SYNTHESIS AND TRANSFORMATIONS OF 1-(4-HYDROXYPHENYL)DIHYDROURACILS

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N-(4-Hydroxyphenyl)-β-alanine and its methyl derivatives, as well as p-hydroxyphenylamino-β,β'-dipropionic acid, were obtained by the reaction of p-aminophenol with methyl acrylate and acrylic, methacrylic, and crotonic acids. The β-alanines were converted to the corresponding hydrazides and 1-(4-hydroxyphenyl)dihydro- and thiodihydrouracils, which were decyclized by the action of alkalis to ureido and thioureido acids and were dehydrogenated by heating with sulfur to give uracils. The dihydro- and thiodihydrouracils were alkylated and acetylated.

1-Arylhexahydropyrimidine derivatives are of interest as stabilizers for polymers. They are readily obtained from the corresponding N-substituted β-alanines [1]. In the present research we used the reaction of p-aminophenol (I) with methyl acrylate to obtain methyl N-(4-hydroxyphenyl)-β-alanine (II) and the reaction of aminophenol I with methacrylic and crotonic acids to give α-methyl- and β-methyl-β-alanines (IIIb,c). Aminophenol I reacts with acrylic acid to give a difficult-to-separate mixture of alanine IIIa and dipropionic acid IV, which was obtained in pure form by the reaction of I with acrylic acid at a molar ratio of the reacting substances of 1:2.

It is apparent from the PMR spectra of alanines III and IV that protonation of the nitrogen atom of the substituted amino group occurs in trifluoroacetic acid, whereas the signals of the protons of the adjacent methylene groups are not split but show up in the form of complex multiplets (Table 1). A broad absorption band of stretching vibrations of OH and NH groups at 2100-3600 cm^{-1}, which indicates the presence of strong hydrogen bonds, is observed in the IR spectra of β-alanines IIIa-c. The stretching vibrations of the OH and NH groups are superimposed and become virtually indistinguishable. In addition, the weaker bands of the CH stretching vibrations are superimposed on the broad absorption band of the OH and NH groups. The absorption band of the carbonyl group of alanines III and IV and their hydrazides V is shifted to the lower-frequency region due to hydrogen bonds and shows up at 1630-1685 cm^{-1}.

When β-alanines III and ester II are heated with hydrazine, they form the corresponding hydrazides V. N-(4-Hydroxyphenyl)-β-alanine hydrazide (Va) at a concentration of 1.0 μg/ml displayed a tuberculostatic effect* on *Mycobacterium tuberculosis*.

The corresponding 1-substituted dihydro- and thiodihydrouracils (VI, VII) were obtained by the action of urea, cyanates, or thiocyanates on N-substituted β-alanines in an acidic medium [2]. The reactions of II and IIIa-c with urea and thiocyanates were carried out in acetic acid with subsequent treatment with hydrochloric acid. In the PMR spectra of dihydrouracils VIb,c and thiodihydrouracils VIIb,c the protons of the methylene group couple with the proton of the CH group to form the typical AB part of an ABX spin system. The chemical shifts and the spin–spin coupling constants (SSCC) are presented in Table 1.

Dihydrouracils VI and thiodihydrouracils VII, inasmuch as they are resistant to the action of acids, readily undergo decyclization under the influence of alkalis to give the corresponding β-ureido acids VIII and IX. Under the influence of hydrochloric acid the latter again undergo cyclization to dihydrouracils VI and VII.

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TABLE 1. Spectral Characteristics of the Synthesized II-XIX*

Compound	IR spectrum, ν, cm^{-1}			PMR spectrum, δ, ppm, J, Hz
	OH	NH	C=O	
1	2	3	4	5
II	3395	3310	1730	
IIIa	3600—2220		1640	2,53 (2H, t, α-CH_2); 3,07—3,57 (2H, m, β-CH_2); 6,43—7,03 (4H, q, arom.); 8,45 (2H, br s, $\overset{+}{N}H_2$)
IIIb	3380—2100		1640	0,93 (3H, d, J=7,5, CH_3); 2,41—2,9 (1H, m, CH); 2,99—3,74 (2H, m, CH_2); 6,50—7,23 (4H, q, arom.); 8,65 (2H, br s, $\overset{+}{N}H_2$)
IIIc	3300—2205		1630	1,03 (3H, d, J=7,5, CH_3); 2,50 (2H, d, J=6,0, CH_2); 3,38—3,89 (1H, m, CH); 6,48—7,04 (4H, q, arom.); 8,41 (2H, br s, $\overset{+}{N}H_2$)
IV	3200—2200		1685	1,80—4,07 [8H, m, 2(CH_2CH_2)]; 6,56—7,13 (4H, q, arom)
Va	3385—2480		1680	
Vb	3600—2700		1685	
Vc	3380—2580		1630	
VIa	3270	3200	1700, 1660	2,56 (2H, t, 5-CH_2); 3,55 (2H, t, 6-CH_2); 6,49—7,16 (4H, q, arom.); 9,36 (1H, s, NH); 10,11 (1H, s, OH)
VIb	3390	3100	1670	0,91 (3H, d, J=7,5, CH_3); 2,53—2,94 (1H, m, CH); 2,94—3,69 (2H, m, CH_2); 6,41—6,91 (4H, q, arom)
VIc	3270	3200	1700, 1670	0,86 (3H, d, J=7,5, CH_3); 2,33 and 2,83 (2H, AB-part of ABX, J_{AB}=18,0, J_{AX}=5,8, J_{BX}=4,8); 3,39—3,89 (1H, m, CH); 6,40—6,93 (4H, q, arom)
VIIa	3290	3195	1700	2,61 (2H, t, 5-CH_2); 3,66 (2H, t, 6-CH_2); 6,53—7,08 (4H, q, arom.); 9,43 (1H, s, NH)
VIIb	3375	3220	1715	0,93 (3H, d, J=7,5, CH_3); 2,53—3,08 (1H, m, CH); 3,41—3,86 (2H, m, CH_2); 6,48—7,04 (4H, q, arom)
VIIc	3350	3180	1700	0,95 (3H, d, J=7,5, CH_3); 2,46 and 2,95 (2H, AB-part of ABX, J_{AB}=18,0, J_{AX}=5,8, J_{BX}=4,8); 3,70—4,18 (1H, m, CH); 6,53—6,98 (4H, q, arom.)
VIIIa	3500—2200		1705	
VIIIb	3510—2200		1680	
VIIIc	3500—2370		1715	
IXa	3500—2520		1720	
IXb	3520—2510		1715	
IXc	3550—2470		1715	
Xc	3370—2730		1640, 1620	1,60 (3H, s, CH_3); 5,68 (1H, s, CH); 6,54—6,93 (4H, q, arom)
XIc	3350—2900		1675	1,60 (3H, s, CH_3); 5,88 (1H, s, CH); 6,68 (4H, s, arom)
XIIa		3210	1750, 1725, 1670	1,94 (3H, s, $OCOCH_3$); 2,61 (2H, t, 5-CH_2); 3,55 (2H, t, 6-CH_2); 6,66—7,09 (4H, q, arom.); 9,10 (1H, s, NH)
XIIb		3195	1755, 1730, 1680	
XIIc		3195	1760, 1720, 1685	
XIIIa		3140	1760, 1715	1,94 (3H, s, $COCH_3$); 2,66 (2H, t, 5-CH_2); 3,68 (2H, t, 6-CH_2); 6,68—7,09 (4H, q, arom)
XIIIb		3200	1755, 1680	
XIIIc		3205	1760, 1705	
XIVa		3200	1710, 1695	2,64 (2H, t, CH_2); 3,53 (3H, s, OCH_3); 3,55 (2H, t, 6-CH_2); 6,54—6,94 (4H, q, arom); 9,09 (1H, s, NH)
XVa		3205	1710, 1715	

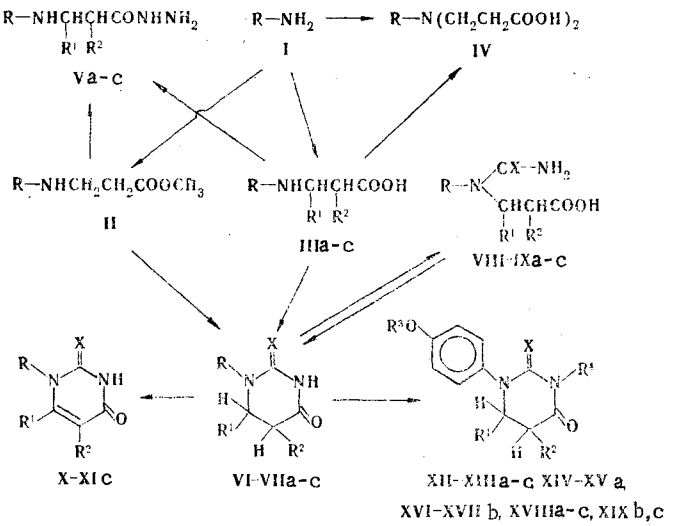
(continued)

TABLE 1 (continued)

1	2	3	4	5
XVIIIa			1715, 1685	2,63 (2H, t, 5-CH_2); 2,86 (3H, s., N—CH_3); 3,42 (2H, t, 6-CH_2); 3,46 (3H, s, O—CH_3); 6,41—6,95 (4H, m, arom.)
XVIIIb			1705, 1675	1,11 (3H, d, J=7,8, CH_3); 2,51—2,85 (1H, m, CH); 2,96 (3H, s, N—CH_3); 3,21—3,90 (2H, m, CH_2); 3,66 (3H, s, O—CH_3); 6,45—7,33 (4H, m, arom.)
XVIIIc			1705, 1680	1,10 (3H, d, J=7,8, 5-CH_3); 2,30—3,4 (2H, m, CH_2); 3,03 (3H, s, N—CH_3); 3,66—4,23 (1H, m, CH); 3,73 (3H, s, O—CH_3); 6,76—7,39 (4H, m, arom.)
XIXb			1715, 1680	
XIXc			1710, 1680	

*The PMR spectra of VIa and VIIa were recorded in d_6-DMSO, the spectra of XVIIIb,c were recorded in deuteroacetone, and the spectra of the remaining compounds were recorded in trifluoroacetic acid.

Dehydrogenation occurred when thiomethyldihydrouracil VIIc was heated with sulfur [3], and we isolated thiouracil XIc, which was converted to 1-(4-hydroxyphenyl)-6-methyluracil (Xc) by the action of chloroacetic acid. Uracil Xc is also formed in the dehydrogenation of dihydrouracil VIc with sulfur. Signals of the methyl group in the form of a singlet appear in the PMR spectra of uracils Xc and XIc. By acetylation of dihydrouracils VI and VII with acetic anhydride we isolated acetoxyphenyl derivatives XII and XIII, whereas the direction of alkylation [4] depends on the reaction conditions. Thus alkoxyphenyl derivatives XIV and XV were obtained when stoichiometric amounts of alkali, dimethyl sulfate, or allyl bromide were used for the alkylation of dihydrouracil VIa, whereas the corresponding 1-(4-alkoxyphenyl)-3-alkyldihydrouracils XVIII and XIX were isolated when the reaction of dihydrouracils VI was carried out with excess dimethyl sulfate.



R=4-HOC_6H_4; a R^1=R^2=H, b R^1=H, R^2=CH_3, c R^1=CH_3, R^2=H; VI, VIII, X, XII, XIV—XIX X=O; VII, IX, XI, XIII X=S; XII R^3=CH_3CO–, R^4=H, X=O; XIII R^3=CH_3CO–, R^4=H; XIV R^3=CH_3, R^4=H; XV R^3=CH_2=CH–CH_2–, R^4=H; XVI R^3=$(C_6H_{11}NH)_2PO$–, R^4=H; XVII R^3=$(C_6H_5NH)_2PO$–, R^4=H; XVIII R^3=R^4=CH_3; XIX R^3=R^4=C_2H_5

The corresponding 4-(5-methyldihydro-1-uracilyl)phenylphosphoric acid amides XVIb and XVIIb were obtained by the reaction of 4-(5-methyldihydro-1-uracilyl)phenylphosphoric acid dichloride, obtained by refluxing VIb with phosphorus oxychloride in dioxane with cyclohexylamine (or aniline).

Signals of methyl groups in the form of a singlet, which corresponds to three protons, are observed in the PMR spectra of the compounds that have a methoxy or acetyl group. By comparing the IR spectra of dihydrouracils VI and thiodihydrouracils VII with the spectra of acetyl derivatives XII and XIII we established that the phenyl hydroxy group in VI and VII

TABLE 2. Characteristics of the Synthesized II-XIX

Compound	mp, °C	Found, %			Empirical formula	Calc., %			Yield, % (synthetic method)
		C	H	N		C	H	N	
II	88—89[a]	61,3	6,6	7,3	$C_{10}H_{13}NO_3$	61,5	6,7	7,2	51
IV	174—175 (dec.)[b]	59,6	6,0	7,7	$C_9H_{11}NO_3$	59,7	5,8	7,7	77
IIIc	171—172 (dec.)[c]	61,2	6,5	6,9	$C_{10}H_{13}NO_3$	61,5	6,7	7,2	53
IIIa	183,5—185 (dec.)[b]	61,3	6,5	6,9	$C_{10}H_{13}NO_3$	61,5	6,7	7,2	64
	192—194 (dec.)[b]	56,7	5,9	5,7	$C_{12}H_{15}NO_5$	56,9	6,0	5,5	90
Va	135—137[a]			21,6	$C_9H_{13}N_3O_2$			21,5	60
Vb	156,5—157,5[d]			20,2	$C_{10}H_{15}N_3O_2$			20,1	32
Vc	155—156[e]			20,3	$C_{10}H_{15}N_3O_2$			20,1	35
VIa	264—266[f]	58,1	5,0	13,6	$C_{10}H_{10}N_2O_3$	58,3	4,9	13,6	80 (A) 80 (B) 100 (C)
VIb	206,5—207,5[g]	60,0	5,6	12,9	$C_{11}H_{12}N_2O_3$	60,0	5,5	12,7	80 (B) 100 (C)
VIc	253,5—254[g]	60,1	5,4	12,9	$C_{11}H_{12}N_2O_3$	60,0	5,5	12,7	36 (B) 100 (C)
VIIa	309—310[h]	54,0	4,4	12,6	$C_{10}H_{10}N_2O_2S$	54,0	4,5	12,6	81 (A) 81 (B) 100 (C)
VIIb	216—217[g]	55,7	5,1	11,8	$C_{11}H_{12}N_2O_2S$	55,9	5,1	11,9	79 (B) 100 (C)
VIIc	218—220[g]	56,0	5,0	11,5	$C_{11}H_{12}N_2O_2S$	55,8	5,1	11,9	40 (B) 100 (C)
VIIIa	191,5—192[i]			11,5	$C_{10}H_{12}N_2O_4 \cdot H_2O$			11,5	70
VIIIb	190,5—191,5[j]			12,0	$C_{11}H_{14}N_2O_4$			11,8	69
VIIIc	179,5—180,5[b]			11,8	$C_{11}H_{14}N_2O_4$			11,8	74
IXa	161 (dec., in a sealed capillary)[c]			11,7	$C_{10}H_{12}N_2O_3S$			11,7	43
IXb	151—152[b]			10,1	$C_{11}H_{14}N_2O_3S \cdot H_2O$			10,3	94
IXc	136—137 (dec., in a sealed capillary)[b]			10,4	$C_{11}H_{14}N_2O_3S \cdot H_2O$			10,3	79
Xc	316—317 (dec.)[k]	60,3	4,5	13,0	$C_{11}H_{10}N_2O_3$	60,6	4,6	12,8	66
XIc	289,5 (dec.)[f]	56,5	4,2	12,3	$C_{11}H_{10}N_2O_2S$	56,4	4,3	12,0	44
XIIa	233,5—234,5[g]	58,0	4,9	11,4	$C_{12}H_{12}N_2O_4$	58,1	4,9	11,3	93 (A) 100 (B)
XIIb	218—219[g]	59,6	5,3	10,7	$C_{13}H_{14}N_2O_4$	59,5	5,4	10,7	76 (A) 100 (B)
XIIc	223—224[g]	59,3	5,5	10,8	$C_{13}H_{14}N_2O_4$	59,5	5,4	10,7	69 (A) 100 (B)
XIIIa	241,5—242,5[g]	54,7	4,5	10,5	$C_{12}H_{12}N_2O_3S$	54,5	4,6	10,6	82 (A) 100 (B)
XIIIb	210—211[g]	57,8	5,0	10,1	$C_{13}H_{14}N_2O_3S$	58,1	5,1	10,1	77 (A) 100 (B)
XIIIc	228—229[g]	58,2	5,0	10,0	$C_{13}H_{14}N_2O_3S$	58,1	5,1	10,1	67 (A) 100 (B)
XIVa	202—204[c,l]	60,3	5,3	12,7	$C_{11}H_{12}N_2O_3$	60,0	5,5	12,7	53
XVa	181—182[d]			11,4	$C_{13}H_{14}N_2O_3$			11,2	60
XVIb	190 (dec.)[m]	57,3	7,3	12,3	$C_{23}H_{37}N_4O_4P$[n]	59,5	8,0	12,1	17
XVIIb	136 (dec.)[o]	60,8	5,1	12,2	$C_{23}H_{23}N_4O_4P$[p]	61,3	5,1	12,4	22
XVIIIa	103—104[d]			12,0	$C_{12}H_{14}N_2O_3$			12,1	80 (A) 77 (B)
XVIIIb	91,5—93,0[q]			11,3	$C_{13}H_{16}N_2O_3$			11,3	77
XVIIIc	63—64[r]			11,3	$C_{13}H_{16}N_2O_3$			11,5	74
XIXb	98—99[c]			9,7	$C_{16}H_{20}N_2O_3$			9,4	57
XIXc	66—67[r]			9,7	$C_{16}H_{20}N_2O_3$			9,6	78

[a]From propanol. [b]From water. [c]From acetone. [d]From ethanol. [e]From isopropyl alcohol. [f]From acetic acid. [g]From dioxane. [h]From ethylene glycol. [i]From methanol. [j]From ethanol—water. [k]From acetic acid—ether. [l]According to the data in [5], this compound has mp 206.5°C. [m]From acetone—ether. [n]Found: P 6.2%. Calculated: P 6.7%. [o]From ethanol-ether. [p]Found: P 6.9%. Calculated: P 6.9%. [q]From hexane. [r]From ether.

gives an absorption band at 3275-3390 cm^{-1}, whereas the bands at 3100-3215 cm^{-1} are related to the NH stretching vibrations. The absorption of the stretching vibrations of the carbonyl groups of the dihydrouracil derivatives is represented in the form of clearly distinguishable bands: the carbonyl group of the acetyl fragment of XII and XIII is observed at 1750-1760 cm^{-1}, whereas the bands at the following lower frequencies correspond to the vibrations of

the carbonyl groups of the amide fragments: the CHRCONH fragment at 1680-1730 cm^{-1} and the =NCONH fragment at 1660-1685 cm^{-1}. Absorption at the frequencies that are characteristic for the stretching vibrations of the NH and OH groups is absent in the spectra of dialkyl derivatives XVIII-XIX, and this confirms their structures.

EXPERIMENTAL

The IR spectra of KBr pellets were recorded with a UR-20 spectrometer. The PMR spectra were obtained with a Tesla BS 487C spectrometer with hexamethyldisiloxane as the internal standard. The individuality of the compounds was determined by TLC on Silufol UV-254 plates in ether–hexane and acetone–hexane systems.

The characteristics of the compounds obtained are presented in Tables 1 and 2.

N-(4-Hydroxyphenyl)-β-alanine Methyl Ester (II). A mixture of 54.6 g (0.05 mole) of p-aminophenol, 48 g (0.55 mole) of methyl acrylate, 5 ml of glacial acetic acid, 0.2 g of hydroquinone and 50 ml of isopropyl alcohol was refluxed for 7 h, after which the mixture was allowed to stand at 5°C for 2 days, and 49.8 g of II was removed by filtration.

N-(4-Hydroxyphenyl)-β-alanine (IIIa). A mixture of 1.95 g (0.01 mole) of ester II and 20 ml of 10% HCl was evaporated on a water bath, and the residue was crystallized to give 1.6 g (73%) of N-(4-hydroxyphenyl)-β-alanine hydrochloride with mp 155-157°C (from water). Found: Cl 16.3%. Calculated: Cl 16.3%.

β-Alanine IIIa was obtained from the hydrochloride by the action of diethylamine on it.

N-(4-Hydroxyphenyl)-α-methyl-β-alanine (IIIb). A 27.3 g (0.25 mole) sample of amine I was refluxed with 28.5 g (0.3 mole) of methacrylic acid in 50 ml of water for 4 h, after which the mixture was cooled, and the precipitated IIIb was removed by filtration to give 25.9 g of IIIb.

N-(4-Hydroxyphenyl)-β-methyl-β-alanine (IIIc). This compound was obtained from 27.3 g (0.25 mole) of amine I and 28.5 g (0.3 mole) of crotonic acid as in the preparation of IIIb. The yield was 31.2 g.

p-Hydroxyphenylamino-β,β'-dipropionic Acid (IV). A mixture of 27.3 g (0.25 mole) of amine I, 100 ml of water, and 40 g (0.55 mole) of acrylic acid was refluxed for 8 h, after which the mixture was cooled, and 57.0 g of crystals of IV was removed by filtration.

N-(4-Hydroxyphenyl)-β-alanine) Hydrazide (Va). A mixture of 3.9 g (0.02 mole) of ester II and 12 ml of 99% hydrazine was refluxed for 30 min at 120°C. The mixture was allowed to stand at 20°C, after which it was worked up to give 2.34 g of Va.

N-(4-Hydroxyphenyl)-α-methyl-β-alanine Hydrazide (Vb). A mixture of 9.8 g (0.05 mole) of alanine IIIb and 20 ml of 99% hydrazine was heated at 120°C for 3 h, after which 10 ml of methanol was added. The mixture was allowed to stand at 5°C, after which 3.35 g of Vb was isolated.

N-(4-Hydroxyphenyl)-β-methyl-β-alanine Hydrazide (Vc). This compound was obtained from IIIc by a procedure similar to that used to prepare Vb.

1-(4-Hydroxyphenyl)dihydrouracil (VIa). A) A mixture of 3.9 g (0.02 mole) of ester II, 2.4 g (0.04 mole) of urea, and 10 ml of glacial acetic acid was refluxed for 20 h, after which 4.0 ml of concentrated HCl was added, and the mixture was refluxed for another 2 h. The reaction mixture was then diluted with water (1:3) and allowed to stand at 20°C. Workup gave 3.26 g of VIa.

B) A 3.26-g sample of VIa was obtained from 3.6 g (0.02 mole) of IIIa and 1.8 g (0.03 mole of sodium cyanate by a procedure similar to that used in method A.

C) A 2.24-g (0.01 mole) sample of VIIIa and 10 ml of concentrated HCl was refluxed for 20 min, after which 20 ml of water was added, the mixture was cooled, and VIa was removed by filtration. The yield was quantitative.

1-(4-Hydroxyphenyl)-5-methyldihydrouracil (VIb) and 1-(4-Hydroxyphenyl)-6-methyldihydrouracil (VIc). These compounds were obtained from, respectively, acids IIIb,c and VIIIb,c by methods B and C for the synthesis of VIa.

1-(4-Hydroxyphenyl)-2-thiodihydrouracil (VIIa). A) A mixture of 3.9 g (0.03 mole) of ester II, 2.4 g (0.025 mole) of KCNS, and 10 ml of glacial acetic acid was heated at 120°C

for 18 h, after which 2.0 ml of concentrated HCl was added, and the mixture was refluxed for another hour. It was then cooled and filtered to give 3.6 g of VIIa.

B) A 3.6-g sample of VIIa was obtained from 3.6 g (0.02 mole) of alanine IIIa and 2.4 g (0.025 mole) of KCNS by method A.

C) A 2.4-g (0.01 mole) sample of IXa was refluxed in 10 ml of concentrated HCl for 20 min, after which 20 ml of water was added, and the mixture was cooled and filtered to give VIIa in quantitative yield.

1-(4-Hydroxyphenyl)-2-thio-5-methyldihydrouracil (VIIb) and 1-(Hydroxyphenyl)-2-thioxo-6-methyldihydrouracil (VIIc). These compounds were obtained from IIIb,c and IXb,c by methods B and C for the synthesis of VIa.

N-(p-Hydroxyphenyl)-N-carbamido- β-alanine (VIIIa). An 8.2-g (0.04 mole) sample of VIa was dissolved in 25 ml of 20% NaOH, after which the solution was allowed to stand at 20°C for 24 h. It was then heated to 50-60°C and filtered, and the filtrate was neutralized to pH 6 with 30% acetic acid. Workup gave 4.0 g of VIIa.

Compounds VIIb,c and IXa-c. These compounds were obtained from VIb,c and VIIa-c by a procedure similar to that used to prepare VIIIa.

1-(4-Hydroxyphenyl)-6-methyluracil (Xc). A 1.18-g (5 mmole) sample of thiouracil XIc was dissolved in 20 ml of acetic acid, 30 ml of 20% perchloric acid was added, and the mixture was refluxed for 7 h. It was then evaporated, and the residue was treated with ethanol to give 0.72 g of Xc.

1-(4-Hydroxy)-2-thio-6-methyluracil (XIc). A 9.5-g (0.04 mole) sample of VIIc was heated with 30 g of sulfur at 220-230°C for 8 h. The resulting solid mass was ground up and extracted (two 150-ml portions) with boiling acetic acid, and the extract was concentrated *in vacuo* to one sixth of its original volume. The concentrate was cooled, and the precipitated sulfur was removed by filtration. Water (50 ml) was added to the filtrate, and the mixture was neutralized to pH 7 with sodium carbonate. Workup gave 4.14 g of uracil XIc.

1-(4-Acetoxyphenyl)dihydrouracil (XIIa). A) A 10.3-g (0.05 mole) sample of VIa and 30 ml of acetic anhydride was heated at 130°C for 20 h, after which 120 ml of water was added, and the mixture was heated to the boiling point. It was then allowed to stand, after which it was worked up to give 11.5 g of uracil XIIa.

B) A 10.3-g (0.05 mole) sample of VIa was dissolved in 100 ml of 5% NaOH, the mixture was cooled to 3-5°C, 15.3 g (0.15 mole) of acetic anhydride was added with stirring, and the mixture was stirred for 15-20 min. The precipitate crystals of XIIa were removed by filtration. The yield was quantitative.

Compounds XIIb,c and XIIIa-c. These compounds were obtained from VIb,c and VIIa-c by the methods used to prepare XIIa.

1-(4-Methoxyphenyl)dihydrouracil (XIVa). A 4.12-g (0.02 mole) sample of dihydrouracil VIIa was dissolved in 32 ml of 2.5% NaOH solution, the solution was diluted with water to 100 ml, and 2.52 g (0.02 mole) of dimethyl sulfate was added with stirring. The reaction mixture was refluxed for 2 h, after which it was cooled and worked up to give 2.33 g of uracil XIVa.

1-(4-Allyloxyphenyl)dihydrouracil (XVa). An 8.7-ml (0.1 mole) sample of allyl bromide was added to a refluxing mixture of 10.3 g (0.05 mole) of dihydrouracil VIa, 3.3 g of 85% powdered potassium hydroxide, and 100 ml of acetone, and the mixture was refluxed for 8 h. The liquid fractions were removed by distillation with a rotary evaporator, the residue was treated with 100 ml of water, and the mixture was filtered to give 7.4 g of XVa.

4-(5-Methyldihydro-1-uracilyl)phenylphosphoric acid Dicyclohexylamide (XVIb). A 51.0-g (0.25 mole) sample of dihydrouracil VIb was dissolved in dry dioxane, 23 ml of phosphorus oxychloride was added dropwise, and the mixture was refluxed for 24 h until a solid deposit of the acid dichloride appeared. The solvent was decanted, the precipitate was pulverized and washed with toluene, and 116 ml (1.0 mole) of cyclohexylamine in 100 ml of dioxane was added dropwise with heating and stirring. The resulting mass was dissolved in chloroform, the solution was poured into petroleum ether, and the resulting precipitate was washed repeatedly with water and crystallized from ether—acetone (1:1). The yield was 20 g.

4-(5-Methyldihydro-1-uracilyl)phenylphosphoric Acid Diphenylamide (XVIIb). This com-

pound was obtained from 51.0 g (0.25 mole) of VIb, 23 ml of $POCl_3$, and 92 ml (1.0 mole) of aniline by a procedure similar to that used to prepare XVIb. The yield was 25 g.

1-(4-Methoxyphenyl)-3-methyldihydrouracil (XVIIIa). A) An 11.4-ml (0.12 mole) sample of dimethyl sulfate was added with stirring to a mixture of 10.3 g (0.05 mole) of VIa, 50 ml of 10% NaOH, and 150 ml of dioxane, and the mixture was stirred at 20-25°C for 30 min. It was then allowed to stand at 20°C for 6 h, after which the liquid fractions were removed by distillation, the residue was treated with water, and the mixture was filtered to give 9.4 g of XVIIIa.

B) A 7.8-ml (0.125 mole) sample of methyl iodide was added to a mixture of 5.15 g (0.025 mole) of dihydrouracil VIa and 6.0 g of powdered KOH in 50 ml of DMF at such a rate that the temperature of the reaction mixture did not exceed 40°C, after which the mixture was stirred for 2 h, and the product was isolated as in method A. The yield was 4.5 g.

1-(4-Methoxyphenyl)-3,5-dimethyldihydrouracil (XVIIIb) and 1-(4-Methoxyphenyl)-3,6-dimethyldihydrouracil (XVIIIc). These compounds were obtained from VIb,c by method A for the synthesis of XVIIIa.

1-(4-Ethoxyphenyl)-3-ethyl-5-methyldihydrouracil (XIXb) and 1-(4-Ethoxyphenyl)-3-ethyl-6-methyldihydrouracil (XIXc). These compounds were obtained from VIb,c and ethyl iodide by a procedure similar to that used to prepare XVIIIa.

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SYNTHESIS AND REACTIONS OF 2-CHLOROHEXAFLUOROCYCLOPENTENE- AND 2-CHLOROOCTAFLUOROCYCLOHEXENE-1-CARBONITRILES

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2-Chlorohexafluorocyclopentene- and 2-chlorooctafluorocyclohexene-1-carbonitriles were synthesized. Products of substitution of the chlorine atoms by a phenylamino group and the fluorine atoms in the α position by a phenylimino group were obtained by reaction of the products with aniline. The reactions with amidines of trifluoro- and trichloroacetic acids, as well as with 2-aminopyridine, lead to pyrimidine derivatives with condensed perfluorinated five- and six-membered rings.

We have previously developed a general method for the preparation of perfluoroalkyl-substituted 1-cyano-2-chloroethylenes, studied their reactions with nucleophilic reagents, and demonstrated that these compounds have high reactivities and are convenient reagents for the preparation of various heterocyclic compounds [1-4]. In the present paper we describe the synthesis of 2-chlorohexafluorocyclopentene- and 2-chlorooctafluorocyclohexene-1-carbonitriles IIa,b that contain a 1-cyano-2-chloroethylene fragment included in a perfluorinated ring.

For the preparation of nitriles IIa,b, 1,2-dichlorohexafluorocyclopentene and 1,2-dichlorooctafluorocyclohexene were converted to the corresponding carboxylic acids by the action of butyllithium and carbon dioxide gas [5]. The indicated cyano compounds were synthesized

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