was treated with glacial acetic acid (250 ml.). The resulting precipitate (34 g.) was washed with a 1% acetic acid solution and then recrystallized successively from methylene chloride and absolute ether; m.p. 143–145°.

Anal. Calcd. for $C_{32}H_{27}NO_7$: C, 71.49; H, 5.06; N, 2.60. Found: C, 71.44; H, 5.32; N, 2.61.

β-(4-Benzoyloxyphenyl)serine Ethyl Ester Hydrochloride Monohydrate.—N-4-Benzoyloxybenzylidene-β-(4-benzoyloxyphenyl)serine ethyl ester (5.0 g.) was treated with dry hydrogen chloride in a 1:1 mixture of methylene chloride–ethyl ether (100 ml.). The resulting hydrochloride was recrystallized 5 times from water; yield, 1.0 g.; m.p. 135–138°.

Anal. Calcd. for $C_{18}H_{22}ClNO_6$: C, 56.32; H, 5.77; N, 3.64. Found: C, 56.61; H, 5.33; N, 3.66.

Pharmacological Test.—Intact male rats were treated with a 0.1% solution of thiouracil in their drinking water for 10 days. Concommitently they were dosed with varying amounts of L-triiodothyronine to show the effect of the hormone on the development of the goiters. The test compounds were administered to groups of animals along with triiodothyronine (different sites of injection to prevent physical mixing) in a ratio of 100 parts of test compound to 1 part of triiodothyronine. After 10 days of treatment the animals were sacrificed and the thyroid glands were removed and weighed. Animals receiving saline or 0.1% solutions of thiouracil in their drinking water served as controls.

Drug	No. of rats	Thyroid gland weight (mean ± S.D.) (mg./100 g.)
None (untreated controls) (0.9% NaCl)	7	6.7 ± 1.4
None (thiouracil 0.1% treated controls) (0.9% NaCl)	8	16.0 ± 4.0
L-TIT[a] (1.25 γ/2 ml./kg.)	8	11.4 ± 2.5
L-TIT (1.75 γ/2 ml./kg.)	8	8.3 ± 2.0
L-TIT (2.45 γ/2 ml./kg.)	7	9.4 ± 2.6
L-TIT (3.45 γ/2 ml./kg.)	8	7.8 ± 2.0
L-TIT (2.45 γ/2 ml./kg.) + IV[b] (245.0 γ/2 ml./kg.)	8	5.7 ± 0.79

[a] L-Triiodothyronine. [b] β-[3,5-Diiodo-4(3,5-diiodo-4-hydroxyphenoxy)phenyl]serine.

Acknowledgment.—The authors wish to thank Smith Kline and French Laboratories for the pharmacological tests reported.

Synthetic Schistosomicides. III. 5-(4-Amino-1-naphthylazo)uracil and Related Heterocyclic Azo Compounds[1]

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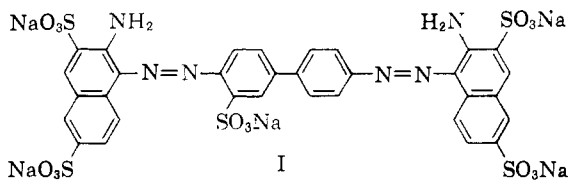
Received January 11, 1963

A variety of 4-amino-1-naphthylazoheterocyclic compounds and 8-amino-5-(heterocyclicazo)quinoline derivatives have been prepared by allowing a diazotized heterocyclic amine to react with the appropriate 1-naphthylamine or 8-aminoquinoline precursor or by coupling 4-acetamido-1-naphthalenediazonium chloride with a substituted pyrimidinol followed by acid hydrolysis. 5-(4-Amino-1-naphthylazo)uracil (ANU) was highly active against experimental *Schistosoma mansoni* infections in the mouse, hamster, and monkey.

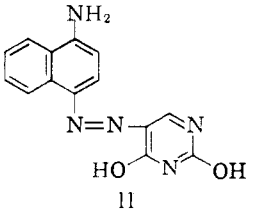
Over half a century ago, Ehrlich demonstrated that the cotton substantive azo dye Trypan Red (I) was capable of sterilizing *Trypanosoma equinum* infections



I

in the mouse when administered in a single subcutaneous dose 24 hr. before the death of untreated controls.[2] Subsequent researches with literally thousands of azo derivatives have demonstrated that certain specific structures among this large class of compounds not only possess antitrypanosomal activity but also possess antibacterial, antimalarial, antiviral, antifungal, and antihaemorrhagic properties.[3] Notable among the azo compounds used as medicinals during this era are chloroazodin, 3,5-diamino-2-[4′-(sulfamylphenyl)azo]-benzoic acid, 4-*o*-tolylazo-*o*-diacetotoluide, salicylazosulfapyridine, 4′-sulfamyl-2,4-diaminoazobenzene hydrochloride, 2,6-diamino-3-phenylazopyridine hydrochloride, and 2′,6′-diamino-2-butyloxy-5,5′-azopyridine.

During the course of a continuing program in these laboratories to develop new schistosomicidal agents, several hundred azo compounds of diverse structure have been tested against *Schistosoma mansoni* in mice. Although most of these compounds were ineffective, unexpected activity was observed with 5-(4-amino-1-naphthylazo)uracil (ANU) (II), which proved to be highly effective against *S. mansoni* in mice, hamsters, and monkeys.[4] The present communication is concerned with the synthesis of ANU and certain closely related compounds.



II

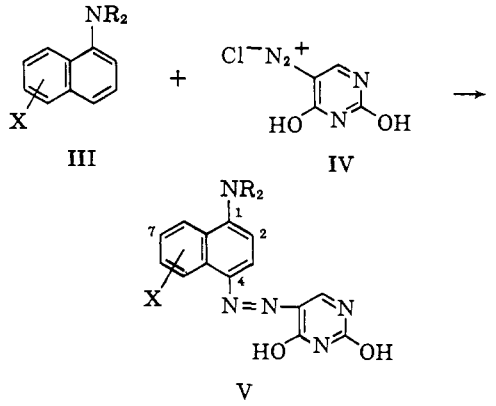
ANU (II) was prepared by allowing diazotized 5-aminouracil (IV) to couple with 1-naphthylamine in aqueous ethanol. In like manner, a variety of substituted 5-(4-amino-1-naphthylazo)uracils of formula V (where X represents a hydrogen atom or a methyl, hydroxy, or ethoxy group and NR_2 represents an amino,

(1) For previous paper in this series, see E. F. Elslager, J. F. Cavalla, W. D. Closson, and D. F. Worth, *J. Org. Chem.*, **26**, 2837 (1961).

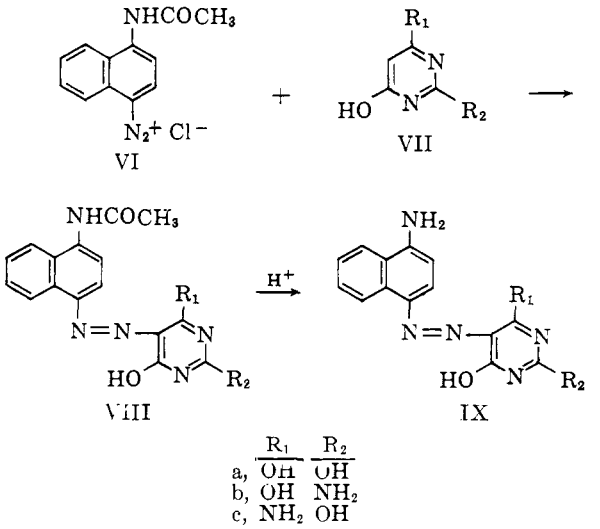
(2) P. Ehrlich, *Berlin. klin. Wochschr.*, **44**, 233 (1907).

(3) G. N. Mahapata, *J. Proc. Inst. Chemists* (India), **29**, 33 (1957).

(4) P. E. Thompson, J. E. Meisenhelder, and H. Najarian, unpublished results, Parke, Davis and Company, Ann Arbor, Michigan.

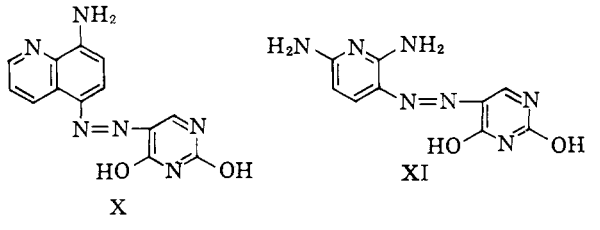


alkylamino or dialkylamino radical) (Table I) were prepared from 5-aminouracil and a 1-naphthylamine derivative of formula III (procedures I and II). Alternatively, 5-(4-amino-1-naphthylazo)barbituric acid (IXa) and related compounds (IXb and IXc) were prepared by allowing 4-acetamido-1-naphthalenediazonium chloride (VI) to react with the appropriate

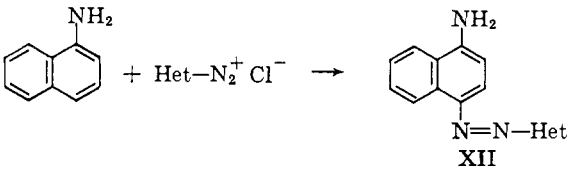


pyrimidinol (VII) followed by acid hydrolysis of the intermediate N-[4-(4-hydroxy-5-pyrimidinylazo)-1-naphthyl]acetamides (VIII, a through c).

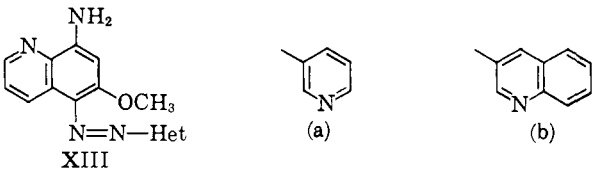
Diazotized 5-aminouracil was also coupled with 8-aminoquinoline and 2,6-diaminopyridine to give 5-(8-amino-5-quinolylazo)uracil (X) and 5-(2,6-diamino-3-pyridylazo)uracil (XI), a uracil analog of 2,6-diamino-3-phenylazopyridine.



In order to study the influence of other heterocyclic groups on antischistosome activity, a series of (4-amino-1-naphthylazo)heterocyclic compounds was prepared in which various other heterocyclic amines were diazotized and coupled with 1-naphthylamine (XII,



where Het represents a pyrazole, pyridine, pyridine-1-oxide, quinoline, or isoquinoline ring) (Table II, procedures I and III). In like manner, 3-(4-amino-5-chloro-3-methyl-1-naphthylazo)pyridine was prepared from diazotized 3-aminopyridine and 8-chloro-2-methyl-1-naphthylamine; 8-amino-6-methoxy-5-(3-pyridylazo)quinoline (XIII a) and 8-amino-6-methoxy-5-(3-quinolylazo)quinoline (XIII b) were prepared from



8-amino-6-methoxyquinoline and diazotized 3-aminopyridine and 3-aminoquinoline, respectively.

A majority of the intermediate heterocyclic amines are commercially available.[5] 6-Aminoquinoline, 5-amino-6-methylquinoline, and 5-aminoisoquinoline were prepared by the catalytic hydrogenation of the corresponding nitro compounds,[6,7] while 2-aminopyridine 1-oxide was synthesized by the method of Adams and Miyano.[8]

All of the substituted 1-naphthylamines employed are commercially available[9] with the exception of 8-chloro-2-methyl-1-naphthylamine, which was prepared by reduction of the corresponding nitro compound with iron and acetic acid.[10]

The heterocyclic azo compounds described herein were tested against *S. mansoni* in mice by Dr. P. E. Thompson and co-workers of these laboratories.[11] When indicated, expanded studies were carried out against *S. mansoni* infections in hamsters and monkeys.[11] It is noteworthy that significant antischistosome activity was observed only with ANU. When given in the diet to mice infected with a Puerto Rican strain of *S. mansoni* in doses ranging from 221 to 804 mg./kg./day for 14 days, ANU caused a 73 to 100% reduction in live worms and was tolerated well. By gavage, the drug was less active and more toxic for mice. When administered to rhesus monkeys infected with the Puerto Rican strain, ANU suppressed egg

(5) 5-Aminouracil, 4-aminoantipyrine, 3-aminoquinoline, and 8-aminoquinoline were purchased from Distillation Products Industries, Rochester 3, N. Y.; 3-aminopyridine, 4-aminopyridine, 2,6-diaminopyridine, and 6-methoxy-8-aminoquinoline from the Aldrich Chemical Company, Milwaukee, Wis.; 2-chloro-5-aminopyridine from Reilly Coal Tar Chemicals, Indianapolis, Ind.

(6) J. J. Craig and W. E. Cass, *J. Am. Chem. Soc.*, **64**, 783 (1942).

(7) A. L. Searles and R. M. Warren, *J. Org. Chem.*, **18**, 1317 (1953).

(8) R. Adams and S. Miyano, *J. Am. Chem. Soc.*, **76**, 2785 (1954).

(9) N-methyl-1-naphthylamine, N-ethyl-1-naphthylamine, and N,N-dimethyl-1-naphthylamine were purchased from Distillation Products Industries, Rochester 3, N. Y.; 8-amino-2-naphthol was purchased from the Aldrich Chemical Company, Milwaukee, Wis.; 2-methyl-1-naphthylamine was obtained through the courtesy of the Union Carbide Chemicals Co., New York, N. Y.; 2-ethoxy-1-naphthylamine was obtained through the courtesy of the National Aniline Division, Allied Chemical Corp., New York, N. Y.

(10) V. Veselý, A. Medvedeva, and E. Müller, *Collection Czech. Chem. Commun.*, **7**, 228 (1935).

(11) For a description of test methods, see P. E. Thompson, J. E. Meisenhelder, and H. Najarian, *Am. J. Trop. Med. Hyg.*, **11**, 31 (1962).

production but was rarely curative at doses ranging from 50 to 200 mg./kg. daily for 10 days.[4]

On the assumption that ANU, like 4′-sulfamyl-2,4-diaminoazobenzene,[12] might be reduced *in vivo* to provide active metabolites, samples of the probable reduction products, 5-aminouracil and 1,4-naphthalenediamine dihydrochloride,[13] were tested against *S. mansoni* in mice. Although both compounds were ineffective at the maximum tolerated doses, 1,4-naphthalenediamine dihydrochloride killed adult *S. mansoni in vitro* at drug concentrations of 25 γ/ml.. Therefore, ANU may well owe its schistosomicidal effects to some unique property that allows adequate blood levels of 1,4-naphthalenediamine.

Experimental.[14]

Procedures for Preparing (4-Amino-1-naphthylazo)Heterocyclic Compounds (Tables I and II). Procedure I.—A solution of 50.8 g. (0.4 mole) of 5-aminouracil[5] in 500 ml. of 50% aqueous ethanol and 90 ml. of concentrated hydrochloric acid was cooled to −5° and diazotized by the addition of a cold solution of 27.6 g. (0.4 mole) of sodium nitrite in 120 ml. of water with vigorous mechanical stirring. The temperature was maintained below 5° during the addition. The diazonium salt mixture was stirred for 15 min. at 0°, then added over a period of 10 min. to a cold solution of 57.2 g. (0.4 mole) of 1-naphthylamine in 500 ml. of 95% ethanol. Subsequently, the reaction mixture was stirred for 1 hr. at 0–5°, the pH was adjusted to 8 by the addition of sodium hydroxide, and the brilliant red dye that separated was collected by filtration, washed with water, and dried *in vacuo* at 60° for 18 hr. Crystallization of the crude product from a dimethylacetamide–water mixture gave 83 g. (70%) of 5-(4-amino-1-naphthylazo)uracil as deep red crystals, m.p. 253° dec.

Procedure II.—5-Aminouracil[5] (19.1 g., 0.15 mole) was diazotized according to the method described under procedure I and the diazonium salt mixture was added with mechanical stirring to a cold solution of 23.9 g. (0.15 mole) of 8-amino-2-naphthol in 200 ml. of glacial acetic acid and 300 ml. of water while maintaining the temperature at 0–5°. The deep purple reaction mixture was stirred for 18 hr. at room temperature, a mixture of 200 g. of sodium acetate and 400 ml. of water was added, and stirring was continued for 24 hr. The crude dye was collected by filtration, washed with water, and dried *in vacuo* at 45° for 18 hr. Crystallization from a dimethylacetamide–water mixture gave 37 g. (74%) of 5-(4-amino-6-hydroxy-1-naphthylazo)uracil as black crystals, m.p. >250°.

Procedure III.—4-Aminopyridine[5] (14.1 g., 0.15 mole) was added slowly with stirring and external cooling to 70 ml. of 85% phosphoric acid. Subsequently, 120 ml. of concentrated nitric acid was diluted with water to a volume of 220 ml. and added with continued stirring and cooling to the phosphoric acid solution. The resulting orange colored solution was cooled to −5° and a cold solution of 10.5 g. (0.15 mole) of sodium nitrite in 75 ml. of water was added over a period of 25 min. Dow Antifoam A was added to suppress foaming. The diazonium salt solution was then poured slowly with stirring into a solution of 20.0 g. (0.15 mole) of 1-naphthylamine in 300 ml. of ethanol over a period of 20 min. while maintaining the temperature at 0 to −5°. The reaction mixture was stirred for 2 hr. at 0 to −10° and was allowed to stand for 18 hr. at room temperature. The mixture was made alkaline by the addition of sodium acetate (300 g. dissolved in 1 l. of water) and 500 ml. of 10% aqueous sodium hydroxide. The reddish black precipitate was collected by filtration, washed thoroughly with warm water, crystallized 3 times from an ethanol–water mixture, dried *in vacuo* at 40°, and allowed to equilibrate in the air. The dark red product, 4-(4-amino-1-naphthylazo)pyridine, weighed 7.5 g. (20%), m.p. 164–166°.

N-[4-(2,4,6-Trihydroxy-5-pyrimidinylazo)-1-naphthyl]acetamide (VIIIa).—Barbituric acid (12.8 g., 0.1 mole) was suspended in a solution of 106 g. (1 mole) of sodium carbonate in 500 ml. of water and 10% sodium hydroxide solution was added slowly until the barbituric acid completely dissolved. This solution was cooled to 0° and to it was added with stirring a cold solution of 4-acetamido-1-naphthalenediazonium chloride prepared from 20.0 g. (0.1 mole) of N-(4-amino-1-naphthyl)-acetamide, 6.9 g. (0.1 mole) of sodium nitrite, and 500 ml. of 5% hydrochloric acid. The mixture was stirred for 2 hr. at 0°, made acid with concentrated hydrochloric acid, and allowed to stir at room temperature for 18 hr. The red precipitate was collected by filtration, washed thoroughly with water, and dried *in vacuo* at 40° for 24 hr.; yield, 33.4 g. (99%), m.p. >300°. Crystallization of the crude dye from a dimethylacetamide–water mixture gave 19.7 g., m.p. >360°.

Anal. Calcd. for $C_{16}H_{13}N_5O_4$: C, 56.63; H, 3.86; N, 20.64. Found: C, 56.44; H, 3.99; N, 20.73.

5-(4-Amino-1-naphthylazo)barbituric Acid (IXa).—A suspension of 15.9 g. (0.047 mole) of N-[4-(2,4,6-trihydroxy-5-pyrimidinylazo)-1-naphthyl] acetamide in a mixture of 100 ml. of water, 100 ml. of concentrated hydrochloric acid, and 200 ml. of glacial acetic acid was boiled under reflux for 6 hr. The reaction mixture was poured onto ice and was made slightly alkaline with sodium hydroxide. The reddish black solid was collected by filtration, washed thoroughly with water, and dried *in vacuo* at 40° for 48 hr. Crystallization of the crude product from a dimethylformamide–water mixture gave 6.0 g. (43%) of a reddish black solid, m.p. >300°.

Anal. Calcd. for $C_{14}H_{11}N_5O_3$: C, 56.56; H, 3.73; N, 23.56. Found: C, 56.49; H, 3.98; N, 23.23.

2-Amino-5-(4-amino-1-naphthylazo)-4,6-pyrimidinediol (IXb).—N-(4-Amino-1-naphthyl)acetamide (20.0 g., 0.1 mole) was diazotized and coupled with 12.7 g. (0.1 mole) of 2-amino-4,6-pyrimidinediol according to the procedure outlined previously for the preparation of VIIIa. The crude N-[4-(2-amino-4,6-dihydroxy-5-pyrimidinylazo)-1-naphthyl]acetamide (VIIIb), weighing 23.0 g. (68%), m.p. >300°, was not purified but was hydrolyzed directly in a mixture of acetic acid and hydrochloric acid (procedure IXa). The pH was adjusted to 7 and the crude product was collected by filtration, washed with water and acetone, and dried *in vacuo* at 100° for 48 hr.; yield, 14.8 g. (49%). Purification from dimethylacetamide gave 4.8 g. of a highly insoluble, dark maroon dye, m.p. >300°.

Anal. Calcd. for $C_{14}H_{12}N_6O_2 \cdot 0.5H_2O$: C, 55.08; H, 4.29; N, 27.53; H_2O, 2.95. Found: C, 55.42; H, 4.34; N, 27.22; H_2O (Karl Fischer), 2.65.

6-Amino-5-(4-amino-1-naphthylazo)uracil (IXc).—Utilizing the experimental conditions described for the preparation of IXb, 20.0 g. (0.1 mole) of N-(4-amino-1-naphthyl)acetamide and 12.7 g (0.1 mole) of 6-aminouracil yielded 27.6 g. (82%) of crude N-[4-(4-amino-2,6-dihydroxy-5-pyrimidinylazo)-1-naphthyl]acetamide (VIIIc), m.p. >300°. Hydrolysis of the crude amide (13.4 g., 0.04 mole) gave 6.0 g. (48%) of IXc. Purification from a dimethylacetamide–water mixture provided 4.9 g. of a black powder, m.p. >300°.

Anal. Calcd. for $C_{14}H_{12}N_6O_2 \cdot 0.75H_2O$: C, 54.27; H, 4.40; N, 27.13; H_2O, 4.36. Found: C, 53.96; H, 4.42; N, 26.71; H_2O (Karl Fischer), 4.37.

5-(8-Amino-5-quinolylazo)uracil (X).—5-Aminouracil[5] (19.1 g., 0.15 mole) was diazotized according to procedure I and coupled with 21.6 g. (0.15 mole) of 8-aminoquinoline in a mixture of 100 ml. of glacial acetic acid and 400 ml. of water. The reaction mixture was treated with a solution of 200 g. of sodium acetate in 500 ml. of water and the crude brown dye was collected by filtration, dried *in vacuo* at 45°, and crystallized from a dimethylacetamide–water mixture; yield, 34.2 g. (74%); m.p. >250°.

Anal. Calcd. for $C_{13}H_{10}N_6O_2 \cdot 1.5H_2O$: C, 50.48; H, 4.23; N, 27.18; H_2O, 8.73. Found: C, 49.98; H, 4.47; N, 26.93; H_2O (Karl Fischer), 8.82.

5-(2,6-Diamino-3-pyridylazo)uracil (XI).—5-Aminouracil[5] (12.7 g., 0.1 mole) was diazotized according to procedure I and coupled with 14.6 g. (0.1 mole) of 2,6-diaminopyridine hydrochloride in 135 ml. of ethanol and 135 ml. of water. The reaction mixture was neutralized with aqueous sodium acetate and the crude red solid was collected by filtration, washed with warm water, dried *in vacuo* at 45°, and crystallized from a dimethylformamide–water mixture; yield, 22.0 g. (89%); m.p. >360°.

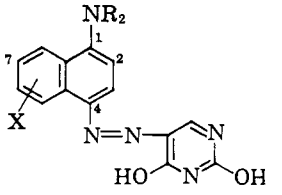
Anal. Calcd. for $C_9H_9N_7O_2$: C, 43.72; H, 3.67. Found: C, 43.72; H, 4.00.

(12) Prontosil®. For a historical summary, see A. Burger, "Medicinal Chemistry", Second Edition, Interscience Publishers, New York, N. Y., 1960, pp. 800–801.

(13) R. Adams and R. A. Wankel, *J. Am. Chem. Soc.*, **73**, 131 (1951).

(14) Melting points are uncorrected.

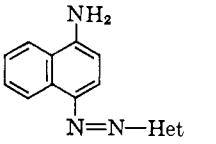
TABLE I
5-(4-AMINO-1-NAPHTHYLAZO)URACILS



NR_2	X	M.p., °C.	λ_{max}	Yield purified, %	Procedure	Purification[a] solvent	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
NH_2	H	253 dec.	485	70	I	A	$C_{14}H_{11}N_5O_2 \cdot 0.5H_2O$[c]	57.92	57.93	4.17	4.22	24.13	23.72
$NHCH_3$	H	263 dec.	492	85	I	A	$C_{15}H_{13}N_5O_2 \cdot 0.1H_2O$[d]	60.64	60.36	4.44	5.02	23.58	23.47
NHC_2H_5	H	247 dec.	498	86	I	A	$C_{16}H_{15}N_5O_2$	62.12	61.97	4.88	5.15	22.64	22.60
$N(CH_3)_2$	H	260 dec.	432	18	I	B	$C_{16}H_{15}N_5O_2 \cdot 0.25H_2O$[e]	61.22	61.38	4.99	5.70	22.31	21.98
NH_2	2-CH_3	266 dec.	490	70	I	A	$C_{15}H_{13}N_5O_2 \cdot 0.75H_2O$	58.34	58.03	4.73	4.99	22.68	22.60
NH_2	2-OC_2H_5	264 dec.	513	56	II	A	$C_{16}H_{15}N_5O_3$	59.07	59.24	4.65	5.18	21.53	21.49
NH_2	7-OH	>250	493	74	II	A	$C_{14}H_{11}N_5O_3 \cdot 2H_2O$[f]	50.45	50.84	4.54	4.98	21.01	21.07

[a] A, dimethylacetamide–water; B, acetone–dimethylacetamide–water. [b] In methanol. [c] Calcd. water determination (Karl Fischer): 3.10; found: 3.15. [d] Calcd.: 0.61; found: 0.33. [e] Calcd.: 1.43; found: 1.27. [f] Calcd.: 10.81; found: 10.52.

TABLE II
(4-AMINO-1-NAPHTHYLAZO) HETEROCYCLIC COMPOUNDS



Het	M.p., °C.	λ_{max}[b]	Yield purified, %	Procedure	Purification solvent[a]	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
2,3-Dimethyl-5-oxo-1-Phenyl-3-pyrazolin-4-yl	173–175	457	58	I	A	$C_{21}H_{19}N_5O \cdot 0.5H_2O$	68.83	68.64	5.50	5.94	19.12	18.87
3-Pyridyl	185–187	470	42	I	B	$C_{15}H_{12}N_4$	72.56	73.10	4.87	5.15	22.57	22.69
4-Pyridyl	164–166	488	20	III	B	$C_{15}H_{12}N_4$	72.56	72.42	4.87	4.77		
6-Chloro-3-pyridyl	170–172	487	44	I	B	$C_{15}H_{11}ClN_4$	63.72	63.78	3.92	4.04	19.82	19.57
2-Pyridyl 1′-oxide	192–193	545	78	I	B	$C_{15}H_{12}N_4O \cdot 0.67H_2O$[c]	65.20	65.56	4.86	5.03	20.28	19.82
3-Quinolyl	238–239	490	37	I	B	$C_{19}H_{14}N_4$	76.49	76.05	4.73	4.97	18.78	18.87
6-Quinolyl	220–225	475	83	I	A	$C_{19}H_{14}N_4 \cdot 0.2H_2O$[d]	75.58	75.79	4.80	4.79	18.56	18.78
6-Methyl-5-quinolyl	208–211	446	81	I	B	$C_{20}H_{16}N_4$	76.90	76.72	5.16	5.30	17.94	17.94
6-Methoxy-8-quinolyl	170–171	480	56	I	B	$C_{20}H_{16}N_4O \cdot 0.6H_2O$[e]	70.82	70.66	5.11	5.23	16.52	16.34
5-Isoquinolyl	243–245	488	75	I	A	$C_{19}H_{14}N_4 \cdot 0.2H_2O$[f]	75.58	75.40	4.80	4.86	18.56	18.46

[a] A, dimethylacetamide-water; B, ethanol-water. [b] In methanol. [c] Calcd. water determination (Karl Fischer): 4.36; found: 4.64. [d] Calcd.: 1.19; found: 0.97. [e] Calcd.: 3.18; found: 2.52. [f] Calcd.: 1.19; found: 1.10.

3-(4-Amino-5-chloro-3-methyl-1-naphthylazo)pyridine.—Diazotized 3-aminopyridine[5] (9.4 g., 0.1 mole) was coupled with 19.2 g. (0.1 mole) of 8-chloro-2-methyl-1-naphthylamine[10] according to procedure I above and the crude dye was crystallized from an ethanol–water mixture. The shiny red-brown needles thus obtained weighed 13.3 g. (45%), m.p. 173–174°.

Anal. Calcd. for $C_{16}H_{13}ClN_4$: C, 64.75; H, 4.41; N, 18.88. Found: C, 64.55; H, 4.67; N, 18.48.

8-Amino-6-methoxy-5-(3-pyridylazo)quinoline (XIIIa.).—3-Aminopyridine[5] (9.4 g., 0.1 mole) was diazotized and coupled with 17.4 g. (0.1 mole) of 8-amino-6-methoxyquinoline according to procedure I. The crude dye was crystallized from a mixture of 2-propanol and 10% ammonium hydroxide to give 6.2 g. (22%) of deep red crystals, m.p. 199–200°.

Anal. Calcd. for $C_{15}H_{13}N_5O$: C, 64.50; H, 4.69; N, 25.08. Found: C, 64.16; H, 4.73; N, 24.82.

8-Amino-6-methoxy-5-(3-quinolylazo)quinoline (XIIIb).—Utilizing procedure I above, 14.5 g. (0.1 mole) of 3-aminoquinoline was diazotized and coupled with 17.4 g. (0.1 mole) of 8-amino-6-methoxyquinoline. Crystallization of the crude dye from a mixture of ethanol and 10% ammonium hydroxide gave 13.0 g. (40%) of maroon crystals, m.p. 204–206°.

Anal. Calcd. for $C_{19}H_{15}N_5O$: C, 69.28; H, 4.59; N, 21.27. Found: C, 69.68; H, 4.78; N, 21.23.

Acknowledgment.—The authors are indebted to Dr. Loren M. Long for encouragement in this investigation, to Dr. Paul E. Thompson, Dr. Haig Najarian, and Dr. D. A. McCarthy for the antischistosome testing, and to Mr. Wilbur F. Kamm and Mrs. Doris R. Thomas for the preparation of several of the compounds described herein. We also thank Mr. Charles E. Childs and associates for the microanalyses, Dr. J. M. Vandenbelt and associates for the determination of the infrared and ultraviolet absorption spectra, and Mr. William Pearlman for carrying out the catalytic hydrogenations.