was repeated with *p*-aminobenzoic acid; yield 70%, m.p. 268°.

Anal. Calcd. for $C_{11}H_{10}NO_3$: N, 6.85. Found: N, 6.76.

p-(2-β-Hydroxyethoxy-3-hydroxymercuributyrylamino)-phenylacetic Acid.—To 15 ml. of ethylene glycol was added 1 g. (0.01 mole) of *p*-crotonylaminophenylacetic acid and 1.5 g. (0.01 mole) of mercuric acetate. The resulting solution was allowed to stand for 5 days. The white solid that had separated was collected and washed with methanol and then with ether; yield 2 g. (50%), m.p. 205° dec.

Anal. Calcd. for $C_{14}H_{16}HgNO_6$: Hg, 40.53. Found: Hg, 40.23.

N-(3-Hydroxymercuri-2-β-hydroxyethoxypropyl)-N'-succinylurea Sodium Salt.—Twenty grams (0.1 mole) of N-allyl-N'-succinylurea[8] was dissolved in 40 ml. of ethylene glycol. Thirty-two grams (0.1 mole) of mercuric acetate was added and stirred. The reaction was exothermic and there was a strong odor of acetic acid. After standing for two days at room temperature, a sample was completely miscible in water and did not turn dark when made basic with sodium hydroxide. The excess ethylene glycol was distilled at 0.1 mm. and at a bath temperature of 120°. The remaining sirup was dissolved in methanol, clarified with carbon and filtered. Ether was added and the mercurial precipitated as an oil. The oil was separated, dissolved in a minimum amount of distilled water, and carefully neutralized with sodium hydroxide to a *p*H of 7.5. The water was evaporated under reduced pressure to give a 60% yield of white solid.

Anal. Calcd. for $C_{10}H_{17}HgN_2NaO_7$: Hg, 40.90. Found: Hg, 40.80.

General Method for the Mercuration of Ethyl *p*-Allyloxybenzoate,[9] Ethyl *p*-(N-Allylcarbamyl)-phenoxyacetate, Ethyl *o*-(N-Allylcarbamyl)-phenoxyacetate, N-Allylphthalimide,[10] α-Allylbenzhydrol[11] and Methyl Cinnamate.—A mixture of 6.4 g. (0.02 mole) of mercuric acetate and 0.02 mole of the allylic compound or of methyl cinnamate was stirred in 10–25 ml. of the appropriate alcohol (methyl Cellosolve, ethyl Cellosolve, butyl Cellosolve, β-chloroethanol, ethyl lactate, ethylene glycol, ethanol or methanol) or in 25 ml. of water. The mixture dissolved and after standing for 2–5 days at room temperature the product crystallized. This was collected and purified by recrystallization from ethyl acetate or a mixture of ethyl acetate and petroleum ether. The mercurials from ethyl *p*-allyloxybenzoate are listed in Table II, and from ethyl N-allylcarbamylphenoxyacetates in Table III. The other products are listed below.

N-(3-Acetoxymercuri-2-β-methoxyethoxypropyl)-phthalimide, yield 9 g. (88%), m.p. 109°. *Anal.* Calcd. for $C_{16}H_{19}HgNO_6$: C, 36.75; H, 3.72; N, 2.69. Found: C, 36.70; H, 3.85; N, 2.83.

N-(3-Acetoxymercuri-2-β-hydroxyethoxypropyl)-phthalimide, yield 9.5 g. (95%), m.p. 126°. *Anal.* Calcd. for $C_{15}H_{17}HgNO_6$: C, 35.50; H, 3.37; N, 2.77. Found: C, 35.57; H, 3.52; N, 2.92.

4-Acetoxymercuri-1,1-diphenyl-3-β-hydroxyethoxybutanol-1, yield 4.5 g. (41%), m.p. 114.5°. *Anal.* Calcd. for $C_{20}H_{24}HgO_5$: C, 44.07; H, 4.44. Found: C, 44.26; H, 4.48.

4-Acetoxymercuri-1,1-diphenyl-3-methoxybutanol-1, yield 7.2 g. (70%), m.p. 135.6–136°. *Anal.* Calcd. for $C_{19}H_{22}HgO_4$: Hg, 38.95. Found: Hg, 38.40.

Methyl 2-hydroxymercuri-3-β-hydroxyethoxyhydrocinnamate, yield 6.9 g. (78%), m.p. 216–218° dec. *Anal.* Calcd. for $C_{12}H_{16}HgO_5$: Hg, 45.40. Found: Hg, 45.70.

Methyl 2-acetoxymercuri-3-β-methoxyethoxyhydrocinnamate, yield 7.9 g. (80%), m.p. 97°. *Anal.* Calcd. for $C_{15}H_{20}HgO_6$: C, 36.30; H, 4.05. Found: C, 36.28; H, 3.97.

Methyl 2-acetoxymercuri-3-β-chloroethoxyhydrocinnamate, yield 7.5 g. (75%), recrystallized from ethanol, m.p. 124°. *Anal.* Calcd. for $C_{14}H_{17}ClHgO_5$: C, 33.48; H, 3.42. Found: C, 32.92; H, 3.34.

Ethyl *m*-(3-Acetoxymercuri-2-β-hydroxyethoxypropyl)-*p*-hydroxybenzoate.—Two grams (0.011 mole) of ethyl *m*-allyl-*p*-hydroxybenzoate[9] and 3.18 g. (0.01 mole) of mercuric acetate were dissolved in 5 ml. of ethylene glycol and allowed to stand at room temperature for three days. Ether was added and the product precipitated. The precipitate was crystallized from a mixture of ethyl acetate and petroleum ether; yield 4 g. (77%), m.p. 99–100°.

Anal. Calcd. for $C_{16}H_{22}HgO_7$: Hg, 38.03. Found: Hg, 37.82.

Ethyl *m*-(3-Acetoxymercuri-2-methoxy)-*p*-hydroxybenzoate.—The procedure in the above paragraph was repeated using methanol rather than ethylene glycol; yield 50%, m.p. 124–125°.

Anal. Calcd. for $C_{15}H_{20}HgO_6$: Hg, 40.25. Found: Hg, 40.22.

2-Acetoxymercuri-5-carbethoxy-2,3-dihydrobenzofurane.—The procedure described in the above paragraph was used with the exception that ethylene glycol was replaced with ethanol, methyl Cellosolve, or benzyl alcohol. The yields varied from 14–50%, m.p. 114–116°.

Anal. Calcd. for $C_{14}H_{16}HgO_5$: Hg, 43.01. Found: Hg, 42.95.

INDIANAPOLIS, INDIANA

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[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES]

Diuretics. II. Alkoxymercuration by Mixed Anion Salts of Mercury

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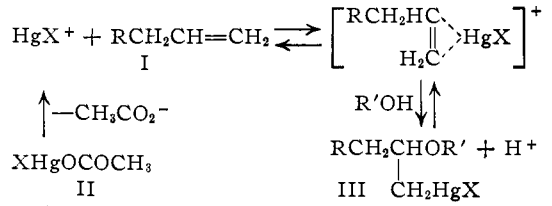
Alkoxymercuration of allylamides by means of mixed anion salts of mercury furnished a convenient and direct synthesis of twenty-one new mercurial diuretics.

Normal mercuric salts of mineral acids, with few exceptions, are not suitable for the alkoxymercuration of olefins. This is due to the insolubility of some mercuric salts and to the instability of the mercury–olefin adduct in the presence of mineral acid.[1] Mixed anion salts of $XHgOCOCH_3$, where X is a mineral acid anion, are moderately soluble in water and the common alcohols and yield predominantly HgX^+ and $CH_3CO_2^-$ ions in solution. Alkoxymercuration of allylic compounds by means of these mixed anion salts yielded the new mercurials $RCH_2CH(OR')CH_2HgX$ (III) reported here.

Mixed anion salts of mercury were prepared from mercuric acetate and each of the following normal salts: mercuric chloride, mercuric bromide, mercuric iodide, mercuric nitrate and mercuric thiocyanate. The mixed anion salts were established as discrete crystalline compounds by observing that their X-ray patterns were completely different from the patterns of the starting normal salts. The allylic compounds I employed

(1) J. Chatt, *Chem. Revs.*, **48**, 13 (1951).



X = Cl, Br, I, SCN or NO_3 R′ = H, CH_3, C_2H_5 or $CH_3O(CH_2)_2$

R is given in Tables I, II and III

in the mercuration studies were allylamides of alkanesulfonic acids, alkanesulfamic acids, hydantoic acid, hippuric acid and 1,3-dimethyluracil-5-carboxylic acid. Two other amide-like derivatives, N-allylurea and 3-allyl-5-carbethoxy-1-methyluracil also were used. The allylamides were prepared from acid chlorides or esters by conventional methods. The two uracils were obtained by methods previously reported.[2]

The mercurials III were obtained by allowing the mixed salts to react with the allylamides in alcoholic or aqueous solution. A number of these mercurials were titrated in 66% aqueous N,N-dimethylformamide. Several were sufficiently soluble to be titrated in water. Titrations of the type $RHgX + OH^- \rightleftarrows RHgOH + X^-$ (eq. 1.), all conformed very closely to the calculated theoretical curve. Attempts to determine the ionization constant of the hydroxymercuri form in water were complicated by the fact that the slope of the titration curve is distinctly greater than the theoretical slope derived from a reaction of the type $RHgOH + H^+ \rightleftarrows RHg^+ + H_2O$ (eq. 2.).[3]

Several authors[4,5] have selected the *p*H of half-conversion without comment concerning the slope of their titration curves.

For this reason the results are expressed in Table IV as the apparent equilibrium constant for eq. 1. defined as the molarity ratio $(X^-)/(OH^-)$ at half-conversion. From the average of several determinations of $pH = f(OH^-)$ in 66% dimethylformamide the constant in the following expression was determined: $pH - \log (OH^-) = 16.8 \pm 0.1$. It is interesting that the quantity $(X^-)/(OH^-)$ is about the same in water and 66% dimethylformamide for the halide compounds that were titrated in both solvents, but that it is much greater in the non-aqueous solvent for the thiocyanate compounds. More favorable solvation of the thiocyanate ion by dimethylformamide and of the halide ions by water, although not demonstrated independently, would seem to be a reasonable explanation.

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Experimental

Preparation of Mixed Anion Mercuric Salts.—A mixture of 0.01 to 0.05 mole (3.18 to 15.9 g.) of mercuric acetate and an equal molar amount of mercuric chloride, mercuric bromide, mercuric iodide, mercuric nitrate or mercuric thiocyanate was added to 100–200 ml. of the appropriate solvent. The solvents that were used were methanol, ethanol, water, methyl Cellosolve, ethyl Cellosolve and ethylene glycol. The resulting mixed mercuric salts were not isolated when used in the mercuration reactions but allowed to react with the allylamides as they existed either suspended or dissolved in the solvent. The crystalline mixed anion salts were obtained from methanol by partial evaporation of the solvent. These were recrystallized from methanol and their X-ray powder patterns determined.[6]

N-Allylalkanesulfonamides (Table I).—The appropriate alkanesulfonyl chloride[7] was added dropwise while stirring to an ether solution containing one mole equivalent of allylamine or N-methylallylamine and one mole equivalent of pyridine. The molar quantities of the reactants varied from 0.1 mole to 2.83 moles. After one hour the ether solution was washed with water and dried over magnesium sulfate. In the case of the water-soluble N-methyl derivatives, the ether solution was cooled and the pyridine hydrochloride collected on a filter. The ether was evaporated and the product distilled through a Vigreux column.

N,N-Dialkyl-N′-allylsulfamates (Table I).—One-half mole of the appropriate N,N-dialkylsulfamyl chloride[8,9] was added dropwise, with stirring, to 57 g. (1.0 mole) of allylamine dissolved in 500 ml. of ether. The ether was washed with water and dried over magnesium sulfate. The ether was evaporated and the product was distilled.

Mercuration of N-Allylalkanesulfonamides.—One-tenth mole of the N-allylalkanesulfonamide was added to 0.1 mole of chloromercuric acetate (see preparation of mercuric salts) in 200 ml. of distilled water. The resulting solution was warmed on the steam-bath to approximately 60° and then allowed to stand at room temperature for 4 days. This same procedure was repeated with 0.1 mole of bromomercuric acetate in water. The products from N-allylmethanesulfonamide and N-allylethanesulfonamide crystallized from solution, were collected and recrystallized from ethanol (Table II). The products from N-allylbutanesulfonamide, N-allyl-N-methylbutanesulfonamide and N-allyl-N-methylmethanesulfonamide could not be induced to crystallize and therefore could not be characterized. When mercurations of N-allylalkanesulfonamides were carried out in methanol or ethanol the products separated as gums and could not be crystallized.

Mercuration of N,N-Dialkyl-N′-allylsulfamates.—The procedure used here was exactly the same as that described above for the mercuration of the N-allylalkanesulfonamides. The only mercurated product that could be crystallized and characterized was obtained from N-(allylsulfamyl)-morpholine (Table II). Products from the other allylsulfamates were sirups or plastics.

Hydantoic Acid Allylamide.—Two hundred and fifty milliliters of allylamine was added to 132 g. of methyl hydantoate[10] and boiled under reflux for 24 hours. The excess allylamine was distilled under reduced pressure. The remaining solid product was recrystallized from ethanol; yield 140 g., m.p. 167–168°.

Anal. Calcd. for $C_6H_{11}N_3O_2$: C, 45.85; H, 7.05; N, 26.74. Found: C, 45.94; H, 7.29; N, 26.51.

Mercuration of Hydantoic Acid Allylamide.—Fifteen and seven-tenths grams (0.1 mole) of hydantoic acid allylamide was added to 0.1 mole of chloromercuric acetate in 200 ml. of methanol, to 0.1 mole of bromomercuric acetate in 100 ml. of methanol, to 0.1 mole of thiocyanatomercuric acetate in 400 ml. of methanol and to 0.1 mole of chloromercuric acetate in 200 ml. of water. The mixtures were agitated until the solids dissolved. The products crystallized from the solutions after standing for 12 hours at room temperature. Each mercurial was collected on a filter and recrystallized from methanol (Table II).

Mercuration of N-Allylhippuramide.—Five and five-

(2) C. W. Whitehead, THIS JOURNAL, **74**, 4267 (1952).

(3) A study of the equilibria of RHg^+ in water is in progress.

(4) R. L. Rowland, THIS JOURNAL, **74**, 5482 (1952), curve 1 in Fig. 2.

(5) T. D. Waugh, H. F. Walton and J. A. Laswick, *J. Phys. Chem.*, **59**, 395 (1955), curves 1a and 1b in Fig. 1.

(6) The *d*, Å. and I/I_1 values for the mixed salts may be obtained by writing the authors.

(7) Supplied by Distillation Products Industries, Rochester 3, N. Y.

(8) L. F. Andrieth and M. von Brauchitsch, *J. Org. Chem.*, **21**, 427 (1955).

(9) L. Deniville, *Bull. soc. chim. France*, [5] **3**, 2143 (1936).

(10) C. Harries and M. Weiss, *Ann.*, **327**, 365 (1903).

TABLE I

N-ALLYLALKANESULFONAMIDES AND N,N-DIALKYL-N'-ALLYLSULFAMATES, $RSO_2NR'CH_2CH{=}CH_2$

R	R'	Formula	B.p. °C.	Mm.	Yield, %	Nitrogen, % Calcd.	Found
CH_3	H	$C_4H_9NO_2S$	103	0.7	72	10.35	10.47
CH_3	CH_3	$C_5H_{11}NO_2S$	92	.5	43	9.39	9.31
C_2H_5	H	$C_5H_{11}NO_2S$	117–120	.5	70	9.41	9.47
$(CH_3)_2N$	H	$C_5H_{12}N_2O_2S$	110	.5	9	17.06	17.37
$C_2H_5(CH_3)N$	H	$C_6H_{14}N_2O_2S$	100	.5	40	14.57	14.76
C_4H_8N[a]	H	$C_7H_{14}N_2O_2S$	135	.7	52	14.72	14.59
C_4H_8ON[b]	H	$C_7H_{14}N_2O_3S$	140[c]		50	40.76[d]	40.94[d]
						6.84[e]	6.86[e]
n-C_4H_9	H	$C_7H_{15}NO_2S$	114	1.5	68	7.90	7.72
$(C_2H_5)_2N$	H	$C_7H_{16}N_2O_2S$	100	0.5	5.5	14.57	14.76
n-C_4H_9	CH_3	$C_8H_{17}NO_2S$	110	.5	30	7.32	7.37

[a] Pyrrolidino. [b] Morpholino. [c] Melting point. [d] Values for carbon. [e] Values for hydrogen.

TABLE II

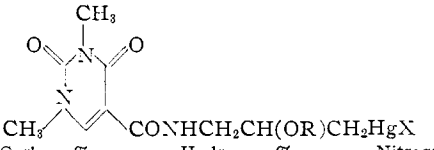
$RNHCH_2CH(OR')CH_2HgX$

No.	R	R'	X	Formula	M.p., °C.	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
							51.67[a]	51.55[a]				
1	CH_3SO_2	H	Cl	$C_4H_{10}ClHgNO_3S$	106	66	12.37	12.92	2.60	2.66	3.61	3.56
2	H_2NCO	CH_3	I	$C_5H_{11}HgIN_2O_2$	165	70	13.09	13.54	2.42	2.53	6.11	5.86
3	$C_2H_5SO_2$	H	Br	$C_5H_{12}BrHgNO_3S$	118	61					3.14	3.07
4	$C_2H_5SO_2$	H	Cl	$C_5H_{12}ClHgNO_3S$	84	90	14.93	15.50	3.01	3.43	49.87[a]	49.90[a]
5	$H_2NCONHCH_2CO$	H	Cl	$C_6H_{12}ClHgN_3O_3$	125–135 d.	42	48.90[a]	49.22[a]			10.03	10.01
6	$H_2NCONHCH_2CO$	CH_3	Br	$C_7H_{14}BrHgN_3O_3$	174 d.	70	17.96	17.99	2.99	2.83	8.96	8.76
7	$H_2NCONHCH_2CO$	CH_3	Cl	$C_7H_{14}ClHgN_3O_3$	171 d.	90	20.59	20.18	3.45	3.49	10.29	10.01
8	$H_2NCONHCH_2CO$	CH_3	SCN	$C_8H_{14}HgN_4O_3S$	132 d.	62	21.50	21.55	3.15	3.21	12.54	12.75
9	O(CH$_2$)$_4$N—SO_2	CH_3	Cl	$C_8H_{17}ClHgN_2O_4S$	118	30	20.30	20.57	3.62	3.21	5.92	5.50
10	$C_6H_5CONHCH_2CO$	H	Cl	$C_{12}H_{15}ClHgN_2O_3$	162	85	30.63	30.91	3.25	3.59	5.96	6.02
11	$C_6H_5CONHCH_2CO$	CH_3	Cl	$C_{13}H_{17}ClHgN_2O_3$	99	98	32.17	31.80	3.53	3.62	5.77	5.75

[a] Values for mercury.

TABLE III

MERCURIALS FROM 1,3-DIMETHYL-5-N-ALLYLCARBAMYLURACIL



No.	R	X	Formula	M.p., °C.	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
12	H	Cl	$C_{10}H_{14}ClHgN_3O_4$	166–168	88	25.22	25.11	2.96	3.11	8.82	8.39
13	CH_3	Br	$C_{11}H_{16}BrHgN_3O_4$	204	90	24.80	25.56	3.02	2.93	7.86	7.96
14	CH_3	Cl	$C_{11}H_{16}ClHgN_3O_4$	215	62	27.00	27.10	3.30	3.41	8.59	8.29
15	CH_3	I	$C_{11}H_{16}HgIN_3O_4$	184	95	22.54	22.89	2.77	2.80	7.22	7.69
16	CH_3	SCN	$C_{12}H_{16}HgN_4O_4S$[a]	150–152	75	28.10	28.11	3.14	3.21	10.92	10.69
17	C_2H_5	Cl	$C_{12}H_{18}ClHgN_3O_4$	178–180	83	28.60	28.46	3.60	3.49	8.33	8.27
18	$CH_3O(CH_2)_2$	Cl	$C_{13}H_{20}ClHgN_3O_5$	154	90	29.20	29.80	3.75	3.85	7.86	7.62

[a] Marked activity at 10 mg. per kg. *per os*.

tenths grams (0.025 mole) of N-allylhippuramide[11] was added to 0.025 mole of chloromercuric acetate in 25 ml. of distilled water and also to 0.025 mole of chloromercuric acetate in 25 ml. of methanol. The resulting solutions were allowed to stand at room temperature for 3–5 days. The products crystallized from solution and were recrystallized from ethanol (Table II).

3-Allyl-5-carbethoxy-1-methyluracil.—To 155 ml. of 1.3 *N* sodium hydroxide was added 22.4 g. (0.1 mole) of 3-allyl-5-carbethoxyuracil.[2] The solution was heated to 40° and stirred while 12.6 g. (0.1 mole) of dimethyl sulfate was added dropwise. The resulting mixture was concentrated under reduced pressure and cooled. The solid was collected and recrystallized from a mixture of ethyl acetate and light petroleum ether, yield 16 g. (69%), m.p. 90°.

Anal. Calcd. for $C_{11}H_{14}N_2O_4$: C, 55.55; H, 5.92; N, 11.76. Found: C, 55.48; H, 6.30; N, 11.84.

5-Carbethoxy-3-(γ-chloromercuri-β-methoxypropyl)-1-methyluracil (Table IV, No. 19).—A mixture of 2.7 g. (0.01 mole) of mercuric chloride and 3.2 g. (0.01 mole) of mercuric acetate was added to 50 ml. of methanol. To this was added 4.6 g. (0.02 mole) of 3-allyl-5-carbethoxy-1-methyluracil. The solution was warmed for 5 minutes on the steam-bath and then filtered. The filtrate was cooled and the product crystallized upon standing; yield 7.5 g. (75%). An analytical sample was prepared by recrystallization from methanol, m.p. 169°.

Anal. Calcd. for $C_{12}H_{17}ClHgN_2O_5$: C, 28.50; H, 3.37; N, 5.55. Found: C, 28.35; H, 3.49; N, 5.34.

5-Carbethoxy-1-methyl-3-(γ-thiocyanatomercuri-β-methoxypropyl)-uracil[12] (Table IV, No. 20).—To a mixture of 3.2 g. (0.01 mole) of mercuric acetate and 2.76 g. (0.01 mole) of mercuric thiocyanate in 50 ml. of methanol was added 4.6 g. (0.02 mole) of 3-allyl-5-carbethoxy-1-methyluracil. This was warmed (50–60°) for 5 minutes, filtered and cooled; yield 5.1 g. (58%), m.p. 150–152°.

(11) C. Harries and I. Petersen, *Ber.*, **43**, 637 (1910).

(12) Oral doses of 2 and 4 mg. per kg. produced marked diuresis without signs of gastric disturbance.

TABLE IV

APPARENT EQUILIBRIUM CONSTANTS FOR $RHgX + OH^- \rightleftarrows RHgOH + X^-$ AT HALF-CONVERSION

Compound	Solvent[a]	(X^-)	pH	(OH^-)	$(X^-)/(OH^-)$
2 (Table II)	D	0.0013	11.8	1.0×10^{-5}	130
6 (Table II)	D	.0013	10.6	6.3×10^{-7}	2.1×10^{3}
	W	.0016	8.4	2.5×10^{-6}	640
8 (Table II)	D	.0017	8.20	2.5×10^{-9}	7×10^{5}
	W	.0036	8.14	1.4×10^{-6}	2.6×10^{3}
	W	.0008	7.5	3×10^{-7}	2.7×10^{3}
10 (Table II)	D	.0016	9.85	1.1×10^{-7}	1.5×10^{4}
	W	.0018	7.10	1.3×10^{-7}	1.4×10^{4}
11 (Table II)	D	.0013	9.95	1.4×10^{-7}	0.9×10^{4}
12 (Table III)	D	.0013	9.85	1.1×10^{-7}	1.2×10^{4}
	W	.0018	7.25	1.8×10^{-7}	1.0×10^{4}
13 (Table III)	D	.0017	11.0	1.6×10^{-6}	1.1×10^{3}
14 (Table III)	D	.0016	10.2	2.5×10^{-7}	6.4×10^{3}
15 (Table III)	D	.0015	12.3	3.2×10^{-5}	47
16 (Table III)	D	.0016	8.65	7.1×10^{-9}	2.3×10^{5}
17 (Table III)	D	.0013	10.0	1.6×10^{-7}	8.1×10^{3}
18 (Table III)	D	.0013	10.0	1.6×10^{-7}	8.1×10^{3}
19 (Exptl.)	D	.0016	9.95	1.4×10^{-7}	1.1×10^{4}
	W	.0017	7.25	1.8×10^{-7}	0.9×10^{4}
20 (Exptl.)	D	.0018	8.55	5.6×10^{-9}	3.2×10^{5}

[a] D = 66% dimethylformamide; W = water.

Anal. Calcd. for $C_{12}H_{16}HgN_4O_4S$: C, 28.10; H, 3.14; N, 10.92. Found: C, 28.11; H, 3.21; N, 10.69.

1,3-Dimethyl-5-N-allylcarbamyluracil.—One hundred grams (0.50 mole) of 1,3-dimethyl-5-carbethoxyuracil[2] was placed in a hydrogenation bomb with 300 ml. of dioxane and 60 g. (1.0 mole) of allylamine and heated overnight at 110°. The dioxane was removed under reduced pressure and the residue was dissolved in a minimum amount of water. The aqueous solution was decolorized with carbon, filtered, and the clear filtrate chilled. The solid was collected and again crystallized from a small volume of water. Forty grams (yield 36%) of white needles, m.p. 133°, was obtained.

Anal. Calcd. for $C_{10}H_{13}N_3O_3$: C, 53.80; H, 5.87; N, 18.83. Found: C, 54.00; H, 5.67; N, 18.59.

Mercurials from 1,3-Dimethyl-5-N-allylcarbamyluracil (Table III).—Eleven and one-tenth grams (0.05 mole) of 1,3-dimethyl-5-(N-allylcarbamyl)-uracil was added to 0.05 mole of chloromercuric acetate in 250 ml. of water, to 0.05 mole of chloromercuric acetate in 150 ml. of methanol, to 0.05 mole of chloromercuric acetate in 150 ml. of ethanol, to 0.05 mole of bromomercuric acetate in 150 ml. of methanol, to 0.05 mole of iodomercuric acetate in 150 ml. of methanol, to 0.05 mole of nitratomercuric acetate in 150 ml. of methanol, to 0.05 mole of thiocyanatomercuric acetate in 150 ml. of methanol, and to 0.05 mole of chloromercuric acetate in 40 ml. of methyl Cellosolve. The mixtures were heated to boiling and the solids dissolved. The resulting solutions were allowed to cool and stand at room temperature. The solid products were collected and separately recrystallized from ethylene dichloride.

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[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES]

Diuretics. III. 4,6-Diaminopyrimidines

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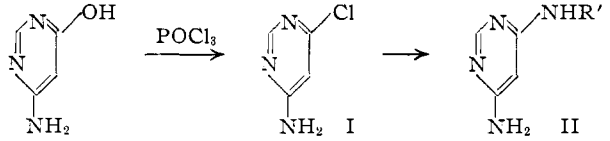
4-Amino-6-hydroxypyrimidine was chlorinated to yield 4-amino-6-chloropyrimidine. The latter was aminated to give 4-amino-6-alkylamino- and 4-amino-6-arylaminopyrimidines. Some of these aminopyrimidines were found to have diuretic activity. The reactions of diethyl malondiimidate with alkylamines yielded N,N''-dialkylmalondiamidines which were in turn cyclized with ethyl formate to 4,6-bis-alkylaminopyrimidines. The amination of 4,6-dichloropyrimidine also yielded 4,6-bis-alkylaminopyrimidines as well as intermediate 4-chloro-6-substituted aminopyrimidines. The pK_a's, the ultraviolet and infrared spectra were determined for a number of the 4,6-diaminopyrimidines and 4,6-bis-alkylaminopyrimidines

Although it has been reported that 4-amino-6-hydroxypyrimidine does not react successfully with phosphorus oxychloride[1] to yield 4-amino-6-chloropyrimidine (I), the latter was considered to be an appropriate intermediate in the synthesis of 4-amino-6-alkylamino- and 4-amino-6-arylaminopyrimidines. This reaction was reinvestigated and the product was found to be moderately soluble in water and easily hydrolyzed by acid. When precautions were taken to prevent this hydrolysis, compound I could be obtained in 48–62% yield. Condensations of I with alkylamines by conventional procedures yielded 4-amino-6-alkylaminopyrimidines (II, R′ = alkyl). The 4-amino-6-arylaminopyrimidines (II, R′ = aryl) were best obtained through their hydrochlorides by the reactions of arylamine hydrochlorides with I.



The parent 4,6-diaminopyrimidine was prepared by the method of Kenner through the condensation of malondiamidine with ethyl formate.[2] The possibility was considered that 4,6-bis-substituted aminopyrimidines could be prepared by a similar condensation of ethyl formate with N,N''-disubstituted malondiamidines (IV). The latter were prepared from diethyl malondiimidate (III) reactions with primary amines. When ethyl formate was allowed to react with IV the isolated products had the composition of 4,6-bis-substituted aminopyrimidines (V). The structure of V was confirmed by comparison with 4,6-bis-substituted aminopyrimidines obtained by the amination of 4,6-dichloropyrimidine. When 4,6-dichloropyrimidine was treated with amines the intermediate 4-chloro-6-substituted aminopyrimidines (VI) were also produced. The yields of both V and VI from the amination of 4,6-dichloropyrimidine depended upon the molar ratio of the reactants as well as the temperature of the reaction.

A number of the 4,6-diaminopyrimidines were titrated in 66% dimethylformamide and all showed one titratable group (Table III). It was impossible to determine pK'_a values of less than 2.5 because of the solvent blank. However, an at-

(1) D. J. Brown, *Rev. Pure Appl. Chem.*, **3**, 124 (1953).

(2) G. W. Kenner, B. Lythgoe, A. R. Todd and A. Topham, *J. Chem. Soc.*, 574 (1943).