of yellow solid, mp 124-125°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.16 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.82 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.53 (d, J = 6 Hz, 1H, pyrimidine H_6), 8.49 (d, J = 8 Hz, 1H, quinoline H_6), 8.33 (d, J = 8 Hz, 1H, quinoline H_7), 7.70 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 6.93 (d, J = 6 Hz, 1H, pyrimidine H_5), 4.02 (q, J = 7 Hz, 2H, CH_2), 3.98 (s, 3H, ester CH_3), 0.95 (t, J = 7 Hz, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 172.0 (pyrimidine C_2), 169.2 (pyrimidine C_4), 166.0 (CO_2), 159.0 (pyrimidine C_6), 150.9 (quinoline C_2), 145.4 (quinoline C_9), 144.2 (quinoline C_8), 134.4 (quinoline C_6), 130.2 (quinoline C_4), 129.3 (quinoline C_{10}), 126.1 (quino-

line C_7), 125.7 (quinoline C_5), 123.7 (quinoline C_3), 109.6 (pyrimidine C_5), 63.0 (CH_2), 52.8 (ester CH_3), 13.6 (CH_3); ir (potassium bromide): 1700 (C=O stretch), 1260 (C-O-C asymmetric stretch), 1130 (C-O-C symmetric stretch), 1040 (S=O stretch) cm^{-1}; ms: m/e (relative intensity) 357 (M^+, 31), 309 (57), 280 (73), 234 (11), 219 (100), 188 (14), 175 (12), 95 (29); high resolution ms: Calcd. for $C_{17}H_{15}N_3O_4S$ m/e 357.0784. Found: m/e 357.0801.

Anal. Calcd. for $C_{17}H_{15}N_3O_4S$: C, 57.13; H, 4.23; N, 11.76. Found: C, 57.03; H, 4.00; N, 11.43.

4-Ethoxy-5-methyl-2-[(5-carboxy-8-quinolyl)thio]pyrimidine (**11a**).

1,5-Diazabicyclo[4.3.0]non-5-ene (0.62 g, 5.0 mmoles), **3** (0.30 g, 1.2 mmoles) and 2-chloro-4-ethoxy-5-methylpyrimidine (0.22 g, 1.3 mmoles) were reacted in methanol (60 ml) to give 1.143 g of yellow oil which was purified by flash chromatography, eluting with 1:1 methanol:ethyl acetate to give 0.522 g (100% yield) of yellow solid, mp 223-224°; ^1H nmr (deuteriodimethyl sulfoxide): δ 9.48 (d, J = 9 Hz, 1H, quinoline H_4), 8.85 (d, J = 4 Hz, 1H, quinoline H_2), 8.20 (d, J = 8 Hz, 1H, quinoline H_6), 8.11 (s, 1H, pyrimidine H_6), 8.09 (d, J = 8 Hz, 1H, quinoline H_7), 7.56 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 3.97 (q, J = 7 Hz, 2H, CH_2), 1.96 (s, 3H, CH_3), 0.99 (t, J = 7 Hz, 3H, ethyl CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 170.4 (pyrimidine C_2), 166.7 (CO_2), 166.5 (pyrimidine C_4), 157.0 (pyrimidine C_6), 150.1 (quinoline C_2), 144.3 (quinoline C_9), 144.2 (quinoline C_8), 134.9 (quinoline C_6), 132.3 (quinoline C_4), 129.5 (quinoline C_7), 127.3 (quinoline C_{10}), 126.6 (quinoline C_5), 122.8 (quinoline C_3), 114.3 (pyrimidine C_5), 62.2 (CH_2), 14.0 (ethyl CH_3), 11.9 (CH_3); ir (potassium bromide): 3500-2400 (OH stretch), 1680 (C=O stretch) cm^{-1}; ms: m/e (relative intensity) 341 (M^+, 83), 312 (73), 280 (15), 253 (100), 226 (28), 205 (46), 173 (78), 156 (28), 144 (21), 126 (19), 116 (52), 89 (19), 54 (47); high resolution ms: Calcd. for $C_{17}H_{15}N_3O_3S$ m/e 341.0834. Found: m/e 341.0829.

4-Ethoxy-2-[(5-methoxycarbonyl-8-quinolyl)thio]pyrimidine (**11b**).

Concentrated hydrochloric acid (10 drops) was added to a solution of **11a** (0.42 g, 1.2 mmoles) in methanol (100 ml) and ethyl acetate (100 ml). The dry ether solution of diazomethane (total 30.5 mmoles) was added in thirds as described above. The reaction was quenched by the addition of 7*M* aqueous acetic acid (18 ml), then evaporated *in vacuo* to give 0.641 g of yellow solid which was purified by flash chromatography, eluting with ethyl acetate to give 0.204 g (47% yield) of yellow solid, mp 158-159°; ^1H nmr (deuteriodimethyl sulfoxide): δ 9.23 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.97 (dd, J = 3 Hz, J = 2 Hz, 1H, quinoline H_2), 8.37 (d, J = 7 Hz, 1H, quinoline H_6), 8.24 (d, J = 7 Hz, 1H, quinoline H_7), 8.21 (s, 1H, pyrimidine H_6), 7.73 (dd, J = 9 Hz, J = 3 Hz, 1H, quinoline H_3), 4.07 (q, J = 7 Hz, 2H, CH_2), 3.96 (s, 3H, ester CH_3), 2.02 (s, 3H, CH_3), 1.08 (t, J = 7 Hz, 3H, ethyl CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 170.1 (pyrimidine C_2), 166.8 (CO_2), 166.3 (pyrimidine C_4), 157.0 (pyrimidine C_6), 150.4 (quinoline C_2), 145.8 (quinoline C_9), 145.0 (quinoline C_8), 134.4 (quinoline C_6), 131.6 (quinoline C_4), 130.1 (quinoline C_7), 127.5 (quinoline C_{10}), 126.2 (quinoline C_5), 123.4 (quinoline C_3), 114.6 (pyrimidine C_5), 62.3 (CH_2), 52.6 (ester CH_3), 14.0 (ethyl CH_3), 11.9 (CH_3); ir (potassium bromide): 1695 (C=O stretch), 1260 (C-O-C asymmetric stretch), 1190 (C-O-C symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 355 (M^+, 100), 326 (78), 294 (12), 267 (65), 240 (22), 219 (19), 187 (46), 159 (29), 128 (12), 54 (13); high resolution ms: Calcd. for $C_{18}H_{17}N_3O_3S$ m/e 355.0991. Found: m/e 355.1002.

Anal. Calcd. for $C_{18}H_{17}N_3O_3S$: C, 60.83; H, 4.82; N, 11.82. Found: C, 60.69; H, 4.72; N, 11.67.

4-Ethoxy-5-methyl-2-(5-methoxycarbonyl-8-quinolylsulfinyl)pyrimidine (**11c**).

m-Chloroperbenzoic acid (70% purity) (0.11 g, 0.4 mmole), sodium bicarbonate (0.16 g, 2.0 mmoles) and **11c** (0.14 g, 0.4 mmole) were reacted in tetrahydrofuran (20 ml) to give 0.413 g of white solid which was purified by flash chromatography, eluting with 49:1 ethyl acetate:triethylamine to give 0.091 g (63% yield) of white solid, mp 174-175°; ^1H nmr (deuteriodimethyl sulfoxide): δ 9.17 (d, J = 9 Hz, 1H, quinoline H_4), 8.82 (d, J = 4 Hz, 1H, quinoline H_2), 8.50 (d, J = 8 Hz, 1H, quinoline H_6), 8.38 (s, 1H, pyrimidine H_6), 8.34 (d, J = 8 Hz, 1H, quinoline H_7), 7.69 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 4.02 (q, J = 7 Hz, 2H, CH_2), 3.98 (s, 3H, ester CH_3), 2.01 (s, 3H, CH_3), 0.92 (t, J = 7 Hz, 3H, ethyl CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 167.5 (pyrimidine C_2), 167.0 (pyrimidine C_4), 166.0 (CO_2), 157.4 (pyrimidine C_6), 150.9 (quinoline C_2), 145.6 (quinoline C_9), 144.2 (quinoline C_8), 134.3 (quinoline C_6), 130.2 (quinoline C_4), 129.2 (quinoline C_{10}), 126.0 (quinoline C_7), 125.6 (quinoline C_5), 123.7 (quinoline C_3), 119.6 (pyrimidine C_5), 62.8 (CH_2), 52.8 (ester CH_3), 13.7 (ethyl CH_3), 12.2 (CH_3); ir (potassium bromide): 1705 (C=O stretch), 1260 (C-O-C asymmetric stretch), 1130 (C-O-C symmetric stretch), 1050 (S=O stretch) cm^{-1}; ms: m/e (relative intensity) 371 (M^+, 19), 323 (16), 294 (40), 219 (100), 188 (13), 109 (16), 54 (12); high resolution ms: Calcd. for $C_{18}H_{17}N_3O_4S$ m/e 371.0939. Found: 371.0886.

Anal. Calcd. for $C_{18}H_{17}N_3O_4S$: C, 58.21; H, 4.61; N, 11.31. Found: C, 58.07; H, 4.44; N, 11.09.

8-Benzylthio-5-carboxyquinoline (**12a**).

1,5-Diazabicyclo[4.3.0]non-5-ene (0.14 g, 1.2 mmoles), **3** (0.07 g, 0.3 mmole) and benzyl bromide (0.05 g, 0.3 mmole) were reacted in methanol (20 ml) to give 0.237 g of yellow oil which was purified by flash chromatography, eluting with 1:4 methanol:ethyl acetate to give 0.086 g (100% yield) of tan solid, mp 201-202°; ^1H nmr (deuteriomethanol): δ 9.49 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.83 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.24 (d, J = 8 Hz, 1H, quinoline H_6), 7.65 (d, J = 8 Hz, 1H, quinoline H_7), 7.63 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 7.52 (d, J = 7 Hz, 2H, phenyl H_2, H_6), 7.34 (dd, J = 7 Hz, J = 7 Hz, 2H, phenyl H_3, H_5), 7.30 (dd, J = 7 Hz, J = 7 Hz, 1H, phenyl H_4), 4.37 (s, 2H, CH_2); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 167.6 (CO_2), 149.0 (quinoline C_2), 145.6 (quinoline C_9), 144.3 (quinoline C_8), 136.5 (phenyl C_1), 134.5 (quinoline C_4), 130.6 (quinoline C_6), 128.9 (phenyl C_2, C_6), 128.4 (phenyl C_3, phenyl C_5), 127.1 (phenyl C_4), 126.0 (quinoline C_{10}), 123.1 (quinoline C_3), 122.7 (quinoline C_5), 122.2 (quinoline C_7), 34.2 (CH_2); ir (potassium bromide): 3200-2500 (OH stretch), 1670 (C=O stretch) cm^{-1}; ms: m/e (relative intensity) 295 (M^+, 71), 262 (91), 218 (20), 204 (7), 186 (26), 173 (44), 116 (10), 91 (100), 65 (22); high resolution ms: Calcd. for $C_{17}H_{13}NO_2S$ m/e 295.0667. Found: m/e 295.0657.

8-Benzylthio-5-methoxycarbonylquinoline (**12b**).

Concentrated hydrochloric acid (4 drops) was added to a solution of **12a** (0.10 g, 0.3 mmole) in methanol (14 ml) and ethyl acetate (14 ml). The dry ether solution of diazomethane (total 25.4 mmoles) was added in thirds as described above. The reaction was quenched by the addition of 7*M* aqueous acetic acid (10

ml), then evaporated *in vacuo* to give 0.167 g of yellow residue which was purified by flash chromatography, eluting with ethyl acetate to give 0.063 g (60% yield) of tan solid. This was recrystallized from hexane (6.0 ml) to give 0.050 g (79% recovery) of tan solid, mp 99-100°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.26 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.91 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.17 (d, J = 8 Hz, 1H, quinoline H_6), 7.71 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 7.71 (d, J = 8 Hz, 1H, quinoline H_7), 7.51 (d, J = 7 Hz, 2H, phenyl H_2, H_6), 7.35 (dd, J = 7 Hz, J = 7 Hz, 2H, phenyl H_3, H_5), 7.30 (dd, J = 7 Hz, J = 7 Hz, 1H, phenyl H_4), 4.37 (s, 2H, CH_2), 3.91 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 166.2 (CO_2), 149.3 (quinoline C_2), 146.4 (quinoline C_9), 144.0 (quinoline C_8), 136.3 (phenyl C_1), 134.2 (quinoline C_4), 130.7 (quinoline C_6), 129.0 (phenyl C_2, C_6), 128.5 (phenyl C_3, C_5), 127.2 (phenyl C_4), 125.7 (quinoline C_{10}), 123.5 (quinoline C_3), 122.1 (quinoline C_7), 121.3 (quinoline C_5), 52.1 (CH_3), 34.1 (CH_2); ir (potassium bromide): 1685 (C=O stretch), 1250 (C-O-C asymmetric stretch), 1170 (C-O-C symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 309 (M^+, 87), 276 (98), 232 (19), 217 (21), 200 (52), 187 (62), 172 (15), 159 (18), 128 (18), 91 (100), 65 (30); high resolution ms: Calcd. for $C_{18}H_{15}NO_2S$ m/e 309.0824. Found: m/e 309.0787.

Anal. Calcd. for $C_{18}H_{15}NO_2S$: C, 69.88; H, 4.89; N, 4.53. Found: C, 70.08; H, 4.87; N, 4.46.

5-Carboxy-8-[1-(2-propenyl)]thioquinoline (**13a**).

1,5-Diazabicyclo[4.3.0]non-5-ene (0.14 g, 1.2 mmoles), **3** (0.07 g, 0.3 mmole) and allyl bromide (0.04 g, 0.3 mmole) were reacted in methanol (20 ml) to give 0.235 g of yellow oil which was purified by flash chromatography, eluting with 1:4 methanol:ethyl acetate to give 0.071 g (100% yield) of tan solid, mp 165-166°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.37 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.90 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.17 (d, J = 8 Hz, 1H, quinoline H_6), 7.67 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 7.60 (d, J = 8 Hz, 1H, quinoline H_7), 5.96 (ddt, J = 16 Hz, J = 11 Hz, J = 7 Hz, 1H, propenyl H_2), 5.41 (dd, J = 16 Hz, J = 2 Hz, 1H, *trans* propenyl H_3), 5.19 (dd, J = 11 Hz, J = 2 Hz, 1H, *cis* propenyl H_3), 3.78 (d, J = 7 Hz, 2H, propenyl CH_2); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 167.6 (CO_2), 149.0 (quinoline C_2), 145.0 (quinoline C_9), 144.4 (quinoline C_8), 134.5 (quinoline C_4), 132.9 (propenyl C_2), 130.6 (quinoline C_6), 126.1 (quinoline C_{10}), 123.1 (quinoline C_3), 122.7 (quinoline C_5), 122.2 (quinoline C_7), 118.4 (propenyl C_3), 32.5 (propenyl CH_2); ir (potassium bromide): 3200-2600 (OH stretch), 1675 (C=O stretch), 1665 (C=C stretch), 995 (CH bend), 925 (CH bend) cm^{-1}; ms: m/e (relative intensity) 245 (M^+, 19), 230 (10), 212 (100), 198 (17), 187 (8), 173 (17), 149 (12), 128 (9), 116 (9); high resolution ms: Calcd. for $C_{13}H_{11}NO_2S$ m/e 245.0510. Found: m/e 245.0526.

8-[1-(2-propenyl)]thio-5-methoxycarbonylquinoline (**13b**).

Concentrated hydrochloric acid (4 drops) was added to a solution of **13a** (0.14 g, 0.6 mmole) in methanol (15 ml) and ethyl acetate (15 ml). The dry ether solution of diazomethane (total 42.8 mmoles) was added in thirds as described above. The reaction was quenched by the addition of 7*M* aqueous acetic acid (25 ml), then evaporated *in vacuo* to give 0.139 g of yellow solid which was purified by flash chromatography, eluting with chloroform to give 0.109 g (74% yield) of tan solid. This was recrystallized from hexane (5.0 ml) to give 0.091 g (83% recovery) of white crystals, mp 93-94°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.26 (d, J = 9 Hz, 1H, quinoline H_4), 8.93 (d, J = 4 Hz, 1H, quinoline H_2), 8.18 (d, J = 8 Hz, 1H, quinoline H_6), 7.72 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 7.63 (d, J = 8 Hz, 1H, quinoline H_7), 5.97 (ddt, J = 17 Hz, J = 10 Hz, J = 6 Hz, 1H, propenyl H_2), 5.43 (d, J = 17 Hz, 1H, *trans* propenyl H_3), 5.21 (d, J = 10 Hz, 1H, *cis* propenyl H_3), 3.91 (s, 3H, CH_3), 3.80 (d, J = 6 Hz, 2H, propenyl CH_2); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 166.2 (CO_2), 149.2 (quinoline C_2), 145.9 (quinoline C_9), 144.2 (quinoline C_8), 134.2 (quinoline C_4), 132.7 (propenyl C_2), 130.6 (quinoline C_6), 125.7 (quinoline C_{10}), 123.5 (quinoline C_3), 122.2 (quinoline C_7), 121.2 (quinoline C_5), 118.6 (propenyl C_3), 52.1 (CH_3), 32.4 (propenyl CH_2); ir (potassium bromide): 1690 (C=O stretch), 1680 (C=C stretch), 1260 (C-O-C asymmetric stretch), 1180 (C-O-C symmetric stretch), 930 (CH bend) cm^{-1}; ms: m/e (relative intensity) 259 (M^+, 27), 244 (21), 226 (100), 212 (33), 201 (13), 187 (32), 172 (16), 167 (29), 159 (29), 128 (26), 115 (10), 101 (10); high resolution ms: Calcd. for $C_{14}H_{13}NO_2S$ m/e 259.0667. Found: m/e 259.0645.

Anal. Calcd. for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40. Found: C, 64.76; H, 4.91; N, 5.38.

8-Hexylthio-5-carboxyquinoline (**14a**).

1,5-Diazabicyclo[4.3.0]non-5-ene (0.29 g, 2.3 mmoles), **3** (0.14 g, 0.6 mmole) and *n*-hexyl bromide (0.10 g, 0.6 mmole) were reacted in methanol (40 ml) to give 0.450 g of yellow oil which was purified by flash chromatography, eluting with 1:4 methanol:ethyl acetate to give 0.095 g (57% yield) of yellow solid, mp 159-160°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.39 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.90 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.20 (d, J = 8 Hz, 1H, quinoline H_6), 7.68 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 7.57 (d, J = 8 Hz, 1H, quinoline H_7), 3.04 (t, J = 7 Hz, 2H, hexyl$_1$ CH_2), 1.72 (tt, J = 7 Hz, J = 7 Hz, 2H, hexyl$_2$ CH_2), 1.48 (tt, J = 7 Hz, J = 7 Hz, 2H, hexyl$_3$ CH_2), 1.30 (tt, J = 7 Hz, J = 7 Hz, 2H, hexyl$_4$ CH_2), 1.29 (tt, J = 7 Hz, J = 7 Hz, 2H, hexyl$_5$ CH_2), 0.86 (t, J = 7 Hz, 3H, hexyl CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 167.8 (CO_2), 149.0 (quinoline C_2), 146.3 (quinoline C_9), 144.4 (quinoline C_8), 134.6 (quinoline C_4), 131.0 (quinoline C_6), 126.2 (quinoline C_{10}), 123.3 (quinoline C_3), 122.1 (quinoline C_5), 121.7 (quinoline C_7), 30.9 (hexyl$_4$ CH_2), 29.5 (hexyl$_1$ CH_2), 28.2 (hexyl$_3$ CH_2), 27.7 (hexyl$_2$ CH_2), 22.1 (hexyl$_5$ CH_2), 13.9 (hexyl CH_3); ir (potassium bromide): 3200-2500 (OH stretch), 2900 (CH stretch), 2830 (CH stretch), 1650 (C=O stretch) cm^{-1}; ms: m/e (relative intensity) 289 (M^+, 9), 256 (100), 232 (39), 219 (64), 205 (29), 200 (17), 186 (11), 173 (23), 160 (8), 116 (8); high resolution ms: Calcd. for $C_{16}H_{19}NO_2S$ m/e 289.1136. Found: m/e 289.1134.

8-Hexylthio-5-methoxycarbonylquinoline (**14b**).

Concentrated hydrochloric acid (2 drops) was added to a solution of **14a** (0.09 g, 0.31 mmole) in methanol (12 ml) and ethyl acetate (12 ml). The dry ether solution of diazomethane (total 23.3 mmoles) was added in thirds as described above. The reaction was quenched by the addition of 7*M* aqueous acetic acid (20 ml), then evaporated *in vacuo* to give 0.348 g of white solid which was purified by flash chromatography, eluting with chloroform to give 0.083 g (88% yield) of yellow solid. This was recrystallized from hexane (3.0 ml) to give 0.071 g (86% recovery) of yellow solid, mp 96-97°; ^{1}H nmr (deuteriochloroform): δ 9.60 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 9.10 (dd, J = 5 Hz, J = 2 Hz, 1H, quinoline H_2), 8.26 (d, J = 8 Hz, 1H, quinoline H_6), 7.65 (dd, J = 9 Hz, J = 5 Hz, 1H, quinoline H_3), 7.51 (d, J = 8 Hz, 1H, quinoline H_7), 3.96 (s, 3H, ester CH_3), 3.07 (t, J = 7 Hz, 2H, hex-

yl$_1$ CH_2), 1.81 (tt, J = 7 Hz, J = 7 Hz, 2H, hexyl$_2$ CH_2), 1.51 (tt, J = 7 Hz, J = 7 Hz, 2H, hexyl$_3$ CH_2), 1.31 (tt, J = 7 Hz, J = 7 Hz, 2H, hexyl$_4$ CH_2), 1.30 (tt, J = 7 Hz, J = 7 Hz, 2H, hexyl$_5$ CH_2), 0.86 (t, J = 7 Hz, 3H, hexyl CH_3); ^{13}C nmr (deuteriochloroform): δ 166.5 (CO_2), 150.1 (quinoline C_9), 148.2 (quinoline C_2), 138.1 (quinoline C_4), 131.7 (quinoline C_6), 127.3 (quinoline C_8), 125.4 (quinoline C_{10}), 124.3 (quinoline C_7), 124.2 (quinoline C_3), 122.1 (quinoline C_5), 52.4 (ester CH_3), 31.9 (hexyl$_1$ CH_2), 31.4 (hexyl$_4$ CH_2), 28.8 (hexyl$_3$ CH_2), 28.2 (hexyl$_2$ CH_2), 22.6 (hexyl$_5$ CH_2), 14.1 (hexyl CH_3); ir (potassium bromide): 2930 (CH stretch), 2900 (CH stretch), 2830 (CH stretch), 1685 (C=O stretch), 1250 (C-O-C asymmetric stretch), 1180 (C-O-C symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 303 (M$^+$, 7), 270 (100), 246 (43), 233 (77), 219 (31), 214 (26), 200 (23), 187 (40), 172 (15), 160 (31), 128 (23), 116 (20), 55 (18); high resolution ms: Calcd. for $C_{17}H_{21}NO_2S$ m/e 303.1293. Found: m/e 303.1313.

Anal. Calcd. for $C_{17}H_{21}NO_2S$: C, 67.29; H, 6.98; N, 4.62. Found: C, 67.07; H, 7.04; N, 4.70.

5-Carboxy-8-[1-(2-phenyl-2-oxo)ethane]thioquinoline (**15a**).

1,5-Diazabicyclo[4.3.0]non-5-ene (0.29 g, 2.3 mmoles), **3** (0.14 g, 0.6 mmole) and 2-chloroacetophenone (0.09 g, 0.6 mmole) were reacted in methanol (40 ml) to give 0.558 g of yellow oil which was purified by flash chromatography, eluting with 1:4 methanol:ethyl acetate to give 0.083 g (44% yield) of yellow solid. This was recrystallized from toluene (20 ml) to give 0.057 g (69% recovery) of yellow solid, mp 214-215°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.38 (dd, J = 8 Hz, J = 2 Hz, 1H, quinoline H_4), 8.93 (dd, J = 5 Hz, J = 2 Hz, 1H, quinoline H_2), 8.18 (d, J = 8 Hz, 1H, quinoline H_6), 8.13 (d, J = 7 Hz, 2H, phenyl H_2, H_6), 7.71 (dd, J = 8 Hz, J = 5 Hz, 1H, quinoline H_3), 7.69 (dd, J = 7 Hz, J = 7 Hz, 1H, phenyl H_4), 7.67 (d, J = 8 Hz, 1H, quinoline H_7), 7.57 (dd, J = 7 Hz, J = 7 Hz, 2H, phenyl H_3, H_5), 4.89 (s, 2H, CH_2); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 194.2 (ketone CO), 167.6 (CO_2), 149.1 (quinoline C_2), 144.7 (quinoline C_9), 144.2 (quinoline C_8), 135.4 (phenyl C_1), 134.5 (quinoline C_4), 133.6 (phenyl C_4), 130.7 (quinoline C_6), 128.7 (phenyl C_3, C_5), 128.6 (phenyl C_2, C_6), 125.9 (quinoline C_{10}), 123.2 (quinoline C_3), 122.6 (quinoline C_5), 122.4 (quinoline C_7), 37.9 (CH_2); ir (potassium bromide): 3200-2450 (OH stretch), 1660 (C=O stretch), 1650 (C=O stretch) cm^{-1}; ms: m/e (relative intensity) 323 (M$^+$, 3), 218 (100), 173 (5), 105 (19), 77 (13); high resolution ms: Calcd. for $C_{18}H_{13}NO_3S$ m/e 323.0616. Found: m/e 323.0577.

Anal. Calcd. for $C_{18}H_{13}NO_3S$: C, 66.86; H, 4.05; N, 4.33. Found: C, 66.59; H, 3.89; N, 4.26.

5-Methoxycarbonyl-8-[1-(2-phenyl-2-oxo)ethane]thioquinoline (**15b**).

Concentrated hydrochloric acid (2 drops) was added to a solution of **15a** (0.06 g, 0.19 mmole) in methanol (10 ml) and ethyl acetate (10 ml). The dry ether solution of diazomethane (total 14.4 mmoles) was added in thirds as described above. The reaction was quenched by the addition of 7*M* aqueous acetic acid (20 ml), then evaporated *in vacuo* to give 0.075 g of yellow solid which was purified by flash chromatography, eluting with chloroform to give 0.051 g (78% yield) of white solid. This was recrystallized from a mixture of hexane (60 ml) and carbon tetrachloride (15 ml) to give 0.032 g (63% recovery) of white solid, mp 140-141°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.26 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.94 (dd, J = 5 Hz, J = 2 Hz, 1H, quinoline H_2), 8.16 (d, J = 8 Hz, 1H, quinoline H_6), 8.13 (d, J = 7 Hz, 2H, phenyl H_2, H_6), 7.73 (dd, J = 9 Hz, J = 5 Hz, 1H, quinoline H_3), 7.69 (dd, J = 7 Hz, J = 7 Hz, 1H, phenyl H_4), 7.68 (d, J = 8 Hz, 1H, quinoline H_7), 7.57 (dd, J = 7 Hz, J = 7 Hz, 2H, phenyl H_3, H_5), 4.90 (s, 2H, CH_2), 3.91 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 194.1 (ketone CO), 166.2 (CO_2), 149.3 (quinoline C_2), 145.4 (quinoline C_9), 144.1 (quinoline C_8), 135.4 (phenyl C_1), 134.2 (quinoline C_4), 133.6 (phenyl C_4), 130.6 (quinoline C_6), 128.7 (phenyl C_3, C_5), 128.6 (phenyl C_2, C_6), 125.6 (quinoline C_{10}), 123.5 (quinoline C_3), 122.4 (quinoline C_7), 121.5 (quinoline C_5), 52.2 (CH_3), 37.9 (CH_2); ir (potassium bromide): 1685 (C=O stretch), 1660 (C=O stretch), 1260 (C-O-C asymmetric stretch), 1175 (C-O-C symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 337 (M$^+$, 3), 232 (100), 173 (8), 105 (20), 77 (14); high resolution ms: Calcd. for $C_{19}H_{15}NO_3S$ m/e 337.0772. Found: m/e 337.0820.

Anal. Calcd. for $C_{19}H_{15}NO_3S$: C, 67.64; H, 4.48; N, 4.15. Found: C, 67.48; H, 4.34; N, 4.00.

Methyl 2-[8-(5-carboxyquinolyl)thio]acetate (**16a**).

1,5-Diazabicyclo[4.3.0]non-5-ene (0.29 g, 2.3 mmoles), **3** (0.14 g, 0.6 mmole) and methyl bromoacetate (0.09 g, 0.6 mmole) were reacted in methanol (40 ml) to give 0.559 g of yellow oil which was purified by flash chromatography, eluting with 1:4 methanol:ethyl acetate to give 0.178 g (100% yield) of yellow solid, mp 198-200°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.43 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.91 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.16 (d, J = 8 Hz, 1H, quinoline H_6), 7.69 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 7.53 (d, J = 8 Hz, 1H, quinoline H_7), 4.11 (s, 2H, CH_2), 3.67 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 171.3 (ester CO_2), 169.6 (acid CO_2), 149.1 (quinoline C_2), 144.2 (quinoline C_9), 143.5 (quinoline C_8), 134.9 (quinoline C_4), 130.5 (quinoline C_6), 126.0 (quinoline C_{10}), 123.2 (quinoline C_3), 122.1 (quinoline C_7), 122.1 (quinoline C_5), 52.5 (CH_3), 32.1 (CH_2); ir (potassium bromide): 3300-2400 (OH stretch), 1690 (CO stretch), 1660 (CO stretch), 1260 (C-O-C asymmetric stretch), 1165 (C-O-C symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 277 (M$^+$, 19), 245 (11), 218 (100), 173 (15), 133 (8), 91 (10), 57 (12), 43 (13); high resolution ms: Calcd. for $C_{13}H_{11}NO_4S$ m/e 277.0408. Found: 277.0407.

Methyl 2-[8-(5-Methoxycarbonylquinolyl)thio]acetate (**16b**).

Concentrated hydrochloric acid (4 drops) was added to a solution of **16a** (0.15 g, 0.5 mmole) in methanol (20 ml) and ethyl acetate (20 ml). The dry ether solution of diazomethane (total 40.5 mmoles) was added in thirds as described above. The reaction was quenched by the addition of 7*M* aqueous acetic acid (20 ml), then evaporated *in vacuo* to give 0.204 g of yellow solid which was purified by flash chromatography, eluting with ethyl acetate to give 0.072 g (46% yield) of yellow solid. This was recrystallized from hexane (70 ml) to give 0.041 g (57% recovery) of yellow crystals, mp 142-143°; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 9.26 (dd, J = 8 Hz, J = 2 Hz, 1H, quinoline H_4), 8.95 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.19 (d, J = 8 Hz, 1H, quinoline H_6), 7.74 (dd, J = 8 Hz, J = 4 Hz, 1H, quinoline H_3), 7.57 (d, J = 8 Hz, 1H, quinoline H_7), 4.13 (s, 2H, CH_2), 3.92 (s, 3H, 5-ester CH_3), 3.68 (s, 3H, 8-ester CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 169.5 (8-ester CO_2), 166.2 (5-ester CO_2), 149.5 (quinoline C_2), 145.1 (quinoline C_9), 144.0 (quinoline C_8), 134.3 (quinoline C_4), 130.8 (quinoline C_6), 125.7 (quinoline C_{10}), 123.7 (quinoline C_3), 122.0 (quinoline C_7), 121.8 (quinoline C_5), 52.5 (8-ester CH_3), 52.3 (5-ester CH_3), 32.1 (CH_2); ir (potassium bromide): 1710 (C=O stretch), 1685 (C=O stretch), 1250 (C-O-C

asymmetric stretch), 1155 (C-O-C symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 291 (M^+, 9), 260 (6), 232 (100), 200 (5), 187 (11), 173 (15), 172 (14), 159 (8), 128 (11); high resolution ms: Calcd. for $C_{14}H_{13}NO_4S$ m/e 291.0565. Found: m/e 291.0362.

Anal. Calcd. for $C_{14}H_{13}NO_4S$: C, 57.72; H, 4.50; N, 4.81. Found: C, 57.77; H, 4.27; N, 4.77.

5-Carboxy-8-methylthioquinoline (**17a**).

1,5-Diazabicyclo[4.3.0]non-5-ene (0.29 g, 2.3 mmoles), **3** (0.14 g, 0.6 mmole) and methyl iodide (0.08 g, 0.6 mmole) were reacted in methanol (40 ml) to give 0.503 g of yellow oil which was purified by flash chromatography, eluting with 1:4 methanol:ethyl acetate to give 0.198 g (100% yield) of yellow solid, mp 232-233°; ^1H nmr (deuteriodimethyl sulfoxide): δ 9.41 (dd, J = 11 Hz, J = 2 Hz, 1H, quinoline H_4), 8.92 (dd, J = 5 Hz, J = 2 Hz, 1H, quinoline H_2), 8.24 (d, J = 10 Hz, 1H, quinoline H_6), 7.70 (dd, J = 11 Hz, J = 5 Hz, 1H, quinoline H_3), 7.54 (d, J = 10 Hz, 1H, quinoline H_7), 2.54 (s, 3H, CH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 167.7 (CO_2), 148.9 (quinoline C_2), 146.9 (quinoline C_9), 144.4 (quinoline C_8), 134.5 (quinoline C_4), 130.7 (quinoline C_6), 125.9 (quinoline C_{10}), 123.0 (quinoline C_3), 122.6 (quinoline C_5), 121.2 (quinoline C_7), 13.4 (CH_3); ir (potassium bromide): 3600-2400 (OH stretch), 1660 (C=O stretch) cm^{-1}; ms: m/e (relative intensity) 219 (M^+, 100), 186 (46), 173 (51), 158 (17), 144 (11), 128 (21); high resolution ms: Calcd. for $C_{11}H_9NO_2S$ m/e 219.0354. Found: m/e 219.0350.

5-Methoxycarbonyl-8-methylthioquinoline (**17b**).

Concentrated hydrochloric acid (4 drops) was added to a solution of **17a** (0.15 g, 0.7 mmole) in methanol (25 ml) and ethyl acetate (25 ml). The dry ether solution of diazomethane (total 51.0 mmoles) was added in thirds as described above. The reaction was quenched by the addition of 7*M* aqueous acetic acid (15 ml), then evaporated *in vacuo* to give 0.412 g of yellow residue which was purified by flash chromatography, eluting with chloroform to give 0.080 g (50% yield) of yellow solid. This was recrystallized from hexane (10 ml) to give 0.063 g (79% recovery) of yellow solid, mp 127-128°; ^1H nmr (deuteriodimethyl sulfoxide): δ 9.27 (dd, J = 9 Hz, J = 2 Hz, 1H, quinoline H_4), 8.93 (dd, J = 4 Hz, J = 2 Hz, 1H, quinoline H_2), 8.20 (d, J = 9 Hz, 1H, quinoline H_6), 7.72 (dd, J = 9 Hz, J = 4 Hz, 1H, quinoline H_3), 7.54 (d, J = 9 Hz, 1H, quinoline H_7), 3.91 (s, 3H, OCH_3), 2.53 (s, 3H, SCH_3); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 166.3 (CO_2), 149.1 (quinoline C_2), 147.9 (quinoline C_9), 144.3 (quinoline C_8), 134.1 (quinoline C_4), 130.7 (quinoline C_6), 125.6 (quinoline C_{10}), 123.4 (quinoline C_3), 121.2 (quinoline C_7), 121.0 (quinoline C_5), 52.0 (OCH_3), 13.4 (SCH_3); ir (potassium bromide): 1690 (C=O stretch), 1255 (C-O-C asymmetric stretch), 1180 (C-O-C symmetric stretch) cm^{-1}; ms: m/e (relative intensity) 233 (M^+, 100), 218 (9), 200 (83), 187 (81), 172 (69), 156 (22), 141 (16), 128 (59), 115 (13), 101 (22), 87 (56), 75 (14), 69 (12), 45 (14); high resolution ms: Calcd. for $C_{12}H_{11}NO_2S$ m/e 233.0511. Found: 233.0471.

Anal. Calcd. for $C_{12}H_{11}NO_2S$: C, 61.78; H, 4.75; N, 6.00. Found: C, 61.48; H, 4.55; N, 5.86.

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