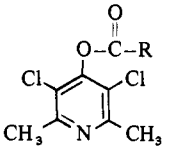
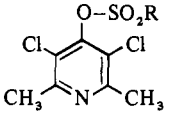
Table I. Esters and Carbonates of Clopidol



No.	R	Yield, %	Crystn solvent	Mp[a] or bp (mm), °C	Formula	Analyses[b]
2	CH_3	93	Hexane	56.5-57	$C_9H_9Cl_2NO_2$	C, H, Cl, N
3	CH_2Cl	15	Hexane	62-63	$C_9H_8Cl_3NO_2$	C, H, Cl, N
4	CH_2CH_3	39	Hexane	46.5-47	$C_{10}H_{11}Cl_2NO_2$	C, H, Cl, N
5	$CH(CH_3)_2$	62		78-79 (0.05)	$C_{11}H_{13}Cl_2NO_2$	C, H, Cl, N
6	$C(CH_3)_3$	81	Hexane	54-55	$C_{12}H_{15}Cl_2NO_2$	C, H, Cl, N
7	$(CH_2)_7CH=CH(CH_2)_7CH_3$	50	Me_2CO	<25	$C_{25}H_{39}Cl_2NO_2$	C, H, N
8	1-Adamantyl	41	Hexane	97.5-98.5	$C_{18}H_{20}Cl_2NO_2$	C, H, Cl, N
9	C_6H_5	88	Me_2CO	142-142.5	$C_{14}H_{11}Cl_2NO_2$	C, H, Cl, N
10	p-ClC_6H_4	82	Me_2CO	178-179	$C_{14}H_{10}Cl_3NO_2$	C, H, Cl, N
11	p-$CH_3OC_6H_4$	82	Me_2CO-$CHCl_3$	181-182	$C_{15}H_{13}Cl_2NO_3$	C, H, Cl, N
12	OCH_3	85	Hexane	67-68	$C_9H_9Cl_2NO_3$	C, H, Cl, N
13	OCH_2CH_3	87	Hexane	67.5-68.5	$C_{10}H_{11}Cl_2NO_3$	C, H, N[c]

[a] All melting points are uncorrected. [b] All analyses were within ±0.3% of the calcd values. [c] Cl: calcd, 26.85; found, 27.3.

Table II. Sulfonates of Clopidol



No.	R	Yield, %	Crystn solvent	Mp, °C[a]	Formula	Analyses[b]
14	CH_3	65	Hexane	111-112	$C_8H_9Cl_2NO_3S$	C, H, Cl, N, S
15	$CH_2CH_2CH_2Cl$	12	Me_2CO	67.5-68.5	$C_{10}H_{12}Cl_3NO_3S$	C, H, Cl, N, S
16	$(CH_2)_{15}CH_3$	66	Hexane	83.5-84	$C_{23}H_{39}Cl_2NO_3S$	C, H, Cl, N, S
17	C_6H_5	43	Me_2CO	117.5-118.5	$C_{13}H_{11}Cl_2NO_3S$	C, H, Cl, N, S
18	p-ClC_6H_4	53	Me_2CO-$CHCl_3$	146.5-147.5	$C_{13}H_{10}Cl_3NO_3S$	C, H, Cl, N[c]
19	p-FC_6H_4	54	Me_2CO	131-133 dec	$C_{13}H_{10}Cl_2FNO_3S$	C, H, Cl, N, S

[a] All melting points are uncorrected. [b] All analyses were within ±0.3% of the calcd values. [c] S: calcd, 8.75; found, 9.11.

Experimental Section

Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Ir spectra were recorded on an Infracord spectrophotometer and nmr on a Varian Associates A-60 instrument (Me_4Si) and are in accord with proposed structures. The synthesis of the propionate ester, 4, and the p-chlorobenzenesulfonate, 18, serves as typical examples.

3,5-Dichloro-2,6-dimethyl-4-pyridylpropionate (4). Clopidol (19.2 g, 0.10 mole) was added slowly to a slurry of NaH (5.4 g, 0.11 mole, 50% mixture in oil) in 50 ml of DMF under N_2. The resulting mixture was cooled to 15° and to it was added CH_3CH_2COCl (9.2 g, 0.11 mole), dissolved in 25 ml of DMF. The reaction mixture was stirred for 1.5 hr and filtered. The filtrate was extracted with hexane, and the hexane solution was washed with H_2O and evaporated yielding the desired material.

3,5-Dichloro-2,6-dimethyl-4-pyridyl p-Chlorobenzenesulfonate (18). To a slurry of NaH (10.8 g, 0.22 mole, 50% mixture in oil) in 100 ml of DMF was added 38.4 g (0.20 mole) of clopidol. The mixture was cooled to 3° and to it was added 46.4 g (0.22 mole) of p-$ClC_6H_4SO_2Cl$, dissolved in 75 ml of DMF. The reaction mixture was stirred 1.5 hr and filtered, and the salt washed with $CHCl_3$. The filtrate was partially reduced *in vacuo* and the remaining solution cooled in ice H_2O causing the desired product to precipitate.

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N-Alkyl Derivatives of Purine-6(1*H*)-thione†

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A number of 9-alkylpurines are cytotoxic to H.Ep.-2 cells in culture, both the wild strain and a strain resistant to purine-6(1*H*)-thione (6-mercaptopurine).[1] Among the most active compounds are the 9-butyl, 9-cyclopentyl, and 9-cyclohexyl derivatives of purine-6(1*H*)-thione. Since these compounds are toxic to H.Ep.-2/MP cells, their mechanism of action, although still not defined, must be different from that of 6-mercaptopurine and could be due to binding to nucleic acid since it is known that the structurally related caffeine does bind to nucleic acids.[2] To shed some light on this activity, we decided to prepare derivatives of 6-mercaptopurine in which the alkyl groups are attached to nitrogens other than N-9.

7-Cyclopentylpurine-6(1*H*)-thione (**3**) was prepared by the route previously used for the preparation of other 7-alkylpurines including the 7-butyl derivatives.[3] *N*-(4-Amino-6-chloro-5-pyrimidinyl)formamide (**1**) was alkylated with

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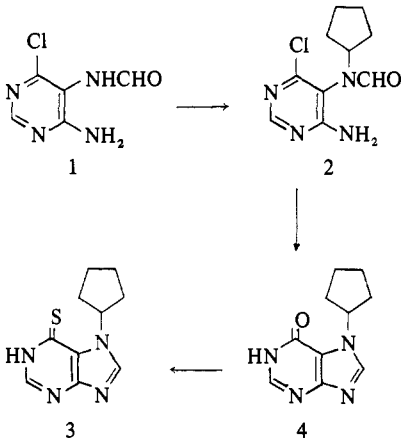
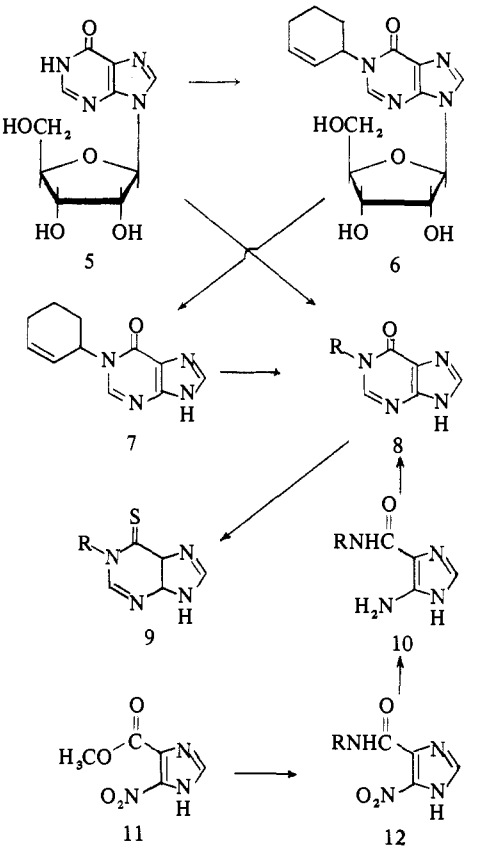
bromocyclopentane, although, not surprisingly, the yield with this secondary bromide was not good.‡ Refluxing formic acid converted *N*-(4-amino-6-chloro-5-pyrimidinyl)-*N*-cyclopentylformamide (**2**) to 7-cyclopentylhypoxanthine (**4**), which was thiated with phosphorous pentasulfide in pyridine to 7-cyclopentylpurine-6(1*H*)-thione (**3**).



Treatment of inosine with 1-iodobutane in DMF containing potassium carbonate according to Shaw[4] gave 1-butylinosine, which was hydrolyzed without purification to 1-butylhypoxanthine (**8a**). Thiation of **8a** gave 1-butylpurine-6(1*H*)-thione (**9a**). Alkylation of inosine with bromocyclopentane in the same way gave 1-cyclopentylinosine, which was hydrolyzed to 1-cyclopentylhypoxanthine (**8b**), in low yield, but gave twice as much of the O-alkylated product, 6-cyclopentyloxy-9-β-D-ribofuranosylpurine. This unexpected result, which has not been observed before,[4-8] must be due to the lower reactivity of the secondary halide. Since it is known that bromocyclohexane does not readily undergo nucleophilic displacement reactions, inosine was next N-alkylated, albeit in low yield, with 2-bromocyclohexene (O-alkylation probably occurred in this case also, but the product was not isolated). The resulting 1-cyclohexenylinosine was hydrolyzed to the hypoxanthine (**7**) which was reduced catalytically to 1-cyclohexylhypoxanthine (**8a**).

Because of the low yields of N-alkylated products encountered with the secondary bromides, a better route for the preparation of the desired 1-substituted hypoxanthines was sought. Treatment of the methyl ester of 5-nitroimidazole-4-carboxylic acid (**11**)[9] with cyclopentyl- and cyclohexylamine in methanol containing sodium methoxide gave the corresponding amides (**12b, c**) in good yield. Catalytic reduction of the nitro group of **12b, c** gave the 5-aminoimidazole-4-carboxamides **10b, c**,§ which were cyclized to the hypoxanthines **8b, c** by refluxing in formamide. Treatment of **10b** with ethyl orthoformate and a catalytic amount of concentrated hydrochloric acid gave *N*-cyclopentyl-5-ethoxymethyleneaminoimidazole-4-carboxamide, which failed to cyclize to the hypoxanthine. Thiation of **8b, c** with phosphorus pentasulfide in pyridine gave 1-cyclopentylpurine-6(1*H*)-thione (**9b**) and 1-cyclohexylpurine-6(1*H*)-thione (**9c**).

Biological Evaluations. The cytotoxicity of the *N*-alkylpurines to human epidermoid carcinoma cells No. 2 in culture[10] is given in Table I. Of the hypoxanthines, only the 9-alkyl derivatives are cytotoxic. In the case of *N*-alkylpurine-6(1*H*)-thiones, the 1-alkyl derivatives are as cytotoxic



a, R = butyl
b, R = cyclopentyl
c, R = cyclohexyl

as the 9-alkyl derivatives, and, although the 7-alkyl derivatives are also cytotoxic, they are only about 0.1 as active as the 1 and 9 derivatives. 1-Cyclopentylpurine-6(1*H*)-thione (**9b**) is slightly active against leukemia L1210 at 22 mg/kg on a chronic schedule (*qd* 1-9). The cytotoxicity of the 7-alkyl and, more particularly, the 1-alkylpurine-6(1*H*)-thiones, which are as cytotoxic as the 9-alkylpurines, is compatible with the idea that the activity of all these *N*-alkylpurines could be due to binding to nucleic acids rather than the ability of the 9-alkylpurines to mimic purine nucleosides.

Experimental Section

Except where indicated (MT = Mel-Temp), melting points were determined with a Kofler Heizbank and are corrected. Uv spectra

Table I. Cytotoxicity

No.	Compound	ED_{50}, μg/ml[a]
8a	1-Butylhypoxanthine	>20[b]
8b	1-Cyclopentylhypoxanthine	>20[b]
8c	1-Cyclohexylhypoxanthine	>20[b]
9a	1-Butylpurine-6(1*H*)-thione	1.0
9b	1-Cyclopentylpurine-6(1*H*)-thione	0.60
9c	1-Cyclohexylpurine-6(1*H*)-thione	1.4
	7-Butylhypoxanthine	>20[b]
4	7-Cyclopentylhypoxanthine	>20[b]
	7-Butylpurine-6(1*H*)-thione	15
3	7-Cyclopentylpurine-6(1*H*)-thione	12
	9-Butylhypoxanthine	18
	9-Cyclopentylhypoxanthine	<10
	9-Cyclohexylhypoxanthine	9.4
	9-Butylpurine-6(1*H*)-thione	5.0
	9-Cyclopentylpurine-6(1*H*)-thione	1.8
	9-Cyclohexylpurine-6(1*H*)-thione	<10

[a] The concentration of compound required to inhibit the growth of treated H.Ep.-2 cells to 50% of that of untreated controls as measured by colony counts (see ref 10). [b] No inhibition at this, the highest level tested.

‡ 3-Bromocyclohexene failed to react with 1 under more strenuous conditions.

§ Compound 10c was kindly provided by Dr. Y. F. Shealy.

were determined in aqueous solution with a Cary Model 14 spectrometer. Chromatographic analyses were carried out on tlc plates of silica gel H (Brinkmann). The spots were detected by uv light after spraying the plates with Ultraphor (WT, highly concd). All compounds were shown to be chromatographically homogeneous.

N-(4-Amino-6-chloro-5-pyrimidinyl)-*N*-cyclopentylformamide (2). To a solution of *N*-(4-amino-6-chloro-5-pyrimidinyl)formamide (1) (2 g, 11.6 mmoles) in DMF (50 ml) containing anhydrous potassium carbonate (1.6 g, 11.6 mmoles) was added bromocyclopentane (2.5 ml, 23 mmoles), and the mixture was stirred at 35° for 18 days. Additional bromocyclopentane (1 ml) and potassium carbonate (0.8 g, 5.8 mmoles) were added on the 13th day. The residue from evaporation of the filtered reaction mixture was triturated with ethanol and chilled in the ice box, and the insoluble solid collected by filtration. The resulting crude product was triturated with H_2O, and the residue was dried *in vacuo*: yield 590 mg (21%); mp 180°.

The analytical sample was prepared from a previous run by chloroform recrystallization of the purified product: mp 184°; λ_{max} ($\epsilon \times 10^{-3}$) 0.1 *N* HCl, 237 (9.8), 277 nm (4.0); pH 7, 236.5 (10.2), 277 nm (3.8); 0.1 *N* NaOH, 236 (10.4), 277 nm (3.9). *Anal.* ($C_{10}H_{13}ClN_4O$) C, H, N.

7-Cyclopentylhypoxanthine (4). A solution of 4-amino-6-chloro-5-pyrimidinyl)-*N*-cyclopentylformamide (500 mg, 2.3 mmoles) in 98% formic acid (75 ml) was refluxed for 4 days before it was evaporated to dryness *in vacuo*, and the residue crystallized from EtOH with charcoal treatment: yield 385 mg (80%). Recrystallization from water gave the pure material: yield 195 mg (42%); mp 188°; λ_{max} ($\epsilon \times 10^{-3}$) 0.1 *N* HCl, 250 nm (9.8); pH 7, 256 nm (9.2); 0.1 *N* NaOH, 263 nm (10.0). *Anal.* ($C_{10}H_{12}N_4O$) C, H, N.

1-Cyclohexenylhypoxanthine (7). To a solution of inosine (15 g, 57 mmoles) in DMF (200 ml) containing K_2CO_3 (7.9 g, 57 mmoles) at 90° was added 3-bromocyclohexene[11] (5 ml, 39 mmoles) in DMF (10 ml) dropwise in 45 min. Two more dropwise additions of bromocyclohexene (5 ml) were made during the next hour, and the mixture was heated for a total of 5 hr. The residue from evaporation of the filtered solution was triturated with butanol (150 ml). The insoluble solid (50% recovery of inosine) was removed by filtration, and the filtrate was concentrated to 75 ml before extraction with water (three 50-ml portions). A solution of the residue from evaporation of the butanol in a mixture of 83 ml of concd HCl and 200 ml of EtOH was refluxed for 1 hr before evaporation to dryness. An aqueous solution (100 ml) of the residue was adjusted to pH 6 with NaOH and the insoluble gum that formed removed by filtration. A butanol extract (two 75-ml portions) of this solution was evaporated to dryness, and the residue crystallized from 50% EtOH (35 ml): yield 690 mg (6% based on unrecovered inosine); mp 255°; λ_{max} ($\epsilon \times 10^{-3}$) 0.1 *N* HCl, 259 nm (9.9); pH 7, 252 nm (8.9); 0.1 *N* NaOH, 262 nm (9.3). *Anal.* ($C_{11}H_{12}N_4O$) C, H, N.

1-Butylhypoxanthine (8a). To a stirred solution of inosine (5.0 g, 18.5 mmoles) in DMF (150 ml) containing K_2CO_3 (2.58 g, 18.5 mmoles) at 90° was added 1-iodobutane (5 ml, 37 mmoles) in 10 ml of DMF, and the mixture was heated for 4 hr before it was filtered and then evaporated to dryness *in vacuo*. A solution of the residue in a mixture of 90 ml of EtOH and 60 ml of concd HCl was refluxed for 1 hr, filtered, and evaporated to dryness *in vacuo*. The residue—1-butylhypoxanthine (2.45 g)—was recrystallized from water to give an analytical sample: yield 1.35 g (38%); mp 220° dec; λ_{max} ($\epsilon \times 10^{-3}$) 0.1 *N* HCl, 249 nm (9.3); pH 7, 251 nm (8.9); 0.1 *N* NaOH, 261 nm (9.55). *Anal.* ($C_9H_{12}N_4O \cdot 0.25H_2O$) C, H, N.

6-Cyclopentyloxy-9-β-D-ribofuranosylpurine and 1-Cyclopentylinosine. To a solution of inosine (10 g, 37.4 mmoles) in 150 ml of DMF containing K_2CO_3 (5.2 g, 37.4 mmoles) at 70° was added bromocyclopentane (8 ml, 74 mmoles) over a period for 20 min. The mixture was heated at 110° for an additional 2.5 hr before it was filtered and evaporated to dryness *in vacuo*. Trituration of the residue with cold butanol gave a white solid, 6-cyclopentyloxy-9-β-D-ribofuranosylpurine, which was recrystallized from EtOH: 3.35 g (27%), mp 137–138° (MT); λ_{max} 0.1 *N* HCl (pH 7)–0.1 *N* NaOH 250 (sh), 252 nm (12.3); no carbonyl absorption in ir. *Anal.* ($C_{15}H_{20}N_4O \cdot 0.5C_2H_5OH$) C, H, N.

The crude 1-cyclopentylinosine (1.6, 13%), λ_{max} 0.1 *N* HCl (pH 7)–0.1 *N* NaOH 249 (sh), 253 nm (9.0), isolated from the butanol was used in the next step without purification.

1-Cyclopentylhypoxanthine (8b). A. A solution of crude 1-cyclopentylinosine (1.6 g) in 100 ml of EtOH and 42 ml of concd HCl was refluxed for 1 hr before it was evaporated to dryness *in vacuo*. A filtered solution of the residue in water (50 ml) was extracted with $CHCl_3$ (125 ml). Evaporation of the dried $CHCl_3$ extract gave a solid: yield 534 mg (55%); mp 232°. A small sample was recrystallized from 50% EtOH for analysis: mp 233°; λ_{max} 0.1 *N* HCl, 251.5 nm (9.4); pH 7, 252 nm (8.8); 0.1 *N* NaOH, 261.5 nm (9.5). *Anal.* ($C_{10}H_{12}N_4O$) C, H, N.

B. *N*-Cyclopentyl-5-nitroimidazole-4-carboxamide (2.24 g, 10 mmoles) in 500 ml of EtOH containing 5 ml of HOAc was reduced at room temperature and atmospheric pressure for 20 hr using 5% Pd/C catalyst (224 mg). After the catalyst was removed by filtration, the solution was evaporated to dryness *in vacuo*. A solution of the residue, 5-amino-*N*-cyclopentylimidazole-4-carboxamide (10b), in formamide (200 ml) was refluxed for 0.5 hr before evaporation to dryness *in vacuo*. A solution of the residue in hot EtOH was poured into acetone, which caused crystallization of starting material (10b). To a solution of the residue from evaporation of the EtOH–acetone was added 10 mmoles of $Pb(OAc)_2$ in H_2O. Addition of NH_4OH caused precipitation of the lead salt, which was collected by filtration and then dissolved in 20% HOAc. The solution was treated with H_2S, the PbS removed by filtration, and the filtrate evaporated to dryness *in vacuo*. The dark syrup was crystallized from acetone with charcoal treatment: yield 635 mg (31%). This material was essentially identical with that prepared by method A described above.

1-Cyclohexylhypoxanthine (8c). A. A solution of 1-cyclohexenylhypoxanthine (745 mg, 3.3 mmoles) in 70% aqueous ethanol (100 ml) containing 5% Pd/C catalyst (100 mg) was hydrogenated at atmospheric pressure for 12 hr. The catalyst was removed by filtration, and the filtrate was taken to dryness *in vacuo*. The residue was crystallized from H_2O (40 ml): yield 613 mg (88%); mp 288°; λ_{max} ($\epsilon \times 10^{-3}$) 0.1 *N* HCl, 250.5 nm (9.6); pH 7, 251.5 nm (9.05); 0.1 *N* NaOH, 260.5 nm (9.8). *Anal.* ($C_{11}H_{14}N_4O$) C, H, N.

B. A solution of 5-amino-*N*-cyclohexylimidazole-4-carboxamide (2.64 g, 1.08 mmoles) in formamide (25 ml) was heated under reflux for 1.75 hr before it was evaporated to dryness *in vacuo*. The residue was crystallized from water and then recrystallized from acetone: yield 775 mg (33%). This material was essentially identical with that prepared by method A described above.

N-Cyclopentyl-5-nitroimidazole-4-carboxamide (12b). A solution of the methyl ester of 5-nitroimidazole-4-carboxylic acid (12.0 g, 0.07 mmole) and cyclopentylamine (59.5 g, 0.7 mmole) in 304 ml of MeOH containing MeONa (3.46 g, 0.064 mmole) was heated at 80° for 6 days before it was evaporated to dryness *in vacuo*. A solution of the residue in 600 ml of water was chilled and acidified with 12 *N* HCl to pH 1. The white precipitate that formed was collected by filtration, washed with water, and dried *in vacuo* over P_2O_5 for 16 hr: yield 11.1 g (71%); mp 247° (HB); λ_{max} ($\epsilon \times 10^{-3}$) 0.1 *N* HCl, 208 (16.6), 304 nm (5.12); pH 7, 203 (13.3), 340 nm (5.15); 0.1 *N* NaOH, 219 (10.3), 352 nm (8.13). *Anal.* ($C_9H_{12}N_4O_3$) C, H, N.

N-Cyclohexyl-5-ethoxymethyleneaminoimidazole-4-carboxamide. A suspension of 5-amino-*N*-cyclohexylimidazole-4-carboxamide hydrochloride (245 mg, 1.0 mmole) in ethyl orthoformate (25 ml) was heated to boiling for 7 min, and the resulting solution

Table II. *N*-Alkylpurine-6(1*H*)-thiones

No.	Alkyl group	Yield, %	Mp, °C	Uv spectra, λ_{max}, nm ($\epsilon \times 10^{-3}$) 0.1 *N* HCl	0.1 *N* NaOH	Formula[a]
3	7-Cyclopentyl	40	214	221 (8.9) 330 (16.7)	228 (11.2) 316 (17.3)	$C_{10}H_{12}N_4S$
9a	1-Butyl	28	182	232 (12.1) 325 (16.2)	238 (10.6) 325 (22.6)	$C_9H_{12}N_4S$
9b	1-Cyclopentyl	59	215	234 (12.9) 325 (16.7)	239 (12.1) 325 (22.7)	$C_{10}H_{12}N_4S$
9c	1-Cyclohexyl	48	238	234 (12.3) 325 (16.2)	238 (11.8) 325 (21.7)	$C_{11}H_{14}N_4S$

[a] *Anal.* C, H, N.

allowed to stand overnight before it was evaporated to dryness *in vacuo*. The residue was recrystallized from EtOH (dried at 100° and 0.07 mmole over P_2O_5): yield 163 mg (62%); mp 144–146° (MT); λ_{max} ($\epsilon \times 10^{-3}$) pH 1, 239 (10.7), 265 nm (12.6); pH 7, 214 (15.2), 277 nm (11.6); pH 13, 226 (12.7), 287 nm (11.4). *Anal.* ($C_{13}H_{20}N_4O$) C, H, N.

***N*-Alkylpurine-6(1*H*)-thiones.** A stirred solution of the *N*-alkylhypoxanthine in pyridine (14 ml/mmole) containing P_2S_5 (3.7 equiv) was heated for 4–8 hr. The filtered mixture was diluted with H_2O, acidified with HOAc, and evaporated to dryness *in vacuo*. Acidification of a filtered solution of the residue in 1 *N* NaOH gave a precipitate, which was recrystallized from EtOH with charcoal treatment. Yields, melting points, and spectra data are given in Table II.

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Medicinal Chemistry of [10]Annulenes and Related Compounds. 2. *N*-(2-Chloroethyl) Derivatives of 11-Azatricyclo[4.4.1.$0^{1,6}$]undecane, 11-Azatricyclo[4.4.1.$0^{1,6}$]undeca-3,8-diene, and 11-Azabicyclo[4.4.1]undeca-1,3,5,7,9-pentaene[1]

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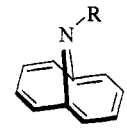
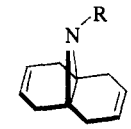
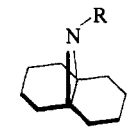
1,6-Imino[10]annulene (**1**) represents an aromatic 10π-electron system with a nitrogen atom held rigidly above the ring. Such a system is unique, and we were interested in investigating the biological activity of compounds containing such a nitrogen atom by studying the series‡ **1**, **2**, and **3**.

The compounds of this series range from the fully aromatic [10]annulene to the saturated decalin. That **1** is a member of this series can be seen from the valence tautomer **4**.§


1, R = H


2, R = H

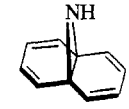

3, R = H

5, R = $ClCH_2C(=O)$
8, R = $ClCH_2CH_2$

6, R = $ClCH_2C(=O)$
9, R = $ClCH_2CH_2$

7, R = $ClCH_2C(=O)$
10, R = $ClCH_2CH_2$
11, R = $HOCH_2CH_2$

This paper discusses the synthesis and α-adrenergic blocking activity of the *N*-(2-chloroethyl) derivatives of these three amines.

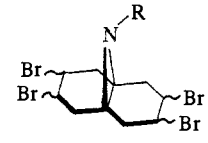

4

Synthesis. Amines **1** and **2** were prepared by modification of literature procedures[1,3] and the synthesis of **3** was reported by us earlier.[1] The general route for the preparation of the β-chloroethyl compounds **8**, **9**, and **10** was *via* the chloroacetyl derivatives **5**, **6**, and **7**.

Aziridine **2** was readily acylated in high yield with chloroacetyl chloride to give **6** as a white crystalline solid. Amide **7** was obtained in low yields (20%) as a yellow oil by similar treatment of aziridine **3**. Much higher yields were obtained in this case if chloroacetic anhydride was used as the acylating agent. The lower basicity[1] of amine **1** made acylation more difficult, but 30% yields (after recrystallization) of amide **5** could be obtained with chloroacetyl chloride.

Reduction of the amide carbonyl without concomitant reduction of the carbon-halogen bond of amides **5**, 6, and 7 was accomplished in yields of 43, 60, and 30%, respectively, with aluminum hydride.[4]

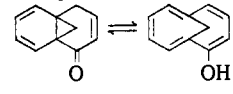
Several alternate synthetic routes were also tried. Treatment of **2** or **3** with methyllithium followed by 1,2-dichloroethane gave only the starting aziridine. Treatment of the lithium salt of **3** with ethylene oxide gave **11**, the *N*-(β-hydroxyethyl) derivative, but in very low yields. Reduction of amide **6** with diimide failed to give amide **7**; starting material was recovered. An alternate route to the aromatic **8** involved conversion of amide 6 to the tetrabromide **12** in high yield. Although the corresponding *N*-acetyl derivative **13** could be dehydrobrominated in base[3] to the aromatic [10]annulene system, similar treatment of **12** failed to give amide **5**.


12, R = $ClCH_2C(=O)$
13, R = Ac

†Taken in part from the thesis submitted by Ann M. Warner to the Graduate School of the University of Kansas in partial fulfillment of the requirement for the Ph.D. degree, Aug 1970. A preliminary account of this work was presented at the Fifth Midwest Regional Meeting of the American Chemical Society, Kansas City, Mo., Oct 31, 1969, Abstract No. 427.

‡The preferred nomenclature is given in the title for 3, 2, and 1, respectively.

§No evidence for the existence of 4 could be found by low-temperature nmr studies on 1. It could be viewed also as a possible minor resonance contributor to 1, in analogy to the Dewar (1,4-bonded) resonance structure of benzene. In some [10]annulenes, however, structures analogous to 4 represent discrete tautomers, such as in the keto-enol pair i and ii.[2]


i ii