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Uracil Derivatives. II.¹⁾ Syntheses and Growth-inhibitory Activity against L-1210 Cells of 5-(4-Substituted-phenylthiomethyl)-6-carbamoyluracils

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5-(Substituted-thiomethyl)-6-carbamoyluracils (IIIa—f and VIa—c) were prepared in two steps from 5-chloromethyl-6-ethoxycarbonyluracil (I). Oxidation of IIIa—c gave the corresponding sulfones (IVa—c).

The compounds thus prepared were examined for growth inhibition of L-1210 cells *in vitro* and some of them exhibited high activity.

Keywords—4-substituted-benzenethiol; nucleophilic substitution; 6-carbamoyluracil; growth inhibition of L-1210 cells; P-388 cells

Over the years there has been a continuous interest in analogs of uracil. Thus, compounds such as 5-fluorouracil,²⁾ 5-trifluoromethyluracil³⁾ and 5-mercaptomethyluracil⁴⁾ are effective as inhibitors of cell growth. As part of our studies on related compounds, we synthesized various 5-(substituted-methyl)-6-carbamoyluracils, and found that among them 5-(4-chlorophenylthiomethyl)-6-carbamoyluracil (IIIa) inhibited the growth of L-1210 cells *in vitro*.¹⁾

As the inhibition of IIIa was weak, we attempted to prepare more active compounds by structural modifications of IIIa as follows: (1) replacement of chlorine by fluorine, bromine, iodine, methyl and methoxyl, (2) oxidation of sulfide, (3) introduction of a methylene group between the sulfur atom and the benzene ring.

Chemistry

We have already reported a general procedure for the preparation of 5-(substituted-thiomethyl)-6-carbamoyluracils.¹⁾ According to this procedure, the first series of target compounds, 5-(4-substituted-phenylthiomethyl)-6-carbamoyluracils (IIIb—f) were prepared by the reaction of 5-chloromethyl-6-ethoxycarbonyluracil (I)¹⁾ with sodium 4-substituted-phenylthiolates followed by treatment with ammonia water (Chart 1).

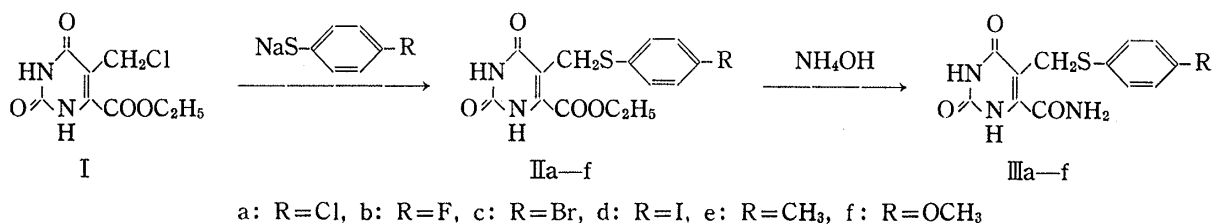
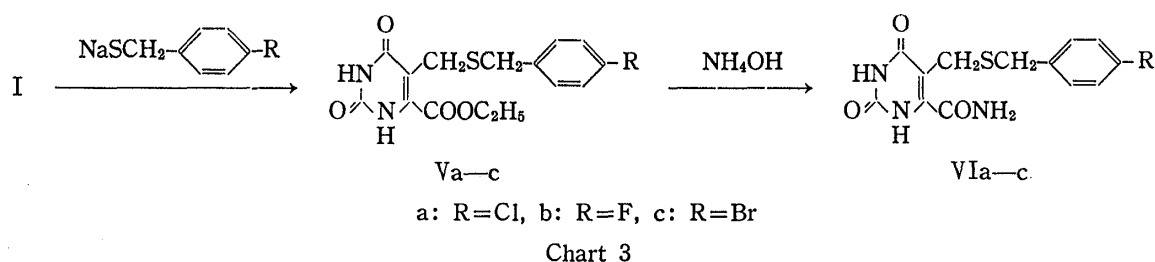
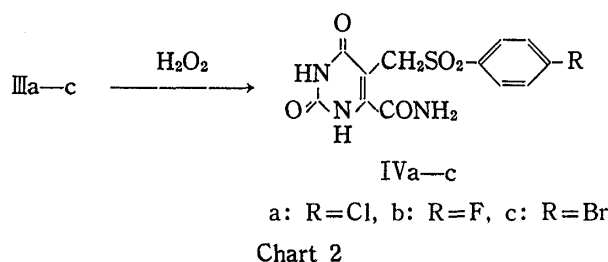


Chart 1

The second series of compounds is 5-(4-substituted-phenylsulfonylmethyl)-6-carbamoyluracils (IVa—c). The sulfones (IVa—c) were prepared by oxidation of the corresponding sulfides (IIIa—c) in an excess of hydrogen peroxide in acetic acid at 80—90°C for 1 h (Chart 2). The infrared (IR) spectra exhibited absorption bands near 1310 and 1145 cm⁻¹ due to sulfone stretching vibrations.

The final target compounds, 5-(4-substituted-benzylthiomethyl)-6-carbamoyluracils (VIa—c) were prepared in two steps *via* the reaction of I with the corresponding sodium thiolates followed by treatment with ammonia water (Chart 3).



Pharmacological Results

The uracil derivatives described above were tested for growth inhibition of L-1210 cells *in vitro*. The results are listed in Table I.

TABLE I. Growth Inhibition of L-1210 Cells *in Vitro*, % Inhibition

Compd. No.	Concentration ($\mu\text{g/ml}$)		
	0.3	3	10
IIa			1
IIb	15	17	11
IIc	42	37	49
IIId	12	10	15
IIIf	6	7	17
IIIa		3	42
IIIb	43	32	32
IIIc	30	33	65
IIId	1	18	71
IIIe	11	13	58
IIIIf	22	24	14
IVa			1
IVb	25	24	25
IVc	29	29	23
Va	31	30	48
Vb	26	29	9
Vc	18	16	17
VIa	28	35	82
VIb	19	15	28
VIc	7	22	12
6-MPR	66	84	91

Almost all the tested compounds showed activity, but their activity was independent of concentration, due to poor solubility. Replacement of chlorine of IIIa by fluorine or bromine resulted in a marked increase in activity at 0.3 $\mu\text{g/ml}$ (IIIb, c), and replacement by iodine, methyl or methoxyl resulted in a slight increase (IIId, e, f). 5-(4-Bromophenylthiomethyl)-6-ethoxycarbonyluracil (IIc) also exhibited high activity. However, in general, the esters (IIIa-f) showed low activity compared with the amides (IIIa-f). The activity of the sulfones (IVa-c) was weak compared with that of the amides (IIIa-c). Introduction of a methylene

group between the sulfur atom and the benzene ring of IIa or IIIa resulted in a marked increase in activity (Va, VIa). However introduction of methylene group in IIb, c or IIIb, c resulted in a slight decrease or almost no change in activity (Vb, c VIb, c).

Compound IIc, which has high activity against L-1210 cells *in vitro* at 0.3 $\mu\text{g/ml}$, was tested for antitumor activity against P-388 *in vivo*, according to the NIH protocol,⁸⁾ but showed no activity.

Experimental

Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were measured with a Hitachi 260-10 spectrometer. Proton nuclear magnetic resonance (¹H-NMR) spectra were taken at 60 MHz with a JEOL JNM-PMX 60 spectrometer using tetramethylsilane (TMS) as an internal standard in dimethyl sulfoxide (DMSO)-*d*₆. Chemical shifts are expressed as δ (ppm) downfield from TMS. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet and br.=broad. Mass spectra (MS) were measured with a JEOL JMS-01SG-2 mass spectrometer. 4-Iodobenzenethiol was prepared from 4-iodobenzene sulfonyl chloride.⁵⁾ According to the method of Pan and Fletcher,⁶⁾ 4-fluoro-⁷⁾ and 4-bromophenylmethanethiol⁶⁾ were prepared from 4-fluorobenzyl chloride and 4-bromobenzyl bromide, respectively.

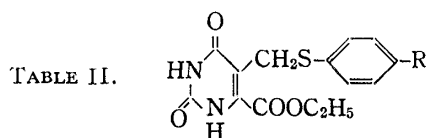
General Procedure for the Preparation of 5-(Substituted-thiomethyl)-6-ethoxycarbonyluracils (IIb—f and Va—c): A Typical Example—5-(4-Bromophenylthiomethyl)-6-ethoxycarbonyluracil (IIc): A solution of sodium (0.49 g, 21.3 mmol) and 4-bromobenzenethiol (4.05 g, 21.5 mmol) in ethanol (300 ml) was refluxed for 1 h. Compound I (5.0 g, 21.5 mmol) was added to the solution after it had cooled, and the mixture was stirred for 5 h at room temperature. The product was filtered off and recrystallized from ethanol to give 7.7 g (93.0%) of IIc: mp 237—240°C. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1730, 1700, 1655, 1260. NMR (DMSO-*d*₆) δ : 1.28 (3H, t, *J*=7 Hz), 4.05 (2H, s), 4.16 (2H, q, *J*=7 Hz), 7.28 (2H, d, *J*=8 Hz), 7.47 (2H, d, *J*=8 Hz), 10.93 (1H, br s), 11.51 (1H, br s). MS *m/e*: 386 (*M*⁺ + 2), 384 (*M*⁺).

Data for the esters IIb—f and Va—c prepared as described above are listed in Tables II and III, respectively. IR, NMR and mass spectral data are given below.

6-Ethoxycarbonyl-5-(4-fluorophenylthiomethyl)uracil (IIb): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1730, 1700, 1655, 1260. NMR (DMSO-*d*₆) δ : 1.23 (3H, t, *J*=7 Hz), 4.01 (2H, s), 4.13 (2H, q, *J*=7 Hz), 6.8—7.6 (4H, m), 10.86 (1H, br s), 11.49 (1H, br s). MS *m/e*: 324 (*M*⁺).

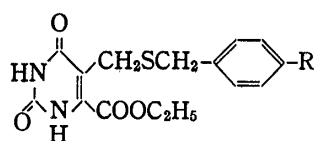
6-Ethoxycarbonyl-5-(4-iodophenylthiomethyl)uracil (IIId): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1730, 1700, 1655, 1260. NMR (DMSO-*d*₆) δ : 1.25 (3H, t, *J*=7 Hz), 4.05 (2H, s), 4.16 (2H, q, *J*=7 Hz), 7.11 (2H, d, *J*=8 Hz), 7.59 (2H, d, *J*=8 Hz), 10.97 (1H, br s), 11.55 (1H, br s). MS *m/e*: 432 (*M*⁺).

6-Ethoxycarbonyl-5-(4-tolylthiomethyl)uracil (IIe): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1730, 1700, 1660, 1265. NMR (DMSO-*d*₆) δ : 1.23 (3H, t, *J*=7 Hz), 2.28 (3H, s), 4.03 (2H, s), 4.12 (2H, q, *J*=7 Hz), 7.14 (2H, d, *J*=8.5 Hz), 7.24 (2H, d, *J*=8.5 Hz), 10.0—11.7 (2H, br.). MS *m/e*: 320 (*M*⁺).



Compd. No.	R	Yield (%)	mp (°C)	Recryst. solv.	Formula	Analysis (%)		
						Calcd (Found)	C	H N
IIb	F	79.0	245—248	EtOH	C ₁₄ H ₁₃ FN ₂ O ₄ S	51.85 (51.74)	4.04 4.27	8.64 8.71
IIc	Br	93.0	237—240	EtOH	C ₁₄ H ₁₃ BrN ₂ O ₄ S	43.65 (43.69)	3.40 3.62	7.27 7.29
IIId	I	89.8	243—246	EtOH	C ₁₄ H ₁₃ IN ₂ O ₄ S	38.90 (38.63)	3.03 2.94	6.48 6.57
IIe	CH ₃	92.0	240—242.5	EtOH	C ₁₅ H ₁₆ N ₂ O ₄ S	56.24 (55.98)	5.30 5.17	8.74 8.54
IIf	OCH ₃	64.4	238—242	EtOH	C ₁₅ H ₁₆ N ₂ O ₅ S	53.56 (53.81)	4.79 4.64	8.33 8.27

TABLE III.



Compd. No.	R	Yield (%)	mp (°C)	Recryst. solv.	Formula	Analysis (%)		
						Calcd (Found)	C	H N
Va	Cl	73.7	213—215	EtOH	C ₁₅ H ₁₅ ClN ₂ O ₄ S	50.78 (50.85)	4.26 4.23	7.90 8.03
Vb	F	41.0	221—223	EtOH	C ₁₅ H ₁₅ FN ₂ O ₄ S	53.25 (53.21)	4.47 4.45	8.28 8.43
Vc	Br	34.9	222—226	EtOH	C ₁₅ H ₁₅ BrN ₂ O ₄ S	45.12 (45.41)	3.79 3.86	7.02 7.21

6-Ethoxycarbonyl-5-(4-methoxyphenylthiomethyl)uracil (IIIf): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1738, 1700, 1660, 1265. NMR (DMSO-*d*₆) δ : 1.20 (3H, t, *J* = 7 Hz), 3.71 (3H, s), 3.93 (2H, s), 4.03 (2H, q, *J* = 7 Hz), 6.83 (2H, d, *J* = 8.6 Hz), 7.22 (2H, d, *J* = 8.6 Hz), 10.77 (1H, br.s), 11.44 (1H, br.s). MS *m/e*: 336 (*M*⁺).

5-(4-Chlorobenzylthiomethyl)-6-ethoxycarbonyluracil (Va): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1725, 1700, 1655, 1260. NMR (DMSO-*d*₆) δ : 1.28 (3H, t, *J* = 7 Hz), 3.60 (2H, s), 3.75 (2H, s), 4.27 (2H, q, *J* = 7 Hz), 7.30 (4H, s), 10.93 (1H, br.s), 11.40 (1H, br.s). MS *m/e*: 356 (*M*⁺ + 2), 354 (*M*⁺).

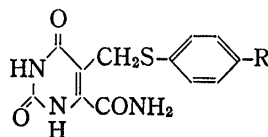
6-Ethoxycarbonyl-5-(4-fluorobenzylthiomethyl)uracil (Vb): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1740, 1720, 1660, 1260. NMR (DMSO-*d*₆) δ : 1.29 (3H, t, *J* = 7 Hz), 3.61 (2H, s), 3.77 (2H, s), 4.27 (2H, q, *J* = 7 Hz), 6.9—7.5 (4H, m), 10.90 (1H, br.s), 11.44 (1H, br.s). MS *m/e*: 338 (*M*⁺).

5-(4-Bromobenzylthiomethyl)-6-ethoxycarbonyluracil (Vc): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1740, 1720, 1660, 1260. NMR (DMSO-*d*₆) δ : 1.32 (3H, t, *J* = 7 Hz), 3.60 (2H, s), 3.73 (2H, s), 4.27 (2H, q, *J* = 7 Hz), 7.26 (2H, d, *J* = 9 Hz), 7.43 (2H, d, *J* = 9 Hz), 10.92 (1H, br.s), 11.48 (1H, br.s). MS *m/e*: 400 (*M*⁺ + 2), 398 (*M*⁺).

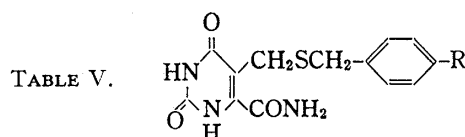
General Procedure for the Preparation of 5-(Substituted-thiomethyl)-6-carbamoyluracils (IIIb—f and VIa—c): A Typical Example—5-(4-Bromophenylthiomethyl)-6-carbamoyluracil (IIIc): A mixture of IIc (3.0 g, 7.8 mmol) and ammonia water (220 ml) was stirred for 2 d at room temperature. Small amounts of insoluble compounds were filtered off and the filtrate was concentrated *in vacuo*. The precipitates were filtered off and recrystallized from MeOH-H₂O to give 2.4 g (86.5%) of IIc: mp 249°C (dec.). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3400, 3350, 1730, 1680, 1660. NMR (DMSO-*d*₆) δ : 3.91 (2H, s), 7.29 (2H, d, *J* = 8 Hz), 7.44 (2H, d, *J* = 8 Hz), 7.97 (1H, br.s), 8.14 (1H, br.s), 11.15 (1H, br.s), 11.29 (1H, br.s). MS *m/e*: 357 (*M*⁺ + 2), 355 (*M*⁺).

Data for the amides IIIb—f and VIa—c prepared as described above are listed in Tables IV and V, respectively. IR, NMR and mass spectral data are given below.

TABLE IV.



Compd. No.	R	Yield (%)	mp (°C) (dec.)	Recryst. solv.	Formula	Analysis (%)		
						Calcd (Found)	C	H N
IIIb	F	85.3	221	MeOH-H ₂ O	C ₁₂ H ₁₀ FN ₃ O ₃ S	48.81 (48.85)	3.41 3.32	14.23 14.34
IIIc	Br	86.5	249	MeOH-H ₂ O	C ₁₂ H ₁₀ BrN ₃ O ₃ S	40.46 (40.25)	2.83 3.06	11.80 11.52
IIId	I	86.0	254	MeOH-H ₂ O	C ₁₂ H ₁₀ IN ₃ O ₃ S	35.75 (35.89)	2.50 2.57	10.42 10.51
IIIe	CH ₃	79.9	241	MeOH-H ₂ O	C ₁₃ H ₁₃ N ₃ O ₃ S	53.60 (53.47)	4.50 4.61	14.42 14.62
IIIf	OCH ₃	62.7	255	MeOH-H ₂ O	C ₁₃ H ₁₃ N ₃ O ₄ S	50.81 (50.81)	4.26 4.15	13.67 13.63



Compd. No.	R	Yield (%)	mp (°C) (dec.)	Recryst. solv.	Formula	Analysis (%)		
						Calcd (Found)	C	H N
VIa	Cl	65.8	238	MeOH-H ₂ O	C ₁₃ H ₁₂ ClN ₃ O ₃ S	47.93 (48.14)	3.71 (3.57)	12.90 (12.62)
VIb	F	69.1	226	MeOH-H ₂ O	C ₁₃ H ₁₂ FN ₃ O ₃ S	50.47 (50.43)	3.91 (4.11)	13.59 (13.39)
VIc	Br	49.7	256	MeOH-H ₂ O	C ₁₃ H ₁₂ BrN ₃ O ₃ S	42.17 (42.43)	3.27 (3.16)	11.35 (11.35)

6-Carbamoyl-5-(4-fluorophenylthiomethyl)uracil (IIIb): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3420, 3350, 1735, 1690, 1660. NMR (DMSO-*d*₆) δ : 3.87 (2H, s), 6.8—7.6 (4H, m), 7.92 (1H, br s), 8.09 (1H, br s), 11.10 (1H, br s), 11.25 (1H, br s). MS *m/e*: 295 (M⁺).

6-Carbamoyl-5-(4-iodophenylthiomethyl)uracil (IIIc): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3400, 3350, 1730, 1680, 1660. NMR (DMSO-*d*₆) δ : 3.90 (2H, s), 7.13 (2H, d, *J* = 8 Hz), 7.57 (2H, d, *J* = 8 Hz), 7.97 (1H, br s), 8.15 (1H, br s), 11.16 (1H, br s), 11.28 (1H, br s). MS *m/e*: 403 (M⁺).

6-Carbamoyl-5-(4-tolylthiomethyl)uracil (IIId): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3400—3300, 1740, 1680, 1650. NMR (DMSO-*d*₆) δ : 2.26 (3H, s), 3.91 (2H, s), 7.13 (2H, d, *J* = 8.5 Hz), 7.28 (2H, d, *J* = 8.5 Hz), 7.97 (1H, br s), 8.15 (1H, br s), 11.17 (1H, br s), 11.31 (1H, br s). MS *m/e*: 291 (M⁺).

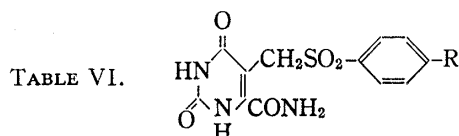
6-Carbamoyl-5-(4-methoxyphenylthiomethyl)uracil (IIIf): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3400, 3300, 1758, 1715, 1665. NMR (DMSO-*d*₆) δ : 3.71 (3H, s), 3.79 (2H, s), 6.92 (2H, d, *J* = 8.6 Hz), 7.29 (2H, d, *J* = 8.6 Hz), 7.89 (1H, br s), 8.01 (1H, br s), 10.97 (1H, br s), 11.15 (1H, br s). MS *m/e*: 307 (M⁺).

6-Carbamoyl-5-(4-chlorobenzylthiomethyl)uracil (VIa): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3350, 1760, 1690, 1650. NMR (DMSO-*d*₆) δ : 3.38 (2H, s), 3.73 (2H, s), 7.30 (4H, s), 7.97 (1H, br s), 8.15 (1H, br s), 11.07 (1H, br s), 11.22 (1H, br s). MS *m/e*: 327 (M⁺ + 2), 325 (M⁺).

6-Carbamoyl-5-(4-fluorobenzylthiomethyl)uracil (VIb): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3350, 1760, 1700, 1660. NMR (DMSO-*d*₆) δ : 3.39 (2H, s), 3.74 (2H, s), 6.9—7.5 (4H, m), 8.00 (1H, br s), 8.18 (1H, br s), 11.09 (1H, br s), 11.23 (1H, br s). MS *m/e*: 309 (M⁺).

5-(4-Bromobenzylthiomethyl)-6-carbamoyluracil (VIc): IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3350, 1760, 1690, 1650. NMR (DMSO-*d*₆) δ : 3.38 (2H, s), 3.72 (2H, s), 7.27 (2H, d, *J* = 9 Hz), 7.46 (2H, d, *J* = 9 Hz), 8.00 (1H, br s), 8.17 (1H, br s), 11.10 (1H, br s), 11.23 (1H, br s). MS *m/e*: 371 (M⁺ + 2), 369 (M⁺).

General Procedure for the Preparation of 5-(4-Substituted-phenylsulfonylmethyl)-6-carbamoyluracils (IVa—c): A Typical Example—5-(4-Bromophenylsulfonylmethyl)-6-carbamoyluracil (IVc): A mixture of IIIc (0.9 g, 2.5 mmol) and 30% hydrogen peroxide (4.0 g, 35 mmol) in acetic acid (7 ml) was heated at 80—90°C for 1 h, then cooled. The product was filtered off and recrystallized from DMSO-MeOH to give



Compd. No.	R	Yield (%)	mp (°C)	Recryst. solv.	Formula	Analysis (%)		
						Calcd (Found)	C	H N
IVa	Cl	67.1	>300	DMSO-MeOH	C ₁₂ H ₁₀ ClN ₃ O ₅ S	41.93 (41.99)	2.93 (3.03)	12.22 (12.01)
IVb	F	57.2	>300	DMSO-MeOH	C ₁₂ H ₁₀ FN ₃ O ₅ S	44.04 (43.95)	3.08 (2.95)	12.84 (12.66)
IVc	Br	74.2	>300	DMSO-MeOH	C ₁₂ H ₁₀ BrN ₃ O ₅ S	37.13 (36.92)	2.60 (2.57)	10.82 (10.64)

0.72 g (74.2%) of IVc: mp > 300°C. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3460, 1703, 1680, 1305, 1140. NMR (DMSO-*d*₆) δ : 4.38 (2H, s), 7.69 (4H, s), 7.97 (1H, br s), 8.12 (1H, br s), 11.19 (2H, br s). MS *m/e*: 389 (M⁺ + 2), 387 (M⁺).

Data for the sulfones IVa—c prepared as described above are listed in Table VI. IR, NMR and mass spectral data are given below.

5-(4-Chlorophenylsulfonylmethyl)-6-carbamoyluracil (IVa): IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3460, 1705, 1690—1675, 1310, 1145. NMR (DMSO-*d*₆) δ : 4.43 (2H, s), 7.63 (2H, d, *J* = 8.4 Hz), 7.75 (2H, d, *J* = 8.4 Hz), 8.02 (1H, brs), 8.16 (1H, br s), 11.29 (2H, br s). MS *m/e*: 345 (M⁺ + 2), 343 (M⁺).

6-Carbamoyl-5-(4-fluorophenylsulfonylmethyl)uracil (IVb): IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3440, 1705, 1690—1675, 1310, 1145. NMR (DMSO-*d*₆) δ : 4.42 (2H, s), 7.2—8.0 (4H, m), 8.02 (1H, br s), 8.19 (1H, br s), 11.27 (2H, br s). MS *m/e*: 327 (M⁺).

Leukemia L-1210 *in Vitro* Screening—Kuwano *et al.* determined the synergistic effect of the combination of 6-methylthioinosine and amphotericin B on deoxyribonucleic acid (DNA) synthesis by measuring the incorporation of ³H-thymidine.⁹ It is also well known that 5-[¹²⁵I]iodo-2'-deoxyuridine (¹²⁵I-dUrd) is incorporated into DNA in the place of thymidine.¹⁰ On the other hand, ³H-thymidine must be measured by the use of a liquid scintillation counter but ¹²⁵I-dUrd can be measured directly with a gamma-counter. Cohen *et al.* measured cell-mediated cytotoxicity by using ¹²⁵I-dUrd.¹¹ Accordingly, we determined the effect of the newly synthesized compounds on the growth of L-1210 cells by measuring the incorporation of ¹²⁵I-dUrd.¹⁾

L-1210 cells were obtained from the Central Research Laboratories of Yamanouchi Co., Ltd. Three samples at concentrations of 3, 30 and 100 µg/ml were prepared in 97.5% saline–2.5% ethanol, and an aliquot of each sample (20 µl) was added to L-1210 cells (1 × 10⁵ cells/180 µl in 10% horse serum supplemented RPMI 1640). 6-Mercaptopurine riboside (6-MPR) was used as a standard. After incubation of the medium in a humidified atmosphere of 5% CO₂–95% air for 18 h at 37°C, ¹²⁵I-dUrd in aqueous solution (0.2 µCi/20 µl) was added. The medium was incubated for a further 6 h, then L-1210 cells were collected with an automatic cell harvester and the radioactivity (cpm) was measured with an autogamma scintillation spectrometer. The incorporation of ¹²⁵I-dUrd into the cells was measured and the percent growth inhibition was calculated by means of the following equation:

$$\% \text{ growth inhibition} = \left(1 - \frac{\text{cpm}_T}{\text{cpm}_C}\right) \times 100$$

where cpm_T is the ¹²⁵I-dUrd radioactivity incorporated in the tested cells and cpm_C is that of the control.

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References and Notes

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