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Synthetic Chemotherapeutic Agents. I. Synthesis of 2-Substituted Thiazolo[5,4-*f*]quinoline Derivatives. (1)¹⁾

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By using 6-aminobenzothiazoles as starting material, a series of 2-substituted 6-ethyl-6,9-dihydro-9-oxothiazolo[5,4-*f*]quinoline-8-carboxylic acids has been prepared through successive steps of, *e.g.* condensation with diethyl ethoxymethylenemalonate, Gould-Jacobs reaction, N-alkylation and hydrolysis. These compounds were evaluated for antibacterial activities *in vitro*. The 2-chloro derivative (10d) showed nearly the same activity with nalidixic acid.

Since the finding of nalidixic acid (1-ethyl-1,4-dihydro-7-methyl-4-oxo-1,8-naphthyridine-3-carboxylic acid) as an unique antibacterial agent,³⁾ many compounds having the 3-carboxy-4-pyridone moiety were synthesized for examination of their antibacterial activities. Several derivatives among them revealed the activities against gram-negative bacteria.⁴⁾

Our work of this series was initiated with the aim of providing a novel drug which would be effective for both gram-negative and gram-positive microorganisms and even for those resistant to the known chemotherapeutic agents. The present paper is concerned with the synthesis of 2-substituted thiazolo[5,4-*f*]quinoline derivatives and their antimicrobial activities.

Thermal cyclization in Dowtherm A of diethyl N-(2-methylthio-6-benzothiazolyl)amino-methylenemalonate (**5a**), prepared from 6-amino-2-methylthiobenzothiazole (**8a**) and diethyl ethoxymethylenemalonate or diethyl dimethylaminomethylenemalonate,⁵⁾ afforded ethyl 6,9-dihydro-2-methylthio-9-oxothiazolo[5,4-*f*]quinoline-8-carboxylate (**6a**). Ethylation of **6a** with ethyl iodide in the presence of potassium carbonate in dimethylformamide (DMF) and hydrolysis of the resulting 6-ethyl ester (**9a**) with diluted hydrochloric acid in acetic acid gave the 6-ethyl acid (**10a**) which could be also obtained by hydrolysis of **6a** and ethylation of the resulting carboxylic acid (**7a**).

It was evident that the cyclization product of **5a** was not ethyl 5,8-dihydro-2-methylthio-5-oxothiazolo[4,5-*g*]quinoline-6-carboxylate (**4**) of a linear type but the thiazolo[5,4-*f*]quinoline derivative (**6a**) of an angular type, from the fact that the nuclear magnetic resonance (NMR) spectrum of the product exhibited no two singlets due to the two protons at 4- and 9-positions of **4**, but two doublets assignable to those at 4- and 5-positions of **6a** (Table I). The 2-methylsulfonyl derivative (**1**) obtained by oxidation of **5a** was also thermally cyclized in Dowtherm A to yield the product (**6g**) of the angular type.

- 1) A part of this work was presented at the 94th Annual Meeting of the Pharmaceutical Society of Japan, Sendai, April 1974.
- 2) Location: Minamifunabori-cho, Edogawa-ku, Tokyo.
- 3) G.Y. Leshner, E.J. Froelich, M.D. Gruett, J.H. Bailey, and R.P. Brundage, *J. Med. Pharm. Chem.*, **5**, 1063 (1962).
- 4) a) D. Kaminsky and R.I. Meltzer, *J. Med. Chem.*, **11**, 160 (1968); b) S. Minami, T. Shono, and J. Matsumoto, *Chem. Pharm. Bull.* (Tokyo), **19**, 1426 (1971); c) M. Antoine, S. Chabassier, S. Geiger, J. le Blevec, J. le Coent, M. Pesson, D. Richer, E. Horvath, M.P. de Lajudie, S. Patte, and B. Pradeau, *Chimica Therapeutica*, **7**, 434 (1972); d) R. Albrecht, *Ann. Chem.*, **762**, 55 (1972); e) R. Albrecht and G.A. Hoyer, *Chimica Therapeutica*, **8**, 346 (1973); f) W.E. Wick, D.A. Preston, W.A. White, and R.S. Gordee, *Antimicrob. Ag. Chemother.*, **4**, 415 (1973); g) M. Pesson, M. Antoine, S. Chabassier, P. Girard, and D. Richer, *Compt. Rend.*, **278C**, 717 (1974).
- 5) N.D. Harris, *Synthesis*, **1971**, 220.

Chart 1

TABLE I. NMR Data for the Aromatic Protons of Benzothiazole and Thiazolo[5,4-*f*]quinoline Derivatives in CF₃COOH^{a)}

Compounds	4-H and 5-H	7-H
5a ^{b)}	7.80 (d, <i>J</i> =9.0 and 2.0), 8.10 (d, <i>J</i> =9.0)	8.16 (d, <i>J</i> =2.0)
6a	8.57 (d, <i>J</i> =9.0), 8.72 (d, <i>J</i> =9.0)	9.56 (s)
7a	8.46 (d, <i>J</i> =9.0), 8.64 (d, <i>J</i> =9.0)	9.49 (s)
9a	8.67 (d, <i>J</i> =9.3), 8.85 (d, <i>J</i> =9.3)	9.62 (s)
10a	8.58 (d, <i>J</i> =9.3), 8.73 (d, <i>J</i> =9.3)	9.50 (s)
10b	8.58 (d, <i>J</i> =9.5), 8.86 (d, <i>J</i> =9.5)	9.52 (s)
10c	8.68 (d, <i>J</i> =9.5), 9.08 (d, <i>J</i> =9.5)	9.56 (s)
10d	8.55 (d, <i>J</i> =9.3), 9.06 (d, <i>J</i> =9.3)	9.65 (s)
10e	8.48 (d, <i>J</i> =9.1), 8.63 (d, <i>J</i> =9.1)	9.45 (s)

^{a)} Measured at 100 MHz-4H-100 (Japan Electron Optics Lab. Tokyo Japan).Chemical shifts are given in ppm from Si(Me)₄ as an internal standard and coupling constant (*J*) in Hz. abbreviation: s=singlet, d=doublet, d.d=doubled doublet^{b)} 8.90 (d, *J*=14.6), -NH-CH=C<

For the synthesis of 4-hydroxyquinoline derivatives by the Gould-Jacobs reaction, several methods using various condensation agents have been known,⁶⁾ but the thermal cyclization

6) ^{a)} H. Agui, T. Mitani, M. Nakashita, and T. Nakagome, *J. Heterocyclic Chem.*, **8**, 357 (1971); ^{b)} N.D. Harris, *Synthesis*, **1971**, 256; ^{c)} D.G. Markees and L.S. Schwab, *Helv. Chim. Acta*, **55**, 1319 (1972).

in Dowtherm A described above proved to be most effective. Treatment of **5a** with polyphosphoric acid (PPA) afforded resinous products and attempts to cyclize with polyphosphoric ester (PPE) or phosphoryl chloride-PPA recovered the starting material. The 9-chloro-thiazolo[5,4-*f*]quinoline derivative (**2**) could be obtained by refluxing a solution of **5a** or **6a** in phosphoryl chloride.

The 9-chloro ester (**2**) was hydrolyzed with mineral acid to give the 9-oxo acid (**7a**), while mild hydrolysis⁷⁾ of **2** with sodium acetate in acetic acid afforded the 9-oxo ester (**6a**). Treatment of **2** with sodium ethoxide gave the corresponding 9-ethoxy ester (**3**) which was converted into the acid (**7a**) by hydrolysis. Since **3** was different from **9a** in the physical properties, it was proved that the ethylation of **6a** described above took place at the N-6 atom. The structure of **9a** was further supported by the fact that **9a** could alternatively be synthesized by cyclization in PPE of the condensation product (**13**) of 6-ethylamino-2-methylthiobenzothiazole (**12**) with diethyl ethoxymethylenemalonate.

TABLE II. 2,6-Disubstituted 6,9-Dihydro-9-oxothiazolo[5,4-*f*]quinoline-8-carboxylic Acids

Compd. No.	Substituents		Yield (%)	mp (°C)	Recrystn. solvents	Formula	Analysis (%)		
	R	R'					Calcd. (Found)	C	H
7a	MeS	H	85 ^{a)}	>300	DMSO	C ₁₂ H ₈ O ₃ N ₂ S ₂	49.30 (48.85)	2.76 (2.45)	9.58 (9.69)
7b	Me	H	85 ^{a)}	>300	DMF	C ₁₂ H ₈ O ₃ N ₂ S	55.38 (55.08)	3.10 (3.41)	10.76 (11.15)
7c	H	H	87 ^{a)}	>300	DMF	C ₁₁ H ₆ O ₃ N ₂ S	53.66 (53.64)	2.46 (2.40)	11.38 (11.73)
7d	Cl	H	92 ^{a)}	>300	DMF	C ₁₁ H ₅ O ₃ N ₂ SCl	47.06 (47.39)	1.80 (2.17)	9.98 (9.98)
10a	MeS	Et	78 ^{b)}	257—259	DMF	C ₁₄ H ₁₂ O ₃ N ₂ S ₂	52.48 (52.29)	3.78 (3.80)	8.75 (8.75)
10b	Me	Et	75 ^{b)}	265—268	DMF	C ₁₄ H ₁₂ O ₃ N ₂ S	58.32 (58.08)	4.20 (4.10)	9.72 (9.83)
10c	H	Et	61 ^{b)}	>300	DMF	C ₁₃ H ₁₀ O ₃ N ₂ S	56.93 (57.10)	3.67 (3.64)	10.21 (10.37)
10d	Cl	Et	49 ^{b)}	238—239	DMF	C ₁₃ H ₉ O ₃ N ₂ SCl	50.57 (50.79)	2.94 (3.27)	9.08 (9.55)
10e	EtO	Et	21 ^{c)}	235—236	DMF	C ₁₅ H ₁₄ O ₄ N ₂ S	56.59 (56.27)	4.43 (4.10)	8.80 (8.95)
11	MeS	DEAE ^{d)}	23 ^{e)}	263—265 (decomp.)	DMF	C ₁₈ H ₂₂ O ₃ N ₃ S ₂ Cl	50.51 (50.12)	5.18 (5.13)	9.82 (9.85)
15	NFV ^{f)}	Et	63 ^{g)}	>300	DMF	C ₁₉ H ₁₃ O ₆ N ₃ S	55.47 (54.99)	3.19 (3.43)	10.12 (10.63)

a) obtained from **6a—e** b) obtained from **9a—d** c) obtained from **6e** via **9e** (based on **6e**) d) (Et)₂N(CH₂)₂ e) obtained from **7a**

f) NO₂- -CH=CH- g) obtained from **14**

The synthetic routes for 2-substituted 6-ethyl-6,9-dihydro-9-oxothiazolo[5,4-*f*]quinoline-8-carboxylic acids were thus established and then the various compounds (**10b—e**) were

7) May and Baker Ltd., Fr. Patent 1531495 (1968) [*C.A.*, **71**, 70509n (1969)].

prepared in a similar manner. Starting from benzothiazole derivatives (8b—f), thiazolo[5,4-f]-quinoline-8-carboxylic acids (10b—e) were obtained through successive steps of condensation with ethyl ethoxymethylenemalonate, thermal cyclization, ethylation at the N-6 atom and finally hydrolysis of the resulting esters (9b—e). Also 7b—d were obtained from 6a—d by hydrolysis. N-Diethylaminoethylation of the ester (6a) failed under the similar N-alkylation conditions as described above, but proceeded in the case of the carboxylic acid (7a) to yield the corresponding 6-diethylaminoethyl derivative (11). The compound (15) was prepared by reaction of 2-methylthiazolo[5,4-f]quinoline derivative (9b) with 5-nitro-2-furfural and hydrolysis of the resulting condensation product (14).

The compounds prepared in this work were tested for their antimicrobial activities against various gram-negative and -positive bacteria *in vitro*. The compound (10d) had nearly the same activities as nalidixic acid but occurrence of the cross-resistance to the two compounds was observed. The others, except 10d, 14 and 15, exhibited inferior activities.

Further details on the antibacterial activities and the structure-activity relationship will be reported in near future.

Experimental⁸⁾

Diethyl N-(2-Methylsulfonyl-6-benzothiazolyl)aminomethylenemalonate (1)—To a suspension of finely powdered 5a (10.0 g) in AcOH (500 ml) was added dropwise a solution of KMnO_4 (20 g) in water (300 ml) at room temperature. The reaction mixture was stirred for 2 hr, treated with NaHSO_3 solution and the crystals remained were collected. Recrystallization from EtOH gave 1 (4.50 g) as yellow needles (see Table III).

Ethyl 9-Chloro-2-methylthiothiazolo[5,4-f]quinoline-8-carboxylate (2)—A mixture of 5a (5.20 g) in POCl_3 (84 g) was stirred at 95° for 3 hr, concentrated and poured onto ice. After neutralization of the solution, the separated precipitate was collected and dissolved in CHCl_3 . The CHCl_3 solution was washed with water and dried over anhyd. Na_2SO_4 . The residue obtained from the extract was crystallized from CHCl_3 -MeOH to give 2 (3.40 g; 48%) as needles, mp 153—156°. *Anal.* Calcd. for $\text{C}_{14}\text{H}_{11}\text{O}_2\text{N}_2\text{S}_2\text{Cl}$: C, 49.62; H, 3.27; N, 8.27. Found: C, 49.46; H, 3.15; N, 8.38.

2 was also obtained from 6a and POCl_3 in the similar procedure described above.

Ethyl 9-Ethoxy-2-methylthiothiazolo[5,4-f]quinoline-8-carboxylate (3)—To a NaOEt solution prepared from Na (0.11 g) and EtOH (28 ml) was added 2 (1.35 g) and the mixture was refluxed for 4 hr. After evaporation of the solvent, the residue was extracted with CHCl_3 . The residue obtained from the dried extract was crystallized from EtOH to give 3 (0.78 g; 57%) as pale yellow needles, mp 148—151°. *Anal.* Calcd. for $\text{C}_{16}\text{H}_{16}\text{O}_3\text{N}_2\text{S}_2$: C, 55.15; H, 4.63; N, 8.04. Found: C, 55.32; H, 4.67; N, 7.81.

Diethyl N-(2-Substituted 6-benzothiazolyl)aminomethylenemalonates (5a—f), cf. Table III—a) A mixture of 8a—f (0.1 mole) and diethyl ethoxymethylenemalonate (23.8 g; 0.11 mole) in Dowtherm A (200 ml) was stirred at 110—130° for 1 hr. After cooling, the precipitated crystals were collected, washed with ether and recrystallized to give the pure products (5a—f).

b) A mixture of 8a (3.20 g) and diethyl dimethylaminomethylenemalonate (2.50 g) in AcOH (20 ml) was stirred at 70—80° for 5 hr, and concentrated to dryness *in vacuo*. The residue was dissolved in water and the solution was neutralized with NaHCO_3 and extracted with CHCl_3 . The product (5a) obtained from the extract was recrystallized from acetone to give the pure sample (4.60 g; 77%), identified with the sample above obtained by comparison of their infrared (IR) spectra and by mixed melting point determination.

General Procedure of Ethyl 2-Substituted 6,9-Dihydro-9-oxothiazolo[5,4-f]quinoline-8-carboxylates (6a—g, cf. Table IV)—a) A mixture of 5a—f or 1 (0.05 mole) in Dowtherm A (150 ml) was refluxed for 40 min and cooled. The resulting precipitate was collected, thoroughly washed with ether and dried. Yield, 75—98%. The thin-layer chromatogram and the NMR spectrum of the crude product showed no evidence of the presence of linear thiazoloquinoline. The crude product was recrystallized from an appropriate solvent described in Table IV.

b) A mixture of 2 (2.0 g), NaOAc (3.3 g) and AcOH (33 ml) was refluxed for 7 hr and cooled. The precipitate was collected, and recrystallized from DMSO to give 6a (1.1 g; 62%), needles.

2-Substituted 6,9-Dihydro-9-oxothiazolo[5,4-f]quinoline-8-carboxylic Acids (7a—d, cf. Table II)—a) A suspension of 6a—d in conc. HCl-90% AcOH (1:11) was treated to give 7a—d as described for the preparation of 10a—c from 9a—c.

b) Hydrolysis of 3 in conc. HCl-90% AcOH was carried out in the similar manner as described in a). IR spectrum of the product obtained by method b) was identical with that of the sample prepared from 6a.

8) All melting points are uncorrected.

TABLE III. Diethyl N-(2-Substituted 6-benzothiazolyl)aminomethylenemalonates

Compd. No.	R	Yield ^{a)} (%)	mp (°C)	Recrystn. solvents	Formula	Analysis (%)		
						Calcd. (Found)	C	H N
5a	MeS	85	132—134	acetone	C ₁₆ H ₁₈ O ₄ N ₂ S ₂	52.44 (52.45)	4.95 (5.08)	7.65 (7.80)
5b	Me	66	139—141	acetone	C ₁₆ H ₁₈ O ₄ N ₂ S	57.47 (57.79)	5.42 (5.78)	8.38 (8.55)
5c	H	62	116—118	MeOH	C ₁₅ H ₁₆ O ₄ N ₂ S	56.23 (56.08)	5.04 (4.92)	8.75 (8.74)
5d	Cl	79	160—162	MeOH	C ₁₅ H ₁₅ O ₄ N ₂ SCl	50.77 (51.10)	4.26 (4.20)	7.90 (8.50)
5e	EtO	66	116—118	EtOH	C ₁₇ H ₂₀ O ₅ N ₂ S	56.03 (56.33)	5.53 (5.29)	7.69 (7.65)
5f	SH	81	255—256	DMF	C ₁₅ H ₁₆ O ₄ N ₂ S ₂	51.12 (50.83)	4.58 (4.70)	7.95 (8.11)
1	MeSO ₂	41 ^{b)}	188—190	EtOH	C ₁₆ H ₁₈ O ₆ N ₂ S ₂	48.22 (47.89)	4.55 (4.48)	7.03 (6.69)

a) obtained from 8a—f b) obtained from 5a

Ethyl 2-Substituted 6-Ethyl-6,9-dihydro-9-oxothiazolo[5,4-f]quinoline-8-carboxylates (9a—e, cf. Table IV)—a) A mixture of 6a—e (0.01 mole), EtI (0.03 mole), powdered K₂CO₃ (0.03 mole) in DMF (65 ml) was stirred at 100—110° for 2 hr. The reaction mixture was filtered and concentrated to dryness *in vacuo*. The resulting residue was extracted with CHCl₃. After evaporation of the solvent, the residue was crystallized from an appropriate solvent. 9e was used in the following step without purification.

b) A mixture of 13 (0.43 g) and PPE (1.20 g) was heated for 15 min at 120°, poured on ice and extracted with CHCl₃. The extract was washed with 2% K₂CO₃ solution and water. After evaporation of the solvent, the resulting residue was chromatographed on silica gel column. Elution with benzene-CHCl₃ (1:1) gave 9a (0.18 g; 48%), mp 200—202°, undepressed on admixture with the sample obtained above.

2-Substituted 6-Ethyl-6,9-dihydro-9-oxothiazolo[5,4-f]quinoline-8-carboxylic Acids (10a—e, cf. Table II)—a) A mixture of 9a—c (0.005 mole) in conc. HCl-90% AcOH (1:11) (25 ml) was refluxed for 1.5 hr and cooled. The precipitate was collected, washed with water, dried and recrystallized.

Hydrolyses of 9d and 9e were carried out in 1N KOH and 0.5N HCl-42% AcOH respectively, and the reaction mixture were worked up according to the usual procedure.

Treatment of 7a with EtI, K₂CO₃ and DMF also gave 10a in the similar manner as described for the alkylation of 6a.

6-(2-Diethylamino)ethyl-6,9-dihydro-2-methylthio-9-oxothiazolo[5,4-f]quinoline-8-carboxylic Acid Hydrochloride (11·HCl)—A mixture of 7a (0.58 g), diethylaminoethyl chloride hydrochloride (0.69 g), KOH (0.44 g), EtOH (12 ml) and water (6 ml) was refluxed for 2 hr. The reaction mixture was acidified with HCl and filtered. Concentration of the filtrate and recrystallization of the residue gave 11 (0.20 g; 23%) as a powder.

6-Ethylamino-2-methylthiobenzothiazole (12)—A suspension of 8a (5.90 g) in trifluoroacetic anhydride (12.6 g) was refluxed for 3 hr and allowed to stand overnight at room temperature. The reaction mixture further added with AcOH (20 ml) was heated for another 3 hr and poured into water (300 ml). The resulting precipitate was recrystallized from petro. ether-benzene to give 2-methylthio-6-trifluoroacetylaminobenzothiazole (5.60 g; 64%) as needles, mp 182—183°. *Anal.* Calcd. for C₁₀H₇ON₂S₂F₃: C, 41.09; H, 2.41; N, 9.59. Found: C, 41.31; H, 2.43; N, 9.60. A mixture of 2-methylthio-6-trifluoroacetylaminobenzothiazole (7.20 g) and K₂CO₃ (13.8 g), EtI (15.6 g) in acetone (150 ml) was refluxed for 3 hr. After concentration of the reaction mixture, the residue was extracted with CHCl₃. The extract was poured on Al₂O₃ column and eluted with CHCl₃. The oil obtained from the eluate was dissolved in EtOH (20 ml), treated with 10% NaOH solution (20 ml), and the reaction mixture was heated 30 min at 90°. After cooling, the resulting precipitate was recrystallized from petro. ether-benzene to give 12 (3.7 g; 56%) as pale yellow needles, mp 92—93°. *Anal.* Calcd. for C₁₀H₁₁N₂S₂: C, 53.53; H, 5.39; N, 12.49. Found: C, 53.95; H, 5.46; N, 12.36.

TABLE IV. Ethyl 2,6-Disubstituted 6,9-Dihydro-9-oxothiazolo[5,4-*f*]quinoline-8-carboxylates

Compd. No.	Substituents		Yield (%)	mp (°C)	Recrystn. solvent	Formula	Analysis (%)		
	R	R'					Calcd. (Found)	C	H N
6a	MeS	H	81 ^{a)}	>300	DMSO	C ₁₄ H ₁₂ O ₃ N ₂ S ₂	52.48 (52.05)	3.78 (3.67)	8.75 (8.94)
6b	Me	H	61 ^{a)}	293 (decomp.)	DMF	C ₁₄ H ₁₂ O ₃ N ₂ S	58.32 (58.23)	4.17 (4.25)	9.72 (9.79)
6c	H	H	64 ^{a)}	>300	DMF	C ₁₃ H ₁₀ O ₃ N ₂ S	56.92 (57.03)	3.68 (3.65)	10.22 (10.32)
6d	Cl	H	86 ^{a)}	>300	DMF	C ₁₃ H ₉ O ₃ N ₂ SCl	50.57 (50.37)	2.94 (2.95)	9.08 (9.37)
6e	EtO	H	92 ^{a)}	>300	DMF	C ₁₅ H ₁₄ O ₄ N ₂ S	56.59 (56.43)	4.43 (4.11)	8.80 (8.96)
6f	SH	H	59 ^{a)}	>300	DMF	C ₁₃ H ₁₀ O ₃ N ₂ S ₂	50.96 (50.67)	3.29 (3.58)	9.15 (9.62)
6g	MeSO ₂	H	81 ^{b)}	>300	DMF- ether	C ₁₄ H ₁₂ O ₅ N ₂ S ₂	47.71 (48.20)	3.43 (3.74)	7.95 (8.24)
9a	MeS	Et	76 ^{c)}	200—202	acetone	C ₁₆ H ₁₆ O ₃ N ₂ S ₂	55.15 (55.11)	4.63 (4.59)	8.04 (7.86)
9b	Me	Et	61 ^{c)}	196—198	EtOH	C ₁₆ H ₁₆ O ₃ N ₂ S	60.74 (60.72)	5.10 (5.02)	8.85 (8.92)
9c	H	Et	84 ^{c)}	201—203	MeOH	C ₁₅ H ₁₄ O ₃ N ₂ S	59.59 (60.04)	4.67 (4.53)	9.27 (9.34)
9d	Cl	Et	74 ^{c)}	219—220	acetone	C ₁₅ H ₁₃ O ₃ N ₂ SCl	53.49 (53.45)	3.89 (3.93)	8.32 (8.63)
14	NFV ^{d)}	Et	63 ^{e)}	285 (decomp.)	acetone- CHCl ₃	C ₂₁ H ₁₇ O ₆ N ₃ S	57.39 (56.95)	3.90 (3.71)	9.56 (9.38)

a) obtained from 5a—f b) obtained from 1 c) obtained from 6a—d d) NO₂- -CH=CH- e) obtained from 9b

Diethyl N-Ethyl-N-(2-methylthio-6-benzothiazolyl)aminomethylenemalonate (13)—A mixture of 12 (1.7 g) and diethyl ethoxymethylenemalonate (1.60 g) was heated at 110—120° for 5 hr. After cooling, the mixture was chromatographed on silica gel. From the fraction eluted with petro. ether-benzene (1:1) 13 was obtained as an oil. The product was used to the next step without purification.

Ethyl 6-Ethyl-6,9-dihydro-2-(5-nitro-2-furyl)vinyl-9-oxothiazolo[5,4-*f*]quinoline-8-carboxylate (14)—In a flask protected from light, a mixture of 9b (0.30 g), 5-nitrofurfural (0.28 g), Ac₂O (5 ml) and AcOH (5 ml) was stirred at 130—140° for 7 hr. After evaporation of the solvent, the residue was extracted with CHCl₃. A brown semi-solid obtained from the extract was chromatographed on Al₂O₃. The fraction eluted with acetone-CHCl₃ (1:1) was concentrated and the residue was crystallized from acetone-CHCl₃ (1:6) to give 14 (0.28 g; 63%) as yellow needles, mp 285° (decomp.).

6-Ethyl-6,9-dihydro-2-(5-nitro-2-furyl)vinyl-9-oxothiazolo[5,4-*f*]quinoline-8-carboxylic Acid (15)—A mixture of 14 (0.22 g) in conc. HCl-90% AcOH (1:11) (5 ml) was refluxed for 1.5 hr in a dark place. After cooling, the precipitate was recrystallized from DMF to give 15 (0.13 g; 63%) as yellow needles, mp >300°.

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