crystals: mp >350°; $\lambda_{max}^{0.1NHCl}$ 238, 266, 305 mμ (E_{max} 13,900, 10,000, 15,900); $\lambda_{max}^{0.1NNaCl}$ 226, 274 (sh), 305 mμ (E_{max} 13,550, 11,100, 16,300); $\lambda_{max}^{0.1NNaOH}$ 237, 318 mμ (E_{max} 18,660, 17,200).

Anal. Calcd for $C_{11}H_9N_5O \cdot 0.5H_2O \cdot HCl$: C, 48.4; H, 4.1; N, 25.7; Cl, 13.0. Found: C, 48.2; H, 4.1; N, 26.2; Cl, 12.7.

2-Amino-6-mercapto-9-phenylpurine.—To 50 ml of $POCl_3$, containing 5 ml of N,N-diethylaniline, was added 2.4 g of 2-amino-6-hydroxy-8-phenylpurine, and the mixture was heated under reflux for 5 hr. The $POCl_3$ was then removed *in vacuo*, and the residue was poured over crushed ice with vigorous stirring. The mixture was made strongly alkaline with 10 *N* KOH, allowed to stand for 20 min, and then shaken with two 100-ml portions of ether to remove the diethylaniline. The aqueous solution was acidified to pH 1 with concentrated HCl and cooled to 0°. The resulting precipitate was filtered and washed with water and acetone to give 2 g of product. The product was extracted from the crude material with 200 ml of absolute ethanol in a Soxhlet extractor for 24 hr. The ethanol solution was concentrated to about 30 ml, from which 1 g of light yellow solid, mp >350°, was obtained upon dilution with 120 ml of water. The 2-amino-6-chloro-8-phenylpurine was thiated without further purification.

To 50 ml of absolute ethanol, containing 2 g of thiourea, was added 1 g of 2-amino-6-chloro-8-phenylpurine, and the mixture was heated under reflux for 1 hr with stirring. The reaction mixture which became a clear solution at the end of that time was cooled to 4°. The crystalline product was isolated by filtration and washed with ethanol to give 1 g of yellow solid. The crude product was recrystallized from 300 ml of 1 *N* HCl, to give 0.9 g (91%) of yellow crystals: mp >350°; $\lambda_{max}^{0.1NHCl}$ 258, 275 (sh), 366 mμ (E_{max} 14,650, 12,300, 16,000); $\lambda_{max}^{0.1NNaOH}$ 246, 264, 349 mμ (E_{max} 18,150, 17,150, 20,200).

Anal. Calcd for $C_{11}H_9N_5S$: C, 54.3; H, 3.7; N, 28.8; S, 13.2. Found: C, 54.1; H, 3.9; N, 28.4; S, 13.3.

Biological Data.—A/JAX female mice weighing 18–20 g were used. The animals in groups of nine or ten, were sensitized and tested for antibody production by a modification of the method of Nathan, *et al.*[2c] Sheep red blood cells stored in Alsever's solution were washed three times with 0.15 *M* pH 7.2 buffered saline solution and a 30% cell suspension was made. Each mouse was given 0.25 ml of the suspension intravenously. Thirteen days later, the mice were bled from the ophthalmic venous plexus and the sera were pooled for each group.

6-MP and TG, in doses of 75 and 2 mg/kg, respectively, were used as standards. The dose levels for 8-PMP and 8-PTG ranged from 2 to 150 and 2 to 75 mg/kg, respectively. All four purine derivatives, both as suspensions in Tween 80 and as solutions in physiological saline achieved by the addition of minimum amounts of 0.1 *N* NaOH, were administered daily by intraperitoneal injection for the first 4 days of the sensitization period.

Before titration for antibody content, the mouse antisera were heated at 56° for 30 min to inactivate the complement. Serial twofold dilutions of antisera were made in diluted normal rabbit serum (1:100 with buffered saline). To each 0.5 ml of diluted antiserum was added 0.05 ml of washed sheep red cells (3%, in buffered saline). The antigen–antibody suspension was thoroughly mixed and allowed to stand at room temperature for 1 hr and then refrigerated for 18 hr. The hemagglutination titer was determined according to the method of Stavitsky.[12] The "antibody index" was calculated as described by Nathan, *et al.*[2c] For each experiment, a group of uninjected mice was included as an additional control. Their sera were always uniformly negative. Sheep cell injected mice not receiving the purine derivatives were the positive controls from which the antibody indices were obtained. The results are listed in Table I.

TABLE I

EFFECT OF MERCAPTOPURINES ON ANTIBODY PRODUCTION

Compd	Dose, mg/kg	Vehicle[a]	Toxicity[b]	Antibody index
None	...	A	1/9	0.97
None	...	A	2/10	0.80
6-MP	75	A	3/9	0.63
6-MP	75	B	3/30	0.25
6-TG	2	A	4/10	0.00
6-TG	2	B	0/10	0.05
8-PMP	2	A	1/9	1.39
8-PMP	10	A	3/9	1.31
8-PMP	75	B	3/10	0.83
8-PMP	150	B	2/10	0.83
8-PMP	150	A	1/10	0.80
8-PTG	2	A	4/10	1.45
8-PTG	10	A	1/10	0.97
8-PTG	10	B	8/9	*c*
8-PTG	20	A	3/10	1.12
8-PTG	25	A	2/9	0.86
8-PTG	50	B	7/9	1.00
8-PTG	75	B	8/9	*c*

[a] A = 13% Tween 80 in physiological saline. B = About 1 ml of 0.1 *N* NaOH was used to dissolve the purines in 6.5 ml of physiological saline. The final pH was 8.5–9.0. [b] Number of mice dead during experiment/number of mice used. [c] Insufficient quantity of serum for measurement.

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Heterocycles Containing (8-Hydroxy-5-methyl-7-quinolyl)vinyl Groups[1]

AL G. MUELLER AND J. P. PHILLIPS

Chemistry Department, University of Louisville, Louisville, Kentucky

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The reactions of 7-formyl-5-methyl-8-quinolinol with various N-methylated pyridines, quinolines, and related heterocycles having an active methyl group adjacent to the nitrogen yielded the compounds reported in Table I. As merocyanines, they are strongly colored and show considerable changes of color as a function of solvent as well as a tendency toward solvation. They were prepared as model compounds of the open form of some photochromic chelating agents,[2] but are themselves only solvatochromic chelating agents.[3]

As compared to a series of similar derivatives of 5-formyl-8-quinolinol,[4] these compounds were similarly rather toxic in cell culture tests, but only one showed any activity in the routine antitumor screen; this was compound **10** of Table I against Sarcoma 180.

The results of Cancer Chemotherapy National Service Center tests are given in Table II for those compounds that were most toxic.

Experimental Section

7-Formyl-5-methyl-8-quinolinol was prepared by Fiedler's method;[5] the appropriate heterocycles for reaction with it were N-methylated, usually with methyl iodide, by standard procedures.[6]

The general preparation of the compounds in Table I consisted in refluxing, for 4 hr, 0.01 molar quantities of 7-formyl-5-methyl-8-quinolinol with the appropriate N-methyl compound in 60 ml of absolute methanol containing 0.8 ml of piperidine. After cooling the solution, the precipitated product was filtered, washed with ether, dried, and recrystallized from methanol or ethanol.

In general, the lower the basicity of the heterocycle the higher the yield, and for compounds **4** and **5**, piperidine as a catalyst was

(1) This work was supported by a grant from the Public Health Service (CA 07403).

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(3) J. W. Faller and J. P. Phillips, *Anal. Chim. Acta*, **32**, 586 (1965).

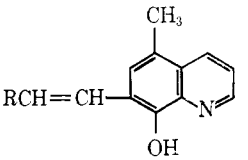
(4) A. Mueller and J. P. Phillips, *J. Med. Chem.*, **9**, 641 (1966).

(5) H. Fiedler, *Arch. Pharm.*, **293**, 609 (1960).

(6) A. B. Prescott, *Am. Chem. J.*, **18**, 91 (1896).

TABLE I

(8-HYDROXY-5-METHYL-7-QUINOLYL)VINYL COMPOUNDS



No.	R	Formula	Mp, °C[a]	Yield, %	—% carbon— Calcd	Found	—% hydrogen— Calcd	Found	—% nitrogen— Calcd	Found
1	1-Methyl-8-hydroxy-2-quinolinium methosulfate[b]	$C_{23}H_{22}N_2O_6S$	193	87					6.16	6.74
2	1-Methyl-5-ethyl-2-pyridinium iodide	$C_{20}H_{21}IN_2O \cdot 0.5H_2O$	250	31	54.43	54.62	5.03	4.87	6.35	6.23
3	1-Methyl-2-quinolinium iodide	$C_{22}H_{19}IN_2O$	242	72	58.16	58.01	4.21	4.20	6.17	6.03
4	3-Methyl-2-benzothiazolium iodide	$C_{20}H_{17}IN_2OS \cdot H_2O$	236	92	50.21	50.70	4.00	4.00	5.86	5.79
5	3-Methyl-2-benzoselenazolium iodide	$C_{20}H_{17}IN_2OSe$	234	81	47.35	47.02	3.38	3.43	5.52	5.50
6	1-Methyl-4-pyridinium iodide	$C_{18}H_{17}IN_2O$	309	57	53.48	53.43	4.24	4.26	6.93	6.97
7	1-Methyl-2-pyridinium iodide	$C_{18}H_{17}IN_2O$	255	43	53.48	53.15	4.24	4.10	6.93	7.01
8	1,6-Dimethyl-2-quinolinium iodide[c]	$C_{23}H_{21}IN_2O$	218	83					5.98	6.39
9	1-Methyl-6-ethoxy-2-quinolinium iodide	$C_{24}H_{23}IN_2O_2$	230	86	57.84	57.80	4.65	4.53	5.62	5.94
10	1-Methyl-4-quinolinium iodide	$C_{22}H_{19}IN_2O \cdot H_2O$	275	61	55.94	55.92	4.48	4.45	5.93	5.89
11	2-Methyl-1-isoquinolinium iodide	$C_{22}H_{19}IN_2O \cdot 0.5H_2O$	232	41	57.03	56.83	4.35	4.19	6.05	5.99

[a] All melting points were with decomposition. [b] The methosulfate was converted to the perchlorate hydroperchlorate, mp above 400°. *Anal.* Calcd for $C_{22}H_{20}Cl_2N_2O_{10}$: N, 5.16. Found: N, 4.95. [c] The iodide was converted to the perchlorate hydroperchlorate, mp 310°, which showed a correct analysis for C, H, and N.

TABLE II

CELL CULTURE TEST RESULTS[a]

No.[b]	ED_{50}, mg/ml	Slope
3	0.63	−0.21
5	4.2	−0.45
8	0.85	−0.79
9	1.40	−0.56
10	0.32	−2.22

[a] Testing by CCNSC on KB 90. [b] Numbers are the same as in Table I.

not even needed. Although full analytical data for 8-hydroxy-1-methyl-2-(8-hydroxy-5-methyl-7-quinolyl)vinylquinolinium methosulfate (**1**, Table I) were not obtained, it is included for comparison with a related compound previously reported.[4]

The Photosensitizing Activity of N,N′-Bis(*p*-formylphenyl)piperazine[1a]

S. N. THAMPI, F. W. SCHUELER,[1b] VERNON B. HAARSTAD,[1c]

Department of Pharmacology, School of Medicine, Tulane University, New Orleans, Louisiana

AND SILAS E. O'QUINN

Department of Dermatology, Louisiana State University School of Medicine, New Orleans, Louisiana

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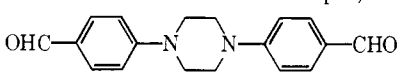
During the course of our continuing program in the polymerization of pharmacophoric moieties, we became interested in the synthesis of a series of piperazines that might be visualized as dimers of *para*-substituted dimethylaminobenzenes. For example, N,N′-bis(*p*-formylphenyl)piperazine (I) might be considered to be a "dimer" of *p*-dimethylaminobenzaldehyde. We proposed to use I as the starting material for the synthesis of this series, utilizing well-known schemes for the preparation of phenethylamines, α-amino acids, *etc.* Bayer[2] ascribes the preparation of I to a procedure patented by Wilson.[3] However, no mention of I was to be found in this patent, in *Chemical Abstracts*, or in Beilstein. Therefore, we decided to attempt its synthesis according to the general procedure described by Wilson.[3] This procedure is a modification of a method originally described by Vilsmier and Haack,[4] for formylation of N,N-disubstituted aromatic amines by a 1:1 complex of N,N-disubstituted formamides and phosphorus oxychloride. However, we found Wilson's conditions to be unsatisfactory. As might be expected, we found it necessary to exclude moisture carefully and to add the $POCl_3$ very slowly to the well-stirred mixture, initially kept at 0° and thereafter not allowed to rise above 20°. The subsequent neutralization step required careful stirring and cooling. Otherwise, a great deal of resinous material was formed. These precautions afforded I in 91% yield.



I

During the course of studies in the synthesis of derivatives of I, it was suspected that one (or all) of

(1) (a) This investigation was supported by a U. S. Public Health Service Research Grant No. CA-03037 from the National Cancer Institute. (b) Deceased. (c) To whom inquiries should be sent.

(2) O. Bayer in "Methoden der Organischen Chemie," Vol VII, E. Müller, Ed., Sauerstoff-Verbindungen II, Teil I, Georg Thieme Verlag, Stuttgart, 1954, p 32.

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(4) A. Vilsmier and A. Haack, *Chem. Ber.*, **60**, 119 (1927).