SYNTHESIS OF (1-URACILYL)ALKYLAMINES AND THEIR TRANSFORMATION TO TWO-RING SYSTEMS

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N-[2(3)-(1-Uracilyl)ethyl(propyl)]alkylamines were synthesized. It is shown that intramolecular cyclization to give imidazo- and pyrimido[1,2-c]pyrimidine systems occurs primarily in the reaction of 5-bromouracil derivatives with primary and secondary amines.

We have previously shown that the same product, viz., 6H-2,8-dioxo-5-carboxy-4,6-dihydroimidazo[1,2-c]pyrimidine, is formed in the reaction of β-(5-bromo-1-uracilyl)-α-alanine with primary and secondary amines [1].

The aim of the present research was to investigate the intramolecular cyclization of (5-bromo-1-uracilyl)alkylamines under the influence of primary and secondary amines with various nucleophilicities as a function of the length of the alkyl group. We used 3-(1-uracilyl)propyl bromide [2] and 2-(1-uracilyl)-ethyl bromide, obtained by alkylation of 2,4-bis(trimethylsilyl)uracil with 1,2-dibromoethane, as the starting compounds for the synthesis of a series of primary and secondary-ω-(1-uracilyl)alkylamines and their 5-bromo derivatives.

3-(1-Uracilyl)propylamine was synthesized by heating 3-(1-uracilyl)propyl bromide and hexamethylenetetramine in chloroform with subsequent cleavage of the intermediate 3-(1-uracilyl)propylhexamethylenetetramine with hydrochloric acid [3]. An attempt to obtain 2-(1-uracilyl)ethylamine by the same method was unsuccessful, since the hexamethylenetetramine derivative is formed in negligible amounts. To obtain this amine we used the Schmidt reaction — 3-(1-uracilyl)propionic acid was heated with sodium azide and concentrated sulfuric acid in chloroform. The reaction gives the product in 50% yield, and the unchanged acid is readily separated from the final amine and can be used again. In order to obtain ω-(1-uracilyl)alkyl-amines II-IX we investigated several methods. We found that the reaction of (1-uracilyl)acetaldehyde [4] with primary amines with subsequent reduction of the imine with sodium borohydride gives the products in very low yields. Better yields (70-80%) were obtained in the reaction of 2-(1-uracilyl)-ethyl and 3-(1-uracilyl)propyl bromides with excess amine (Table 1).

TABLE 1. N-[2-(1-Uracilyl)ethyl]- and N-[3-(1-Uracilyl)-propyl]alkylamines

Compound	UV spectrum (H_2O), nm	R_f (system A)	Found, %			Empirical formula	Calc., %		
			C	H	N		C	H	N
II	264	0,70*	40,9	5,7	24,5	$C_6H_9N_3O_2 \cdot H_2O$	41,6	5,2	24,3
III	267	0,25	54,3	7,6	20,9	$C_9H_{15}N_3O_2$	54,9	7,6	21,3
IV	268	0,26	52,5	7,9	18,2	$C_{10}H_{17}N_3O_2 \cdot H_2O$	52,4	8,3	18,4
V	263	0,24	47,4	4,9	13,1	$C_{13}H_{15}N_3O_2 \cdot HBr$	47,8	4,9	12,9
VI	266	0,70*	49,2	6,6	24,7	$C_7H_{11}N_3O_2$	49,7	6,5	24,8
VII	266	0,12	40,3	6,3	14,1	$C_{10}H_{17}N_3O_2 \cdot HBr$	41,1	6,1	14,4
VIII	266	0,20	42,8	6,6	13,4	$C_{11}H_{19}N_3O_2 \cdot HBr$	43,1	6,5	13,7
IX	265	0,25	49,3	5,3	12,3	$C_{14}H_{17}N_3O_2 \cdot HBr$	49,4	5,3	12,4

*In system B.

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TABLE 2. PMR Spectra of N-[2-(1-Uracilyl)ethyl]- and N-[3-(1-Uracilyl)propyl]alkylamines (II-IX)

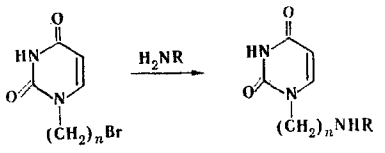
Compound	δ, ppm									
	6-H (d)	5-H (d)	2′-H	1′-H (m)	3′-H (t)	1″-H (m)	2″-H (m)	3″-H (m)	CH_3 (m)	C_6H_5 (s)
II	7,50	5,42	3,15 t	2,71	—	—	—	—	—	—
III	7,22	5,37	3,72 t	3,55	—	3,17	1,48	—	0,85	—
IV	7,25	5,33	4,10 t	3,86	—	3,22	1,41	1,11	0,86	—
V	7,22	5,40	3,70 t	3,53	—	3,17	—	—	—	7,29
VI	7,40	5,50	2,00 m	3,40	3,20	—	—	—	—	—
VII	7,57	5,53	2,01 m	3,35	3,81	2,87	1,35	—	—	—
VIII	7,66	5,51	1,99 m	3,06	3,75	2,62	1,56	1,15	0,86	—
IX	7,60	5,48	1,94 m	3,66	4,08	2,84	—	—	—	7,40

TABLE 3. Characteristic Ions in the Mass Spectra of II-IX, XXVI, and XXVII [m/z (relative intensities, %)]

Compound	M+	a	b	c	d	M—C_7H_7	C_7H_7 m/z 91	m/z 73	m/z 71	m/z 69	m/z 67	m/z 57	m/z 55	m/z 43	m/z 41
III	197	125	—	168	58	—	—	(18)	(16)	(20)	(15)	—	(53)	(51)	(100)
	(0)	(22)		(68)	(26)	—	—	(15)							
IV	211	125	—	168	72	—	—	(15)	(18)	(20)		(29)	(33)	(26)	(33)
	(7)	(48)		(100)	(12)										
V	245	—	120	—	106	154	(100)	—	—	—	—	—	—	—	(5)
	(1)		(46)		(17)	(5)									
VII	211	125	72	182	—	—	—	(20)	(32)	(17)	—	(7)	—	(20)	(68)
	(0)	(15)	(65)	(54)											
VIII	225	125	86	182	—	—	—	(23)	(48)	(42)	(30)	(77)	(63)	(68)	(80)
	(0)	(14)	(33)	(63)											
IX	259	125	120	—	106	168	(100)	—	(7)	(7)	(6)	(11)	(10)	(11)	(14)
	(1)	(5)	(20)		(73)	(13)									
XXVI	282	196	—	253	72	—	—	(13)	(11)	(9)	(14)	(97)	(80)	(94)	(100)
	(14)	(16)		(14)	(6)										
XXVII	316	182	120	—	106	225	(100)	(20)	(35)	(32)	(21)	(49)	(41)	(41)	(44)
	(14)	(5)	(12)		(38)	(5)									

Well-resolved characteristic doublets of 6- and 5-H protons of the pyrimidine ring at 7.25-7.66 and 5.33-5.51 ppm, respectively, are noted in the PMR spectra of II-IX (Table 2). Molecular ions are either absent or have low intensities in the mass spectra of III-IX; this is associated with facile α cleavage with respect to the side chain nitrogen atom. In connection with the presence of alkylamino substituents in the molecules (III, IV, VII, and VIII) intense ions with even numbers of electrons are observed in the spectra in the low-mass region (Table 3). Cleavage with respect to the side chain nitrogen atom (b and c ions) is a characteristic fragmentation process if $R \neq C_6H_5$. Ion c is not formed when a phenyl group is present, since

Scheme A



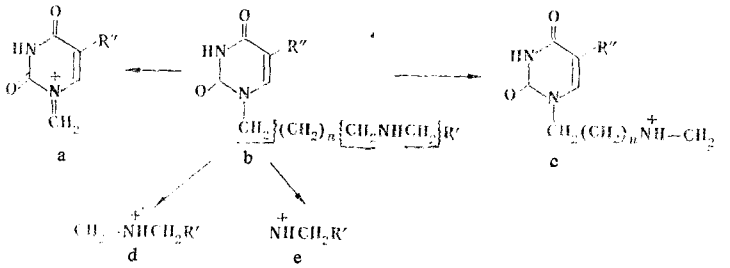
II-IX

II $n=2$, VI $n=3$, R=H; III $n=2$, VII $n=3$, R=C_3H_7; IV $n=2$, VIII $n=3$, R=C_4H_9; V $n=2$, IX $n=3$, R=$CH_2C_6H_5$

cleavage of the N–C bond to give $C_7H_7^+$ and $(M - C_7H_7)^+$ ions is energetically more favorable. Also characteristic is α cleavage with respect to the nitrogen atom in the 1 position of the ring (ion *a*).

TABLE 4. N-[1-(5-Bromo-1-uracilyl)ethyl]- and N-[3-(5-Bromo-1-uracilyl)propyl]alkylamine (X-XVII) Hydrobromides

Compound	UV spectrum (H_2O), λ_{max}, nm	R_f (system A)	δ, ppm								
			6-H (s)	2′-H (m)	1′-H (m)	3′-H	1″-H (m)	2″-H (m)	3″-H (m)	CH_3 (m)	C_6H_5 (s)
X	278	0,38	7,70	3,70	3,60	—	—	—	—	—	—
XI	282	0,32	7,70	3,77	3,57	—	3,13	1,46	—	0,86	—
XII	282	0,36	7,73	3,99	3,57	—	3,17	1,63	1,10	0,86	—
XIII	280	0,44	8,08	4,20	3,75	—	3,24	—	—	—	7,33
XIV	280	0,36	7,98	2,15	3,22	3,73 t	—	—	—	—	—
XV	280	0,26	8,06	1,78	3,28	3,70 t	2,80	1,55	—	0,89	—
XVI	280	0,36	8,19	1,83	3,00	3,72 m	2,65	1,57	1,11	0,91	—
XVII	280	0,39	8,17	1,94	3,66	4,08 m	2,87	—	—	—	7,35

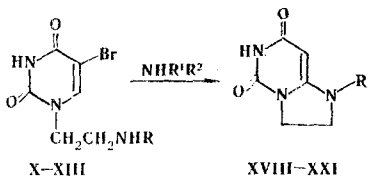


III—IX R″ -H; III—V $n=1$; VII—IX $n=2$; III, VII R′=C_2H_5; IV, VIII R′=C_3H_7; V, IX R′=C_6H_5; XXVI R″=NHC_4H_9, R′=C_3H_7, $n=2$; XXVII R″=NHC_3H_7, R′=C_6H_5, $n=2$

ω-(5-Bromo-1-uracilyl)alkylamines X-XVII were obtained by halogenation of (1-uracilyl)-alkylamines II-IX with bromine in glacial acetic acid. These compounds are relatively unstable. Bromine is split out to give the starting ω-(1-uracilyl)alkylamines in most cases when they are heated with water. The structure of the synthesized X-XVII is confirmed by data from the UV spectra, in which the absorption maximum characteristic for 5-bromouracils at 280 nm appears. The doublet signals of protons attached to the $C_{(5)}$ and $C_{(6)}$ atoms vanish in the PMR spectra, and a new signal, which is related to the 6-H proton of the pyrimidine ring, appears at 7.70-8.17 ppm. Multiplet signals due to the protons of the alkyl chain and the substituents attached to the amino group are observed in the same regions as in the case of II-IX (Table 4).

The reaction proceeds via two pathways when the ω-(5-bromo-1-uracilyl)alkylamines are heated with excess amounts of primary and secondary amines: Primarily either replacement of the halogen atom by an amino group to give 5-alkylaminouracil derivatives or transformation to two-ring systems occurs, depending on the length of the alkyl group attached to the $N_{(1)}$ atom of the pyrimidine ring. Elimination of hydrogen bromide to give the imidazo-[1,2-c]pyrimidine system (XVIII-XXI) and traces of N-[2-(5-alkyl-amino-1-uracilyl)ethyl]-alkylamines occurs in all cases in the reaction of N-[2-(5-bromo-1-uracilyl)ethyl]alkylamines (X-XIII) with primary amines. Only imidazo[1,2-c]pyrimidine and pyrimido[1,2-c]-pyrimidine derivatives, respectively, are formed with morpholine. The halogen atom is replaced by an amino group (XXVI and XXVII) when the N-[3-(5-bromo-1-uracilyl)propyl]-alkylamines are heated with primary amines, but intramolecular cyclization products can also be isolated. N-[3-(5-Bromo-1-uracilyl)propyl]amine reacts with both primary and secondary amines to give 7H-2,9-dioxo-4,5,6,7-tetrahydropyrimido[1,2-c]pyrimidine (XXII) (Table 5).

Scheme B



X-XIII XVIII-XXI

X, XVIII R=H; XI, XIX R=C_3H_7; XII, XX R=C_4H_9; XIII, XXI R=$CH_2C_6H_5$

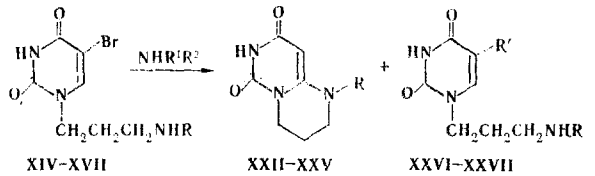
TABLE 5. Imidazo[1,2-c]pyrimidines (XVIII-XXI) and Pyrimido[1,2-c]pyrimidines (XXII-XXV)

Compound	UV spectrum (H_2O) λ_{max}, nm	Found				Empirical formula	Calc.				PMR spectrum, δ, ppm								
		C, %	H, %	N, %	M^+		C, %	H, %	N, %	M	7(8)-H (s)	4H (t)	5-H	6-H	1′-H	2′-H (m)	3′-H (m)	CH_3 (m)	C_6H_5 (s)
XVIII	264	46,7	4,7	27,1	153	$C_6H_7N_3O_2 \cdot 0{,}5H_2O$	46,8	4,5	27,3	153	4,45	3,79	3,55 m	—	—	—	—	—	—
XIX	276	54,8	6,8	21,5	195	$C_9H_{13}N_3O_2$	55,1	6,6	21,4	195	4,52	3,79	3,57 m	—	3,11 m	1,48	—	0,86	—
XX	276	57,4	7,4	20,7	209	$C_{10}H_{15}N_3O_2$	57,4	7,2	20,1	209	4,45	3,86	3,44 m	—	2,84 m	1,57	1,08	0,86	—
XXI	269	63,9	5,5	17,0	243	$C_{13}H_{13}N_3O_2$	64,3	5,4	17,3	243	4,65	3,94	3,35 t	—	4,36 s	—	—	—	7,22
XXII	273	50,1	5,5	24,9	167	$C_7H_9N_3O_2$	50,3	5,4	25,2	167	4,40	3,79	2,00 m	3,60 m	—	—	—	—	—
XXIII	276	57,2	7,3	19,8	209	$C_{10}H_{15}N_3O_2$	57,4	7,2	20,1	209	4,47	3,72	2,01 m	3,35 t	2,87 m	1,19	—	0,86	—
XXIV	276	59,3	7,8	18,6	223	$C_{11}H_{17}N_3O_2$	59,1	7,6	18,8	223	4,47	3,72	1,88 m	3,37 t	2,89 m	1,63	1,11	0,91	
XXV	270	65,2	6,0	16,2	257	$C_{14}H_{15}N_3O_2$	65,4	5,8	16,3	257	4,36	3,81	1,99 m	3,39 t	4,47 t	—	—	—	7,22

TABLE 6. Characteristic Ions in the Mass Spectra of XVIII-XXV [m/z (relative intensities, %)]

Compound	M^+	$(M-C_2H_4)^{+\cdot}$	$(M-C_2H_4NH)^{+\cdot}$	$(M-CH_3)^+$	$(M-C_2H_5)^+$	$(M-C_3H_7)^+$	$(M-C_7H_7)^+$	$(C_7H_7)^+$	m/z 71	m/z 69	m/z 57	m/z 55	m/z 43	m/z 41
XVIII	153 (100)	129 (12)	110 (60)	—	—	—	—	—	(43)	(55)	(88)	(90)	(96)	(98)
XIX	167 (6)	195		180 (3)	166 (6)	—	—	—	(62)	(66)	—	(100)	(77)	(90)
XXI	243 (24)	—	—	—	—		152 (6)	91 (100)	—	—	—	—	—	(6)
XXII	167 (100)	139 (8)	124 (18)	—	—	—	—	—	(12)	(16)	(22)	(19)	(24)	(23)
XXIII	209 (8)	181 (8)	—	194 (4)	—	166 (8)	—	—	(53)	(35)	(90)	(91)	(84)	(100)
XXIV	223 (18)	195 (7)	—	208 (9)	194 (11)	180 (7)	—	—	(42)	(41)	(67)	(56)	(100)	(77)
XXV	257 (58)	—	—	—	—	—	166 (7)	91 (100)	(42)	(39)	(67)	(50)	(56)	(61)

Scheme C

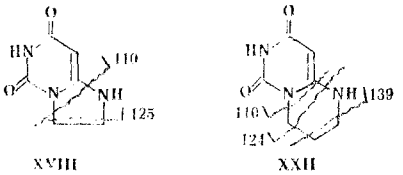


XIV-XVII XXII-XXV XXVI-XXVII

XIV, XXII R=H; XV, XXIII R=C_3H_7; XVI, XXIV R=C_4H_9; XXV, XVII R=$CH_2C_6H_5$; XXVI R=C_3H_7, R′=NHC_4H_9 XXVII R=$CH_2C_6H_5$, R′=NHC_3H_7

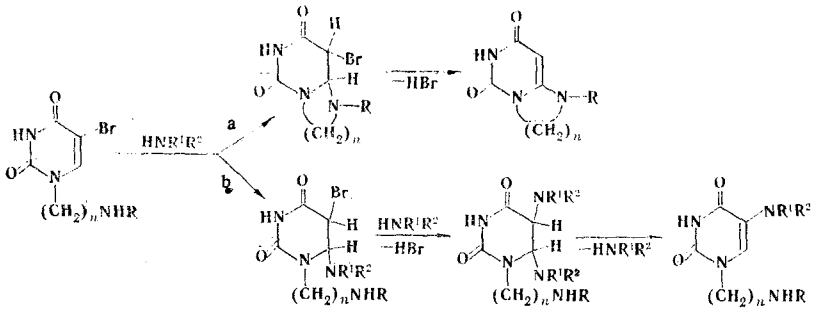
It is apparent from the PMR spectral data that the singlet signal of the proton attached to the $C_{(6)}$ atom that is characteristic for 5-bromouracils vanishes in the formation of the imidazo- and pyrimido[1,2-c]pyrimidine systems, and a new signal, which can be assigned to the 7- and 8-H protons, respectively, appears at 4.36-4.65 ppm. A multiplet due to the 4- and 5-H (XVIII-XXI) or 4- and 6-H (XXII-XXV) protons, which was shifted slightly to the weak-field region as compared with II-IX with an open alkyl chain, is observed at 3.35-3.94 ppm. A singlet signal of the 6-H proton of the pyrimidine ring of XXVI and XXVII is observed at 6.47-6.54 ppm and is shifted to the strong-field region as compared with starting XV and XVII.

The molecular-ion peak is the maximum peak in the mass spectra of XVIII and XXII, and this constitutes evidence for the cyclic structure of these compounds.* The saturated ring is most readily cleaved (Table 2) with the elimination of a molecule of ethylene, ethylenimine, or propyleneimine (XXII).



XVIII XXII

When there was an alkyl substituent attached to the nitrogen atom in the 6 (XIX) or 7 (XXIII, XXIV) position, the intensity of the molecular ion was reduced (6-18%) as compared with unsubstituted XVIII and XXII as a consequence of the ease of homolytic cleavage of the aliphatic chain to give $(M - CH_3)^+$, $(M - C_2H_5)^+$, and $(M - C_3H_7)^+$ ions. A benzyl substituent in the 6 (XXI) or 7 (XXV) position stabilizes the molecule somewhat with respect to electron impact – the intensities of the molecular ions (XXI and XXV) are 24 and 58%, respectively. Cleavage of the C–N bond to give $C_7H_7^+$ (the maximum peak in the spectrum) and $(M - C_7H_7)^+$ ions is a characteristic fragmentation process. The mass spectra of XXVI and XXVII are characterized by molecular ions with medium intensities (14-36%). Like II-IX, XXVI and XXVII under electron impact form products of α cleavage of the side chain in the 1 position, but $C_7H_7^+$ and $(M - C_7H_7)^+$ ions are formed instead of c ions if R′ = C_6H_5 (Table 6). The mechanism of nucleophilic substitution in the 5-halopyrimidine series has not yet been adequately studied in connection with the fact that in many cases the reaction proceeds via different pathways, and both 5- or 6-substituted pyrimidines and mixtures of them are formed. However, in all cases the first act is attack by the nucleophile on the $C_{(6)}$ atom of the pyrimidine ring [5].



*The m/z values are given for the ion peaks.

The reasons for reaction via pathways *a* or b will be the subject of future investigations.

EXPERIMENTAL

The UV spectra of aqueous solutions of the compounds were recorded with a Spectramom 204 spectrophotometer. The PMR spectra of solutions of the compounds in d_6-DMSO were recorded with a Brucker spectrometer (90 MHz) with hexamethyldisiloxane as the internal standard. The mass spectra were recorded with an MS-50 AEI spectrometer with direct introduction of the samples into the ion source; the ionizing-electron energy was 70 eV, and the ionization-chamber temperature was 150°C. Chromatographic purification was carried out with a modified Jobin Ivon Chromatospak chromatograph; Merck H60 silica gel and Merck Silicagel 60F-254 plates for preparative thin-layer chromatography (TLC) with a layer thickness of 2 mm were used as the sorbents. The individuality of the compounds obtained was monitored by means of TLC on Silufol UV-254F plates. The substances were detected on the chromatograms from the absorption in UV rays and by development with ninhydrin. The following systems were used in chromatography: system A [butanol—acetic acid—water (8:1:2)], system B [methylcellosolve—propionic acid—water saturated with NaCl (70:15:15)], system C [ethanol—water (7:3)], and system D [2-propanol—25% ammonium hydroxide—water (7:1:2)]. The melting points of the compounds were determined with a Kofler apparatus.

2-(1-Uracilyl)ethyl Bromide (I). A mixture of 28.8 g (0.116 mole) of 2,4-bis(trimethylsilyl)uracil [6] and 279 g (1.5 mole) of 1,2-dibromoethane was heated with stirring at 105°C for 1.5 h, after which it was cooled, and the unchanged bis(trimethylsilyl)uracil was decomposed with 50 ml of water. The precipitated uracil was removed by filtration and washed with chloroform. The aqueous layer was separated and extracted with chloroform (three 30-ml portions). The extracts were added to the organic layer, and the mixture was evaporated to a volume of 100 ml and allowed to stand overnight. The precipitate was removed by filtration and recrystallized from 2-propanol to give 15.0 g (59%) of a product with mp 145-146°C and R_f 0.77 (system B). UV spectrum (in water): λ_{max} 274 nm. PMR spectrum: 11.25 (1H, s, 3-H), 7.60 (1H, d, 6-H), 5.51 (1H, d, 5-H), 3.95 (2H, t, 2'-H), and 3.64 ppm (2H, t, 1'-H). Found: C 33.0; H 3.3; Br 36.7; N 12.6%. $C_6H_7BrN_2O_2$. Calculated: C 32.8; H 3.2; Br 36.5; N 12.8%.

2-(1-Uracilyl)ethylamine (II). A 4.42-g (0.024 mole) sample of 3-(1-uracilyl)propionic acid [7] was dissolved in a mixture of 80 ml of chloroform and 41 ml of sulfuric acid at 40°C, 1.82 g (0.042 mole) of sodium azide was added in portions with stirring, and the mixture was maintained at 50-55°C for 4 h. It was then cooled, and the sulfuric acid layer was separated and treated with 200 g of ground ice and neutralized with barium oxide. The barium sulfate was removed by filtration and washed with water, and the filtrates were evaporated. The reaction product was purified with a preparative liquid chromatograph. The unchanged 3-(1-uracilyl)propionic acid was eluted with system C, and the amine was eluted with system D to give 1.49 g (40%) of amine II with mp 160-162°C and 1.76 g (40%) of 3-(1-uracilyl)propionic acid.

N-[2-(1-Uracilyl)ethyl]propylamine (III). A 1.6-g (7.3 mmole) sample of I was added to 10 ml of propylamine, and the mixture was stirred for 45 min. The solution was evaporated in vacuo to dryness, and the residue was washed with absolute ether. The yield of amide III, with mp 138-140°C (from 2-propanol), was 1.12 g (80%).

N-[2-(1-Uracilyl)ethyl]butylamine (IV). This compound, with mp 130-132°C (from 2-propanol), was obtained in 80% yield from I and butylamine by a procedure similar to that used to obtain amine III.

N-[2-(1-Uracilyl)ethyl]benzylamine (V) Hydrobromide. A 1.6-g (7.3 mmole) sample of I was added to 8 ml of a mixture of benzylamine and triethylamine (1:3), and the mixture was stirred at room temperature for 2 h and allowed to stand in a refrigerator for 24 h. The precipitated amine salt was removed by filtration and washed with absolute ether to give 1.54 g (65%) with mp 260-262°C (from a mixture of methanol with 2-propanol).

3-(1-Uracilyl)propylamine (VI). A 1.84-g (0.008 mole) sample of 3-(1-uracilyl)propyl bromine [3] was added to a hot solution of 2.15 g (0.015 mole) of urotropin in 20 ml of chloroform, and the mixture was stirred for 1 h. The precipitate was removed by filtration and washed with hot chloroform to give 3.24 g (87%) of the quaternary salt with mp 202-203°C (from 2-propanol). Found: C 41.6; H 5.8; N 22.3%. $C_{13}H_{21}BrN_6O_2$. Calculated: C 41.8; H 5.6; N 22.5%.

A 3.0-g (0.008 mole) sample of this salt was suspended in 20 ml of a mixture of ethanol and concentrated hydrochloric acid (8:1), and the suspension was stirred at room temperature for 2 days. The precipitate was removed by filtration, washed with absolute ethanol, dissolved in 5 ml of distilled water, and separated on Dowex-1-X8 ion-exchange resin (in the formate form) by elution with water. The aqueous solution was evaporated to dryness, and the residue was subjected to lyophilization (in vacuo at 0.1 mm) to give 1.45 g (88%) of amine VI with mp 164-166°C.

N-[3-(1-Uracilyl)propyl]propylamine (VII) Hydrobromide. This compound, with mp 165-168°C (from 2-propanol), was obtained in 70% yield from 3-(1-uracilyl)propyl bromide and propylamine by a procedure similar to that used to prepare amine III.

N-[3-(1-Uracilyl)propyl]butylamine (VIII) Hydrobromide. This compound, with mp 195-197°C (from 2-propanol), was obtained in 60% yield from 3-(1-uracilyl)propyl bromide and butylamine by a procedure similar to that used to prepare amine III.

N-[3-(1-Uracilyl)propyl]benzylamine (IX) Hydrobromide. This compound with mp 232°C (from methanol–2-propanol), was obtained in 65% yield from 3-(1-uracilyl)propyl bromide and benzylamine by a procedure similar to that used to obtain amine V.

N-(5-Bromo-1-uracilyl)ethylamine (X) Hydrobromide. A 1.55-g (0.01 mole) sample of amine II was dissolved in 4 ml of glacial acetic acid, 0.1 ml of bromine was added, and the mixture was maintained at room temperature for 12 h. The precipitate was removed by filtration, washed with absolute ether, and dried in vacuo to give 1.99 g (92%) of a product with mp 279-280°C.

N-[2-(5-Bromo-1-uracilyl)ethyl]propylamine (XI) Hydrobromide. This compound, with mp 186-187°C (from water), was obtained in 70% yield from amine III by a procedure similar to that used to prepare X. Found: C 30.1; H 4.2; Br 45.2; N 11.6%. $C_9H_{14}BrN_3O_2 \cdot HBr$. Calculated: C 30.2; H 3.9; Br 44.8; N 11.8%.

N-[2-(5-Bromo-1-uracilyl)ethyl]butylamine (XII) Hydrobromide. This compound, with mp 165-167°C, was obtained in 70% yield from amide IV by a procedure similar to that used to prepare X. Found C 32.2; H 4.4; Br 43.3; N 11.4%. $C_{10}H_{16}BrN_3O_2 \cdot HBr$. Calculated: C 32.3; H 4.3; Br 43.4; N 11.3%.

N-[2-(5-Bromo-1-uracilyl)ethyl]benzylamine (XIII) Hydrobromide. This compound, with mp 158-160°C, was obtained in 80% yield from amine V by a procedure similar to that used to prepare X.

3-(5-Bromo-1-uracilyl)propylamine (XIV) Hydrobromide. This compound with mp 254°C, was obtained in 70% yield from amine VI by a procedure similar to that used to prepare X.

N-[3-(5-Bromo-1-uracilyl)propyl]propylamine (XV) Hydrobromide. This compound with mp 174-175°C, was obtained in 72% yield from amine VII by a procedure similar to that used to prepare X.

N-[3-(5-Bromo-1-uracilyl)propyl]butylamine (XVI) Hydrobromide. This compound, with mp 154-156°C, was obtained in 70% yield from amine VIII by a procedure similar to that used to prepare X.

N-[3-(5-Bromo-1-uracilyl)propyl]benzylamine (XVII) Hydrobromide. This compound, with mp 167°C, was obtained in 78% yield from amine IX by a procedure similar to that used to prepare X.

2,8-Dioxo-4,5-dihydro-6H-imidazo[1,2-c]pyrimidine (XVIII). A mixture of 0.23 g (0.001 mole) of the hydrobromide of X and 3 ml of an amine (morpholine, butylamine) was refluxed with stirring for 1-3 h, after which the solution was evaporated in vacuo to dryness. The residue was washed with absolute ether and allowed to stand under acetone in a refrigerator for 24 h. The resulting crystals were removed by filtration and washed with cold acetone to give 0.084-0.092 g (54-59%) of a product with mp 312-314°C.

2,8-Dioxo-6-propyl-4,5-dihydroimidazo[1,2-c]pyrimidine (XIX). A 0.39-g (0.0011 mole) sample of the hydrobromide of XI was suspended in 6 ml of butylamine (propylamine, morpholine), and the suspension was refluxed with stirring for 3 h. The solution was evaporated in vacuo to dryness, and the residue was treated with ether. The resinous reaction product was purified by means of preparative TLC (system A). Compound XIX was extracted with hot water from the band (R_f 0.4) detected in UV light. The extracts were evaporated in vacuo to

dryness, and the residue was washed with anhydrous acetone and removed by filtration to give 0.087 g (40%) of a product with mp 300-302°C.

2,8-Dioxo-6-butyl-4,5-dihydroimidazo[1,2-c-]pyrimidine (XX). This compound, with mp 308-310°C, was obtained in 50% yield from XII and 6 ml of butylamine (propylamine, morpholine).

2,8-Dioxo-6-benzyl-4,5-dihydroimidazo[1,2-c]pyrimidine (XXI). This compound, with mp 350°C, was obtained in 40% yield from XIII and butylamine (propylamine, morpholine) by a procedure similar to that used to prepare XIX.

2,9-Dioxo-4,5,6,7-tetrahydro-7H-pyrimido[1,2-c]pyrimidine (XXII). This compound, with mp 313-315°C, was obtained in 55% yield from XIV and propylamine (butyalmine, morpholine) by a procedure similar to that used to prepare XVIII.

7-Propyl-2,9-dioxo-4,5,6,7-tetrahydropyrimido[1,2-c]pyrimidine (XXIII). This compound, with mp 220-222°C, was obtained in 40% yield from the hydrobromide of XV and morpholine by a procedure similar to that used to prepare XIX.

7-Butyl-2,9-dioxo-4,5,6,7-tetrahydropyrimido[1,2-c]pyrimidine (XXIV). This compound, with mp 220°C, was obtained in 45% yield from the hydrobromide of XVI and morpholine by a procedure similar to that used to prepare XIX.

7-Benzyl-2,9-dioxo-4,5,6,7-tetrahydropyrimido[1,2-c]pyrimidine (XXV). This compound, with mp 223°C, was obtained in 45% yield from XVII and morpholine by a procedure similar to that used to prepare XIX.

N-[3-(5-Butylamino-1-uracilyl)propyl]propylamine (XXVI). This compound was obtained from XV and butylamine by a procedure similar to that used to prepare XIX. The bands with R_f 0.55 and R_f 0.4, which were detected in UV light, were extracted with hot water, and the extracts were evaporated in vacuo to dryness to give XXIII in 20% yield and amine XXVI, with mp 110-112°C, in 40% yield. UV spectrum (in water): λ_{max} 272 nm. PMR spectrum: 6.54 ppm (s, 6-H). Found: C 59.8; H 9.1; N 19.7%. $C_{14}H_{25}N_4O_2$. Calculated C 59.8; H 8.9; N 19.9%.

N-[3-(5-Propylamino-1-uracilyl)propyl]benzylamine (XXVII). This compound, with mp 116-117°C, was obtained in 40% yield from the hydrobromide of XVII and propylamine by a procedure similar to that used to prepare XIX. PMR spectrum: 6.47 ppm (s, 6-H). Found: C 64.2; H 7.8; H 17.5%. $C_{17}H_{24}N_4O_2$. Calculated: C 64.5; H 7.6; N 17.7%.

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