Practical Synthesis of Iminochlorothioformates: Application of Iminochlorothioformates in the Synthesis of Novel 2,3,4,9-Tetrahydroisothiazolo[5,4-*b*][1,8]naphthyridine-3,4-diones and 2,3,4,9-Tetrahydroisothiazolo[5,4-*b*]quinoline-3,4-dione Derivatives

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The synthesis of 6-fluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*][1,8]naphthyridine-3,4-dione and 6,8-difluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*]quinoline-3,4-dione are described. The key step includes the one-pot formation of 2-phenylthio derivatives of 1,4-dihydro-4-oxo[1,8]naphthyridine-3-carboxylic acid ester (**18a**) and its corresponding quinoline derivative **18b** by condensation of a β-ketoester with phenyl iminochlorothioformate. A simple and practical synthesis of iminochlorothioformates utilizing isothiocyanates and mercaptans is also described.

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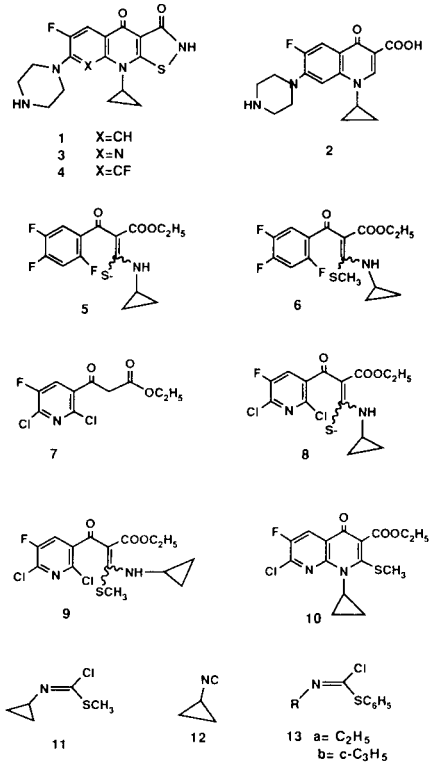
Recently, we discovered that 6-fluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*]quinoline-3,4-dione (**1**) [1] possesses antibacterial activity 4 to 10 times more potent that ciprofloxacin (**2**) [2], a clinically useful antimicrobial agent. The chemical synthesis of **1** has been recently disclosed [3]. As a continuation on research for better antibacterial agents and based upon known structure-activity-relationship established in the quinolone antibacterial research area, we investigated the chemical syntheses of 6-fluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4,9-tetrahydrothiazolo[5,4-*b*][1,8]naphthyridine-3,4-dione (**3**) and 6,8-difluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4-9-tetrahydro[5,4-*b*]quinoline-3,4-dione (**4**). Compound **3** is a bioisostere of the potent antibacterial **1**. Compound **4** is a C_8-fluoro substituted derivative of **1** and C_8-fluoro substituted quinolone analogs are known to improve the *in vivo* efficacy over their parent quinolones. In this paper, we wish to report a practical synthesis of iminochlorothioformates and their application in the synthesis of **3** and **4**.

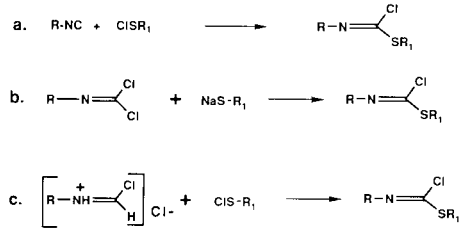
The previously reported synthesis of **1** involved the condensation of ethyl 2,4,5-trifluorobenzoylacetate with cyclopropyl isothiocyanate in the presence of one molar equivalent of sodium hydride to produce the intermediate **5** which, without isolation, was transformed to the desired compound **6** by alkylation of methyl iodide [3]. Similar condensation of ethyl 2,6-dichloro-5-fluoronicotinyl acetate (**7**) [4] with cyclopropyl isothiocyanate followed by alkylation of the intermediate **8** with methyl iodide, however, gave the desired compound **9** in extremely low yield. A substantial amount of side product was formed from an intramolecular displacement of the C_2 chlorine atom of **8** by its thiolate anion. It was apparent that the C_2-chlorine atom in the intermediate **8** was much more labile and susceptible to nucleophilic displacement than the C_2-fluorine atom in **5**. Repeated experimentation did not improve the yield of **9**. Although **9** can lead to the key intermediate **10**, because of the low yield of the above reaction, it became apparent that an alternate methodology to generate **9** or similar analogs was required. Our synthetic strategy required a synthetic route utilizing the β-ketoester **7** as starting material since it is readily available in our laboratories. To avoid the presence of a thiolate anion, our alternate approach may require the condensation of **7** with an iminochlorothioformate **11** to yield **9**.



Iminochlorothioformates are generally prepared by three well established routes [5] as outlined in Scheme I. The first method (a) requires the addition of sulfenyl chlorides to isocyanides. The second approach (b) involves the

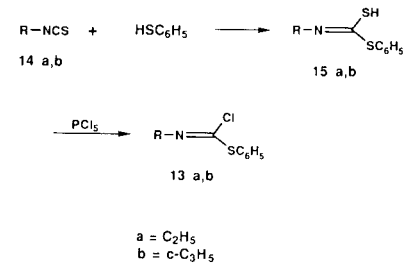
displacement reaction in which the chlorine atom of an isocyanodichloride (phosgeneimine) is displaced by a thiolate anion [6]. In the third route (c), iminochlorothioformates are prepared by reacting formamides with thionyl chloride to yield the imidoyl chloride which was reacted with a sulfenyl chloride. Isocyanides are known to possess malodorous property [7]. The required cyclopropyl isocyanide (**12**) may be prepared by triethyl phosphite or trisubstituted phosphine reduction of isocyanate or isothiocyanate. However, these methods are expected to give poor yield since the elevated temperature involved tends to result in subsequent isocyanide → nitrile rearrangement [8,9]. The route (b) is limited to the preparation of aromatic phosgeneimines yielding *N*-aryl instead of *N*-alkyliminochlorothioformates. Although route (c) can provide both *N*-aryl or *N*-alkyliminochlorothioformate, the yield for *N*-alkyliminochlorothioformate is generally low. For example, the reported yield for phenyl *N*-ethyliminochlorothioformate **13a** prepared by this route was 21% [5]. These limitations precluded our use of the above approaches to synthesize the required *N*-cyclopropyliminochlorothioformate.

Scheme I



In searching for a practical synthesis of iminochlorothioformates, we discovered that they can be prepared conveniently by a two step synthetic sequence exemplified by the synthesis of phenyl iminochlorothioformates outlined in Scheme II. If necessary, the reactions may be carried out in an one-pot procedure.

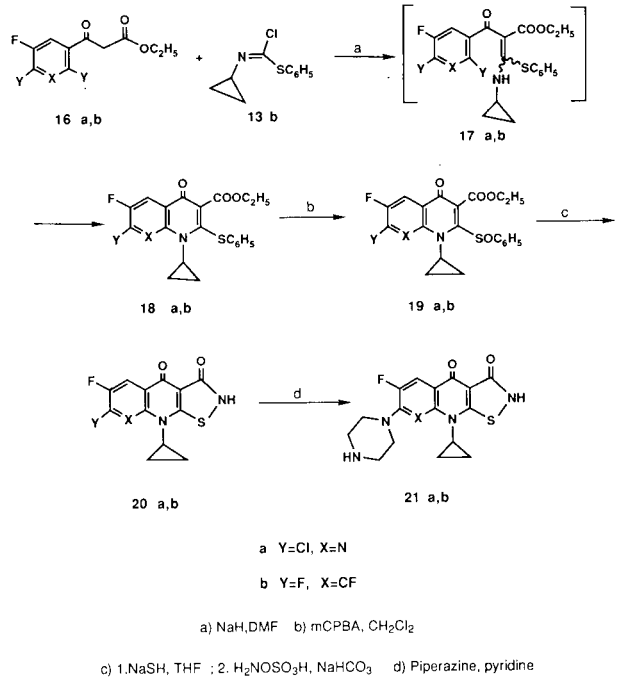
Scheme II



Reaction of ethyl isothiocyanate (**14a**) with thiophenol yielded the phenyl *N*-ethyliminomercaptothioformate (**15a**). Compound **15a** was found to be unstable towards distillation. Without purification, **15a** was allowed to react with phosphorous pentachloride to give phenyl *N*-ethyliminochlorothioformate (**13a**) (bp 68°/0.2 mm Hg) in an overall yield of 52%. Addition of thiophenol to cyclopropylisothiocyanate (**14b**) yielded phenyl *N*-cyclopropyliminomercaptothioformate (**15b**) (mp 67-68°, 93%). Treatment of **15b** with phosphorus pentachloride gave the desired phenyl *N*-cyclopropyliminochlorothioformate (**13b**) (bp 75-80°/0.2 mm Hg, 82%). In addition to simplicity and convenience, the above preparative procedure for iminochlorothioformates utilizes readily available isothiocyanates and mercaptans and provides the desired product in high yield.

With the discovery of this facile synthesis of iminochlorothioformates, we explored the application of phenyl *N*-cyclopropyliminochlorothioformate (**13b**) for the syntheses of **3** and **4** as outlined in Scheme III.

Scheme III



Treatment of ethyl 2,6-dichloro-5-fluoronicotinylacetate (**16a**) [4] with one molar equivalent of sodium hydride in xylene and phenyl *N*-cyclopropyliminochlorothioformate (**13b**) at 20° and then at high temperatures yielded the ethyl 1-cyclopropyl-2-phenylthio-6-fluoro-7-chloro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate (**18a**) (mp 170°, 51%) in one chemical step with compound **17a** as a possible intermediate. Similar treatment of ethyl 2,3,4,5-tetrafluorobenzoylacetate (**16b**) [10] gave ethyl 1-cyclopropyl-2-phenylthio-6,7,8-trifluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate (**18b**) (mp 135-137°, 42%).

Oxidation of the 3-carboxylic acid ester **18a** and **18b** with *m*-chloroperoxybenzoic acid (m-CPBA) in methylene chloride at room temperature yielded ethyl 1-cyclopropyl-2-phenylsulfinyl-6-fluoro-7-chloro-1,4-dihydro-4-oxo-1,8-

naphthyridine-3-carboxylate (**19a**) (mp 188-189°, 83%) or ethyl 1-cyclopropyl-2-phenylsulfinyl-6,7,8-trifluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate (**19b**) (mp 189.5°, 78%). Regiospecific displacement of the sulfinyl group of the sulfoxide **19a** with freshly opened sodium hydrosulfide in aqueous tetrahydrofuran (THF) yielded a 2-mercapto intermediate which, without purification, was allowed to react with hydroxylamine-*O*-sulfonic acid in the presence of sodium bicarbonate at room temperature to give a hydrosulfamine derivative which was cyclized *in situ* to yield the desired heterocycle 6-fluoro-7-chloro-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*][1,8]naphthyridine-3,4-dione (**20a**) (mp >250°, 71%). Similar treatment of **19b** with sodium hydrosulfide and hydroxylamine-*O*-sulfonic acid yielded the 6,7,8-trifluoro-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*]quinoline-3,4-dione (**20b**) (mp 243-245°, 67%).

Displacement of **20a** with an excess of piperazine in pyridine at 60° yielded 6-fluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*][1,8]naphthyridine-3,4-dione (**3**) (mp >250°, 98%). Treatment of **20b** with piperazine in pyridine produced the 6,8-difluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo-[5,4-*b*]quinoline-3,4-dione (**4**) (mp >250°, 74%). Both **3** and **4** were found to possess antibacterial activity more potent than ciprofloxacin (**2**). The biological activities of these compounds will be reported elsewhere.

In summary, we have discovered a practical synthesis of iminochlorothioformate as well as an efficient route to 2,3,4,9-tetrahydroisothiazolo[5,4-*b*][1,8]naphthyridine-3,4-dione and 2,3,4,9-tetrahydroisothiazolo[5,4-*b*]quinoline-3,4-dione systems.

EXPERIMENTAL

Melting points were taken in a Thomas-Hoover capillary apparatus and are uncorrected. Elemental analyses were performed by the Abbott analytical department. The nmr spectra were obtained on a General Electric QE 300 spectrometer using tetramethylsilane as an internal standard. The nmr peaks were designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiple; dq, double quartet; b, broad. Mass spectra were recorded on a Kratos MS-50 mass spectrometer at Abbott Laboratories. The ir spectra were recorded on a Perkin-Elmer Model 710 A infrared spectrometer. The ir, nmr, and ms data of all compounds were consistent with the assigned structures. Solutions were dried over magnesium sulphate. E. Merck silica gel (230-400 mesh) obtained from VWR Scientific was used for column chromatography and yields of the reactions were not optimized.

Phenyl *N*-Ethyliminochlorothioformate (**13a**).

To a solution of thiophenol (63.2 g, 574 mmoles) in carbon tetrachloride (500 ml), ethyl isothiocyanate (50 g, 574 mmoles) was added in dropwise. The reaction mixture was allowed to stand overnight at ambient temperature. The solvent was removed by distillation under reduced pressure. The residual liquid was mixed with 116 g of phosphorus pentachloride at ambient temperature and stirred until a liquid results. It was heated at 60° for 2 hours and the hydrogen chloride and thiophosphoryl chloride byproducts were removed *in vacuo*. The residual liquid was distilled to give 60.5 g (52%) of phenyl *N*-ethyliminochlorothioformate as a yellowish oil, bp 68° (0.2 mm Hg) (Lit bp 151-158° at 30 mm Hg [5]); ^{1}H nmr (deuteriochloroform): δ 1.15 (t, J = 7 Hz, 3, ethyl CH_3), 3.50 (q, J = 7 Hz, 2, ethyl CH_2), 7.40 (m, 5, aromatic H).

Cyclopropyl Isothiocyanate (**14b**).

Carbon disulfide (61 ml, 1.01 moles) was added to a solution of 40 g (1 mole) of sodium hydroxide in 90 ml of water at 10°. After stirring this solution for 10 minutes at 10°, 57 g (1 mole) of cyclopropylamine was added dropwise over a 30 minute period. The reaction mixture was heated at 60° for 1 hour and then was allowed to cool to ambient temperature. To the reaction mixture was added 98 ml (1 mole) of ethyl chloroformate portionwise over 1 hour. During the addition gas evolution has observed and heat was produced. After the addition was complete, the reaction mixture was heated at 55° for 1 additional hour until evolution of gas ceased. The reaction mixture was dried and concentrated under reduced pressure and the crude product was distilled to give 56.8 g (57%) of *N*-cyclopropyl isothiocyanate (**14b**), mp 80-88°/68 mm Hg; ^{1}H nmr (deuteriochloroform): δ 0.87 (m, 2, CH_2), 0.93 (m, 2, CH_2), 2.91 (m, 1, CH).

Phenyl *N*-Cyclopropyliminomercaptothioformate (**15b**).

Cyclopropylisothiocyanate (**14b**) (40.9 g, 410 mmoles) and thiophenol (42.3 ml, 412 mmoles) were mixed together in an ice bath. After 20 minutes, the mixture became a white solid. It was broken up and washed with hexane to give 80 g (93%) of phenyl *N*-cyclopropyliminomercaptothioformate (**15b**), mp 67-68°. (It should be mentioned that in a particular run, one drop of triethylamine was required to initiate the reaction.); ^{1}H nmr (deuteriochloroform): δ 0.49 (m, 2, CH_2), 0.85 (m, 2, CH_2), 3.12 (m, 1, CH), 6.58 (bs, 1, SH), 7.53 (m, 5, aromatic H).

Phenyl *N*-Cyclopropyliminochlorothioformate (**13b**).

Phenyl *N*-cyclopropyliminomercaptothioformate (**15b**) (105.9 g, 506 mmoles) and 105 g (505 mmoles) of phosphorus pentachloride were combined at ambient temperature and stirred. The reaction mixture was then heated at 65° for 6 hours. The hydrogen chloride and thiophosphoryl chloride byproducts were removed *in vacuo* and the residual liquid was distilled to give 88 g (82%) of phenyl *N*-cyclopropyliminochlorothioformate (**13b**) as a yellowish oil (bp 75-80°/0.2 mm Hg); ^{1}H nmr (deuteriochloroform): δ 0.75 (m, 2, CH_2), 0.83 (m, 2, CH_2), 3.27 (m, 1, CH), 7.36 (m, 3, aromatic H), 7.52 (m, 2, aromatic H).

Ethyl 1-Cyclopropyl-2-phenylthio-6-fluoro-7-chloro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate (**18a**).

To a solution of 9.41 g (33.6 mmoles) of ethyl 2,6-dichloro-5-fluoronicotinylacetate [4] in 200 ml of xylene at room temperature under nitrogen atmosphere was added 1.47 g of 60% sodium hydride in mineral oil. After 20 minutes, 10.7 g (50.4 mmoles) of phenyl *N*-cyclopropyliminochlorothioformate (**13b**) was added. The reaction mixture was heated at 50° for 4 hours and then at 125° for 20 hours. The solvent was removed *in vacuo* and the residue was dissolved in methylene chloride. The methylene chloride solution was washed with water, dried over anhydrous magnesium sulfate and concentrated *in vacuo*. Purification through

silica gel column using 4% ethyl acetate in methylene chloride as eluent yielded 7.51 g (51%) of ethyl 1-cyclopropyl-2-phenylthio-6-fluoro-7-chloro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate (**18a**), mp 170°; ^{1}H nmr (deuteriochloroform): δ 1.04 (m, 2, CH_2), 1.33 (t, J = 7 Hz, 3 ethyl CH_3), 1.38 (m, 2, CH_2), 2.62 (m, 1, CH), 4.32 (q, J = 7 Hz, 2, ethyl CH_2), 7.34 (m, 3, aromatic H), 7.42 (m, 2, aromatic H), 8.32 (d, J_{H-F} = 7 Hz, aromatic H).

Anal. Calcd. for $C_{20}H_{16}ClFN_2O_3S \cdot 1/5\ H_2O$: C, 56.86; H, 3.89; N, 6.63. Found: C, 56.70; H, 3.89; N, 6.63.

Using the above procedure, with ethyl 2,3,4,5-tetrafluorobenzoylacetate [10] instead of ethyl 2,6-dichloro-5-fluoronicotinylacetate and toluene as solvent instead of xylene ethyl 1-cyclopropyl-2-phenylthio-6,7,8-trifluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate (**18b**) was prepared in 42% yield, mp 135-137°; ^{1}H nmr (deuteriochloroform): δ 0.93 (bs, 2, CH_2), 1.20 (m, 2, CH_2), 1.36 (t, J = 7 Hz, 3, ethyl CH_3), 4.36 (q, J = 7 Hz, 2, ethyl CH_2), 7.38 (m, 3, aromatic H), 7.43 (m, 2, aromatic H), 7.91 (m, 1, aromatic H).

Anal. Calcd. for $C_{21}H_{16}F_3NO_3S \cdot 1/10\ H_2O$: C, 59.89; H, 3.85; N, 3.33. Found: C, 59.58; H, 3.77; N, 3.24.

Ethyl 1-Cyclopropyl-2-phenylsulfinyl-6-fluoro-7-chloro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate (**19a**).

To a solution of ethyl 1-cyclopropyl-2-phenylthio-6-fluoro-7-chloro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate (**18a**) (2.89 g, 6.9 mmoles) in methylene chloride (75 ml) was added *m*-chloroperoxybenzoic acid (1.59 g of Aldrich 80% peroxy acid, 7.4 mmoles). After 16 hours, the solution was diluted with 100 ml of methylene chloride and the solution was extracted with 2 × 50 ml of dilute sodium bicarbonate solution and then water containing 2 g of sodium bisulfite. The organic solvent was dried over magnesium sulfate and the solvent was removed under reduced pressure. Crystallization of the residue in ethanol yielded 2.5 g (83%) of ethyl 1-cyclopropyl-2-phenylsulfinyl-6-fluoro-7-chloro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate (**19a**), mp 188-189°; ^{1}H nmr (deuteriochloroform): δ 0.96 (m, 1, CH_2), 1.14 (m, 2, CH_2), 1.42 (t, J = 7 Hz, 3, ethyl CH_3), 1.50 (m, 1, CH_2), 2.67 (m, 1, CH), 4.42 (dq, J = 7 Hz, 2, ethyl CH_2), 7.54 (m, 3, aromatic H), 7.99 (m, 2, aromatic H), 8.31 (d, J_{H-F} = 7.5 Hz, 1, aromatic H).

Anal. Calcd. for $C_{20}H_{16}ClFN_2O_4S$: C, 55.24; H, 3.71; N, 6.44. Found: C, 55.65; H, 3.77; N, 6.51.

Using a similar procedure with ethyl 1-cyclopropyl-2-phenylthio-6,7,8-trifluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate (**18b**), ethyl 1-cyclopropyl-2-phenylsulfinyl-6,7,8-trifluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate (**19b**) was prepared in 78% yield. The crystallization solvent was ether instead of ethanol, mp 189.5°; ^{1}H nmr (deuteriochloroform): δ 0.86 (m, 1, CH_2), 1.21 (m, 2, CH_2), 1.32 (m, 1, CH_2), 1.41 (t, J = 7 Hz, 3, ethyl CH_3), 3.37 (m, 1, CH), 4.46 (dq, J = 7 Hz, 2, ethyl CH_3), 7.57 (m, 3, aromatic H), 7.90 (m, 1, aromatic H), 7.96 (m, 2, aromatic H).

Anal. Calcd. for $C_{21}H_{16}F_3NO_4S$: C, 57.93; H, 3.70; N, 3.22. Found: C, 58.06; H, 3.74; N, 3.19.

6-Fluoro-7-chloro-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo-[5,4-*b*][1,8]naphthyridine-3,4-dione (**20a**).

To an ice-sold solution of ethyl 1-cyclopropyl-2-phenylsulfinyl-6-fluoro-7-chloro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate (**19a**) (645 mg, 1.485 mmoles) in 40 ml of tetrahydrofuran was added a solution of sodium hydrosulfide (freshly opened bottle from Aldrich having approximately 3 moles of water (164 mg, 1.49 mmoles) in 6 ml of water). One fifth volume of a sodium bicarbonate solution (1.37 g in 34 ml of water) was then added into the reaction flask. After 1 hour ice-bath, the remaining sodium bicarbonate solution was added and then followed by the addition of 754 mg (3.3 mmoles) of hydroxylamine-*O*-sulfonic acid. The ice-bath was removed. After being stirred at ambient temperature for 3 hours, 25 ml of 1*N* hydrochloric acid was added and the reaction mixture was diluted with 100 ml of water and filtered. The residue was washed with water and then a small amount of ether yielding 330 mg (71%) of 6-fluoro-7-chloro-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*][1,8]naphthyridine-3,4-dione (**20a**), mp >250°; ^{1}H nmr (DMSO-d_6): δ 1.21 (m, 2, CH_2), 1.27 (m, 2, CH_2), 3.47 (m, 1, CH), 8.49 (d, J_{H-F} = 7.5 Hz, 1 aromatic H), 12.3 (bs, 1, NH). (Trace amount of signals corresponding to diethyl ether were present in the spectrum.).

Anal. Calcd. for $C_{12}H_7ClFN_3O_2S \cdot 1/10$ ether: C, 46.31; H, 2.40; N, 13.29. Found: C, 46.68; H, 2.46; N, 12.93.

Using a similar procedure with **19b**, 6,7,8-trifluoro-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*]quinoline-3,4-dione (**20b**) was prepared in 67% yield, mp 243-245°; the product was crystallized from ethanol; ^{1}H nmr (DMSO-d_6): δ 1.22 (s, 2, CH_2), 1.24 (m, 2, CH_2), 3.85 (m, 1, CH), 8.0 (m, 1, aromatic H), 12.01 (bs, 1, NH).

Anal. Calcd. for $C_{13}H_7F_3N_2O_2S \cdot 1/2\ H_2O$: C, 48.60; H, 2.49; N, 8.72. Found: C, 48.93; H, 2.62; N, 8.57.

6-Fluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*][1,8]naphthyridine-3,4-dione (**3**).

To a suspension of 175 mg (0.562 mmole) of 6-fluoro-7-chloro-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*][1,8]naphthyridine-3,4-dione (**20a**) in 5 ml of 1-methyl-2-pyrrolidinone at 60° under nitrogen atmosphere was added 225 mg (2.26 mmoles) of piperazine. After a few minutes a clear solution was formed. After a while, a suspension appeared. After being stirred for 4 hours at 60°, the reaction was cooled to ambient temperature and the mixture was filtered. The solid was washed with ethanol to give 210 mg (94%) of 6-fluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*][1,8]naphthyridine-3,4-dione hydrochloride salt (**3**), mp >250°; ^{1}H nmr (trifluoroacetic acid, perdeuterioacetic acid): δ 1.47 (m, 2, CH_2), 1.58 (m, 2, CH_2), 3.77 (m, 4, NCH_2), 4.59 (m, 4, NCH_2), 8.26 (d, J_{H-F} = 13 Hz, 1, aromatic H).

Anal. Calcd. for $C_{16}H_{16}FN_5FO_2S \cdot HCl \cdot 1/4\ H_2O$: C, 47.76; H, 4.10; N, 17.41. Found: C, 47.67; H, 4.29; N, 17.19.

Similarly prepared using pyridine as a solvent instead of 1-methyl-2-pyrrolidinone was 6,8-difluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-*b*]quinoline-3,4-dione (**4**), mp >250° (74% yield); ^{1}H nmr (trifluoroacetic acid, perdeuterioacetic acid): δ 1.49 (bs, 2, CH_2), 1.61 (m, 2, CH_2), 3.72 (m, 4, NCH_2), 4.01 (m, 4, NH_2), 4.24 (m, 1, CH), 8.13 (d, J_{H-F} = 10 Hz, 1, aromatic H).

Anal. Calcd. for $C_{17}H_{16}F_2N_4O_2S$: C, 53.93; H, 4.23; N, 14.81. Found: C, 54.34; H, 4.32; N, 14.84.

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