Condensed Thienopyrimidines. II.[1] Synthesis and Gastric Antisecretory Activity of Thiazole and Polymethylene Condensed Thienopyrimidine Derivatives

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Thiazolo[3,2-*a*]thieno[3,2-*d*]-, [3,4-*d*]- and [2,3-*d*]pyrimidin-5-one derivatives (6, 11 and 16), and polymethylene condensed thieno[3,2-*d*]-, [3,4-*d*]- and [2,3-*d*]pyrimidin-5-one derivatives (19—21), in which the oxygen atom of the oxazolidine moiety in 3 was replaced by a sulfur atom or methylene groups, were synthesized and evaluated for gastric antisecretory activity in pylorus-ligated rats. The structure–activity relationships of these compounds are discussed.

Keywords aminothiophenecarboxylate; thiophosgene; thiazolothienopyrimidine; lactam; polymethylene condensed thienopyrimidine; gastric antisecretory activity; structure–activity relationship

Some thiazolo[3,2-*a*]thieno[2,3-*d*]pyrimidines (**1**) and polymethylene condensed (*e.g.* pyrrolo-, piperidino-, azepino- and others) thieno[2,3-*d*]pyrimidines (**2**) have been synthesized,[2,3] and reported to possess significant biological activities, for example, antiinflammatory activity (**1a** and **2a**),[2a,3a] gastric antisecretory activity (**1b**)[2b] and antidermatomycosis activity (**2b**).[3b]

In treatment of peptic ulcer, it is generally considered to be important to improve the imbalance between aggressive factors (*e.g.* gastric acid secretion and pepsin secretion) and defensive factors (*e.g.* gastric mucosal blood flow, bicarbonate secretion, and mucus secretion).[4] Since the discovery of histamine H_2 receptor antagonists, control of gastric acid secretion has received much attention from a clinical viewpoint because of its superior healing rate and efficacy. In spite of this clinical usefulness, a high recurrence rate of peptic ulcer has been reported after cessation of treatment with H_2 receptor antagonists.[5] On the other hand, more emphasis has recently been placed on the important roles of gastric defensive factors in protection against and healing of peptic ulcer.

We have carried out the preparation of 2,3-dihydro-5*H*-oxazolo[3,2-*a*]thieno[3,2-*d*]pyrimidin-5-one (**3**), which exhibits potent gastric antisecretory activity.[1]

However, no work has been done on the syntheses and biological evaluation of thiazolo[3,2-*a*]thieno[3,2-*d*]- or [3,4-*d*]pyrimidines, though thiazolo[3,2-*a*]thieno[2,3-*d*]pyrimidines have been reported.[2] As for polymethylene condensed thienopyrimidines, only thieno[2,3-*d*]pyrimidine derivatives have been reported.[3]

In this paper, we wish to describe the synthesis and gastric antisecretory activity of various thiazole and polymethylene condensed thienopyrimidin-5-ones (**6a—o**, **11a—k**, **16a—d**, **19a—n**, **20a—l** and **21a—i**), which include new heterocyclic systems such as thiazolo[3,2-*a*]thieno[3,2-*d*]-, [3,4-*d*]pyrimidines and pyrrole, pyridine, azepine, azocine, and azonine condensed thieno[3,2-*d*]-, and [3,4-*d*]pyrimidines.

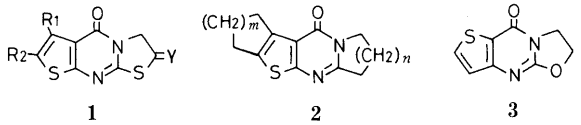


Fig. 1

Chemistry Thiazole and polymethylene condensed

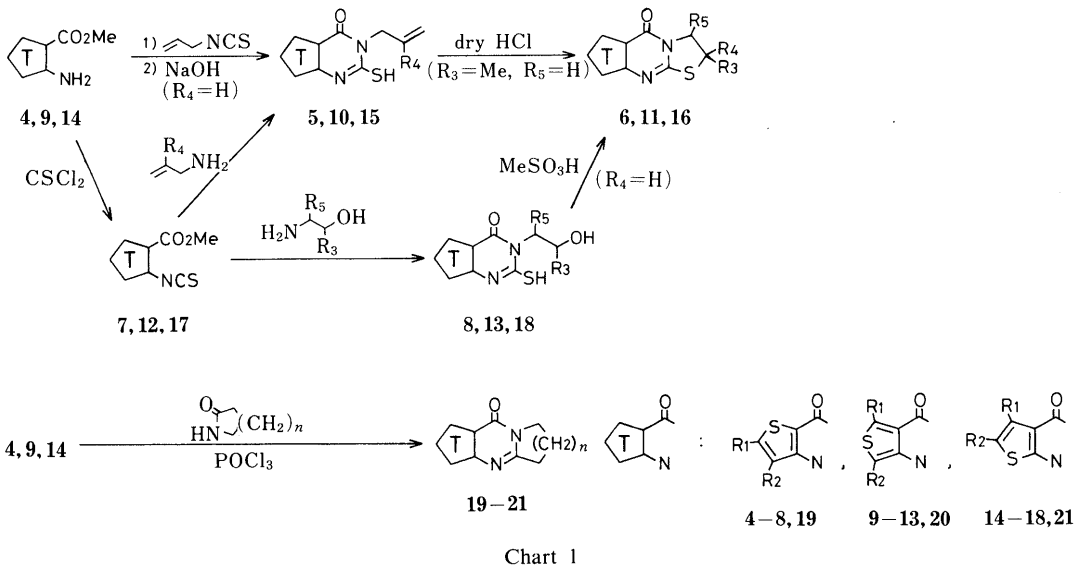


Chart 1

thienopyrimidines were synthesized according to procedures similar to those used for tricyclic thieno[2,3-*d*]pyrimidines.[2,3] Two methods were utilized for synthesis of thiazolothienopyrimidines. Heating of methyl 3-aminothiophene-2-carboxylate derivatives (**4a**, **h**, **m**, **n**) with allyl isothiocyanate in ethanol (EtOH) followed by treatment with sodium hydroxide (NaOH) gave 3-allyl-2-mercaptothieno[3,2-*d*]pyrimidin-4(3*H*)-one derivatives (**5b**, **i**, **m**, **o**). Cyclization of **5b**, **i**, **m**, **o** with hydrogen chloride afforded the desired 2,3-dihydro-2-methyl-5*H*-thiazolo[3,2-*a*]thieno-[3,2-*d*]pyrimidin-5-one derivatives (**6b**, **i**, **m**, **o**) in excellent yields. An alternative convenient method for facile synthesis of a number of 2,3-dihydro-5*H*-thiazolo[3,2-*a*]-thieno[3,2-*d*]pyrimidin-5-one derivatives (**6**) was investigated. Treatment of **4a**, **h**, **l**, **n** with thiophosgene ($CSCl_2$)

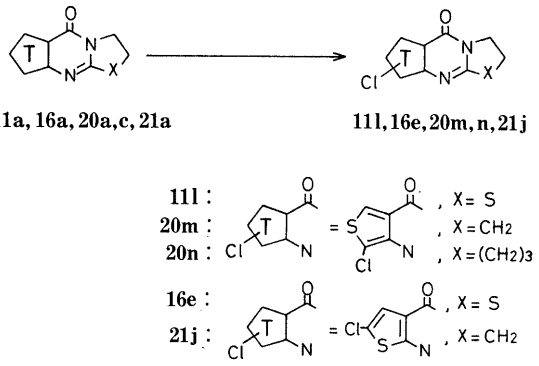


Chart 2

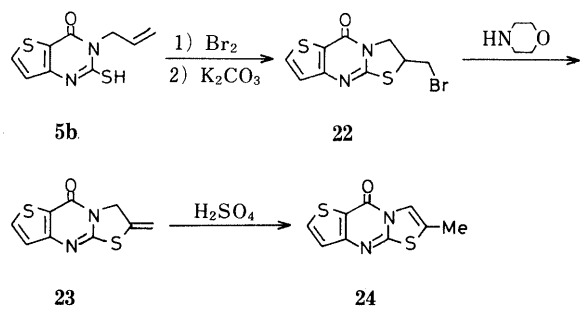
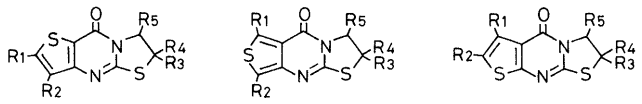


Chart 3

TABLE I. Substituted 2,3-Dihydro-5*H*-thiazolothienopyrimidin-5-ones (**6**, **11**, and **16**)



6 **11** **16**

Compd. No.	R_1	R_2	R_3	R_4	R_5	Yield (%)	mp (°C) (Recryst. solv.)[a]	Formula	Analysis (%) Calcd C	H	Cl	N	S	Found C	H	Cl	N	S
6a	H	H	H	H	H	72	187—189 (E)	$C_8H_6N_2OS_2$	45.70	2.88		13.32	30.49	45.47	2.82		13.05	30.46
6b	H	H	Me	H	H	69	95—97 (H)	$C_9H_8N_2OS_2$	48.19	3.60		12.49	28.59	48.25	3.60		12.53	28.70
6c	H	H	Et	H	H	67	98—100 (C–H)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.22	4.04		11.79	26.97
6d	H	H	Ph	H	H	85	126—128 (E–EA)	$C_{14}H_{10}N_2OS_2$	58.72	3.52		9.78	22.39	58.68	3.24		9.83	22.62
6e	H	H	Me	Me	H	86	121—123 (C–H)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.12	3.96		11.70	26.98
6f	H	H	H	H	Me	83	147—149 (C–H)	$C_9H_8N_2OS_2$	48.19	3.60		12.49	28.59	48.31	3.46		12.72	28.57
6g	H	H	H	H	Ph	80	Oil	$C_{14}H_{10}N_2OS_2 \cdot 3/4\,H_2O$	56.08	3.87		9.34	21.38	56.40	3.96		8.99	21.48
6h	Me	H	H	H	H	87	193—194 (E)	$C_9H_8N_2OS_2$	48.19	3.60		12.49	28.59	48.15	3.45		12.42	28.61
6i	Me	H	Me	H	H	93	182—184 (EA–H)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.29	4.05		11.72	26.78
6j	Me	H	H	H	Me	91	177—180 (E–EA)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.72	3.88		11.83	27.06
6k[b]	Me	H	H	H	iso-Bu	94	197—199 (E)	$C_{13}H_{16}N_2OS_2 \cdot HCl$	49.28	5.41	11.19	8.84	20.24	49.36	5.42	11.46	8.92	20.52
6l	Et	H	H	H	H	91	138—139 (EA–H)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.39	4.11		11.94	26.98
6m	H	Me	Me	H	H	80	110—112 (EA–H)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.70	4.22		12.16	26.84
6n	Me	Me	H	H	H	76	160—162 (E–EA)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.20	4.31		11.39	26.93
6o	Me	Me	Me	H	H	64	156—158 (EA–H)	$C_{11}H_{12}N_2OS_2$	52.35	4.79		11.10	25.41	52.40	4.86		11.08	25.56
11a	H	H	H	H	H	83	198—200 (E)	$C_8H_6N_2OS_2$	45.70	2.88		13.32	30.49	45.79	2.77		13.35	30.25
11b	H	H	Me	H	H	85	107—109 (EA–H)	$C_9H_8N_2OS_2$	48.19	3.60		12.49	28.59	47.95	3.43		12.49	28.41
11c	Me	H	Me	H	H	85	95—96 (EA–H)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.29	4.19		11.85	27.10
11d	H	Me	Me	H	H	88	113—114 (C–H)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.30	4.10		11.67	26.94
11e	H	Me	Me	Me	H	80	146—147 (EA–H)	$C_{11}H_{12}N_2OS_2$	52.35	4.79		11.10	25.41	52.28	4.59		11.27	25.47
11f	H	Et	H	H	H	90	146—148 (EA–H)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.22	3.95		11.94	26.62
11g	H	Et	Me	H	H	92	82—84 (EA–H)	$C_{11}H_{12}N_2OS_2$	52.35	4.79		11.10	25.41	52.42	4.74		11.16	25.47
11h	H	Et	Me	Me	H	Quant.	56—57 (EA–H)	$C_{12}H_{14}N_2OS_2$	54.11	5.30		10.52	24.07	53.90	5.00		10.69	24.13
11i	Me	Me	H	H	H	86	170—172 (E–EA)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.54	3.95		11.76	27.05
11j	Me	Me	Me	H	H	88	119—121 (EA–H)	$C_{11}H_{12}N_2OS_2$	52.35	4.79		11.10	25.41	52.34	4.63		11.10	25.65
11k	Me	Me	Me	Me	H	88	191—193 (EA–H)	$C_{12}H_{14}N_2OS_2$	54.11	5.30		10.52	24.07	53.94	5.07		10.51	23.95
11l	H	Cl	H	H	H	80	169—170 (E)	$C_8H_5ClN_2OS_2$	39.26	2.06	14.49	11.45	26.20	39.11	1.93	14.40	11.31	25.95
16a	H	H	H	H	H	82	202—204 (C–E)	$C_8H_6N_2OS_2$	45.70	2.88		13.32	30.49	45.63	2.78		13.26	30.30
16b	H	H	Me	H	H	56	123—125 (C–H)	$C_9H_8N_2OS_2$	48.19	3.60		12.49	28.59	48.11	3.55		12.31	28.41
16c	Me	H	Me	H	H	63	140—142 (EA–H)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.29	4.27		11.84	26.88
16d	H	Me	Me	H	H	50	124—126 (EA)	$C_{10}H_{10}N_2OS_2$	50.40	4.23		11.75	26.91	50.35	4.18		11.81	27.16
16e	H	Cl	H	H	H	43	160—162 (E)	$C_8H_5ClN_2OS_2$	39.26	2.06	14.49	11.45	26.20	39.26	1.87	14.78	11.34	26.16

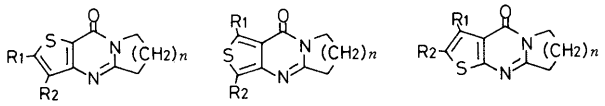
a) C, $CHCl_3$; E, EtOH; EA, AcOEt; H, hexane; M, MeOH. *b*) HCl salt.

afforded isothiocyanate analogues (**7a**, **h**, **l**, **n**) according to the procedure of Kienzle *et al.*[2b] Reaction of **7a**, **h**, **l**, **n** with various 2-aminoethanols afforded 3-(2-hydroxyethyl)-2-mercaptothieno[3,2-*d*]pyrimidin-4(3*H*)-one derivatives (**8a**, **c**, **d**, **f**—**h**, **j**—**l**, **n**), which were cyclized to **6a**, **c**, **d**, **f**—**h**, **j**—**l**, **n** by heating with methanesulfonic acid. 2,3-Dihydro-2,2-dimethyl-5*H*-thiazolo[3,2-*a*]thieno[3,2-*d*]-pyrimidin-5-one (**6e**) was obtained by the treatment of **7a** with 2-methylallylamine followed by cyclization with hydrogen chloride. 2,3-Dihydro-5*H*-thiazolo[3,2-*a*]thieno-[3,4-*d*]- and [2,3-*d*]pyrimidin-5-one derivatives (**11a**—**k** and **16a**—**d**) were prepared from methyl aminothiophenecarboxylates (**9** and **14**, respectively) using the methods described above.

Polymethylene condensed thieno[3,2-*d*]pyrimidines **19a**—**n** were prepared with facility by condensation of **4a**, **h**, **l**, **n** with various lactams in the presence of catalytic amounts of phosphorus oxychloride. Using a method similar to that used to synthesize **19**, other isomers **20a**—**l** or **21a**—**i** were obtained from **9** or **14**, respectively. These derivatives are listed in Tables I and II.

Other thiazolo-, pyrrolo- or azepinothienopyrimidine derivatives (**11 l**, **16e**, **20m**, **n**, and **21j**) having a chloro substituent on the thiophene ring were synthesized by treatment of tricyclic thienopyrimidines (**11a**, **16a**, **20a**, **c** and **21a**) with sulfuryl chloride (SO_2Cl_2) or *N*-chlorosuccinimide (NCS). The thiazolo[3,2-*a*]thieno[3,2-*d*]pyrimidine derivatives, **23** and **24**, possessing an *exo*- or *endo*-double bond in the thiazolidine moiety of 2,3-dihydro-2-methyl-5*H*-thiazolo[3,2-*a*]theino[3,2-*d*]pyrimidin-5-one (**6b**) were synthesized by the procedure shown in Chart 3. Bromination of **5b** followed by treatment with potassium carbonate (K_2CO_3) gave the cyclized 2-bromomethyl derivative **22** in 86% yield. Treatment of **22** with morpholine

TABLE II. Polymethylene Condensed Thienopyrimidines (**19**, **20**, and **21**)



19 **20** **21**

Compd. No.	R_1	R_2	*n*	Yield (%)	mp (°C) (Recryst. solv.)[a]	Formula	Analysis (%) Calcd C	H	Cl	N	S	Found C	H	Cl	N	S
19a	H	H	1	40	150—152 (E–EA)	$C_9H_8N_2OS$	56.23	4.19		14.57	16.68	56.38	3.98		14.67	16.49
19b	H	H	2	71	102—103 (EA–H)	$C_{10}H_{10}N_2OS \cdot 1/3\,H_2O$	56.58	5.07		13.20	15.10	56.55	5.26		13.40	15.05
19c	H	H	3	81	110—111 (EA)	$C_{11}H_{12}N_2OS$	59.97	5.49		12.72	14.56	59.92	5.56		12.64	14.46
19d	Me	H	1	90	170—172 (E–EA)	$C_{10}H_{10}N_2OS$	58.23	4.89		13.58	15.54	58.39	4.75		13.83	15.21
19e	Me	H	2	85	96—97 (EA–H)	$C_{11}H_{12}N_2OS \cdot 1/5\,H_2O$	59.01	5.58		12.51	14.32	59.12	5.33		12.63	14.38
19f	Me	H	3	82	113—115 (EA–H)	$C_{12}H_{14}N_2OS$	61.51	6.02		11.96	13.68	61.47	5.97		11.92	13.75
19g	Me	H	4	66	120—121 (EA–H)	$C_{13}H_{16}N_2OS$	62.87	6.49		11.28	12.91	62.71	6.43		11.11	13.23
19h	Me	H	5	72	113—114 (EA–H)	$C_{14}H_{18}N_2OS$	64.09	6.92		10.68	12.22	64.03	6.88		10.84	12.07
19i	Et	H	1	63	89—90 (EA)	$C_{11}H_{12}N_2OS$	59.97	5.49		12.72	14.56	59.91	5.44		12.59	14.53
19j	Et	H	2	64	78—79 (EA–H)	$C_{12}H_{14}N_2OS$	61.51	6.02		11.96	13.68	61.32	5.74		11.92	13.55
19k	Et	H	3	78	70—73 (EA)	$C_{13}H_{16}N_2OS$	62.87	6.49		11.28	12.91	62.78	6.46		11.11	13.15
19l	Me	Me	1	84	157—159 (EA)	$C_{11}H_{12}N_2OS$	59.97	5.49		12.72	14.56	59.93	5.39		12.74	14.61
19m	Me	Me	2	71	164—166 (EA)	$C_{12}H_{14}N_2OS$	61.51	6.02		11.96	13.68	61.27	5.71		12.05	13.92
19n	Me	Me	3	82	154—156 (EA–H)	$C_{13}H_{16}N_2OS$	62.87	6.49		11.28	12.91	62.97	6.30		11.41	12.88
20a	H	H	1	50	144—146 (EA)	$C_9H_8N_2OS$	56.23	4.19		14.57	16.68	56.35	3.95		14.49	16.69
20b	H	H	2	82	126—128 (EA)	$C_{10}H_{10}N_2OS \cdot 1/5\,H_2O$	57.23	5.00		13.35	15.28	57.40	4.77		13.32	15.25
20c	H	H	3	70	154—156 (EA)	$C_{11}H_{12}N_2OS$	59.97	5.49		12.72	14.56	59.98	5.68		12.79	14.60
20d	H	Me	1	67	128—129 (EA)	$C_{10}H_{10}N_2OS$	58.23	4.89		13.58	15.54	58.18	4.85		13.64	15.81
20e	H	Me	2	50	108—109 (EA–H)	$C_{11}H_{12}N_2OS$	59.97	5.49		12.72	14.56	59.89	5.41		12.70	14.54
20f	H	Me	3	57	113—115 (EA–H)	$C_{12}H_{14}N_2OS$	61.51	6.02		11.96	13.68	61.70	5.96		11.98	13.67
20g	H	Et	1	50	90—91 (EA–H)	$C_{11}H_{12}N_2OS$	59.97	5.49		12.72	14.56	59.93	5.25		12.79	14.57
20h[b]	H	Et	2	29	255—257 (E)	$C_{12}H_{14}N_2OS \cdot HCl$	53.23	5.21	13.09	10.35	11.84	53.21	5.41	12.80	10.29	11.76
20i	H	Et	3	13	67—70 (EA–H)	$C_{13}H_{16}N_2OS$	62.87	6.49		11.28	12.91	62.55	6.36		11.26	13.06
20j	Me	Me	1	80	77—79 (EA–H)	$C_{11}H_{12}N_2OS \cdot 2/3\,H_2O$	56.87	5.79		12.06	13.80	56.89	5.63		12.00	13.77
20k	Me	Me	2	50	72—73 (EA–H)	$C_{12}H_{14}N_2OS$	61.51	6.02		11.96	13.68	61.32	5.86		11.73	13.65
20l	Me	Me	3	39	103—104 (EA–H)	$C_{13}H_{16}N_2OS$	62.87	6.49		11.28	12.91	62.87	6.52		11.43	12.88
20m	H	Cl	1	68	116—118 (EA–H)	$C_9H_7ClN_2OS$	47.69	3.11	15.64	12.36	14.14	47.87	3.19	15.66	12.36	14.22
20n	H	Cl	3	52	106—108 (EA–H)	$C_{11}H_{11}ClN_2OS$	51.87	4.35	13.92	11.00	12.59	51.92	4.28	13.93	11.08	12.72
21a	H	H	1	70	172—174 (EA)	$C_9H_8N_2OS$	56.23	4.19		14.57	16.68	56.13	4.07		14.74	16.66
21b	H	H	2	56	103—105 (EA)	$C_{10}H_{10}N_2OS$	58.23	4.89		13.58	15.54	58.12	4.73		13.35	15.59
21c	Me	H	1	97	116—118 (EA)	$C_{10}H_{10}N_2OS$	58.23	4.89		13.58	15.54	58.35	4.73		13.60	15.80
21d	H	Me	1	83	144—145 (C–H)	$C_{10}H_{10}N_2OS$	58.23	4.89		13.58	15.54	58.13	4.85		13.70	15.52
21e	H	Me	2	78	108—111 (EA–H)	$C_{11}H_{12}N_2OS$	59.98	5.49		12.72	14.55	59.81	5.50		12.80	14.42
21f	H	Me	3	47	100—102 (M)	$C_{12}H_{14}N_2OS$	61.51	6.02		11.95	13.68	61.44	5.95		11.99	13.59
21g	H	iso-Pr	1	82	93—95 (C–H)	$C_{12}H_{14}N_2OS$	61.51	6.02		11.95	13.68	61.67	5.95		12.09	13.79
21h	H	iso-Pr	2	96	113—115 (EA–H)	$C_{13}H_{16}N_2OS$	62.87	6.50		11.28	12.91	62.63	6.27		11.49	13.07
21i	H	iso-Pr	3	38	97—98 (M)	$C_{14}H_{18}N_2OS$	64.09	6.91		10.68	12.22	63.94	7.05		10.66	12.01
21j	H	Cl	1	36	154—156 (E–EA)	$C_9H_7ClN_2OS$	47.69	3.11	15.64	12.36	14.14	47.67	2.96	15.97	12.44	14.22

a) C, CH_2Cl_2; E, EtOH; EA, AcOEt; H, hexane; M, MeOH. *b*) HCl salt.

TABLE III. Gastric Antisecretory Activity of Tricyclic Thienopyrimidine Derivtives

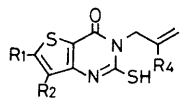
Compd. No.	Gastric antisecretory activity (%, 50 mg/kg, i.d.)	Compd. No.	Gastric antisecretory activity (%, 50 mg/kg, i.d.)
6a	66	**19a**	83
6b	46	**19b**	92
6h	81	**19d**	95
6i	34	**19e**	82
6k	79	**19f**	68
6m	41	**19h**	22
6o	60	**19i**	80
11a	67	**19m**	41
11b	82	**19n**	17
11c	58	**20c**	77
11d	60	**20d**	65
11f	45	**20e**	90
11g	68	**20f**	85
11h	86	**20g**	81
11i	76	**20h**	79
11j	62	**20i**	82
11l	71	**20j**	64
16a	78	**20k**	62
16b	64	**20l**	55
16c	10	**20m**	85
16d	44	**21a**	82
23	50	**21d**	52
24	50	**21e**	73
1a[a]	47	**21f**	58
Cimetidine	46	**21g**	80
		21i	61

a) Ref. 2a.

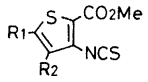
afforded the dehydrobrominated compound, *exo*-methylene substituted thiazolothienopyrimidine **23**. The isomerization of **23** with sulfuric acid (H_2SO_4) afforded the *endo*-methylene analogue (**24**).

Pharmacology and Structure–Activity Relationships The tricyclic compounds prepared in the present study were tested for gastric antisecretory activity in pylorus-ligated rats, by intraduodenal (i.d.) injection at a dose of 50 mg/kg. The results are shown in Table III. The structure–activity relationships in these derivatives are as follows. Gastric antisecretory activities of thiazolothienopyrimidines (**6**, **11** and **16**) were somewhat lower than those of the previously reported oxazolothienopyrimidine derivatives,[1a] while polymethylene condensed thienopyrimidine derivatives exhibited the most potent activities in these series. As for the positional isomers of the condensed thiophene ring, thieno[2,3-*d*]pyrimidine derivatives (**16** and **21**) exhibited reduced activity compared with thieno[3,2-*d*]pyrimidine derivatives (**6** and **19**) or thieno[3,4-*d*]pyrimidines derivatives (**11** and **20**). It was noted that this activity was profoundly influenced by the substituents on the thiophene ring. Decreasing the number of substituents on the thiophene ring resulted in a marked increase of the activity. These structure–activity relationships are in accordance with previous observations of the oxazolothienopyrimidine series.[1a] With regard to the size of the polymethylene ring on **19**—**21**, a marked enhancement of activity was observed in the case of the thienopyrimidine derivatives condensed with a five- or six-membered ring.

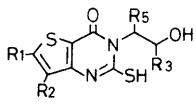
TABLE IV. Intermediates (**5**, **7**, and **8**) to 2,3-Dihydro-5*H*-thiazolo[3,2-*a*]thieno[3,2-*d*]pyrimidin-5-one Derivatives (**6**)



5



7



8

Compd. No.	R_1	R_2	R_3	R_4	R_5	Yield (%)	mp (°C) (Recryst. solv.)[a]	Formula	Analysis (%) Calcd C	H	N	S	Found C	H	N	S
5b	H	H		H		47	212—216 (M)	$C_9H_8N_2OS_2$	48.19	3.60	12.49	28.59	48.29	3.47	12.52	28.71
5e	H	H		Me		72	207—210 (M)	$C_{10}H_{10}N_2OS_2$	50.40	4.23	11.75	26.91	50.39	3.99	11.66	26.78
5i	Me	H		H		34	239—241 (E)	$C_{10}H_{10}N_2OS_2$	50.40	4.23	11.75	26.91	50.25	4.02	11.82	26.72
5m	H	Me		H		18	202—204 (E)	$C_{10}H_{10}N_2OS_2$	50.40	4.23	11.75	26.91	50.53	4.07	11.74	27.26
5o	Me	Me		H		24	184—187 (E)	$C_{11}H_{12}N_2OS_2$	52.35	4.79	11.10	25.41	52.58	4.68	11.12	25.42
7a[b,c]	H	H				84	54—56	$C_7H_5NO_2S_2$								
7h	Me	H				93	63—64 (H)	$C_8H_7NO_2S_2$	45.05	3.31	6.57	30.07	44.73	3.15	6.56	29.78
7l	Et	H				75	60—61 (H)	$C_9H_9NO_2S_2$	47.56	3.99	6.16	28.21	47.48	3.80	6.40	27.97
7n	Me	Me				76	70—71 (H)	$C_9H_9NO_2S_2$	47.56	3.99	6.16	28.21	47.61	3.84	6.43	28.32
8a[b]	H	H	H		H	83	255—257	$C_8H_8N_2O_2S_2$								
8c	H	H	Et		H	51	170—172 (M) (dec.)	$C_{10}H_{12}N_2O_2S_2$	46.85	4.72	10.93	25.02	46.81	4.66	10.95	25.37
8d	H	H	Ph		H	98	215—217 (E)	$C_{14}H_{12}N_2O_2S_2$	55.24	3.97	9.20	21.07	55.20	3.80	9.29	21.21
8f	H	H	H		Me	40	176—178 (M–EA)	$C_9H_{10}N_2O_2S_2 \cdot 1/2\,H_2O$	43.01	4.41	11.15	25.51	42.98	4.31	11.20	25.26
8g	H	H	H		Ph	98	193—195 (E)	$C_{14}H_{12}N_2O_2S_2$	55.24	3.97	9.20	21.07	55.03	3.87	9.24	21.08
8h	Me	H	H		H	79	253—255 (E) (dec.)	$C_9H_{10}N_2O_2S_2$	44.61	4.16	11.56	26.46	44.38	4.12	11.60	26.60
8j	Me	H	H		Me	93	210—213 (E)	$C_{10}H_{12}N_2O_2S_2$	46.85	4.72	10.93	25.02	46.63	4.42	10.63	24.98
8k	Me	H	H		iso-Bu	Quant.	172—174 (E)	$C_{13}H_{18}N_2O_2S_2 \cdot 1/4\,H_2O$	51.69	6.14	9.28	21.23	51.67	5.86	9.25	21.26
8l	Et	H	H		H	71	235—237 (M–A)	$C_{10}H_{12}N_2O_2S_2$	46.85	4.72	10.93	25.02	46.94	4.60	11.18	24.98
8n[d]	Me	Me	H		H	71	150—153	$C_{10}H_{12}N_2O_2S_2$								

a) A, acetone; C, $CHCl_3$; D, dimethylformamide; E, EtOH; EA, AcOEt; H, hexane; M, MeOH. b) Ref. 1b. c) Ref. 2b. d) The material was used for the subsequent step without further purification.

Further studies on the synthesis and the structure–activity relationship of tricyclic thienopyrimidines as new anti-ulcer agents are being continued.

Experimental

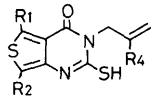
All melting points are uncorrected. Infrared (IR) spectra were measured on a JASCO A-102 spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded with a Varian T-60A (60 MHz) or EM-390

TABLE V. Spectral Data for Intermediates (**5**, **7** and **8**) to 2,3-Dihydro-5*H*-thiazolo[3,2-*a*]thieno[3,2-*d*]pyrimidin-5-one Derivatives (**6**)

Compd. No.	IR (KBr) cm^{-1}	NMR	
		Solvent	δ: ppm
5b	1675	DMSO-d_6	4.99—5.15 (3H, m, $NCH_2C=CH$), 5.20—5.35 (1H, m, $CC=CH$), 5.73—6.20 (1H, m, $CCH=C$), 7.06 and 8.18 (each 1H, d, J=5.4 Hz, ArH×2), 13.2—13.8 (1H, br, SH)
5e	1652	DMSO-d_6	1.77 (3H, s, CH_3), 4.51 (1H, br s, $CC=CH$), 4.73—4.83 (1H, m, $CC=CH$), 4.96 (2H, br s, $NCH_2C=C$), 7.08 and 8.20 (each 1H, d, J=5.4 Hz, ArH×2), 11.0—11.9 (1H, br, SH)
5i	1685[a]	DMSO-d_6	2.56 (3H, d, J=1.5 Hz, $ArCH_3$), 4.95—5.13 (3H, m, $NCH_2C=CH$), 5.18—5.30 (1H, m, $CC=CH$), 5.71—6.20 (1H, m, $CCH=C$), 6.81 (1H, d, J=1.5 Hz, ArH), 13.1—13.8 (1H, br, SH)
5m	1690[b]	DMSO-d_6	2.30 (3H, s, $ArCH_3$), 4.97—5.13 (3H, m, $NCH_2C=CH$), 5.17—5.31 (1H, m, $CC=CH$), 5.69—6.30 (1H, m, $CCH=C$), 7.80 (1H, s, ArH), 11.8—12.5 (1H, br, SH)
5o	1685 (sh), 1680[b]	DMSO-d_6	2.21 and 2.43 (each 3H, s, $ArCH_3$×2), 4.98—5.13 (3H, m, $NCH_2C=CH$), 5.20—5.28 (1H, m, $CC=CH$), 5.73—6.18 (1H, m, $CCH=C$), 10.9—11.2 (1H, br, SH)
7h	1705[a]	$CDCl_3$	2.45 (3H, d, J=1.5 Hz, $ArCH_3$), 3.91 (3H, s, $COOCH_3$), 6.62 (1H, d, J=1.5 Hz, ArH)
7l	1705[a]	$CDCl_3$	1.31 (3H, t, J=7.5 Hz, $ArCH_2CH_3$), 2.80 (2H, q, J=7.5 Hz, $ArCH_2CH_3$), 3.91 (3H, s, $COOCH_3$), 6.67 (1H, s, ArH)
7n	1705[a]	$CDCl_3$	2.10 and 2.36 (each 3H, s, $ArCH_3$×2), 3.90 (3H, s, $COOCH_3$)
8c	1652	CD_3OD	1.02 (3H, t, J=6.8 Hz, CH_2CH_3), 1.40—1.78 (2H, m, CH_2CH_3), 4.04—5.10 (5H, m, NCH_2CHOH, SH), 7.00 and 8.00 (each 1H, d, J=6.0 Hz, ArH×2)
8d	1658	DMSO-d_6	4.37 (1H, dd, J=12.9, 3.9 Hz, NCHCOH), 4.79 (1H, dd, J=12.9, 9.2 Hz, NCHCOH), 5.35 (1H, dd, J=9.2, 3.9 Hz, NCCHOH), 7.06 and 8.17 (each 1H, d, J=5.4 Hz, ArH×2), 7.27—7.56 (5H, m, PhH×5)
8f	1672	CD_3OD	1.54 (3H, d, J=6.9 Hz, CH_3), 3.87—4.42 (2H, m, $NCCH_2OH$), 5.09—7.30 (1H, m, NCHCOH), 6.99 and 7.99 (each 1H, d, J=5.4 Hz, ArH×2)
8g	1657	DMSO-d_6	4.23—4.53 (2H, m, $NCCH_2OH$), 5.03 (1H, br s, NCHCOH), 7.06 and 8.16 (each 1H, d, J=5.4 Hz, ArH×2), 7.13—7.53 (5H, m, PhH×5)
8h	1644	DMSO-d_6	2.58 (3H, s, $ArCH_3$), 3.66 (2H, t, J=6.6 Hz, $NCCH_2OH$), 4.50 (2H, t, J=6.6 Hz, NCH_2COH), 6.82 (1H, s, ArH)
8j	1661	DMSO-d_6	1.40 (3H, d, J=6.9 Hz, CH_3), 2.57 (3H, s, $ArCH_3$), 3.61—4.16 (2H, m, $NCCH_2OH$), 4.77 (1H, t, J=5.7 Hz, OH), 5.97 (1H, q, J=6.9 Hz, NCHCOH), 6.81 (1H, s, ArH), 11.30 (1H, br s, SH)
8k	1651	DMSO-d_6	0.66—1.12 (6H, m, $CH_2CH(CH_3)_2$), 1.27—2.20 (3H, m, $CH_2CH(CH_3)_2$), 2.52 (3H, s, $ArCH_3$), 3.57—3.96 (2H, m, $NCCH_2OH$), 5.83—6.23 (1H, m, NCHCOH), 6.77 (1H, s, ArH), 4.72 and 11.27 (each 1H, br s, OH, SH)
8l	1647	DMSO-d_6	1.27 (3H, t, J=7.5 Hz, $ArCH_2CH_3$), 2.91 (2H, q, J=7.5 Hz, $ArCH_2CH_3$), 3.33 (2H, t, J=6.9 Hz, $NCCH_2OH$), 4.50 (2H, t, J=6.9 Hz, NCH_2COH), 6.83 (1H, s, ArH)

a) $CHCl_3$. b) Liquid film.

TABLE VI. Intermediates (**10**, **12**, and **13**) to 2,3-Dihydro-5*H*-thiazolo[3,2-*a*]thieno[3,4-*d*]pyrimidin-5-one Derivatives (**11**)



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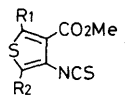
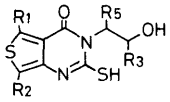


12



13

Compd. No.	R_1	R_2	R_3	R_4	R_5	Yield (%)	mp (°C) (Recryst. solv.)[a]	Formula	Analysis (%) Calcd C	H	N	S	Found C	H	N	S
10b	H	H		H		67	201—203 (E)	$C_9H_8N_2OS_2$	48.19	3.60	12.49	28.59	48.06	3.45	12.50	28.67
10c	Me	H		H		79	212—213 (E)	$C_{10}H_{10}N_2OS_2$	50.40	4.23	11.75	26.91	50.51	4.29	11.86	27.10
10d	H	Me		H		69	177—179 (E)	$C_{10}H_{10}N_2OS_2$	50.40	4.23	11.75	26.91	50.17	4.30	11.74	26.85
10e	H	Me		Me		80	178—179 (E)	$C_{11}H_{12}N_2OS_2$	52.35	4.79	11.10	25.41	52.13	4.72	11.14	25.61
10g	H	Et		H		69	172—175 (E)	$C_{11}H_{12}N_2OS_2$	52.35	4.79	11.10	25.41	52.31	4.61	10.99	25.24
10h	H	Et		Me		96	172—173 (EA–H)	$C_{12}H_{14}N_2OS_2$	54.11	5.30	10.52	24.07	54.03	5.15	10.33	23.83
10j	Me	Me		H		34	209—212 (E)	$C_{11}H_{12}N_2OS_2$	52.35	4.79	11.10	25.41	52.25	4.65	11.07	25.69
10k	Me	Me		Me		86	179—182 (E)	$C_{12}H_{14}N_2OS_2$	54.11	5.30	10.52	24.07	53.85	5.02	10.51	23.87
12a	H	H				74	103—104 (H)	$C_7H_5NO_2S_2$	42.20	2.53	7.03	32.18	42.19	2.46	7.14	32.14
12f	H	Et				Quant.	Oil[b]	$C_9H_9NO_2S_2$	47.56	3.99	6.16	28.21	47.33	4.03	6.15	28.22
12i	Me	Me				72	<35 (H)	$C_9H_9NO_2S_2$	47.56	3.99	6.16	28.21	47.51	4.07	6.16	28.04
13a	H	H	H		H	93	232—234 (dec.) (D–A)	$C_8H_8N_2O_2S_2$	42.09	3.53	12.27	28.09	42.22	3.49	12.38	27.75
13f	H	Et	H		H	77	181—183 (M)	$C_{10}H_{12}N_2O_2S_2 \cdot 1/5\,H_2O$	46.21	4.81	10.78	24.66	46.36	4.56	10.91	24.35
13i	Me	Me	H		H	74	210—212 (M)	$C_{10}H_{12}N_2O_2S_2 \cdot 1/4\,H_2O$	46.06	4.83	10.74	24.59	45.83	4.63	10.78	24.71

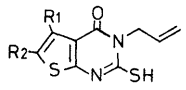
a) See footnote *a* in Table IV. b) bp 165 °C/7 mmHg.

TABLE VII. Spectral Data for Intermediates (**10**, **12** and **13**) to 2,3-Dihydro-5*H*-thiazolo[3,2-*a*]thieno[3,4-*d*]pyrimidine-5-one Derivatives (**11**)

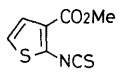
Compd. No.	IR (KBr) cm^{-1}	NMR	
		Solvent	δ: ppm
10b	1656, 1605	DMSO-d_6	4.95—5.12 (3H, m, $NCH_2C=CH$), 5.17—5.27 (1H, m, $CC=CH$), 5.70—6.13 (1H, m, $CCH=C$), 7.10 and 8.48 (each 1H, d, $J=3.0$ Hz, ArH × 2), 12.92 (1H, br s, SH)
10c	1702, 1607	DMSO-d_6	2.79 (3H, s, $ArCH_3$), 4.92—5.11 (3H, m, $NCH_2C=CH$), 5.16—5.28 (1H, m, $CC=CH$), 5.69—6.17 (1H, m, $CCH=C$), 6.76 (1H, s, ArH), 11.75 (1H, br s, SH)
10d	1687, 1606	DMSO-d_6	2.52 (3H, s, $ArCH_3$), 4.96—5.10 (3H, m, $NCH_2C=CH$), 5.16—5.27 (1H, m, $CC=CH$), 5.70—6.15 (1H, m, $CCH=C$), 8.26 (1H, s, ArH), 11.63 (1H, br s, SH)
10e	1693, 1603	DMSO-d_6	1.75 (3H, br s, CH_3), 2.53 (3H, s, $ArCH_3$), 4.46 (1H, br s, $CC=CH$), 4.70—4.82 (1H, m, $CC=CH$), 4.95 (2H, br s, $NCH_2C=C$), 8.30 (1H, s, ArH), 11.69 (1H, br s, SH)
10g	1705, 1605	DMSO-d_6	1.21 (3H, t, $J=7.5$ Hz, $ArCH_2C\underline{H}_3$), 3.01 (2H, q, $J=7.5$ Hz, $ArC\underline{H}_2CH_3$), 4.97—5.12 (3H, m, $NCH_2C=CH$), 5.16—5.27 (1H, m, $CC=CH$), 5.70—6.17 (1H, m, $CCH=C$), 8.30 (1H, s, ArH), 11.61 (1H, br s, SH)
10h	1690, 1600	$CDCl_3$	1.35 (3H, t, $J=7.5$ Hz, $ArCH_2C\underline{H}_3$), 1.83 (3H, br s, CH_3), 2.89 (2H, q, $J=7.5$ Hz, $ArC\underline{H}_2CH_3$), 4.67 (1H, br s, $CC=CH$), 4.82—4.93 (1H, m, $CC=CH$), 5.07 (2H, br s, $NCH_2C=C$), 8.07 (1H, s, ArH), 9.88 (1H, br s, SH)
10j	1695, 1610[a]	DMSO-d_6	2.44 and 2.73 (each 3H, s, $ArCH_3$ × 2), 4.93—5.12 (3H, m, $NCH_2C=CH$), 5.14—5.30 (1H, m, $CC=CH$), 5.70—6.15 (1H, m, $CCH=C$), 11.43 (1H, br s, SH)
10k	1689, 1615	DMSO-d_6	1.75 (3H, br s, CH_3), 2.46 and 2.72 (each 3H, s, $ArCH_3$ × 2), 4.48 (1H, br s, $CC=CH$), 4.71—4.82 (1H, m, $CC=CH$), 4.93 (2H, br s, $NCH_2C=C$), 11.46 (1H, br s, SH)
12a	1710	$CDCl_3$	3.91 (3H, s, $COOCH_3$), 7.15 and 8.08 (each 1H, d, $J=3.6$ Hz, ArH × 2)
12f	1710[a]	$CDCl_3$	1.30 (3H, t, $J=7.5$ Hz, $ArCH_2C\underline{H}_3$), 2.86 (2H, q, $J=7.5$ Hz, $ArC\underline{H}_2CH_3$), 3.91 (3H, s, $COOCH_3$), 7.90 (1H, s, ArH)
12i	1715[a]	$CDCl_3$	2.36 and 2.63 (each 3H, s, $ArCH_3$ × 2), 3.91 (3H, s, $COOCH_3$)
13a	1660, 1600	DMSO-d_6	3.67 (2H, t, $J=6.6$ Hz, $NCH_2C\underline{H}_2O$), 4.51 (2H, t, $J=6.6$ Hz, $NC\underline{H}_2CH_2O$), 7.09 and 8.48 (each 1H, d, $J=3.0$ Hz, ArH × 2), 4.4—5.1 and 11.2—12.6 (each 1H, br, OH, SH)
13f	1669, 1602	DMSO-d_6	1.19 (3H, t, $J=7.5$ Hz, $ArCH_2C\underline{H}_3$), 3.01 (2H, q, $J=7.5$ Hz, $ArC\underline{H}_2CH_3$), 3.46—3.84 (2H, m, $NCH_2C\underline{H}_2O$), 4.50 (2H, t, $J=6.8$ Hz, $NC\underline{H}_2CH_2O$), 8.30 (1H, s, ArH), 4.6—4.9 and 11.8—12.5 (each 1H, br, SH, OH)
13i	1680, 1612	DMSO-d_6	2.42 and 2.73 (each 3H, s, $ArCH_3$ × 2), 3.62 (2H, t, $J=7.2$ Hz, $NCH_2C\underline{H}_2O$), 4.47 (2H, t, $J=7.2$ Hz, $NC\underline{H}_2CH_2O$), 4.3—5.3 (1H, br, OH or SH)

a) $CHCl_3$.

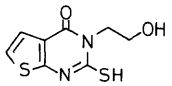
TABLE VIII. Intermediates (**15**, **17**, and **18**) to 2,3-Dihydro-5*H*-thiazolo[3,2-*a*]thieno[2,3-*d*]pyrimidin-5-one Derivatives (**16**)



15



17



18

Compd. No.	R_1	R_2	Yield (%)	mp (°C) (Recryst. solv.)[a]	Formula	Analysis (%) Calcd				Found			
						C	H	N	S	C	H	N	S
15b	H	H	63	203—205 (E)	$C_9H_8N_2OS_2$	48.19	3.60	12.49	28.59	48.11	3.56	12.24	28.37
15c	Me	H	52	205—207 (E)	$C_{10}H_{10}N_2OS_2$	50.40	4.23	11.75	26.91	50.27	4.39	11.53	26.60
15d	H	Me	66	218—221 (E)	$C_{10}H_{10}N_2OS_2$	50.40	4.23	11.75	26.91	50.34	4.13	11.72	26.68
17			39	61—62 (H)	$C_7H_5NO_2S_2$	42.20	2.53	7.03	32.18	42.11	2.29	6.97	31.99
18			68	232—234 (dec.) (D–A)	$C_8H_8N_2O_2S_2$	42.09	3.53	12.27	28.09	42.28	3.41	12.41	27.81

a) See footnote *a* in Table IV.

TABLE IX. Spectral Data for Intermediates (**15**, **17** and **18**) to 2,3-Dihydro-5*H*-thiazolo[3,2-*a*]thieno[2,3-*d*]pyrimidin-5-one Derivatives (**16**)

Compd. No.	IR (KBr) cm^{-1}	NMR	
		Solvent	δ: ppm
15b	1650 (sh), 1645	DMSO-d_6	4.94—5.13 (3H, m, $NCH_2C=CH$), 5.17—5.29 (1H, m, $CC=CH$), 5.70—6.15 (1H, m, $CCH=C$), 7.24 and 7.29 (each 1H, d, $J=6.0$ Hz, ArH × 2)
15c	1690[a]	DMSO-d_6	2.39 (3H, d, $J=1.2$ Hz, $ArCH_3$), 4.95—5.13 (3H, m, $NCH_2C=CH$), 5.17—5.30 (1H, m, $CC=CH$), 5.70—6.16 (1H, m, $CCH=C$), 6.87 (1H, d, $J=1.2$ Hz, ArH), 11.70 (1H, br s, SH)
15d	1655 (sh), 1645	DMSO-d_6	2.42 (3H, d, $J=0.9$ Hz, $ArCH_3$), 4.93—5.12 (3H, m, $NCH_2C=CH$), 5.17—5.28 (1H, m, $CC=CH$), 5.70—6.13 (1H, m, $CCH=C$), 6.93 (1H, d, $J=0.9$ Hz, ArH), 11.3—12.0 (1H, br, SH)
17	1705	$CDCl_3$	3.91 (3H, s, $COOCH_3$), 6.97 and 8.15 (each 1H, d, $J=6.0$ Hz, ArH × 2)
18	1650 (sh), 1640	DMSO-d_6	3.64 (2H, t, $J=7.2$ Hz, $NCH_2C\underline{H}_2O$), 4.49 (2H, t, $J=7.2$ Hz, $NC\underline{H}_2CH_2O$), 7.20 and 7.30 (each 1H, d, $J=4.5$ Hz, ArH × 2), 4.3—5.0 and 12.3—13.1 (each 1H, br, OH, SH)

a) $CHCl_3$.

(90 MHz) spectrometer and the chemical shifts are expressed in ppm from tetramethylsilane as an internal standard; s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; m, multiplet; br, broad. Mass spectra (MS) were obtained with a JEOL JMS-01SG or JMS-G300 mass spectrometer. Merck silica gel (Kieselgel 60 Art. 7734) was employed for column chromatography.

3-Allyl-2-mercaptothieno[3,2-*d*]pyrimidin-4(3*H*)-one(5b) (General Procedure) A solution of methyl 3-aminothiophene-2-carboxylate (**4a**) (26.00 g) and allylisothiocyanate (32.68 g) in *n*-PrOH (200 ml) was refluxed for 24 h and then the solvent was removed *in vacuo*. A 10% NaOH solution was added to the residue and the mixture was washed with AcOEt. The aqueous layer was acidified with 10% HCl solution, and the resulting

TABLE X. Spectral Data for Various Substituted 2,3-Dihydro-5*H*-thiazolothienopyrimidin-5-ones (**6**, **11**, and **16**)

Compd. No.	IR ($CHCl_3$) cm^{-1}	NMR	
		Solvent	δ: ppm
6a	1690 (sh), 1680[a)]	DMSO-d_6	3.58 (2H, t, J=7.5 Hz, $NCH_2C\underline{H}_2S$), 4.44 (2H, t, J=7.5 Hz, $NC\underline{H}_2CH_2S$), 7.22 and 8.11 (each 1H, d, J=5.1 Hz, ArH×2)
6b	1670[a)]	$CDCl_3$	1.60 (3H, d, J=6.0 Hz, CH_3), 3.95—4.33 (2H, m, $NC\underline{H}_2CHS$), 4.43—4.77 (1H, m, $NCH_2C\underline{H}S$), 7.14 and 7.74 (each 1H, d, J=5.1 Hz, ArH×2)
6c	1658[a)]	$CDCl_3$	1.10 (3H, t, J=7.4 Hz, $CH_2C\underline{H}_3$), 1.91 (2H, q, J=7.4 Hz, $C\underline{H}_2CH_3$), 3.89 (1H, q, J=6.9 Hz, $NCH_2C\underline{H}S$), 4.26 (1H, dd, J=12.0, 6.0 Hz, $NC\underline{H}CHS$), 4.61 (1H, dd, J=12.0, 7.8 Hz, $NC\underline{H}CHS$), 7.20 and 7.75 (each 1H, d, J=5.4 Hz, ArH×2)
6d	1670	$CDCl_3$	4.50 (1H, dd, J=12.3, 7.8 Hz, $NC\underline{H}CHS$), 4.91 (1H, dd, J=12.3, 7.5 Hz, $NC\underline{H}CHS$), 5.18 (1H, dd, J=7.8, 7.5 Hz, $NCH_2C\underline{H}S$), 7.23 and 7.76 (each 1H, d, J=5.4 Hz, ArH×2), 7.33—7.57 (5H, m, PhH×5)
6e	1671[a)]	$CDCl_3$	1.67 (6H, s, CH_3×2), 4.29 (2H, s, NCH_2), 7.20 and 7.74 (each 1H, d, J=5.7 Hz, ArH×2)
6f	1672[a)]	$CDCl_3$	1.59 (3H, d, J=6.3 Hz, CH_3), 3.03 (1H, d, J=11.7 Hz, $NCHC\underline{H}S$), 3.84 (1H, dd, J=11.7, 7.8 Hz, $NCHC\underline{H}S$), 5.29 (1H, q, J=6.6 Hz, $NC\underline{H}CHS$), 7.18 and 7.76 (each 1H, d, J=5.4 Hz, ArH×2)
6g	1725 (sh), 1675	$CDCl_3$	3.28 (1H, dd, J=11.1, 1.8 Hz, $NCHC\underline{H}S$), 4.12 (1H, dd, J=11.1, 8.4 Hz, $NCHC\underline{H}S$), 6.16 (1H, dd, J=8.4, 1.8 Hz, $NC\underline{H}CHS$), 7.23 and 7.74 (each 1H, d, J=5.4 Hz, ArH×2)
6h	1680 (sh), 1665	$CDCl_3$	2.59 (3H, s, $ArCH_3$), 3.48 (2H, t, J=7.5 Hz, $NCH_2C\underline{H}_2S$), 4.53 (2H, t, J=7.5 Hz, $NC\underline{H}_2CH_2S$), 6.88 (1H, s, ArH)
6i	1680 (sh), 1665	$CDCl_3$	1.57 (3H, d, J=6.3 Hz, CH_3), 2.57 (3H, d, J=2.4 Hz, $ArCH_3$), 3.90—4.31 (2H, m, $NC\underline{H}_2CHS$), 4.44—4.74 (1H, m, $NCH_2C\underline{H}S$), 6.85 (1H, d, J=2.4 Hz, ArH)
6j	1675 (sh), 1670	$CDCl_3$	1.57 (3H, d, J=6.0 Hz, CH_3), 2.57 (3H, s, $ArCH_3$), 2.98 (1H, d, J=11.7 Hz, $NCHC\underline{H}S$), 3.80 (1H, dd, J=11.7, 7.5 Hz, $NCHC\underline{H}S$), 5.27 (1H, q, J=6.9 Hz, $NC\underline{H}CH_2S$), 6.88 (1H, s, ArH)
6k	1805, 1690, 1608[a)]	DMSO-d_6	0.82—1.10 (6H, m, CH_3×2), 1.43—1.97 (3H, m, $C\underline{H}_2C\underline{H}Me_2$), 2.57 (3H, d, J=1.5 Hz, $ArCH_3$), 3.33 (1H, d, J=11.7 Hz, $SC\underline{H}CHN$), 3.80 (1H, dd, J=11.7, 7.5 Hz, $SC\underline{H}CHN$), 4.96—5.28 (1H, m, $SCHC\underline{H}N$), 6.99 (1H, d, J=1.5 Hz, ArH)
6l	1680 (sh), 1665	$CDCl_3$	1.35 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 2.91 (2H, q, J=7.5 Hz, $C\underline{H}_2CH_3$), 3.48 (2H, t, J=7.5 Hz, $NCH_2C\underline{H}_2S$), 4.54 (2H, t, J=7.5 Hz, $NC\underline{H}_2CH_2S$), 6.91 (1H, s, ArH)
6m	1670	$CDCl_3$	1.59 (3H, d, J=6.9 Hz, CH_3), 2.32 (3H, s, $ArCH_3$), 3.90—4.30 (2H, m, $NC\underline{H}_2CHS$), 4.44—4.76 (1H, m, $NCH_2C\underline{H}S$), 7.37 (1H, s, ArH)
6n	1670	$CDCl_3$	2.20 and 2.48 (each 3H, s, $ArCH_3$×2), 3.48 (3H, t, J=7.5 Hz, $NCH_2C\underline{H}_2S$), 4.55 (2H, t, J=7.5 Hz, $NC\underline{H}_2CH_2S$)
6o	1665, 1655 (sh)	$CDCl_3$	1.57 (3H, d, J=6.3 Hz, CH_3), 2.21 and 2.47 (each 3H, s, $ArCH_3$×2), 3.38—4.30 (2H, m, $NC\underline{H}_2CHS$), 4.43—4.74 (1H, m, $NCH_2C\underline{H}S$)
11a	1665[a)]	DMSO-d_6	3.50 (2H, t, J=7.2 Hz, $NCH_2C\underline{H}_2S$), 4.33 (2H, t, J=7.2 Hz, $NC\underline{H}_2CH_2S$), 7.52 and 8.42 (each 1H, d, J=3.0 Hz, ArH×2)
11b	1680 (sh), 1675	$CDCl_3$	1.57 (3H, d, J=6.3 Hz, CH_3), 3.85—4.20 (2H, m, $NC\underline{H}_2CHS$), 4.37—4.70 (1H, m, $NCH_2C\underline{H}S$), 7.31 and 8.21 (each 1H, d, J=3.3 Hz, ArH×2)
11c	1675	$CDCl_3$	1.38 (3H, d, J=6.6 Hz, CH_3), 2.89 (3H, s, $ArCH_3$), 3.80—4.13 (2H, m, $NC\underline{H}_2CHS$), 4.32—4.62 (1H, m, $NCH_2C\underline{H}S$), 6.96 (1H, s, ArH)
11d	1670	DMSO-d_6	1.47 (3H, d, J=6.3 Hz, CH_3), 2.50 (3H, s, $ArCH_3$), 3.87—4.56 (3H, m, NCH_2CHS), 8.15 (1H, s, ArH)
11e	1705 (sh), 1670	$CDCl_3$	1.64 (6H, s, CH_3×2), 2.60 (3H, s, $ArCH_3$), 4.16 (2H, s, $NC\underline{H}_2CS$), 7.97 (1H, s, ArH)
11f	1675	$CDCl_3$	1.34 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 3.07 (2H, q, J=7.5 Hz, $C\underline{H}_2CH_3$), 3.41 (2H, t, J=7.2 Hz, $NCH_2C\underline{H}_2S$), 4.43 (2H, t, J=7.2 Hz, $NC\underline{H}_2CH_2S$), 8.00 (1H, s, ArH)
11g	1670	$CDCl_3$	1.32 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 1.55 (3H, d, J=6.3 Hz, CH_3), 3.05 (2H, q, J=7.5 Hz, $C\underline{H}_2CH_3$), 3.80—4.17 (2H, m, $NC\underline{H}_2CHS$), 4.33—4.64 (1H, m, $NCH_2C\underline{H}S$), 7.97 (1H, s, ArH)
11h	1675[a)]	$CDCl_3$	1.33 (3H, t, J=7.7 Hz, $CH_2C\underline{H}_3$), 1.64 (6H, s, CH_3×2), 3.07 (2H, q, J=7.7 Hz, $C\underline{H}_2CH_3$), 4.18 (2H, s, $NC\underline{H}_2CS$), 8.01 (1H, s, ArH)
11i	1675	$CDCl_3$	2.50 and 2.82 (each 3H, s, $ArCH_3$×2), 3.34 (2H, t, J=7.2 Hz, $NCH_2C\underline{H}_2S$), 4.24 (2H, t, J=7.2 Hz, $NC\underline{H}_2CH_2S$)
11j	1775	$CDCl_3$	1.54 (3H, d, J=6.3 Hz, CH_3), 2.50 and 2.83 (each 3H, s, $ArCH_3$×2), 3.78—4.12 (2H, m, $NC\underline{H}_2CHS$), 4.28—4.78 (1H, m, $NCH_2C\underline{H}S$)
11k	1675	$CDCl_3$	1.62 (6H, s, CH_3×2), 2.50 and 2.74 (each 3H, s, $ArCH_3$×2), 4.10 (2H, s, $NC\underline{H}_2CS$)
11l	1690	$CDCl_3$	3.45 (2H, t, J=7.5 Hz, $NCH_2C\underline{H}_2S$), 4.45 (2H, t, J=7.5 Hz, $NC\underline{H}_2CH_2S$), 8.01 (1H, s, ArH)
16a	1685[a)]	DMSO-d_6	3.58 (2H, t, J=7.5 Hz, $NCH_2C\underline{H}_2S$), 4.42 (2H, t, J=7.5 Hz, $NC\underline{H}_2CH_2S$), 7.34 and 7.37 (each 1H, d, J=6.0 Hz, ArH×2)
16b	1660[a)]	DMSO-d_6	1.50 (3H, d, J=6.0 Hz, CH_3), 4.01—4.68 (3H, m, NCH_2CHS), 7.33 and 7.43 (each 1H, d, J=5.7 Hz, ArH×2)
16c	1675, 1665 (sh)[a)]	$CDCl_3$	1.58 (3H, d, J=6.0 Hz, CH_3), 2.52 (3H, d, J=1.8 Hz, $ArCH_3$), 3.90—4.28 (2H, m, $NC\underline{H}_2CHS$), 4.41—4.72 (1H, m, $NCH_2C\underline{H}S$), 6.65 (1H, d, J=1.8 Hz, ArH)
16d	1680, 1660[a)]	$CDCl_3$	1.57 (3H, d, J=6.3 Hz, CH_3), 2.48 (3H, d, J=1.8 Hz, $ArCH_3$), 3.89—4.27 (2H, m, $NC\underline{H}_2CHS$), 4.40—4.73 (1H, m, $NCH_2C\underline{H}S$), 7.01 (1H, d, J=1.8 Hz, ArH)
16e	1675	$CDCl_3$	3.51 (2H, t, J=7.7 Hz, $NCH_2C\underline{H}_2S$), 4.54 (2H, t, J=7.7 Hz, $NC\underline{H}_2CH_2S$), 7.24 (1H, s, ArH)

a) KBr.

TABLE XI. Spectral Data for Various Polymethylene Condensed Thienopyrimidines (**19**, **20**, and **21**)

Compd. No.	IR ($CHCl_3$) cm^{-1}	NMR	
		Solvent	δ: ppm
19a	1680 (sh), 1670, 1655 (sh)	$CDCl_3$	2.11—2.48 (2H, m, 7-CH_2), 3.17 (2H, t, J=8.0 Hz, 8-CH_2), 4.22 (2H, t, J=7.4 Hz, 6-CH_2), 7.26 and 7.75 (each 1H, d, J=5.4 Hz, ArH×2)
19b	1675, 1660	$CDCl_3$	1.83—2.11 (4H, m, 7-CH_2, 8-CH_2), 2.90—3.12 (2H, m, 9-CH_2), 4.02—4.24 (2H, m, 6-CH_2), 7.24 and 7.74 (each 1H, d, J=5.4 Hz, ArH×2)
19c	1665	$CDCl_3$	1.63—2.00 (6H, m, 7-CH_2, 8-CH_2, 9-CH_2), 2.96—3.17 (2H, m, 10-CH_2), 4.30—4.55 (2H, m, 6-CH_2), 7.25 and 7.75 (each 1H, d, J=5.4 Hz, ArH×2)
19d	1660	$CDCl_3$	2.08—2.50 (2H, m, 7-CH_2), 2.59 (3H, d, J=1.8 Hz, $ArCH_3$), 3.16 (2H, t, J=8.0 Hz, 8-CH_2), 4.21 (2H, J=7.1 Hz, 6-CH_2), 6.94 (1H, d, J=1.8 Hz, ArH)
19e	1665	$CDCl_3$	1.77—2.11 (4H, m, 7-CH_2, 8-CH_2), 2.59 (3H, s, $ArCH_3$), 2.80—3.02 (2H, m, 9-CH_2), 3.93—4.13 (2H, m, 6-CH_2), 6.92 (1H, s, ArH)
19f	1660	$CDCl_3$	1.67—1.96 (6H, m, 7-CH_2, 8-CH_2, 9-CH_2), 2.59 (3H, d, J=1.5 Hz, $ArCH_3$), 2.93—3.17 (2H, m, 10-CH_2), 4.30—4.53 (2H, m, 6-CH_2), 6.91 (1H, d, J=1.5 Hz, ArH)
19g	1660	$CDCl_3$	1.60—1.75 (4H, m, 8-CH_2, 9-CH_2), 1.75—2.18 (4H, m, 7-CH_2, 10-CH_2), 2.59 (3H, s, $ArCH_3$), 2.92—3.13 (2H, m, 11-CH_2), 4.26—4.46 (2H, m, 6-CH_2), 6.95 (1H, s, ArH)
19h	1665	$CDCl_3$	1.24—1.68 (6H, m, 8-CH_2, 9-CH_2, 10-CH_2), 1.80—2.15 (4H, m, 7-CH_2, 11-CH_2), 2.59 (3H, s, $ArCH_3$), 2.93—3.11 (2H, m, 12-CH_2), 4.26—4.43 (2H, m, 6-CH_2), 6.94 (1H, s, ArH)
19i	1665	$CDCl_3$	1.36 (3H, t, J=7.5 Hz, $ArCH_2C\underline{H}_3$), 2.07—2.51 (2H, m, 7-CH_2), 2.93 (2H, q, J=7.5 Hz, $ArC\underline{H}_2CH_3$), 3.15 (2H, t, J=8.1 Hz, 8-CH_2), 4.20 (2H, t, J=6.9 Hz, 6-CH_2), 6.98 (1H, s, ArH)
19j	1665	$CDCl_3$	1.36 (3H, t, J=7.5 Hz, $ArCH_2C\underline{H}_3$), 1.80—2.10 (4H, m, 7-CH_2, 8-CH_2), 2.74—3.08 (4H, m, $ArC\underline{H}_2CH_3$, 9-CH_2), 4.00—4.19 (2H, m, 6-CH_2), 6.95 (1H, s, ArH)
19k	1665	$CDCl_3$	1.37 (3H, t, J=7.5 Hz, $ArCH_2C\underline{H}_3$), 1.85 (6H, br s, 7-CH_2, 8-CH_2, 9-CH_2), 2.93 (2H, q, J=7.5 Hz, $ArC\underline{H}_2$-CH_3), 2.94—3.15 (2H, m, 10-CH_2), 4.33—4.50 (2H, m, 6-CH_2), 6.97 (1H, s, ArH)
19l	1665	$CDCl_3$	2.09—2.53 (2H, m, 7-CH_2), 2.25 and 2.49 (each 3H, s, $ArCH_3$×2), 3.18 (2H, t, J=7.7 Hz, 8-CH_2), 4.21 (2H, t, J=7.1 Hz, 6-CH_2)
19m	1665	$CDCl_3$	1.77—2.10 (4H, m, 7-CH_2, 8-CH_2), 2.24 and 2.48 (each 3H, s, $ArCH_3$×2), 2.88—3.13 (2H, m, 9-CH_2), 4.01—4.20 (2H, m, 6-CH_2)
19n	1660	$CDCl_3$	1.85 (6H, br s, 7-CH_2, 8-CH_2, 9-CH_2), 2.25 and 2.48 (each 3H, s, $ArCH_3$×2), 2.96—3.20 (2H, m, 10-CH_2), 4.33—4.52 (2H, m, 6-CH_2)
20a	1690 (sh), 1675, 1630	$CDCl_3$	2.05—2.43 (2H, m, 7-CH_2), 3.06 (2H, t, J=8.0 Hz, 8-CH_2), 4.10 (2H, t, J=7.1 Hz, 6-CH_2), 7.43 and 8.25 (each 1H, d, J=3.6 Hz, ArH×2)
20b	1690 (sh), 1670, 1610	$CDCl_3$	1.74—2.15 (4H, m, 7-CH_2, 8-CH_2), 2.82—3.03 (2H, m, 9-CH_2), 3.95—4.14 (2H, m, 6-CH_2), 7.42 and 8.25 (each 1H, d, J=3.6 Hz, ArH×2)
20c	1675	$CDCl_3$	1.67—2.01 (6H, m, 7-CH_2, 8-CH_2, 9-CH_2), 2.85—3.13 (2H, m, 10-CH_2), 4.18—4.34 (2H, m, 6-CH_2), 7.43 and 8.24 (each 1H, d, J=3.6 Hz, ArH×2)
20d	1685, 1670, 1625	$CDCl_3$	2.02—2.41 (2H, m, 7-CH_2), 2.64 (3H, s, $ArCH_3$), 3.06 (2H, t, J=7.8 Hz, 8-CH_2), 4.08 (2H, t, J=7.4 Hz, 6-CH_2), 7.98 (1H, s, ArH)
20e	1665, 1605	$CDCl_3$	1.80—2.05 (4H, m, 7-CH_2, 8-CH_2), 2.63 (3H, s, $ArCH_3$), 2.80—3.03 (2H, m, 9-CH_2), 3.93—4.14 (2H, m, 6-CH_2), 8.00 (1H, s, ArH)
20f	1675 (sh), 1665	$CDCl_3$	1.67—2.00 (6H, m, 7-CH_2, 8-CH_2, 9-CH_2), 2.63 (3H, s, $ArCH_3$), 2.88—3.11 (2H, m, 10-CH_2), 4.17—4.39 (2H, m, 6-CH_2), 7.98 (1H, s, ArH)
20g	1670, 1625	$CDCl_3$	1.36 (3H, t, J=7.5 Hz, $ArCH_2C\underline{H}_3$), 2.01—2.40 (2H, m, 7-CH_2), 3.03 (2H, t, J=6.3 Hz, 8-CH_2), 3.11 (2H, q, J=7.5 Hz, $ArC\underline{H}_2CH_3$), 4.08 (2H, t, J=7.3 Hz, 6-CH_2), 8.03 (1H, s, ArH)
20h	1723, 1631[a]	DMSO-d_6	1.29 (3H, t, J=7.5 Hz, $ArCH_2C\underline{H}_3$), 1.75—2.04 (4H, m, 7-CH_2, 8-CH_2), 3.10—3.33 (2H, m, 9-CH_2), 3.26 (2H, q, J=7.5 Hz, $ArC\underline{H}_2CH_3$), 3.85—4.04 (2H, m, 6-CH_2), 8.54 (1H, s, ArH)
20i	1665	$CDCl_3$	1.37 (3H, t, J=7.5 Hz, $ArCH_2C\underline{H}_3$), 1.65—2.38 (6H, m, 7-CH_2, 8-CH_2, 9-CH_2), 2.88—3.08 (2H, m, 10-CH_2), 3.15 (2H, q, J=7.5 Hz, $ArC\underline{H}_2CH_3$), 4.16—4.40 (2H, m, 6-CH_2), 8.02 (1H, s, ArH)
20j	1665, 1630	$CDCl_3$	1.99—2.35 (2H, m, 7-CH_2), 2.56 and 2.89 (each 3H, s, $ArCH_3$×2), 3.02 (2H, t, J=8.0 Hz, 8-CH_2), 4.03 (2H, t, J=7.4 Hz, 6-CH_2)
20k	1670, 1610	$CDCl_3$	1.78—2.03 (4H, m, 7-CH_2, 8-CH_2), 2.55 and 2.88 (each 3H, s, $ArCH_3$×2), 2.75—2.98 (2H, m, 9-CH_2), 3.87—4.08 (2H, m, 6-CH_2)
20l	1665	$CDCl_3$	1.64—1.97 (6H, m, 7-CH_2, 8-CH_2, 9-CH_2), 2.56 and 2.88 (each 3H, s, $ArCH_3$×2), 2.78—3.08 (2H, m, 10-CH_2), 4.10—4.35 (2H, m, 6-CH_2)
20m	1690 (sh), 1680, 1630	$CDCl_3$	2.04—2.43 (2H, m, 7-CH_2), 3.11 (2H, t, J=7.8 Hz, 8-CH_2), 4.09 (2H, t, J=7.2 Hz, 6-CH_2), 8.04 (1H, s, ArH)
20n	1675	$CDCl_3$	1.68—2.00 (6H, m, 7-CH_2, 8-CH_2, 9-CH_2), 2.94—3.17 (2H, m, 10-CH_2), 4.20—4.39 (2H, m, 6-CH_2), 8.03 (1H, s, ArH)
21a	1665	$CDCl_3$	2.10—2.48 (2H, m, 7-CH_2), 3.17 (2H, t, J=8.0 Hz, 8-CH_2), 4.20 (2H, t, J=6.8 Hz, 6-CH_2), 7.17 and 7.47 (each 1H, d, J=6.0 Hz, ArH×2)
21b	1675	$CDCl_3$	1.82—2.20 (4H, m, 7-CH_2, 8-CH_2), 2.86—3.13 (2H, m, 9-CH_2), 3.99—4.20 (2H, m, 6-CH_2), 7.14 and 7.47 (each 1H, d, J=6.0 Hz, ArH×2)
21c	1660	$CDCl_3$	2.56—2.92 (2H, m, 7-CH_2), 2.58 (3H, d, J=1.5 Hz, $ArCH_3$), 3.15 (2H, t, J=8.0 Hz, 8-CH_2), 4.16 (2H, t, J=7.2 Hz, 6-CH_2), 6.73 (1H, d, J=1.5 Hz, ArH)
21d	1670	$CDCl_3$	2.06—2.45 (2H, m, 7-CH_2), 2.52 (3H, d, J=1.5 Hz, $ArCH_3$), 3.15 (2H, t, J=7.8 Hz, 8-CH_2), 4.18 (2H, t, J=7.5 Hz, 6-CH_2), 7.10 (1H, d, J=1.5 Hz, ArH)
21e	1665	$CDCl_3$	1.84—2.10 (4H, m, 7-CH_2, 8-CH_2), 2.51 (3H, d, J=1.5 Hz, $ArCH_3$), 2.87—3.10 (2H, m, 9-CH_2), 3.97—4.16 (2H, m, 6-CH_2), 7.08 (1H, d, J=1.5 Hz, ArH)
21f	1665	$CDCl_3$	1.70—1.98 (6H, m, 7-CH_2, 8-CH_2, 9-CH_2), 2.50 (3H, d, J=1.2 Hz, $ArCH_3$), 2.97—3.16 (2H, m, 10-CH_2), 4.28—4.50 (2H, m, 6-CH_2), 7.07 (1H, d, J=1.2 Hz, ArH)

TABLE XI. (continued)

Compd. No.	IR ($CHCl_3$) cm^{-1}	NMR	
		Solvent	δ: ppm
21g	1665	$CDCl_3$	1.35 (6H, d, J=7.2 Hz, $CH(C\underline{H}_3)_2$), 2.09—2.45 (2H, m, 7-CH_2), 2.96—3.39 (3H, m, $C\underline{H}(CH_3)_2$, 8-CH_2), 4.18 (2H, t, J=7.2 Hz, 6-CH_2), 7.16 (1H, s, ArH)
21h	1665	$CDCl_3$	1.36 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 1.80—2.15 (4H, m, 7-CH_2, 8-CH_2), 2.84—3.36 (3H, m, $C\underline{H}(CH_3)_2$, 9-CH_2), 3.95—4.19 (2H, m, 6-CH_2), 7.15 (1H, s, ArH)
21i	1665	$CDCl_3$	1.35 (6H, d, J=7.2 Hz, $CH(C\underline{H}_3)_2$), 1.63—1.97 (6H, m, 7-CH_2, 8-CH_2, 9-CH_2), 2.90—3.38 (3H, m, $C\underline{H}(CH_3)_2$, 10-CH_2), 4.27—4.50 (2H, m, 6-CH_2), 7.14 (1H, s, ArH)
21j	1670	$CDCl_3$	2.08—2.45 (2H, m, 7-CH_2), 3.15 (2H, t, J=7.8 Hz, 8-CH_2), 4.18 (2H, t, J=7.4 Hz, 6-CH_2), 7.30 (1H, s, ArH)

a) KBr.

precipitate was collected by filtration and recrystallized from MeOH to give **5b** (17.52 g, 47%) as colorless needles. Other compounds (**5**, **10** and **15**) were similarly prepared. Other data are listed in Tables IV—IX.

Methyl 3-Isothiocyanato-5-methylthiophene-2-carboxylate(7h) (General Procedure) A solution of $CSCl_2$ (2.5 ml) in $CHCl_3$ (60 ml) and then a solution of methyl 3-amino-5-methylthiophene-2-carboxylate (**4h**) (5.00 g) in $CHCl_3$ (30 ml) were added dropwise to an aqueous $NaHCO_3$ solution [prepared from $NaHCO_3$ (3.70 g) and water (23 ml)] at room temperature and the whole was stirred at room temperature for 4 h. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. A residue obtained from the $CHCl_3$ extracts was chromatographed on silica gel and eluted with $CHCl_3$–hexane (1 : 1) to give **7h** (6.80 g, 93%) as yellow needles. Other compounds (**7**, **12** and **17**) were similarly prepared. Other data are listed in Tables IV—IX.

2-Mercapto-3-(2-methyl-2-propenyl)thieno[3,2-*d*]pyrimidin-4(3*H*)-one (5e) (General Procedure) A mixture of **7a**[2b] (2.00 g), 2-methylallylamine hydrochloride (1.30 g) and Et_3N (2.03 g) in CH_2Cl_2 (30 ml) was refluxed for 1 h. After evaporation of the solvent, 10% NaOH solution was added and the mixture was washed with AcOEt. The aqueous layer was acidified with 10% HCl solution and the resulting crystalline solid was collected by filtration. Recrystallization from EtOH afforded **5e** (1.72 g, 72%) as colorless needles. Other compounds (**10e, h, k**) were similarly prepared. Other data are listed in Tables IV—VII.

3-(2-Hydroxybutyl)-2-mercaptothieno[3,2-*d*]pyrimidin-4(3*H*)-one (8c) (General Procedure) A solution of **7a**[2b] (1.02 g) in tetrahydrofuran (THF) (5 ml) was added dropwise to a stirred solution of 1-amino-2-butanol (0.8 ml) in THF (25 ml) at room temperature. The mixture was stirred for 2.5 h, then THF was evaporated off *in vacuo*, and 10% NaOH solution was added to the residue. The mixture was washed with AcOEt. The aqueous layer was acidified with 10% HCl solution and the resulting crystalline solid was collected. Recrystallization from MeOH gave **8c** (0.67 g, 51%) as colorless prisms. Other compounds (**8**, **13** and **18**) were similarly prepared. Other data are listed in Tables IV—IX.

2,3-Dihydro-2-methyl-5*H*-thiazolo[3,2-*a*]thieno[3,2-*d*]pyrimidin-5-one (6b) (General Procedure) A solution of **5b** (2.00 g) in AcOH (20 ml) was refluxed for 2.5 h, with bubbling of anhydrous hydrogen chloride, and then allowed to stand at room temperature overnight. Water (*ca.* 70 ml) was added to the mixture, the resulting precipitate was filtered off, and the filtrate was extracted with $CHCl_3$. A residue obtained from the $CHCl_3$ extracts was chromatographed on silica gel and eluted with AcOEt–hexane (1 : 1). Recrystallization from CH_2Cl_2–hexane gave **6b** (1.38 g, 69%) as colorless needles. Other compounds (**6b, e, i, m, o**, **11b—e**, **g**, **h**, **j**, **k** and **16b—d**) were similarly prepared. Other data are listed in Tables I and X.

2,3-Dihydro-5*H*-thiazolo[3,2-*a*]thieno[3,2-*d*]pyrimidin-5-one (6a) (General Procedure) A solution of **8a**[1b] (1.50 g) and methanesulfonic acid (15 ml) was heated at 120—130 °C for 30 min and then poured into ice-water (*ca.* 60 ml). The mixture was neutralized with 10% NaOH solution. The resulting precipitate was collected by filtration, washed with water and recrystallized from EtOH to give **6a** (1.00 g, 72%) as colorless needles. Other compounds (**6c**, **d**, **f—h**, **j—l**, **n**, **11a**, **f**, **i** and **16a**) were similarly prepared. Other date are listed in Tables I and X.

6,7,8,9-Tetrahydro-4*H*-pyrido[1,2-*a*]thieno[3,2-*d*]pyrimidin-4-one (19b) (General Procedure) $POCl_3$ (1 ml) was added dropwise to a solution of **4a** (1.50 g) and 2-piperidone (1.10 g) in 1,2-dichloroethane (8 ml) and the whole was refluxed for 10 min. The reaction mixture was poured into ice-water, basified with saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2. A residue obtained from the CH_2Cl_2 extracts was recrystallized from AcOEt to afford **19b** (1.40 g, 71%) as colorless needles. Other compounds (**19—21**, except **20m**, **n** and **21j**) were similarly prepared. Other data are listed in Tables II and XI.

8-Chloro-2,3-dihydro-5*H*-thiazolo[3,2-*a*]thieno[3,4-*d*]pyrimidin-5-one (11 l) (General Procedure for 16e and 20m) NCS (200 mg) was added to a solution of **11a** (300 mg) in $CHCl_3$ (15 ml) and the whole was refluxed for 5 h. After cooling, the reaction mixture was poured into ice-water and extracted with CH_2Cl_2. A residue obtained from the CH_2Cl_2 extracts was recrystallized from EtOH to give **11 l** (270 mg, 80%) as colorless needles. Other compounds (**16e** and **20m**) were similarly prepared. Other data are listed in Tables I, II, X, and XI.

1-Chloro-7,8,9,10-tetrahydro-4*H*-azepino[1,2-*a*]thieno[3,4-*d*]pyrimidin-4-one (20n) SO_2Cl_2 (300 mg) was added dropwise to a stirred solution of **20c** (500 mg) in $CHCl_3$ (20 ml) at room temperature. After being stirred for 4 h, the mixture was poured into saturated $NaHCO_3$ solution and extracted with CH_2Cl_2. A residue obtained from the CH_2Cl_2 extracts was chromatographed on silica gel and eluted with AcOEt–hexane (2 : 1). Recrystallization of the product from AcOEt–hexane gave **20n** (301 mg, 52%) as colorless needles. Compound **21j** was similarly prepared. Other data are listed in Tables I, II, X, and XI.

2-Bromomethyl-2,3-dihydro-5*H*-thiazolo[3,2-*a*]thieno[3,2-*d*]pyrimidin-5-one (22) A solution of bromine (2.30 ml) in AcOH (15 ml) was added dropwise to an ice-cooled suspension of **5b** (10.00 g) in AcOH (80 ml) during 10 min and then the whole was stirred at room temperature for 1 h. The resulting crystalline solid was collected by filtration, washed with AcOH and Et_2O, and dried to give crude dibromide intermediate (16.78 g). K_2CO_3 (6.16 g) was added to a suspension of the dibromide in acetone (50 ml) at 0 °C. Water (*ca.* 150 ml) was gradually added to the reaction mixture at 0 °C, and the whole was stirred for 5 min. The precipitate was collected by filtration and recrystallized from MeOH to afford **22** (11.59 g, 86%) as colorless needles. mp 145—148 °C. *Anal.* Calcd for $C_9H_7BrN_2OS_2$: C, 35.65; H, 2.33; Br, 26.35; N, 9.24; S, 21.15. Found: C, 35.76; H, 2.25; Br, 26.67; N, 9.23; S, 21.41. IR (KBr): 1670 cm^{-1}. NMR (DMF-d_7) δ: 3.98—4.11 (2H, m, CH_2Br), 4.38—4.72 (3H, m, NCH_2CHS), 7.24 and 8.15 (each 1H, d, J=5.4 Hz, ArH×2). MS *m/z*: 304 (M^+).

2,3-Dihydro-2-methylene-5*H*-thiazolo[3,2-*a*]thieno[3,2-*d*]pyrimidin-5-one (23) A mixture of **22** (5.00 g) and morpholine (30 ml) was heated to 100 °C for 15 min with stirring, and then cooled. Water was added to the reaction mixture and the resulting precipitate was collected by filtration. Recrystallization from MeOH gave **23** (2.38 g, 65%) as colorless needles. mp 175—177 °C. *Anal.* Calcd for $C_9H_6N_2OS_2$: C, 48.63; H, 2.72; N, 12.60; S, 28.85. Found: C, 48.53; H, 2.58; N, 12.60; S, 28.64. IR (KBr): 1680 cm^{-1}. NMR (DMSO-d_6) δ: 5.09—5.20 (2H, m, NCH_2), 5.41—5.53 and 5.53—5.67 (each 1H, m, $=CH_2$), 7.27 and 8.15 (each 1H, d, J=5.4 Hz, ArH×2). MS *m/z*: 222 (M^+).

2-Methyl-5*H*-thiazolo[3,2-*a*]thieno[3,2-*d*]pyrimidin-5-one (24) A solution of **23** (506 mg) in concentrated H_2SO_4 (2 ml) was stirred at 40 °C for 15 min and the mixture was poured into ice-water. The solution was extracted with $CHCl_3$ and the extract was dried over $MgSO_4$. Evaporation of the solvent gave the crystalline residue, which was recrystallized from $CHCl_3$–hexane to afford **24** (417 mg, 82%) as colorless needles. mp 200—202 °C. *Anal.* Calcd for $C_9H_6N_2OS_2$: C, 48.63; H, 2.72; N, 12.60; S, 28.85. Found: C, 48.52; H, 2.77; N, 12.64; S, 29.03. IR (KBr): 1695, 1680 cm^{-1} (sh). NMR ($CDCl_3$) δ: 2.04 (3H, d, J=1.5 Hz, CH_3), 7.27 and 7.85 (each 1H, d, J=5.4 Hz, ArH×2), 7.70 (1H, d, J=1.5 Hz, NCH=CS). MS *m/z*: 202 (M^+).

Gastric Secretion in Pylorus-Ligated Rats Sprague Dawley (Charles River Co., Ltd.) male rats, weighing 200—230 g, were divided into groups of four animals each and fasted for 24 h with free access to water before the

experiment. The animals were anesthetized with ether and the pylorus was ligated by the method of Shay *et al.*[6] A dose of 50 mg/kg of a test compound suspended in 0.5% carboxymethylcellulose solution was given intraduodenally immediately after ligation of the pylorus in a volume of 2 ml/kg of body weight. Four hours later, the animals were sacrificed by carbon dioxide. The gastric contents were centrifuged at 3000 rpm for 10 min, after which the volume of gastric juice was measured. The volume was then expressed as ml/100 g body weight.

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