[Chem. Pharm. Bull. 24(1) 130—135 (1976)]

UDC 547.789'831.057.09 : 615.31.076.7

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

Renzo Dohmori, Shizuo Kadoya, Isao Takamura, and Norio Suzuki

Research Institute, Daiichi Seiyaku Co., Ltd.[2]

(Received April 3, 1975)

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)aminomethylenemalonate (**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. Lesher, 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.

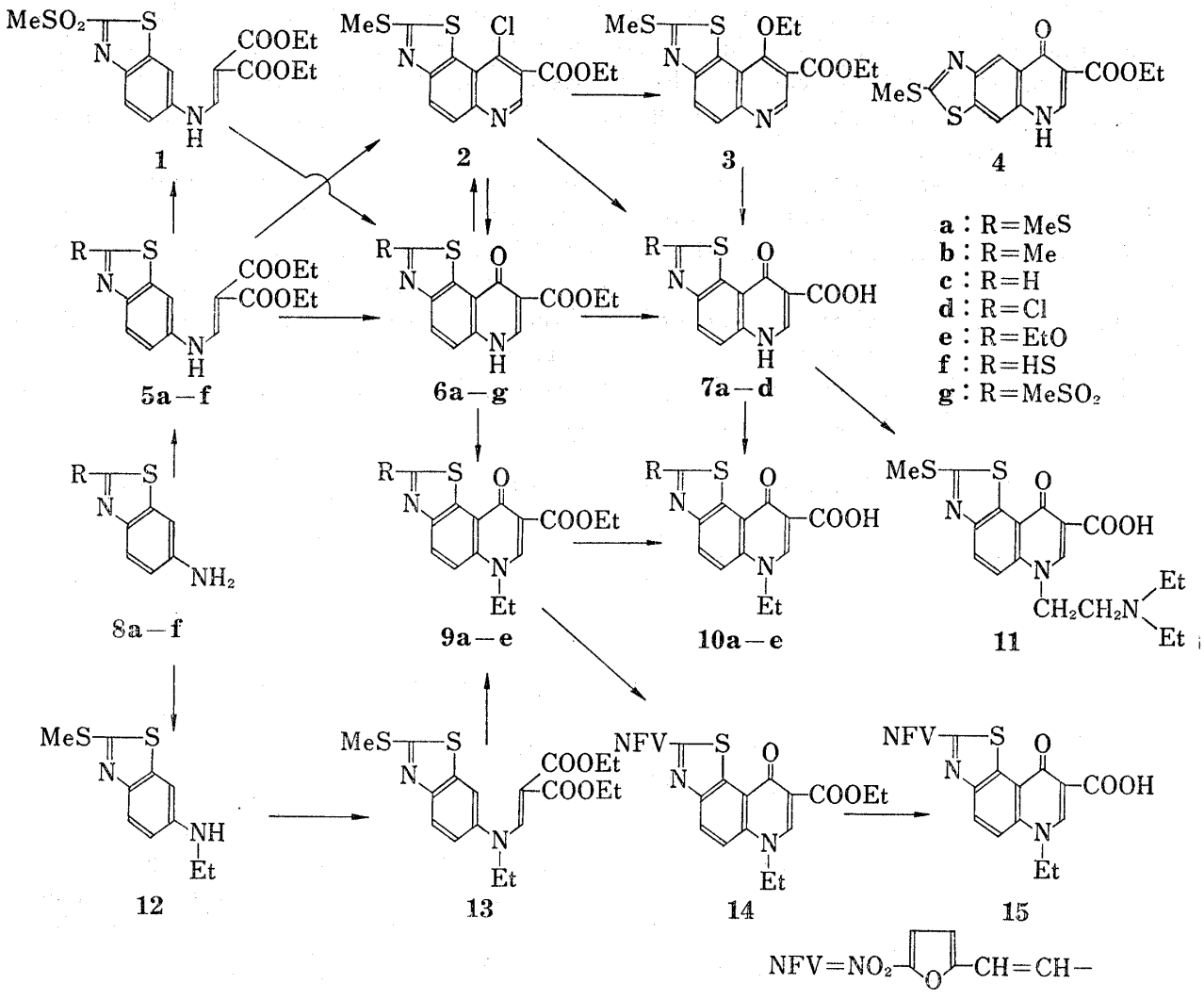


Chart 1

Table I. NMR Data for the Aromatic Protons of Benzothiazole and Thiazolo[5,4-*f*]quinoline Derivatives in CF_3COOH[a)]

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

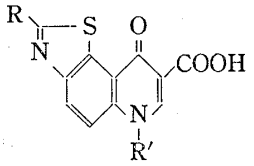
For the synthesis of 4-hydroxyquinoline derivatives by the Gould-Jacobs reaction, several methods using various condensation agents have been known,[6)] but the thermal cyclization

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-chlorothiazolo[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 hydrolysis[7] 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 R	Substituents R′	Yield (%)	mp (°C)	Recrystn. solvents	Formula	Analysis (%) Calcd. (Found) C	H	N
7a	MeS	H	85[a]	>300	DMSO	$C_{12}H_8O_3N_2S_2$	49.30 (48.85)	2.76 (2.45)	9.58 (9.69)
7b	Me	H	85[a]	>300	DMF	$C_{12}H_8O_3N_2S$	55.38 (55.08)	3.10 (3.41)	10.76 (11.15)
7c	H	H	87[a]	>300	DMF	$C_{11}H_6O_3N_2S$	53.66 (53.64)	2.46 (2.40)	11.38 (11.73)
7d	Cl	H	92[a]	>300	DMF	$C_{11}H_5O_3N_2SCl$	47.06 (47.39)	1.80 (2.17)	9.98 (9.98)
10a	MeS	Et	78[b]	257—259	DMF	$C_{14}H_{12}O_3N_2S_2$	52.48 (52.29)	3.78 (3.80)	8.75 (8.75)
10b	Me	Et	75[b]	265—268	DMF	$C_{14}H_{12}O_3N_2S$	58.32 (58.08)	4.20 (4.10)	9.72 (9.83)
10c	H	Et	61[b]	>300	DMF	$C_{13}H_{10}O_3N_2S$	56.93 (57.10)	3.67 (3.64)	10.21 (10.37)
10d	Cl	Et	49[b]	238—239	DMF	$C_{13}H_9O_3N_2SCl$	50.57 (50.79)	2.94 (3.27)	9.08 (9.55)
10e	EtO	Et	21[c]	235—236	DMF	$C_{15}H_{14}O_4N_2S$	56.59 (56.27)	4·43 (4.10)	8.80 (8.95)
11	MeS	DEAE[d]	23[e]	263—265 (decomp.)	DMF	$C_{18}H_{22}O_3N_3S_2Cl$	50.51 (50.12)	5.18 (5.13)	9.82 (9.85)
15	NFV[f]	Et	63[g]	>300	DMF	$C_{19}H_{13}O_6N_3S$	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*) $(Et)_2N(CH_2)_2$- *e*) obtained from **7a**

f) NO_2-  -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**, 70509*n* (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.

Experimental[8)]

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 $C_{14}H_{11}O_2N_2S_2Cl$: 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 $C_{16}H_{16}O_3N_2S_2$: 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.

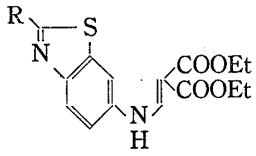
2-Substituted 6,9-Dihydro-9-oxothiazolo[5,4-*f*]quinoline-8-carboxylic Acids (7a—d, *cf.* Table II)——a) A suspension of **6a—d** in conc. HCl–90% AcOH (1: 11) was treated to give **7a—d** as described for the preparation of **10a—c** from **9a—c**.

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	$C_{16}H_{18}O_4N_2S_2$	52.44 (52.45)	4.95 (5.08)	7.65 (7.80)
5b	Me	66	139—141	acetone	$C_{16}H_{18}O_4N_2S$	57.47 (57.79)	5.42 (5.78)	8.38 (8.55)
5c	H	62	116—118	MeOH	$C_{15}H_{16}O_4N_2S$	56.23 (56.08)	5.04 (4.92)	8.75 (8.74)
5d	Cl	79	160—162	MeOH	$C_{15}H_{15}O_4N_2SCl$	50.77 (51.10)	4.26 (4.20)	7.90 (8.50)
5e	EtO	66	116—118	EtOH	$C_{17}H_{20}O_5N_2S$	56.03 (56.33)	5.53 (5.29)	7.69 (7.65)
5f	SH	81	255—256	DMF	$C_{15}H_{16}O_4N_2S_2$	51.12 (50.83)	4.58 (4.70)	7.95 (8.11)
1	$MeSO_2$	41[b]	188—190	EtOH	$C_{16}H_{18}O_6N_2S_2$	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 K_2CO_3 (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 $CHCl_3$. 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 $CHCl_3$. The extract was washed with 2% K_2CO_3 solution and water. After evaporation of the solvent, the resulting residue was chromatographed on silica gel column. Elution with benzene–$CHCl_3$ (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.

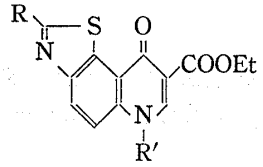
Hydrolyses of **9d** and **9e** were carried out in 1N KOH and 0.5N HCl–42% AcOH respectively, and the reaction mixture were worked up according to the usual procedure.

Treatment of **7a** with EtI, K_2CO_3 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 $C_{10}H_7ON_2S_2F_3$: 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 K_2CO_3 (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 $CHCl_3$. The extract was poured on Al_2O_3 column and eluted with $CHCl_3$. 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 $C_{10}H_{12}N_2S_2$: 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 R	Substituents R′	Yield (%)	mp (°C)	Recrystn. solvent	Formula	Analysis (%) Calcd. (Found) C	H	N
6a	MeS	H	81[a]	>300	DMSO	$C_{14}H_{12}O_3N_2S_2$	52.48 (52.05)	3.78 (3.67)	8.75 (8.94)
6b	Me	H	61[a]	293 (decomp.)	DMF	$C_{14}H_{12}O_3N_2S$	58.32 (58.23)	4.17 (4.25)	9.72 (9.79)
6c	H	H	64[a]	>300	DMF	$C_{13}H_{10}O_3N_2S$	56.92 (57.03)	3.68 (3.65)	10.22 (10.32)
6d	Cl	H	86[a]	>300	DMF	$C_{13}H_9O_3N_2SCl$	50.57 (50.37)	2.94 (2.95)	9.08 (9.37)
6e	EtO	H	92[a]	>300	DMF	$C_{15}H_{14}O_4N_2S$	56.59 (56.43)	4.43 (4.11)	8.80 (8.96)
6f	SH	H	59[a]	>300	DMF	$C_{13}H_{10}O_3N_2S_2$	50.96 (50.67)	3.29 (3.58)	9.15 (9.62)
6g	$MeSO_2$	H	81[b]	>300	DMF–ether	$C_{14}H_{12}O_5N_2S_2$	47.71 (48.20)	3.43 (3.74)	7.95 (8.24)
9a	MeS	Et	76[c]	200—202	acetone	$C_{16}H_{16}O_3N_2S_2$	55.15 (55.11)	4.63 (4.59)	8.04 (7.86)
9b	Me	Et	61[c]	196—198	EtOH	$C_{16}H_{16}O_3N_2S$	60.74 (60.72)	5.10 (5.02)	8.85 (8.92)
9c	H	Et	84[c]	201—203	MeOH	$C_{15}H_{14}O_3N_2S$	59.59 (60.04)	4.67 (4.53)	9.27 (9.34)
9d	Cl	Et	74[c]	219—220	acetone	$C_{15}H_{13}O_3N_2SCl$	53.49 (53.45)	3.89 (3.93)	8.32 (8.63)
14	NFV[d]	Et	63[e]	285 (decomp.)	acetone–$CHCl_3$	$C_{21}H_{17}O_6N_3S$	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*) NO_2-(furyl)-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), Ac_2O (5 ml) and AcOH (5 ml) was stirred at 130—140° for 7 hr. After evaporation of the solvent, the residue was extracted with $CHCl_3$. A brown semi-solid obtained from the extract was chromatographed on Al_2O_3. The fraction eluted with acetone–$CHCl_3$ (1: 1) was concentrated and the residue was crystallized from acetone–$CHCl_3$ (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°.

Acknowledgement The authors are indebted to Dr. N. Koga, director of this institute, Dr. G. Ohta for their support and encouragement. Thanks are due to the members of the analytical section of this institute for elemental analysis.