Reaction of Enaminones with Carbon Disulfide: Synthesis of Heterocycles Using Enamino Dithiocarboxylates

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Received January 24, 1991

Reaction of various types of enaminones, which are prepared by the condensation of 1,3-dicarbonyl compounds with aromatic amines, with carbon disulfide in the presence of sodium hydroxide as the base in dimethyl sulfoxide to give the corresponding enamino dithiocarboxylates, 1,3-thiazines and trithiones. Enamino dithiocarboxylates are cyclized under refluxing in diphenyl ether to give the fused quinoline derivatives. The reaction of 6-arylamino-1,3-dimethyluracils with excess carbon disulfide in the presence of sodium hydroxide and subsequent methylation with dimethyl sulfate gave directly the corresponding 1,3-dimethyl-5-methylthiopyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-diones.

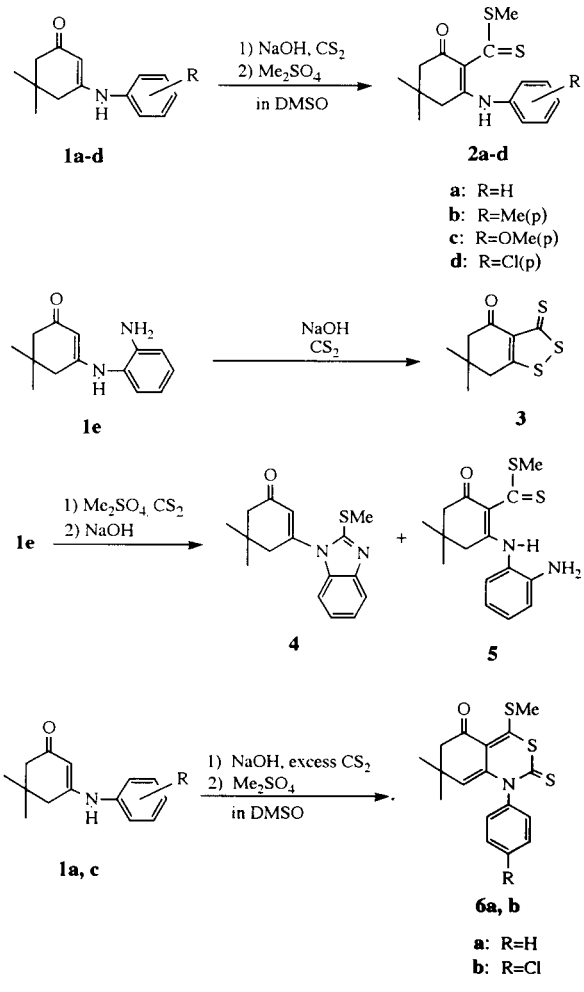
J. Heterocyclic Chem., **28**, 1245 (1991).

Enamino dithiocarboxylate derivatives, which are readily prepared by the reaction of the various enamines with carbon disulfide in the presence of an appropriate base, are extensively utilized in organic synthesis, especially the preparation of heterocyclic compounds [1-7]. Enaminones are also very useful and versatile starting materials in organic synthesis [8-10]. We have previously reported the synthesis of enamino dithiocarboxylates, methyl 1,3-dimethyl-6-aminouracil-5-dithiocarboxylates, by the reaction of enaminone derivatives, 5-aminouracils, with carbon disulfide followed by methylation with dimethyl sulfate. These enamino dithiocarboxylates are very useful intermediates for the synthesis of pyrimido[3,4-*d*]pyrimidines and isothiazoles[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-diones [11-14].

As a continuation of our studies of some potential uses of carbon disulfide for the synthesis of heterocyclic compounds [15], we now wish to report the synthesis of enamino dithiocarboxylate derivatives from the various *N*-arylenaminone compounds and some syntheses of heterocyclic compounds such as acridine, pyrimidoquinoline and indenoquinoline derivatives using the above enamino dithiocarboxylates.

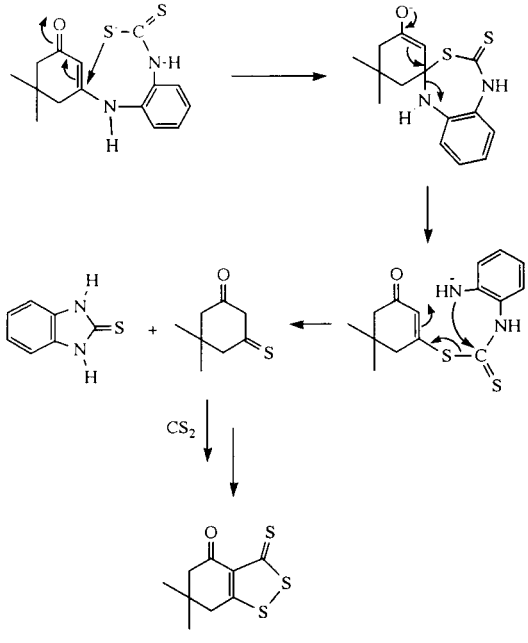
Reaction of **1a-d** with carbon disulfide in the presence of sodium hydroxide in dimethyl sulfoxide (DMSO) followed by methylation with dimethyl sulfate at room temperature gave the corresponding enamino dithiocarboxylates **2a-d** in 32-50% yields. The reaction of 3-(*o*-aminoanilino)-5,5-dimethylcyclohex-2-en-1-one (**1e**) derived from dimedone and *o*-phenylenediamine with carbon disulfide in the presence of sodium hydroxide in DMSO gave the benzo[1,2]dithiole-3-thione **3** in 46% yield [16]. This procedure displays promising preparative value as a method of fused 1,2-dithiole-3-thione derivatives. The outline of reaction pathway is shown in Scheme 2. When **1e** reacted with carbon disulfide in the presence of dimethyl sulfate and sodium hydroxide, a mixture of **4** and **5** was obtained in 27% and 17% yield, respectively. When excess of carbon disulfide and sodium hydroxide were used, cyclized products, benzothiazine derivatives **6a,b** were obtained instead of dithiocarboxylates in good yield.

Scheme 1



It is well known that *N*-phenyl-*o*-aminobenzoates are the key intermediates for the synthesis of acridinone derivatives in good results [17,18]. As a similar cyclization,

Scheme 2

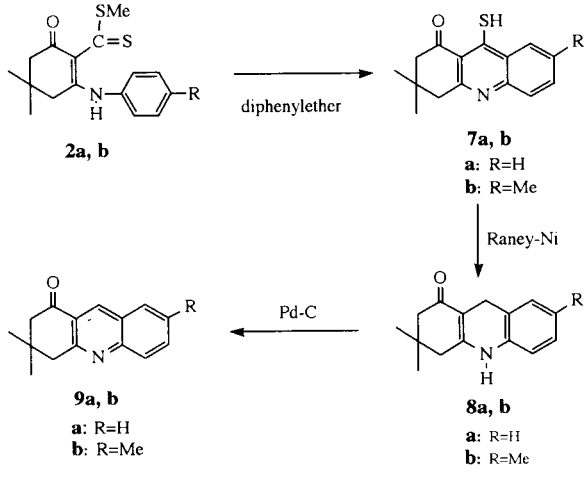


3

Gould-Jacobs reaction is also popular method for the preparation of quinoline derivaties [19,20], which are formed by the cyclization of the ester carbonyl group at the *o*-position of the amino group.

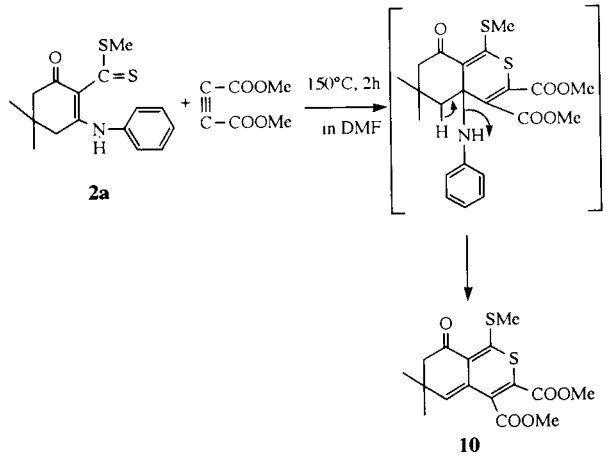
Enamino dithiocarboxylates **2a,b** were readily cyclized by refluxing in diphenyl ether to give the corresponding acridine derivatives **7a,b** in good yields. Compounds **9a** and **9b** were prepared by dehydration of **8a** and **8b** which were obtained by the desulfurization of **7a** and **7b** with Raney-nickel in ethanol.

Scheme 3

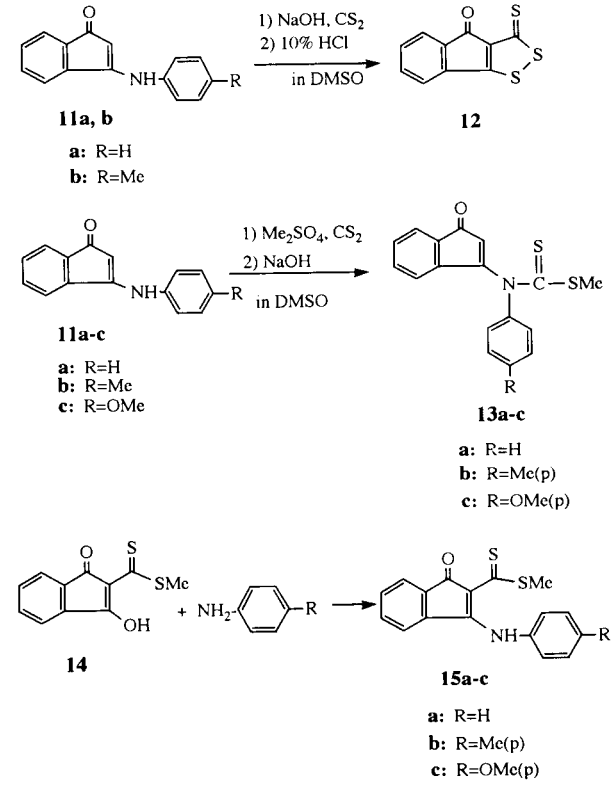


We have previously reported that enamino dithiocarboxylate derivatives act as the "Hetero Diene" in the Diels-Alder reaction with appropriate alkenes, affording either 4-amino-2,3-dihydro-4*H*-thiapyranes or 2*H*-thiapyranes, depending on the nature of the substitutions [21-24]. The above enamino dithiocarboxylates have a diene system in the thiocarbonyl group of their dithiocarboxylic acid and a double bond of enamine. Reaction of **2a** with dimethyl acetylendicarboxylate in benzene was readily carried out followed by the elimination of anilino group to give the corresponding Diels-Alder product **10** in 21% yield.

Scheme 4

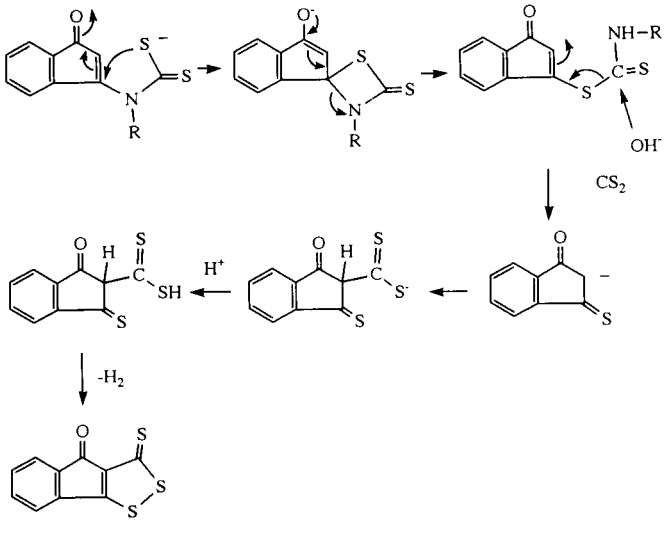


Scheme 5



When enaminone, 3-anilinoinden-1-one (**11a**) was allowed to react with carbon disulfide in the presence of sodium hydroxide in dimethyl sulfoxide followed by treatment with 10% hydrochloric acid, a trithione, 4-oxoindeno[1,2-*c*][1,2]dithiole-3-thione (**12**) was obtained in 78% yield, though the expected enamino dithiocarboxylate was not detected in the reaction mixture. Similarly, the reaction of **11b** with carbon disulfide gave the same trithione **12** in 82% yield. When the reaction was carried out in the presence of dimethyl sulfate, methyl *N*-phenyldithiocarbamate derivatives **13a-c** were obtained from the corresponding enaminones **11a-c** in 54, 62, and 58% yields, respectively. Therefore the reaction was assumed to proceed by the addition of the amino group to carbon disulfide followed by the nucleophilic attack of the thiolate anion. Decomposition of the 3-azathiethane ring produced the corresponding *β*-oxothione derivative which works as a key intermediate for the formation of the trithione. The 3-oxoindene-1-thione, thus formed, reacts again with carbon disulfide and by air oxidation of the resultant dithiocarboxylate gave the desired trithione **12**. The outline of reaction pathway is shown in Scheme 6.

Scheme 6



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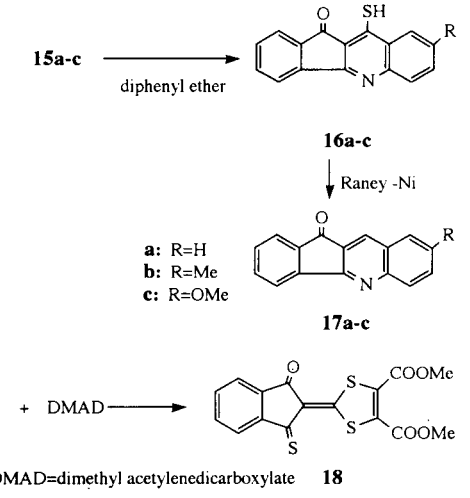
We have reported the synthesis of methyl 3-amino-1-oxoindan-2-dithiocarboxylate by the reaction of methyl indan-1,3-dione-2-dithiocarboxylate (**14**) with ammonia [15]. In a similar synthesis of the above enamino dithiocarboxylate, reaction of **14** with arylamine derivatives (aniline, *p*-toluidine, *p*-anisidine) gave the corresponding methyl 1-arylamino-3-oxoindan-2-dithiocarboxylates **15a-c** which were converted to indenoquinoline derivatives **16a-c** under refluxing in diphenyl ether. Desulfurization of **16a-c** with Raney-nickel gave the corresponding indeno[1,2-*b*]-quinolin-11-one derivatives **17a-c** in good yields.

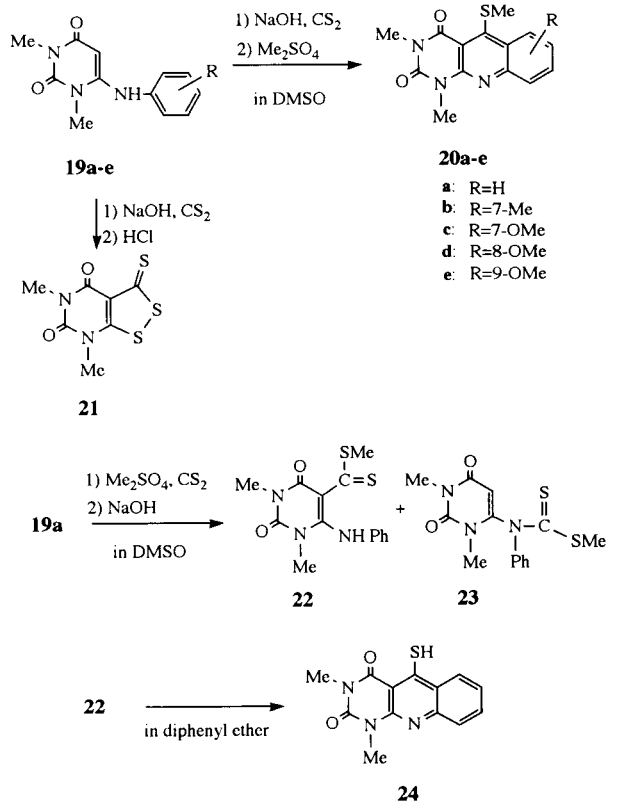
It is well known that 1,3-dipolar cyclization reactions of trithione with various activated dipolarphiles such as maleic anhydride and dimethyl acetylenedicarboxylate occurred in appropriate solvent to give the corresponding 1,2-dithiole derivatives [26,27]. Compound **12** also reacted with dimethyl acetylenedicarboxylate to yield dimethyl indan-2-ylidene-1,2-dithiole-4,5-carboxylate (**18**) in 21% yield *via* 1,3-dipolar cyclization reaction.

Scheme 7



DMAD=dimethyl acetylenedicarboxylate **18**

Scheme 8



Yoneda *et al.* have reported the synthesis of pyrimido-[4,5-*d*]quinoline derivatives by the Vilsmeir reaction of 6-*N*-arylaminouracils with dimethylformamide and phosphorus oxychloride with good results [28,29]. This reaction suggests the possibility of the direct preparation of pyrimido[4,5-*b*]quinoline *via* condensation of *N*-aryl enaminones with carbon disulfide followed by cyclization of the enamino dithiocarboxylic acids. In fact, enaminones **19a-e** readily reacted with carbon disulfide followed by methylation with dimethyl sulfate in the presence of sodium hydroxide in dimethyl sulfoxide to give the expected cyclized products, 1,3-dimethyl-5-methylthiopyrimido[4,5-*b*]quinolines **20a-e** in 20-47% yields. When **19a** was allowed to react excess carbon disulfide in the presence of an excess sodium hydroxide in DMSO at room temperature, trithione derivative, 5,7-dimethyl-1,2-dithiolo[3,4-*d*]pyrimidine-4,6(5*H*,-7*H*)-dione (**21**) was obtained in 40% yield.

When a solution of sodium hydroxide was added to a solution of **19a**, carbon disulfide, and dimethyl sulfate in dimethyl sulfoxide, methyl 4-anilino-1,3-dimethyluracil-5-dithiocarboxylate (**22**) and methyl *N*-phenyl-*N*-((1,3-dimethyl)-6-uracilyl)dithiocarbamate (**23**) were obtained in 28 and 33% yields, respectively. Heating **22** in diphenyl ether at 250° for 20 minutes gave a cyclized product **24**.

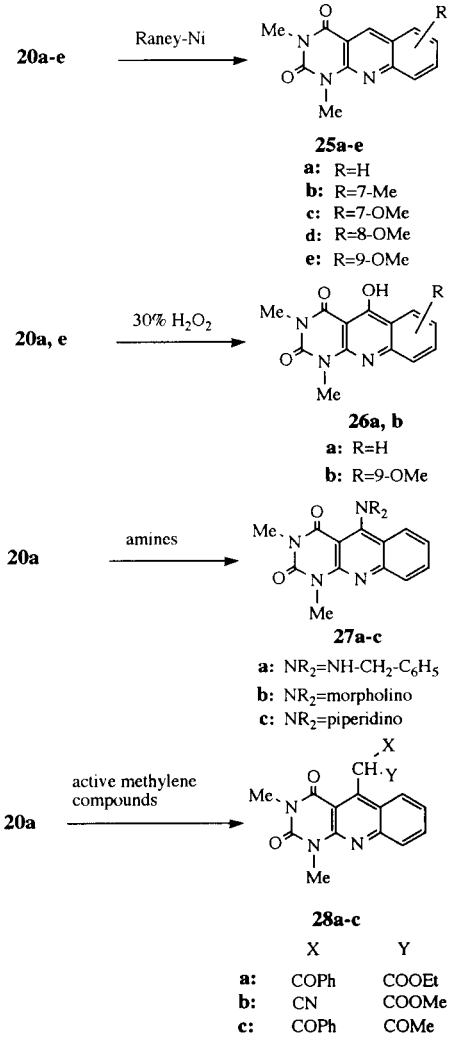
It is well known that the methylthio group on a heterocyclic ring reacts with nucleophilic reagents to give the corresponding substituted products [31-33]. However, prior to our work, there was no report on the substitution reaction of the methylthio group on pyrimido[4,5-*d*]quinoline. At first we attempted the desulfurization of compounds **20a-e**. The desulfurization of **20a-e** with Raney-nickel occurred readily to give the expected 1,3-dimethylpyrimido[4,5-*d*]quinoline derivatives **26a-c** in good yields. The treatment of **20** with hydrogen peroxide in acetic acid gave 5-hydroxy derivatives **26a,b** in good yields.

Substitution of the methylthio group in compound **20a** with amines (benzylamine, morpholine, piperidine) occurred easily. The corresponding 5-amino-1,3-dimethylaminopyrimido[4,5-*d*]quinoline derivatives **27a-c** were obtained in good yields.

The reaction of **20a** with active methylene compounds (ethyl benzoylacetate, methyl cyanoacetate, acetylacetone) in the presence of potassium carbonate gave the corresponding displacement products **28a-c** of 4-methylthio group in **20a**.

In conclusion, the reaction of carbon disulfide with the various *N*-aryl-substituted enaminones may be concluded to have wide utility for the synthesis of heterocyclic compounds, fused trithiones, thiazines, and pyrimido[4,5-*d*]-quinolines derivatives. Especially, *N*-aryl-substituted enamino dithiocarboxylates derived from the reaction of enaminones with carbon disulfide are the key intermediates for the fused quinoline derivatives bearing a methylthio group at the 4-position of the quinoline ring.

Scheme 9



EXPERIMENTAL

All melting points were determined in a capillary tube and are uncorrected. Infrared (ir) spectra were recorded in potassium bromide pellets on a JASCO IRA-2 spectrometer and ultraviolet (uv) absorption spectra were determined in 95% ethanol on a Hitachi EP-S2 spectrometer. Nuclear magnetic resonance (nmr) spectra were obtained on JNM-PS-100(100 MHz) and JNM-FX-90Q(90 MHz) spectrometers with tetramethylsilane as an internal standard. Mass spectra (ms) were recorded on a JEOL-01SG mass spectrometer.

Methyl 3-Anilino-5,5-dimethyl-1-oxo-2-cyclohexene-2-dithiocarboxylate (**2a**).

In a 200 ml of three-necked flask, filtered with a mechanical stirrer, a condenser, and a dropping funnel, was placed a solution of 4.30 g (20 mmoles) of 3-anilino-5,5-dimethyl-2-cyclohexen-1-one (**1a**), and sodium hydroxide solution (sodium hydroxide, 0.80 g, 20 mmoles, water 2 ml) in 50 ml of dimethyl sulfoxide. To the

vigorously stirred mixture, 2.28 g (30 mmoles) of carbon disulfide was added in the course of 30 minutes. The mixture became warm and the temperature soon approached the boiling points of carbon disulfide. Cooling with ice-water may be necessary to keep the reaction under control. The mixture was stirred for 20 minutes below 10° over 20 minutes. After stirring at room temperature for 1 hour, the reaction mixture was diluted with water (200 ml) and acidified with 10% hydrochloric acid. The resulting precipitate was collected by filtration. After drying, this compound was recrystallized from methanol to give 3.10 g (10 mmoles, 50% yield) of yellow needles, mp 161-164°; ir (potassium bromide): ν max cm^{-1} 3400 (NH), 1630; uv (ethanol): λ max nm (log ϵ) 222 (4.01), 285 (4.36), 364 (4.19); ^{1}H-nmr (deuteriochloroform): δ 1.01 (6H, s, Me x 2), 2.40 (2H, s, 6-H), 2.48 (2H, s, 4-H), 2.50 (3H, s, SMe), 7.28 (5H, m, phenyl-H), 15.95 (1H, bs, NH).

Anal. Calcd. for $C_{16}H_{19}NOS_2$: C, 62.91; H, 6.27; N, 4.59; S, 20.99. Found: C, 62.85; H, 6.36; N, 4.50; S, 20.94.

Methyl 5,5-Dimethyl-1-oxo-3-(*p*-toluidino)-2-cyclohexene-2-dithiocarboxylate (**2b**).

This compound (1.37 g, 4.32 mmoles) was prepared from 5,5-dimethyl-3-(*p*-toluidino)-2-cyclohexen-1-one (**1b**) (2.29 g, 10 mmoles) and carbon disulfide (1.14 g, 15 mmoles) in 43% yield in a manner similar to that described for the preparation of **2a**. An analytical sample was recrystallized from methanol to give orange needles, mp 185-187°; ir (potassium bromide): ν max cm^{-1} 3400 (NH), 1625 (CO); uv (ethanol): λ max nm (log ϵ) 224 (4.05), 285 (4.39), 364 (4.22); ^{1}H-nmr (deuteriochloroform): δ 1.01 (6H, s, 5-Me x 2), 2.40 (2H, s, 6-H), 2.48 (2H, s, 4-H), 2.52 (3H, s, SMe), 7.06 (2H, d, J = 9.0 Hz, 2', 6'-H), 7.26 (2H, d, J = 9.0 Hz, 3', 5'-H), 16.44 (1H, bs, NH).

Anal. Calcd. for $C_{17}H_{21}NOS_2$: C, 63.91; H, 6.63; N, 4.39; S, 20.07. Found: C, 63.84; H, 6.71; N, 4.39; S, 20.24.

Methyl 3-(*p*-Anisidino)-5,5-dimethyl-1-oxo-2-cyclohexene-2-dithiocarboxylate (**2c**).

This compound (1.07 g, 3.21 mmoles) was prepared from 3-(*p*-anisidino)-5,5-dimethyl-2-cyclohexen-1-one (**1c**) (2.29 g, 10 mmoles) and carbon disulfide) (1.146 g, 15 mmoles) in 32% yield in a manner similar to that described for the preparation of **2a**. An analytical sample was recrystallized from methanol to give orange prisms, mp 168-172°; ir (potassium bromide): ν max cm^{-1} 3400 (NH), 1628 (CO); uv (ethanol): λ max nm (log ϵ) 229 (4.07), 285 (4.39), 364 (4.21); ^{1}H-nmr (deuteriochloroform): δ 1.00 (6H, s, 5-Me x 2), 2.44 (2H, s, 6-H), 2.49 (2H, s, 4-H), 2.56 (3H, s, SMe), 3.86 (3H, s, OMe), 6.95 (2H, d, J = 9.0 Hz, 2', 6'-H), 7.13 (2H, d, J = 9.0 Hz, 3', 5'-H), 16.44 (1H, bs, NH).

Anal. Calcd. for $C_{17}H_{21}NO_2S_2$: C, 60.86; H, 6.31; N, 4.18; S, 19.11. Found: C, 60.72; H, 6.45; N, 4.14; S, 19.30.

Methyl 3-(*p*-Chlorophenyl)amino-5,5-dimethyl-1-oxo-2-cyclohexene-2-dithiocarboxylate (**2d**).

This compound (1.36 g, 4.0 mmoles) was prepared from 3-(*p*-chlorophenyl)amino-5,5-dimethyl-2-cyclohexen-1-one (**1d**) (2.50 g, 10 mmoles) and carbon disulfide (1.14 g, 15 mmoles) in 40% yield in a manner similar to that described for the preparation of **2a**. An analytical sample was recrystallized from methanol to give yellow prisms, mp 160-162°; ir (potassium bromide): ν max cm^{-1} 3040 (NH), 1625 (CO); uv (ethanol): λ max nm (log ϵ) 287 (4.34), 364 (4.16); ^{1}H-nmr (deuteriochloroform): δ 1.13 (6H, s, 5-Me x 2), 2.58 (2H, s, $-CH_2-$), 2.62 (2H, s, $-CH_2-$), 2.77 (3H, s, SMe), 7.20 (2H, d, J = 8.6 Hz, phenyl-H), 7.55 (2H, d, J = 8.6 Hz, phenyl-H), 15.00 (1H, bs, NH).

Anal. Calcd. for $C_{16}H_{18}ClNOS_2$: C, 56.53; H, 5.34; N, 4.12; S, 18.87. Found: C, 56.26; H, 5.43; N, 4.09; S, 18.89.

6,6-Dimethyl-4-oxo-4,5,6,7-tetrahydrobenzo-1,2-dithiole-3-thione (**3**).

To a solution of 2.30 g (10 mmoles) of 3-(*o*-amino)anilino-5,5-dimethyl-2-cyclohexen-1-one (**1e**) and a solution of sodium hydroxide (sodium hydroxide 1.60 g, 40 mmoles, water 5 ml) in 30 ml of dimethyl sulfoxide, was added 2.28 g (30 mmoles) of carbon disulfide below 5° over 30 minutes. After stirring at room temperature for 4 hours, *ca.* 10 ml of 10% hydrochloric acid was added to the reaction mixture was poured into 200 ml of ice-water and the resulting precipitate was recyrstallized from methanol to give 1.08 g (4.70 mmoles, 47%) of red leaflets, mp 176-177° [lit [16] mp 169°]; ir (potassium bromide): ν max cm^{-1} 1667 (CO); uv (ethanol): λ max nm (log ϵ) 227 (4.17), 262 (3.92), 312 (3.86), 335 (3.76), 420 (3.82); ^{1}H-nmr (deuteriochloroform): δ 1.16 (6H, s, Me x 2), 2.51 (2H, s, $-CH_2-$), 2.93 (2H, s, $-CH_2-$); ms: m/z 230 (M^+, 100), 215 (7), 187 (10), 174 (40), 82 (45), 55 (25), 43 (25).

3-(2-Methylthiobenzimidazo-1-yl)-5,5-dimethyl-2-cyclohexen-1-one (**4**) and Methyl 3-(2-Aminophenyl)amino-5,5-dimethyl-1-oxo-2-cyclohexene-2-dithiocarboxylate (**5**).

To a solution of 2.30 g (10 mmoles) of **1e**, 1.14 g (15 mmoles) of carbon disulfide, and 1.89 g (15 mmoles) of dimethyl sulfate in 100 ml of dimethyl sulfoxide, a solution of sodium hydroxide (sodium hydroxide 0.8 g, 15 mmoles, water 3 ml) was added at below 5° over 20 minutes. After stirring at room temperature for 2 hours, the reaction mixture was diluted with water (200 ml) and acidified with 10% hydrochloric acid. The resulting precipitate was collected by filtration. After drying, a mixture of **4** and **5** was recrystallized from ethanol. The methyl dithiocarboxylate **5** (0.42 g, 1.31 mmoles, 13%) was separated from a mixture of the reaction products by recrystallization from ethanol to give tan needles, mp 164-165°. This mother liquor of recrystallization consists of imidazole **4** and methyl dithiocarboxylate **5** derivatives. After evaporation of ethanol, the residue was chromatographed on a neutral alumina-column using benzene as an eluent to give 0.76 g (2.66 mmoles, 27%) of imidazole derivative **4** and ethanol as an eluent to give 0.12 g (0.38 mmole, 3.8%) of **5**. Compound **4** was recrystallized from ethanol to give colorless prisms.

Compound **4**.

This compound had mp 134-135°; ir (potassium bromide): ν max cm^{-1} 1660 (CO), 1620, 1450, 1373, 1265, 743; uv (ethanol): λ max nm (log ϵ) 215 (4.63), 277 (4.37); ^{1}H-nmr (deuteriochloroform): δ 1.52 (6H, s, Me x 2), 2.45 (2H, s, $-CH_2-$), 2.73 (2H, d, J = 1.3 Hz, $-CH_2-$), 6.27 (1H, bs, $=CH-$), 7.20-7.26 (3H, m, aromatic-H), 7.64 (1H, m, 7'-H).

Anal. Calcd. for $C_{16}H_{18}N_2OS$: C, 67.11; H, 6.34; N, 9.78; S, 11.17. Found: C, 66.95; H, 6.47; N, 9.86; S, 11.19.

Compound **5**.

This compound had mp 164-165°; ir (potassium bromide): ν max cm^{-1} 3400, 3330, 3220 (NH), 1602, 1550, 1450, 1304, 1285, 1144, 730: uv (ethanol): λ max nm (log ϵ) 240 (4.07), 282 (4.31), 360 (4.14); ^{1}H-nmr (deuteriochloroform): δ 1.02 (6H, s, Me x 2), 2.44 (2H, s, $-CH_2-$), 2.47 (2H, s, $-CH_2-$), 2.53 (3H, s, SMe), 3.65 (2H, bs, NH_2), 6.74-7.24 (4H, m, aromatic-H), 15.04 (1H, bs, NH).

Anal. Calcd. for $C_{16}H_{20}N_2OS_2$: C, 59.99; H, 6.29; N, 8.75; S, 19.97. Found: C, 60.06; H, 6.40; N, 8.69; S, 20.06.

7,7-Dimethyl-4-methylthio-5-oxo-1-phenyl-1,5,6,7-tetrahydro-2*H*-3,1-benzothiazine-2-thione (**6a**).

To a solution of 2.15 g (10 mmoles) of **1a** and a solution of sodium hydroxide (sodium hydroxide 1.60 g, 40 mmoles, water 5 ml) in 30 ml of dimethyl sulfoxide, was added 2.28 g (30 mmoles) of carbon disulfide below 5° over 20 minutes. After stirring at room temperature for 2 hours, dimethyl sulfate (1.80 g, 15 mmoles) was added dropwise to the reaction mixture with stirring for 1 hour at room temperature. The reaction mixture was poured into 200 ml of ice-water and acidified with 10% hydrochloric acid. The resulting precipitate was collected by filtration. After drying, the product was recrystallized from methanol to give 1.81 g (0.52 mmole) of orange needles, mp 198-200°, in 52% yield; ir (potassium bromide): ν max cm^{-1} 1650 (CO), 1600, 1480, 1340; uv (ethanol): λ max nm (log ϵ) 314 (4.51), 410 (3.19); ^{1}H-nmr (deuteriochloroform): δ 0.96 (6H, s, Me x 2), 2.34 (2H, s, 6-H), 2.50 (3H, s, SMe), 4.53 (1H, s, 8-H), 7.12-7.27 (2H, m, phenyl-H), 7.44-7.62 (3H, m, phenyl-H).

Anal. Calcd. for $C_{17}H_{17}NOS_3$: C, 58.76; H, 4.93; N, 4.01; S, 27.51. Found: C, 58.82; H, 4.98; N, 4.01; S, 27.51.

1-(*p*-Chlorophenyl)-7,7-dimethyl-4-methylthio-5-oxo-1,5,6,7-tetrahydro-2*H*-3,1-benzothiazine-2-thione (**6b**).

This compound (1.83 g, 4.80 mmoles) was prepared from **1d** (2.49 g, 10 mmoles) and carbon disulfide (2.28 g, 30 mmoles) in 48% yield in a manner similar to that described for the preparation of **6a**. An analytical sample was recrystallized from methanol to give an orange powder, mp 181-182°; ir (potassium bromide): ν max cm^{-1} 1653 (CO); uv (ethanol): λ max nm (log ϵ) 218 (4.31), 313 (4.52), 413 (3.21); ^{1}H-nmr (deuteriochloroform): δ 0.99 (6H, s, Me x 2), 2.36 (2H, s, 7-H), 2.51 (3H, s, SMe), 4.48 (1H, s, 4-H), 7.45 (4H, m, aromatic-H).

Anal. Calcd. for $C_{17}H_{16}ClNOS_3$: C, 53.46; H, 4.22; N, 3.67; S, 25.18. Found: C, 53.41; H, 4.28; N, 3.51; S, 25.12.

Cyclization of Enamino Dithiocarboxylate **2a** to Acridine Derivative **9a**.

A solution of 1.03 g (5 mmoles) of **2a** in 20 ml of diphenyl ether was refluxed for 30 minutes. After cooling, 30 ml of petroleum ether was added to this reaction mixture. The brown precipitate that appeared was collected by filtration was washed with petroleum ether. This compound is 1,2,3,4,9,10-hexahydro-3,3-dimethyl-1-oxoacridine-9-thione (**7a**) of mp 339-341° in 76% (3.80 mmoles) yield; m/s: 257 (M^+, 100), 242 (10), 201 (20), 170. This material was used in the next step without purification.

A mixture of this product, *ca.* 3 g of Raney-nickel (W-2), and 50 ml of ethanol was refluxed for 20 hours. After removal of the Raney-nickel and solvent, the residue was chromatographed on an alumina column using benzene as an eluent to give 0.622 g of a mixture of **8a** and **9a** in ratio 9:1 (in ^{1}H-nmr spectrum). The mixture was used in the next step without purification. An analytical sample of **8a** was purified by recrystallization from methanol to give colorless needles, mp 245-247°; ir (potassium bromide): ν max cm^{-1} 3240 (NH), 1618, 1580 (CO); uv (ethanol): λ max nm (log ϵ) 234 (4.23), 355 (4.24); ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 1.00 (6H, Me x 2), 2.11 (2H, s, $-CH_2-$), 2.28 (2H, s, $-CH_2-$), 3.51 (2H, s, $-CH_2-$), 6.70-7.10 (4H, m, 5, 6, 7, 8-H), 9.10 (1H, bs, NH).

Anal. Calcd. for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.25; H, 7.48; N, 6.09.

A mixture of the above products, **8a** and **9a**, and 0.2 g of 10% palladium on charcoal, and 30 ml of dry *m*-xylene was refluxed for 30 hours with stirring. The reaction mixture was cooled to below 20° and the catalyst removed by filtration. The *m*-xylene was removed under reduce pressure. The residue was chromatographed on silica gel using benzene as an eluent giving 0.54 g (2.4 mmoles, 48% yield from **2a**) of colorless needles of **9a**, mp 98-99°; ir (potassium bromide): ν max cm^{-1} 1662 (CO), 1545, 1505, 760; uv (ethanol): λ max nm (log ϵ) 216 (4.37), 253 (4.36), 279 (4.20), 325 (3.89), 334 (3.86), 368 (3.71), 382 (3.72); ^{1}H-nmr (deuteriochloroform): δ 1.16 (6H, s, Me x 2), 3.23 (2H, s, $-CH_2-$), 7.68 (1H, m, 6 or 7-H), 7.98 (1H, m, 7 or 6-H), 8.12 (1H, nd, J = 8.2 Hz, 8-H), 8.26 (1H, nd, J = 8.2 Hz, 5-H).

Anal. Calcd. for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.95; H, 6.72; N, 6.21.

1,2,3,4,9,10-Hexahydro-3,3,7-trimethyl-1-oxoacridine-9-thione (**7b**).

This compound (0.883 g, 3.26 mmoles) was prepared from **2b** (1.60 g, 5.0 mmoles) in 65% yield in a manner similar to that described for the preparation of **7a**. This compound was used in the next step without purification, mp 267-271°; ir (potassium bromide): ν max cm^{-1} 3040 (NH), 1650 (CO); uv (ethanol): λ max nm (log ϵ) 245 (3.58), 290 (3.76); ^{1}H-nmr (trifluoroacetic acid): δ 1.30 (6H, s, Me x 2), 2.71 (3H, s, 7-Me), 2.98 (2H, s, $-CH_2-$), 3.42 (2H, s, $-CH_2-$), 7.97 (2H, bs, aromatic-H), 8.45 (1H, bs, 8-H).

1,2,3,4,9,10-Hexahydro-3,3,7-trimethyl-1-oxoacridine (**8b**).

This compound (0.509 g, 2.12 mmoles) was prepared from **7b** (0.883 g, 3.26 mmoles) in 65% yield in a manner similar to that described for the preparation of **7a**. This compound was obtained as a mixture of **8b** and **9b** (**8b**:**9b** = 9:1). A mixture was used in the next step without purification. An analytical sample was recrystallized from methanol to give pale yellow needles, mp 245-248°; ir (potassium bromide): ν max cm^{-1} 3250 (NH), 1613 (CO); uv (ethanol): λ max nm (log ϵ) 237 (4.23), 360 (4.23); ^{1}H-nmr (deuteriochloroform): δ 1.01 (6H, s, Me x 2), 2.11 (2H, s, $-CH_2-$), 2.17 (3H, s, 7-Me), 2.27 (2H, s, $-CH_2-$), 3.47 (2H, s, $-CH_2-$), 6.70 (1H, s, 9-H), 6.85 (2H, m, 5, 6-H), 9.06 (1H, bs, NH).

Anal. Calcd. for $C_{16}H_{19}NO$: C, 79.6; H, 7.94; N, 5.80. Found: C, 79.59; H, 7.88; N, 5.68.

1,2,3,4-Tetrahydro-3,3,7-trimethylacridin-1-one (**9b**).

This compound (0.263 g, 1.10 mmoles) was prepared from the above products (a mixture of **8b** and **9b**) in 42% yield (from **7b**) in a manner similar to that described for the preparation of **9a**. An purified sample was recyrstallized from methanol to give pale yellow needles, mp 97-98°; ir (potassium bromide): ν max cm^{-1} 1672 (CO), 1585, 1206, 825; uv (ethanol): λ max nm (log ϵ) 225 (4.31), 252 (4.67); ^{1}H-nmr (deuteriochloroform): δ 1.14 (6H, s, Me x 2), 2.49 (3H, s, 7-Me), 2.60 (2H, s, $-CH_2-$), 3.14 (2H, s, $-CH_2-$), 7.63 (1H, d, J = 8.0 Hz, 6-H), 7.68 (1H, s, 8-H), 7.94 (1H, d, J = 8.0 Hz, 5-H), 8.74 (1H, s, 9-H).

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.28; H, 7.18; N, 5.78.

Dimethyl 6,7-Dihydro-8*H*-6,6-dimethyl-1-methylthio-8-oxobenzothiapyran-3,4-dicarboxylate (**10**).

A mixture of 0.50 g (1.64 mmoles) of **2a**, 0.47 g (3.31 mmoles) of dimethyl acetylenedicarboxylate, and 3 ml of dimethylformamide was heated at 150° for 2 hours. Ice-water (50 ml) was added to the reaction mixture and then 10% hydrochloric acid was added to

the mixture. The resulting dark precipitate was collected by filtration. The product was purified by the chromatography on alumina column using benzene as an eluent to give 0.12 g (0.339 mmole, 21%) of yellow needles, mp 151-152°; ir (potassium bromide): ν max cm^{-1} 1725, 1646 (CO), 1455, 1425, 1270, 1240; uv (ethanol): λ max nm (log ϵ) 264 (3.97), 312 (4.26), 336 (4.20), 450 (2.69); ^{1}H-nmr (deuteriochloroform): δ 1.03 (6H, s, Me x 2), 2.35 (2H, s, $-CH_2-$), 2.48 (3H, s, SMe), 3.81 (3H, s, OMe), 3.88 (3H, s, OMe), 5.35 (1H, s, 5-H); ms: m/z 354 (M^+, 38), 339 (100), 322 (10), 307 (12), 279 (13).

Anal. Calcd. for $C_{16}H_{18}O_5S_2$: C, 54.22; H, 5.12; S, 18.09. Found: C, 54.53; N, 5.10; S, 17.77.

4-Oxo-4*H*-indeno-1,2-dithiole-3-thione (**12**).

To a solution of 2.21 g (10 mmoles) of 3-anilinoinden-1-one (**11a**) and a solution of sodium hydroxide (sodium hydroxide 1.60 g, 40 mmoles, water 5 ml) in 30 ml of dimethyl sulfoxide, 2.28 g (30 mmoles) of carbon disulfide was added at below 5° over 20 minutes. After stirring at room temperature for 2 hours, *ca.* 10 ml of 10% hydrochloric acid was added to the reaction mixture with stirring at 0°. The reaction mixture was poured into 200 ml of ice-water and the resulting precipitate was collected by filtration. After drying, the product was recrystallized from methanol to give 1.84 g (7.80 mmoles) of dark violet needles, mp 297-298°, in 78% yield. This compound **11** was also synthesized in 82% yield from 3-(*p*-toluidinoinden-1-one) (**11b**) under same above reaction condition; ir (potassium bromide): ν max cm^{-1} 1700 (CO), 1464, 1425, 1330, 1278, 1075, 980, 902, 804; uv (ethanol): λ max nm 227, 290, 329, 490; min 258, 305, 425; ms: m/z 236 (M^+, 100), 192 (28), 160 (35), 144 (63), 70 (23), 57 (27), 44 (29).

Anal. Calcd. for $C_{10}H_4OS_3$: C, 50.82; H, 1.71; S, 40.70. Found: C, 50.81; H, 1.72; S, 40.67.

Methyl *N*-(3-Oxo-3*H*-1-indenyl)-*N*-phenyldithiocarbamate (**13a**).

To a solution of 2.21 g (10 mmoles) of 3-anilinoinden-1-one (**11a**), 2.28 g (30 mmoles) of carbon disulfide, 1.89 g (15 mmoles) of dimethyl sulfate in 50 ml of dimethyl sulfoxide, a solution of sodium hydroxide (sodium hydroxide 1.60 g, 40 mmoles, water 6 ml) was added at below 5° over 20 minutes. After stirring at room temperature for 4 hours, the reaction mixture was poured into 200 ml of ice-water and the resulting precipitate was collected by filtration. After drying, this compound was recrystallized from methanol to give 1.593 g (5.4 mmoles, 54%) of orange needles, mp 240-241°; ir (potassium bromide): ν max cm^{-1} 1685 (CO); uv (ethanol): λ max nm (log ϵ) 231 (4.39), 267 (4.11), 305 (4.28), 359 (4.43), 430 (3.81); ^{1}H-nmr (deuteriochloroform): δ 2.65 (3H, s, SMe), 6.45 (1H, d, J = 8.0 Hz, 4-H), 7.08-7.68 (9H, m, aromatic-H, 2-H).

Anal. Calcd. for $C_{17}H_{13}NOS_2$: C, 65.57; H, 4.21; N, 4.50; S, 20.59. Found: C, 65.48; H, 4.28; N, 4.35; S, 20.51.

Methyl *N*-(3-Oxo-3*H*-1-indenyl)-*N*-(*p*-toluidino)dithiocarbamate (**13b**).

This compound (1.98 g, 5.81 mmoles) was prepared from 3-(*p*-toluidino)inden-1-one (**1b**) (2.51 g, 10 mmoles) in 58% yield in a manner similar to that described for the preparation of **12a**. An analytical sample was recrystallized from methanol to give orange needles, mp 231-233°; ir (potassium bromide): ν max cm^{-1} 1682 (CO); uv (ethanol): λ max nm (log ϵ) 232 (4.52), 266 (4.19), 274 (4.16), 303 (4.11), 315 (4.13), 368 (4.44), 434 (3.83); ^{1}H-nmr (deuteriochloroform): δ 2.64 (3H, s, SMe), 3.90 (3H, s, OMe), 6.48 (1H, d, J = 8.0 Hz, 4-H), 6.95-7.73 (8H, m, aromatic-H).

Anal. Calcd. for $C_{18}H_{15}NO_2S_2$: C, 63.32; H, 4.43; N, 4.10; S, 18.71. Found: C, 63.27; H, 4.37; N, 4.05; S, 18.78.

Methyl *N*-(*p*-Anisidino)-*N*-(3-oxo-3*H*-2-indenyl)dithiocarbamate (**13c**).

This compound (1.98 g, 5.81 mmoles) was prepared from 3-(*p*-anisidino)inden-1-one (**1c**) (2.51 g, 10 mmoles) in 58% yield in a manner similar to that described for the preparation of **12a**. An analytical sample was recrystallized from methanol to give orange needles, mp 231-233°; ir (potassium bromide): ν max cm^{-1} 1682 (CO); uv (ethanol): λ max nm (log ϵ) 232 (4.52), 266 (4.19), 274 (4.16), 303 (4.11), 315 (4.13), 368 (4.44), 434 (3.83); ^{1}H-nmr (deuteriochloroform): δ 2.64 (3H, s, SMe), 3.90 (3H, s, OMe), 6.48 (1H, J = 8.0 Hz, 4-H), 6.95-7.73 (8H, m, aromatic-H).

Anal. Calcd. for $C_{18}H_{15}NO_2S_2$: C, 63.32; H, 4.43; N, 4.10; S, 18.71. Found: C, 63.27; H, 4.37; N, 4.05; S, 18.78.

Methyl 3-Anilino-3-oxo-3*H*-indene-2-dithiocarboxylate (**15a**).

A mixture of 2.36 g (10 mmoles) of methyl 1,3-dioxoindan-2-dithiocarboxylate (**14**), 1.40 g (15 mmoles) of aniline, and 50 ml of methanol was refluxed 5 hours. After removal of the solvent, the residue was washed with 5 ml of methanol and resulting crystallized product was collected by filtration and recrystallized from methanol to give 2.24 g (7.20 mmoles, 72%) of orange needles, mp 242-244°; ir (potassium bromide): ν max cm^{-1} 3400 (NH), 1681 (CO); uv (ethanol): λ max nm (log ϵ) 231 (4.39), 266 (4.11), 303 (4.26), 315 (4.23), 369 (4.42), 433 (3.77); ^{1}H-nmr (deuteriochloroform): δ 2.67 (3H, s, SMe), 6.46 (1H, d, J = 7.0 Hz, 4-H), 7.14 (1H, dt, J = 1.0, 7.0 Hz, 5-H), 7.34-7.94 (5H, m, aromatic-H), 7.65 (1H, dt, J = 1.0, 7.0 Hz, 6-H), 7.68 (1H, dd, J = 1.0, 7.0 Hz, 7-H), 15.65 (1H, bs, NH).

Anal. Calcd. for $C_{17}H_{13}NOS_2$; C, 65.57; H, 4.21; N, 4.50; S, 20.59. Found: C, 65.26; H, 4.16; N, 4.52; S, 20.20.

Methyl 3-(*p*-Toluidino)-3-oxo-3*H*-indene-2-dithiocarboxylate (**15b**).

This compound (2.24 g, 6.89 mmoles) was prepared from **14** (2.36 g, 10 mmoles) and *p*-toluidine (1.61 g, 15 mmoles) in 69% yield in a manner similar to that described for the preparation of **15a**. An analytical sample was recrystallized from a mixture of methanol and benzene to give orange needles, mp 250-251°; ir (potassium bromide): ν max cm^{-1} 3380 (NH), 1691 (CO); uv (ethanol): λ max nm (log ϵ) 228 (4.51), 250 (4.27, shoulder), 269 (4.31, shoulder), 304 (4.20, shoulder), 315 (4.24), 368 (4.34), 440 (3.70, shoulder); ^{1}H-nmr (deuteriochloroform): δ 2.48 (3H, s, Me), 2.66 (3H, s, SMe), 6.51 (1H, d, J = 7.6 Hz, 4-H), 7.31 (4H, s, phenyl-H), 7.16 (1H, m, 6-H), 7.47 (1H, m, 5-H), 7.67 (1H, d, J = 7.3 Hz, 7-H), 15.23 (1H, bs, NH).

Anal. Calcd. for $C_{18}H_{15}NOS_2$: C, 66.43; H, 4.64; N, 4.26; S, 19.70. Found: C, 66.27; H, 4.57; N, 4.22; S, 19.60.

Methyl 3-*p*-Anisidino-3-oxo-3*H*-indene-2-dithiocarboxylate (**15c**).

This compound (2.22 g, 6.51 mmoles) was prepared from **14** (2.36 g, 10 mmoles) and *p*-anisidine (1.85 g, 15 mmoles) in 65% yield in a manner similar to that described for the preparation of **15a**. An analytical samples was recrystallized from methanol to give orange needles, mp 233-235°; ir (potassium bromide): ν max cm^{-1} 3380, 3260 (NH), 1692 (CO); uv (ethanol): λ max nm (log ϵ) 244 (4.40), 254 (4.40, shoulder), 262 (4.45), 300 (4.01, shoulder), 320 (3.93, shoulder), 386 (4.21), 558 (4.11); ^{1}H-nmr (deuteriochloroform): δ 2.66 (3H, s, SMe), 3.90 (3H, s, OMe), 6.50 (1H, d, J =

7.5 Hz, 4-H), 7.01 (2H, d, J = 8.8 Hz, 2', 4'-H), 7.33 (2H, d, J = 8.8 Hz, 3', 5'-H), 7.16-7.72 (3H, m, aromatic-H), 15.65 (1H, bs, NH).

Anal. Calcd. for $C_{18}H_{15}NO_2S_2$: C, 63.32; H, 4.43; N, 4.10; S, 18.71. Found: C, 63.14; H, 4.41; N, 4.10; S, 18.69.

5,10-Dihydro-10-mercapto-11*H*-indeno[1,2-*b*]quinolin-11-one (**16a**).

A solution of 1.57 g (5.0 mmoles) of **15a** in 200 ml of diphenyl ether was refluxed for 30 minutes. After cooling, 30 ml of petroleum-ether was added to this reaction mixture. The resulting brown precipitate was collected by filtration and washed with petroleum ether. This material was used in the next step without purification, mp 357-360° [lit [24] mp 360°]; ir (potassium bromide): ν max cm^{-1} 3400 (broad, NH or OH), 1690 (CO), 1620, 1545, 1460, 1418, 1254, 750; uv (ethanol: λ max nm 226, 286, 395: λ min 248, 345; ms: m/z 263 (M^+, 100), 219 (20), 190 (10), 170 (15).

11*H*-Indeno[1,2-*b*]quinolin-1-one (**17a**).

A mixture of the above crude **16a**, *ca.* 3 g of Raney-nickel (W-2), and 50 ml of ethanol was refluxed for 20 hours. After removal of the Raney-nickel and solvent, the residue was chromatographed on an alumina column using benzene as an eluent to give 0.89 g (3.85 mmoles, 77%) of pale yellow needles. A pure sample was recrystallized from methanol to give pale yellow needles, mp 181-182° [lit [35] mp 175°]; ir (potassium bromide): ν max cm^{-1} 1712 (CO), 1618, 1508, 762, 728; uv (ethanol): λ max nm (log ϵ) 223 (4.38), 228 (4.39), 243 (4.27), 289 (4.73); ^{1}H-nmr (deuteriochloroform): δ 7.42-7.94 (6H, m, aromatic-H), 8.04-8.19 (2H, m, aromatic-H), 8.39 (1H, s, 10-H); ms: m/z 231 (M^+, 100), 202 (30), 175 (10).

8-Methyl-11*H*-indeno[1,2-*b*]quinolin-11-one (**17b**).

This compound (0.81 g, 3.31 mmoles) was prepared from **15b** (1.63 g, 5.0 mmoles) in 66% yield in a manner similar to that described for the preparation of **17a**. An analytical sample was recrystallized from methanol to give yellow needles, mp 187-188°; ir (potassium bromide): ν max cm^{-1} 1710 (CO), 1618, 1340, 1215, 821, 731; uv (ethanol): λ max nm (log ϵ) 231 (4.36), 245 (4.27), 257 (4.28), 295 (4.73); ^{1}H-nmr (deuteriochloroform): δ 2.54 (3H, s, 8-Me), 7.48 (1H, dt, J = 1.3, 7.3 Hz, 2-H), 7.57-7.77 (2H, m, 3, 7-H), 7.63 (1H, d, J = 0.7 Hz, 9-H), 7.81 (1H, m, 4-H), 8.01 (1H, d, J = 9.0 Hz, 6-H), 8.05 (1H, m, 1-H), 8.28 (1H, d, J = 0.7 Hz, 10-H).

Anal. Calcd. for $C_{17}H_{11}NO$: C, 83.24; H, 4.52; N, 5.71. Found: C, 83.16; H, 4.45; N, 5.57.

8-Methoxy-11*H*-indeno[1,2-*b*]quinolin-11-one (**17c**).

This compound (1.10 g, 3.85 mmoles) was prepared from **15c** (1.71 g, 5.0 mmoles) in 77% yield in a manner similar to that described for the preparation of **17a**. An analytical sample was recrystallized from methanol to give yellow needles, mp 217-219°; ir (potassium bromide): ν max cm^{-1} 1708 (CO), 1615, 1505, 1354, 1236; uv (ethanol): λ max nm (log ϵ) 234 (4.40), 247 (4.35), 259 (4.39), 299 (4.78); ^{1}H-nmr (deuteriochloroform): δ 3.95 (3H, s, OMe), 7.15 (1H, d, J = 2.9 Hz, 9-H), 7.40 (1H, dd, J = 2.9, 9.8 Hz, 7-H), 7.46 (1H, m, 2-H), 7.66 (1H, m, 3-H), 7.81 (1H, m, 4-H), 8.02 (1H, d, J = 9.5 Hz, 6-H), 8.04 (1H, m, 1-H).

Anal. Calcd. for $C_{17}H_{11}NO_2$: C, 78.15; H, 4.24; N, 5.36. Found: C, 78.01; H, 4.23; N, 5.21.

Dimethyl 2-(3-Oxo-1-thioxoindan-2-ylidene)-1,3-dithiole-4,5-dicarboxylate (**18**).

A solution of 2.36 g (10 mmoles) of trithione **12** and 1.50 g (1.06 mmoles) of dimethyl acetylenedicarboxylate in 30 ml of benzene was refluxed for 2 hours. After removal of the solvent, the residue was recrystallized from methanol to give 2.21 g (6.39 mmoles, 64%) of yellow needles, mp 231-233°; ir (potassium bromide): ν max cm^{-1} 1740, 1710, 1680 (CO); uv (ethanol): λ max nm 243, 335, 420, 454; λ min nm 230, 283, 360, 420; ^{1}H-nmr (deuteriochloroform): δ 3.97 (6H, s, OMe), 7.54-7.94 (4H, m, aromatic-H).

Anal. Calcd. for $C_{16}H_{10}O_5S_2$: C, 55.48; H, 2.91; S, 18.51. Found: C, 55.48; H, 2.90; N, 18.50.

1,3-Dimethyl-5-methylthiopyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**20a**).

To a solution of 1.66 g (5.0 mmoles) of **19a** and *ca.* 20% solution of sodium hydroxide (sodium hydroxide: 0.80 g, 20 mmoles, water: 4.5 ml) in 20 ml of dimethyl sulfoxide, stirred at room temperature, 0.76 g (10 mmoles) of carbon disulfide was added in several portions during 30 minutes. After another 4 hours at room temperature under stirring, 2.13 g (15 mmoles) of methyl iodide was slowly added to the stirring solution over a period of 10 minutes and stirring was continued for 2 hours at room temperature. The reaction mixture was poured into 100 ml of ice-water. The precipitate that appeared was collected by filtration and washed several times with water. This crude product was recrystallized from methanol to give 0.26 g (0.91 mmole, 18%) of yellow needles, mp 165-166°; ir (potassium bromide): ν max cm^{-1} 1705, 1655 (CO); uv (ethanol): λ max nm (log ϵ) 220 (4.33), 246 (4.54), 268 (4.54), 322 (3.85); ^{1}H-nmr (deuteriochloroform): δ 2.60 (3H, s, SMe), 3.50 (3H, s, NMe), 3.78 (3H, s, NMe), 7.52 (1H, m, 9-H), 7.78 (1H, m, 8-H), 7.96 (1H, d, J = 8.0 Hz, 10-H), 8.62 (1H, nd, J = 8.0 Hz, 7-H).

Anal. Calcd. for $C_{14}H_{13}N_3O_2S$: C, 58.53; H, 4.56; N, 14.63; S, 11.14. Found: C, 58.39; H, 4.51; N, 14.68; S, 11.14.

1,3,7-Trimethyl-5-methylthiopyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**20b**).

This compound (0.377 g, 1.25 mmoles) was prepared from **19b** (1.23 g, 5.0 mmoles) in 25% yield in a manner similar to that described for the preparation of **20a**. An analytical sample was recrystallized from methanol to give yellow needles, mp 230-231°, ir (potassium bromide): ν max cm^{-1} 1705, 1660 (CO); uv (ethanol): λ max nm (log ϵ) 226 (4.29), 254 (4.55), 270 (4.58), 324 (3.80); ^{1}H-nmr (deuteriochloroform): δ 2.52 (3H, d, J = 1.0 Hz, 7-Me), 2.57 (3H, s, SMe), 3.49 (3H, s, NMe), 3.74 (3H, s, NMe), 7.58 (1H, dd, J = 1.5, 8.1 Hz, 8-H), 7.81 (1H, d, J = 8.1 Hz, 9-H), 8.39 (1H, d, J = 1.5 Hz, 6-H).

Anal. Calcd. for $C_{15}H_{15}N_3O_2S$: C, 59.79; H, 5.02; N, 13.95; S, 10.62. Found: C, 59.75; H, 4.99; N, 13.90; S, 10.88.

1,3-Dimethyl-7-methoxy-5-methylthiopyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**20c**).

This compound (0.491 g, 1.55 mmoles) was prepared from **19c** (1.31 g, 5.0 mmoles) in 31% yield in a manner similar to that described for the preparation of **20a**. An analytical sample was recrystallized from methanol to give yellow needles, mp 211-212°, ir (potassium bromide): ν max cm^{-1} 1705, 1660 (CO); uv (ethanol): λ max nm (log ϵ) 224 (4.32), 268 (4.67), 317 (3.71), 406 (3.71); ^{1}H-nmr (deuteriochloroform): δ 2.58 (3H, s, SMe), 3.48 (3H, s, NMe), 3.76 (3H, s, NMe), 3.96 (3H, s, OMe), 7.44 (1H, dd, J = 1.5, 8.0 Hz, 8-H), 7.85 (1H, d, J = 8.0 Hz, 9-H), 7.91 (1H, d, J = 1.5 Hz, 6-H).

Anal. Calcd. for $C_{15}H_{15}N_3O_3S$: C, 56.78; H, 4.77; N, 13.24; S, 10.00. Found: C, 56.69; H, 4.72; N, 13.24; S, 10.04.

1,3-Dimethyl-8-methoxy-5-methylthiopyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**20d**).

This compound (0.71 g, 2.30 mmoles) was prepared from **19d** (1.31 g, 5.0 mmoles) in 46% yield in a manner similar to that described for the preparation of **20a**. An analytical sample was recrystallized from methanol to give yellow needles, mp 217-218°, ir (potassium bromide): ν max cm^{-1} 1700, 1655 (CO); uv (ethanol): λ max nm (log ϵ) 270 (4.65), 355 (4.22); ^{1}H-nmr (deuteriochloroform): δ 2.59 (3H, s, SMe), 3.50 (3H, s, NMe), 3.78 (3H, s, NMe), 3.99 (3H, s, OMe), 7.19 (1H, dd, J = 1.5, 8.1 Hz, 7-H), 7.30 (1H, d, J = 1.5 Hz, 9-H), 8.61 (1H, d, J = 8.1 Hz, 6-H).

Anal. Calcd. for $C_{15}H_{15}N_3O_3S$: C, 56.78; H, 4.77; N, 13.24; S, 10.00. Found: C, 56.79; H, 4.76; N, 13.21; S, 9.98.

1,3-Dimethyl-9-methoxy-5-methylthiopyrimido[4,5-*b*]quinoline-2,4-(1*H*,3*H*)-dione (**20e**).

This compound (0.082 g, 0.26 mmole) was prepared from **19e** (0.261 g, 0.10 mmole) in 26% yield in a manner similar to that described for the preparation of **20a**. An analytical sample was recrystallized from methanol to give yellow needles, mp 183-184°, ir (potassium bromide): ν max cm^{-1} 1706, 1650 (CO); uv (ethanol): λ max nm (log ϵ) 230 (4.34), 248 (4.39), 283 (4.63), 324 (3.78), 400 (3.67); ^{1}H-nmr (deuteriochloroform): δ 2.61 (3H, s, SMe), 3.53 (3H, s, NMe), 3.85 (3H, s, NMe), 4.07 (3H, s, OMe), 7.09 (1H, d, J = 8.0 Hz, 8-H), 7.49 (1H, t, J = 8.0 Hz, 7-H), 8.23 (1H, d, J = 8.0 Hz, 6-H).

Anal. Calcd. for $C_{15}H_{15}N_3O_3S$: C, 56.78; H, 4.77; N, 13.24; S, 10.00. Found: C, 56.61; H, 4.78; N, 13.24; S, 10.00.

5,7-Dimethyl-1,2-dithiolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (**21**).

To a solution of 1.66 g (5.0 mmoles) of **19a** and *ca.* 20% solution of sodium hydroxide (sodium hydroxide: 1.60 g, 40 mmoles, water: 9.0 ml) in 30 ml of dimethyl sulfoxide stirring at room temperature, 1.52 g (20 mmoles) of carbon disulfide was added in several portions during 30 minutes. After another 4 hours at room temperature under stirring, 20 ml of 10% hydrochloric acid was slowly added to the stirring solution over a period of 10 minutes and stirring was continued for 2 hours at room temperature. The reaction mixture was poured into 100 ml of ice-water. The precipitate that appeared was collected by filtration and washed several times with water. This crude product was recrystallized from methanol to give 0.369 g (1.5 mmoles, 30%) of yellow needles, mp 231-233°; ir (potassium bromide): ν max cm^{-1} 1708, 1665 (CO); uv (ethanol): λ max nm (log ϵ) 235 (4.10), 291 (4.32), 398 (3.75); ^{1}H-nmr (deuteriochloroform): δ 3.54 (3H, s, NMe), 3.85 (3H, s, NMe).

Anal. Calcd. for $C_7H_6N_2O_2S_3$: C, 34.13; H, 2.46; N, 11.38; S, 39.05. Found: C, 34.05; H, 2.42; N, 11.35; S, 39.01.

Methyl 4-Anilino-1,3-dimethyluracil-5-dithiocarboxylate (**22**) and Methyl *N*-Phenyl-*N*-(1,3-dimethyluracil-4-yl)dithiocarbamate (**23**).

To a solution of 2.31 g (10 mmoles) of 4-anilino-1,3-dimethyluracil (**19a**), 2.28 g (30 mmoles) of carbon disulfide, and 1.89 g (15 mmoles) of dimethyl sulfate in 50 ml of dimethyl sulfoxide, a solution of sodium hydroxide (sodium hydroxide: 1.60 g, 40 mmoles, water: 6 ml) was added at below 5° over 20 minutes. After stirring at room temperature for 4 hours, the reaction mixture was poured into 200 ml of ice-water and the resulting precipitates which are a mixture of **22** and **23** was collected by filtration. After drying, this compound was recrystallized from methanol to give 1.05 g (33%) of pale yellow needles of **23**. After evaporation of the mother liquid, the residue was recrystallized from methanol to give 0.3 g (0.57 mmole, 6%) of the colorless needles of **23**. The filtrate was extracted by 50 ml of dichloromethane. After removal of solvent, the residue was recrystallized from methanol to give 0.75 g (2.15 mmoles, 22%) of **22**.

Compound **22**.

This compound was obtained as yellow needles, mp 220-222°; ir (potassium bromide): ν max cm^{-1} 1708, 1645 (CO); uv (ethanol): λ max nm (log ϵ) 295 (4.24), 364 (4.03); ^{1}H-nmr (deuteriochloroform): δ 2.58 (3H, s, SMe), 3.10 (3H, s, NMe), 6.96-7.48 (5H, m, phenyl-H), 14.08 (1H, bs, NH).

Anal. Calcd. for $C_{14}H_{15}N_3O_2S_2$: C, 52.33; H, 4.71; N, 13.05; S, 19.92. Found: C, 51.27; H, 4.77; N, 13.20; S, 20.22.

Compound **23**.

This compound was obtained as colorless prisms, mp 170-172°; ir (potassium bromide): ν max cm^{-1} 1695, 1660 (CO); uv (ethanol): λ max nm (log ϵ) 288 (4.24); ^{1}H-nmr (deuteriochloroform): δ 2.58 (3H, s, SMe), 3.31 (3H, s, NMe), 3.46 (3H, s, NMe), 5.78 (1H, s, 5-H), 7.28-7.52 (5H, m, phenyl-H).

Anal. Calcd. for $C_{14}H_{15}N_3O_2S_2$: C, 52.33; H, 4.71; N, 13.05; S, 19.92. Found: C, 52.32; H, 4.67; N, 13.20; S, 20.11.

5-Mercapto-1,3-dimethylpyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**24**).

This compound (0.26 g, 0.095 mmole) was prepared from **22** (0.32 g, 1.0 mmole) in 95% yield in a manner similar to that described for the preparation of **7a**. An analytical sample was recrystallized from methanol to give yellow needles, mp 226-228°; ir (potassium bromide): ν max cm^{-1} 1695, 1620 (CO), 1562, 1460, 1285; uv (ethanol): λ max nm (log ϵ) 238 (4.51), 251 (4.54), 266 (4.56), 323 (3.95), 395 (3.84); ms: m/z 273 (M^+, 20), 258 (30), 256 (100), 241 (15), 192 (30).

Anal. Calcd. for $C_{13}H_{11}N_3O_2S$: C, 57.13; H, 4.06; N, 15.37; S, 11.73. Found: C, 56.97; H, 3.95; N, 15.45; S, 11.68.

1,3-Dimethylpyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**25a**).

This compound (0.187 g, 0.78 mmole) was prepared from **20a** (0.287 g, 1.0 mmole) in 78% yield in a manner similar to that described for the preparation of **17a**. An analytical sample was recrystallized from methanol to give colorless needles, mp 196-197° [lit [28] mp 212°]; ir (potassium bromide): ν max cm^{-1} 1705, 1650 (CO); uv (ethanol): λ max nm (log ϵ) 220 (4.47), 242 (4.67), 254 (4.57), 300 (3.88), 310 (3.91), 360 (3.46); ^{1}H-nmr (deuteriochloroform): δ 3.52 (3H, s, NMe), 3.82 (3H, s, NMe), 7.56 (1H, m, 7 or 8-H), 7.56 (1H, m, 8 or 7-H), 7.99 (1H, d, J = 8.0 Hz, 6 or 9-H), 8.08 (1H, d, J = 8.0 Hz, 9 or 6-H), 9.08 (1H, s, 5-H).

1,3,7-Trimethylpyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**25b**).

This compound (0.183 g, 0.72 mmole) was prepared from **20b** (0.287 g, 1.0 mmole) in 72% yield in a manner similar to that described for the preparation of **17a**. An analytical sample was recrystallized from methanol to give colorless needles, mp 229-230° [lit [28] mp 224°]; ir (potassium bromide): ν max cm^{-1} 1700, 1655 (CO); uv (ethanol): λ max nm (log ϵ) 225 (4.32), 246 (4.56), 276 (4.66), 310 (3.77), 368 (3.57); ^{1}H-nmr (deuteriochloroform): δ 2.51 (3H, s, 7-Me), 3.50 (3H, s, NMe), 3.80 (3H, s, NMe), 7.68 (1H, dd, J = 1.5, 9.0 Hz, 8-H), 7.74 (1H, s, 7-H), 7.96 (1H, d, J

= 9.0 Hz, 9-H), 9.02 (1H, s, 5-H).

1,3-Dimethyl-7-methoxypyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**25c**).

This compound (0.211 g, 0.78 mmole) was prepared from **20c** (0.287 g, 1.0 mmole) in 78% yield in a manner similar to that described for the preparation of **17a**. An analytical sample was recrystallized from methanol to give colorless needles, mp 213-214° [lit [30] mp 211°]; ir (potassium bromide): ν max cm^{-1} 1705, 1650 (CO).

1,3-Dimethyl-8-methoxypyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**25d**).

This compound (0.19 g, 0.70 mmole) was prepared from **20d** (0.317 g, 5.0 mmoles) and in 70% yield in a manner similar to that described for the preparation of **17a**. An analytical sample was recrystallized from methanol to give colorless needles, mp 252-254° [lit [28] mp 258°]; ir (potassium bromide): ν max cm^{-1} 1700, 1655 (CO); uv (ethanol): λ max nm (log ϵ) 234 (4.59), 244 (4.64), 258 (4.67), 350 (4.15); ^{1}H-nmr (deuteriochloroform): δ 3.48 (3H, s, NMe), 3.79 (3H, s, NMe), 3.97 (3H, s, OMe), 7.17 (1H, dd, J = 1.5, 9.0 Hz, 7-H), 7.32 (1H, d, J = 1.5 Hz, 9-H), 7.86 (1H, d, J = 9.0 Hz, 6-H).

1,3-Dimethyl-9-methoxypyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**25e**).

This compound (0.15 g, 0.52 mmole) was prepared from **20e** (0.287 g, 1.0 mmole) in 52% yield in a manner similar to that described for the preparation of **17a**. An analytical sample was recrystallized from methanol to give colorless needles, mp 213-214°; ir (potassium bromide): ν max cm^{-1} 1705, 1660 (CO); uv (ethanol): λ max nm (log ϵ) 220 (4.41), 244 (4.42), 278 (4.64), 320 (3.76), 380 (3.31).

Anal. Calcd. for $C_{14}H_{13}N_3O_3$: C, 61.98; H, 4.83; N, 15.49. Found: C, 61.63; H, 4.81; N, 15.42.

5-Hydroxy-1,3-dimethylpyrido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**26a**).

A solution of 0.287 g (1.0 mmole) of **20a**, 3 ml of 30% hydrogen peroxide in 15 ml of acetic acid was heated 70° for 3 hour. After evaporation of the solvent, the residue was washed with 3 ml of water, the product was dried in air and recrystallized from a mixture of benzene and methanol to give 0.162 g (0.63 mmole, 63%) of colorless needles, mp 204-205°; ir (potassium bromide): ν max cm^{-1} 1730-1670 (CO, broad); uv (ethanol): λ max nm 272, 259, 271, 291, 303, 350; λ min nm 274, 269, 286, 298, 320; ^{1}H-nmr (deuteriochloroform): δ 3.46 (3H, s, NMe), 3.72 (3H, s, NMe), 7.36-7.56 (1H, m, aromatic-H), 7.78-7.88 (2H, m, aromatic-H), 8.26 (1H, d, J = 8.0 Hz, 6-H), 11.86 (1H, s, OH).

Anal. Calcd. for $C_{13}H_{11}N3O_3$: C, 60.69; H, 4.31; N, 16.34. Found: C, 60.30; H, 4.16; N, 16.11.

5-Hydroxy-1,3-dimethyl-9-methoxypyrido[4,5-*b*]quinoline-2,4-(1*H*,3*H*)-dione (**26b**).

This compound (0.71 g, 2.62 mmoles) was prepared from **20e** (1.58 g, 5.0 mmoles) in 52% yield in a manner similar to that described for the preparation of **26a**. An analytical sample was recrystallized from methanol to give colorless needles, mp 213-214°; ir (potassium bromide): ν max cm^{-1} 1705, 1660 (CO); uv (ethanol): λ max nm (log ϵ) 220 (4.41), 244 (4.42), 278 (4.64), 320 (3.76), 380 (3.31).

Anal. Calcd. for $C_{14}H_{13}N_3O_3$: C, 61.98; H, 4.83; N, 15.49. Found: C, 61.63; H, 4.81; N, 15.42.

5-Benzylamino-1,3-dimethylpyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**27a**).

A mixture of 0.287 g (1.0 mmole) of **20a** and 0.154 g (1.5 mmoles) of benzylamine was heated at 150° for 30 minutes. After cooling, the crude product was recrystallized form methanol to give 0.218 g (0.63 g, 63%) of colorless needles, mp 237-238°; ir (potassium bromide): ν max cm^{-1} 3040 (NH), 1680, 1630 (CO); uv (ethanol): λ max nm: 246, 257, 305, 315, 368, 386; λ min nm 217, 252, 296, 312, 330, 278.

Anal. Calcd. for $C_{20}H_{18}N_4O_2$: C, 69.35; H, 5.24; N, 16.18. Found: C, 69.81; H, 5.19; N, 16.06.

1,3-Dimethyl-5-morpholinopyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**27b**).

This compound (0.63 g, 0.50 mmole) was prepared from **20a** (0.287 g, 1.0 mmole) and morpholine (0.15 g, 1.5 mmoles) in 50% yield in a manner similar to that described for the preparation of **27a**. An analytical sample was recrystallized from methanol to give colorless needles, mp 197-198°; ir (potassium bromide): ν max cm^{-1} 1705, 1655 (CO); uv (ethanol): λ max nm (log ϵ) 241 (4.56), 266 (4.46), 312 (3.68), 340 (3.64), 390 (3.71).

Anal. Calcd. for $C_{17}H_{18}N_4O_3$: C, 62.56; H, 5.56; N, 17.18. Found: C, 62.18; H, 5.56; N, 16.95.

1,3-Dimethyl-5-piperidinopyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (**27c**).

This compound (0.139 g, 0.43 mmole) was prepared from **20a** (0.287 g, 1.0 mmole) and morpholine (0.128 g, 1.5 mmoles) in 43% yield in a manner similar to that described for the preparation of **27a**. An analytical sample was recrystallized from methanol to give colorless needles, mp 241-242°; ir (potassium bromide): ν max cm^{-1} 1703, 1655 (CO); uv (ethanol): λ max nm (log ϵ) 240 (4.56), 264 (4.40), 275 (4.38), 340 (3.59), 400 (3.87).

Anal. Calcd. for $C_{18}H_{20}N_4O_2$: C, 66.65; H, 6.22; N, 17.27. Found: C, 66.27; H, 6.15; N, 17.23.

Ethyl α-Benzoyl-1,3-dimethyl-2,4-dioxo-2*H*,4*H*-pyrimido[4,5-*b*]-quinoline-5-acetate (**28a**).

A mixture of 0.287 g (1.0 mmole) of **20a**, 0.23 g, (1.2 mmoles) of ethyl benzoylacetate, 0.276 g (2.0 mmoles) of potassium carbonate, and 20 ml of dimethyl sulfoxide was heated at 100° for 1 hour. After cooling, the reaction mixture was poured into 100 ml of ice-water and acidified with 10% hydrochloric acid. The resulting precipitate was collected by filtration and recrystallized from ethanol to give 0.156 g (0.36 mmole, 36%) of yellow needles, mp 348-353°; ir (potassium bromide): ν max cm^{-1} 3400 (OH), 1705 (CO), 1650, 1625 (CO); uv (etahnol, insufficient solubility): λ max nm 245, 305, 370; min nm 280, 345; ^{1}H-nmr (deuteriochloroform): δ 1.03 (3H, t, J = 7.0 Hz, O-CH_2-CH_3), 3.47 (3H, s, NMe), 3.84 (3H, s, NMe), 4.15 (2H, q, J = 7.0 Hz, O-CH_2-), 6.97-7.94 (9H, m, 6, 7, 8, 9-H, phenyl-H), 10.10 (1H, s, CH).

Anal. Calcd. for $C_{24}H_{21}N_3O_5$: C, 66.81; H, 4.91; N, 9.74. Found: C, 66.80; H, 4.86; N, 9.66.

Methyl α-Cyano-1,3-dimethyl-2,4-dioxo-2*H*,4*H*-pyrimido[4,5-*b*]-quinoline-5-acetate (**28b**).

This compound (0.226 g, 0.669 mmole) was prepared from **20a** (0.287 g, 1.0 mmole) and methyl cyanoacetate (0.149 g, 1.5 mmoles) in 67% yield in a manner similar to that described for the preparation of **28a**. An analytical sample was recrystallized

from methanol to give yellow needles, mp 207-209°; ir (potassium bromide): ν max cm^{-1} 3200 (NH), 1700, 1620 (CO); uv (ethanol): λ max nm (log ϵ) 280 (4.37); ^{1}H-nmr (deuteriochloroform): δ 3.54 (3H, s, NMe), 3.84 (3H, s, NMe or OMe), 3.87 (3H, s, NMe or OMe), 7.26 (1H, s, CH), 7.61-8.17 (4H, m, 6, 7, 8, 9-H).

Anal. Calcd. for $C_{17}H_{14}N_4O_4$: C, 60.35; H, 4.17; N, 16.56. Found: C, 60.11; H, 4.08; N, 16.75.

α-Benzoyl-α-(1,3-dimethyl-2,4-dioxo-2*H*,4*H*-pyrimido[4,5-*b*]quinolin-5-yl)acetone (**28c**).

This compound (0.60 g, 0.15 mmole) was prepared from **20a** (0.287 g, 1.0 mmole) and benzoylacetone (0.243 g, 1.5 mmoles) in 15% yield in a manner similar to that described for the preparation of **28a**. An analytical sample was recrystallized from methanol to give yellow needles, mp 211-213°; ir (potassium bromide): ν max cm^{-1} 1700, 1650 (CO); uv (ethanol, insufficient solubility): λ max nm 246, 310; λ min nm 227, 280; ^{1}H-nmr (deuteriochloroform): δ 3.24 (3H, s, CO-Me), 3.48 (3H, s, NMe), 3.80 (3H, s, NMe), 5.61 (1H, s, CH), 7.38-8.22 (9H, m, 6, 7, 8, 9-H, phenyl-H).

Anal. Calcd. for $C_{23}H_{19}N_3O_4$: C, 68.82; H, 4.77; N, 10.47. Found: C, 68.79; H, 4.76; N, 10.33.

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