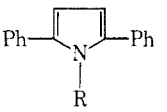
TABLE I
1-SUBSTITUTED 2,5-DIPHENYLPYRROLES



R	Method	Yield, %	Mp, °C	Formula	Analysis[c]
3-(N-Morpholino)propyl	A	40	78	$C_{23}H_{26}N_2O$	C, H
2-(N-Morpholino)ethyl	A	75	72	$C_{22}H_{24}N_2O$	C, H
3-Dimethylaminopropyl	A	38	48	$C_{21}H_{24}N_2$	C, H
2-Dimethylaminoethyl	A	68	54	$C_{20}H_{22}N_2$	C, H
2-(N-Methylpiperazino)ethyl	A	46	97	$C_{23}H_{27}N_3$	C, H
3-(N-Hydroxyethylpiperazino)propyl	A	35	92	$C_{25}H_{31}N_3O$	C, H
3-Diethylamino-2-hydroxypropyl	A	55	65	$C_{23}H_{28}N_2O$	C, H
4-Dimethylaminophenyl	B	82	216	$C_{24}H_{22}N_2$	C, H
3-N-Methyl-N-phenylaminopropyl	A	68	84	$C_{26}H_{26}N_2$	C, H, N
3-(2-Hydroxyethylamino)propyl	A	89	38	$C_{21}H_{24}N_2O$	C, H
Amino[a]		14	155[b]	$C_{16}H_{14}N_2$	C, H, N
2-Aminoethyl	C	73	78	$C_{18}H_{18}N_2$	C, H
3-Aminopropyl	C	80	82	$C_{19}H_{20}N_2$	C, H
4-Aminobutyl·HCl	C	23	143	$C_{20}H_{22}N\cdot HCl$	C, H, Cl
2,3-Dihydroxypropyl	C	87	108	$C_{19}H_{19}NO_2$	C, H
3-Hydroxypropyl	C	72	56	$C_{19}H_{19}NO$	C, H
2-Hydroxyethyl	C	75	105	$C_{18}H_{17}NO$	C, H
Acetamido	A	32	212[b]	$C_{18}H_{16}N_2O$	C, H, N

[a] Acidic hydrolysis. [b] The preparation of these compounds has been previously reported by H. Beyer, T. Pyl, and C. E. Volker, *Ann.*, **638**, 150 (1960), by a different method. They gave 214° as the melting point of the 1-amino compound and 137° for its acetyl derivative. [c] Compounds were analyzed for the elements indicated. The analytical results obtained for those elements were within ±0.3% of the theoretical values.

The crude product separated as an oil when the acidic extract was made basic with NaOH. Upon cooling, the oil solidified and was isolated by filtration. After being dried over KOH, the crude product was either sublimed at reduced pressure or recrystallized from 3:1 C_6H_6–hexane.

Method B.—A mixture of 0.05 mole of 1,4-diphenyl-1,4-butanedione and 0.08 mole of N,N-dimethyl-*p*-phenylenediamine was heated under N_2 for 3 hr at 160–170°. The cooled, amorphous reaction product was triturated with Et_2O and then filtered. The residue was dissolved in toluene and treated with 250 ml of 0.1 *N* HCl to give the crude product as the hydrochloride. The filtered amine hydrochloride was dissolved in hot H_2O to which Na_2CO_3 was then added. The product was recrystallized from 5:1 C_6H_6–Et_2O.

Method C.—A mixture of 0.05 mole of 1,4-diphenyl-1,4-butanedione, 0.25 mole of the amine, and 100 ml of ethylene glycol was refluxed for 2 hr. The cooled mixture was diluted with 500 ml of H_2O, extracted once with C_6H_6, and then made strongly basic. The crude product separated as an oil and slowly solidified. Purification was accomplished by recrystallization from 3:1 C_6H_6–hexane.

Some 6,8-Dibromo-S-substituted-2-mercapto-3-aryl- (or alkyl-) 4-quinazolones

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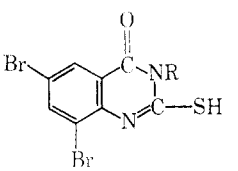
In view of the broad spectrum of biological activities associated with 4-quinazolones,[1-5] it seemed of interest to synthesize 6,8-dibromo-3-aryl- (or alkyl-) S-substituted-2-mercapto-4-quinazolones and evaluate them for their antimalarial activity. Their syntheses by condensation of 3,5-dibromoanthranilic acid[6] and aryl (or alkyl) isothiocyanates followed by alkylation with alkyl halides is reported in this communication. None of the compounds tested showed any chemotherapeutic activity in standard tests in chicks infected with *Plasmodium gallinaceum*.

Experimental Section

6,8-Dibromo-2-mercapto-3-phenyl-4-quinazolone.—A mixture of phenyl isothiocyanate (6.00 ml), 3,5-dibromoanthranilic acid

TABLE I
6,8-DIBROMO-2-MERCAPTO-3-ARYL- (OR ALKYL-) 4-QUINAZOLONES



R	% yield	Mp, °C	Formula[a]
C_6H_5	98	298 dec	$C_{14}H_8Br_2N_2OS$
o-$CH_3C_6H_4$	85	225	$C_{15}H_{10}Br_2N_2OS$
m-$CH_3C_6H_4$	95	215	$C_{15}H_{10}Br_2N_2OS$
p-$CH_3C_6H_4$	94	305 dec	$C_{15}H_{10}Br_2N_2OS$
m-ClC_6H_4	90	218	$C_{14}H_7Br_2ClN_2OS$
p-ClC_6H_4	98	207	$C_{14}H_7Br_2ClN_2OS$
o-$OCH_3C_6H_4$	75	235	$C_{15}H_{10}Br_2N_2O_2S$
p-$OCH_3C_6H_4$	87	228	$C_{15}H_{10}Br_2N_2O_2S$
p-$OC_2H_5C_6H_4$	90	222	$C_{16}H_{12}Br_2N_2O_2S$
CH_3	95	229	$C_9H_6Br_2N_2OS$
C_2H_5	80	180	$C_{10}H_8Br_2N_2OS$
n-C_4H_9	96	234	$C_{12}H_{12}Br_2N_2OS$
$C_6H_5CH_2$	88	228	$C_{15}H_{10}Br_2N_2OS$

[a] All compounds were analyzed for N, S, and the analytical results were within ±0.3% of the theoretical values.

(1) F. J. Wolf, U. S. Patent, 2,473,931 (1949); *Chem. Abstr.*, **43**, 7042 (1949).
(2) B. R. Baker, F. J. McEvoy, R. E. Schaub, J. P. Joseph, and J. H. Williams, *J. Org. Chem.*, **18**, 178 (1953).
(3) M. L. Gujral, P. N. Saxena, and R. S. Tiwari, *Indian J. Med. Res.*, **43**, 637 (1955); *Chem. Abstr.*, **50**, 662 (1956).
(4) Br. Pawlewski, *Ber.*, **38**, 131 (1905).
(5) T. N. Ghosh, *J. Indian Chem. Soc.*, **7**, 981 (1930).
(6) A. S. Wheeler and W. M. Oates, *J. Am. Chem. Soc.*, **32**, 770 (1910).

(16.00 g), and absolute EtOH (70.00 ml) was refluxed for 6 hr. The product was washed with EtOH, dissolved in 10% NaOH, precipitated with HCl, washed several times with H_2O, and dried. It was crystallized from EtOH.

TABLE II

6,8-DIBROMO-2-*p*-XYLYLTHIO-3-ARYL- (OR ALKYL-) 4-QUINAZOLONES

R	% yield	Mp, °C	Formula[a]
C_6H_5	50	187	$C_{22}H_{16}Br_2N_2OS$
o-$CH_3C_6H_4$	55	139	$C_{23}H_{18}Br_2N_2OS$
m-$CH_3C_6H_4$	60	181	$C_{23}H_{18}Br_2N_2OS$
p-$CH_3C_6H_4$	45	145	$C_{23}H_{18}Br_2N_2OS$
m-ClC_6H_4	60	165	$C_{22}H_{15}Br_2ClN_2OS$
p-ClC_6H_4	56	152	$C_{22}H_{15}Br_2ClN_2OS$
p-$OCH_3C_6H_4$	50	182	$C_{23}H_{18}Br_2N_2O_2S$
p-$OC_2H_5C_6H_4$	55	166	$C_{24}H_{20}Br_2N_2O_2S$
CH_3	60	124	$C_{17}H_{14}Br_2N_2OS$
C_2H_5	65	140	$C_{18}H_{16}Br_2N_2OS$
n-C_4H_9	45	120	$C_{20}H_{20}Br_2N_2OS$
$C_6H_5CH_2$	70	151	$C_{23}H_{18}Br_2N_2OS$

[a] See Table I, footnote *a*.

TABLE III

6,8-DIBROMO-2-*n*-BUTYLTHIO-3-ARYL- (OR ALKYL-) 4-QUINAZOLONES

R	% yield	Mp, °C	Formul .[a]
C_6H_5	70	185	$C_{18}H_{16}Br_2N_2OS$
o-$CH_3C_6H_4$	40	215	$C_{19}H_{18}Br_2N_2OS$
m-$CH_3C_6H_4$	48	190	$C_{19}H_{18}Br_2N_2OS$
p-$CH_3C_6H_4$	60	235	$C_{19}H_{18}Br_2N_2OS$
m-ClC_6H_4	55	250	$C_{18}H_{15}Br_2ClN_2OS$
p-ClC_6H_4	58	270 dec	$C_{18}H_{15}Br_2ClN_2OS$
o-$OCH_3C_6H_4$	45	265 dec	$C_{18}H_{18}Br_2N_2O_2S$
p-$OCH_3C_6H_4$	54	252	$C_{19}H_{18}Br_2N_2O_2S$
p-$OC_2H_5C_6H_4$	50	248 dec	$C_{20}H_{20}Br_2N_2O_2S$
CH_3	55	270 dec	$C_{13}H_{14}Br_2N_2OS$
C_2H_5	60	225 dec	$C_{14}H_{16}Br_2N_2OS$
n-C_4H_9	52	255 dec	$C_{16}H_{20}Br_2N_2OS$
$C_6H_5CH_2$	60	265 dec	$C_{19}H_{18}Br_2N_2OS$

[a] See Table I, footnote *a*.

TABLE IV

6,8-DIBROMO-2-ALLYLTHIO-3-ARYL- (OR ALKYL-) 4-QUINAZOLONES

R	% yield	Mp, °C	Formula[a]
C_6H_5	50	276	$C_{17}H_{12}Br_2N_2OS$
o-$CH_3C_6H_4$	48	152	$C_{18}H_{14}Br_2N_2OS$
m-$CH_3C_6H_4$	45	222	$C_{18}H_{14}Br_2N_2OS$
p-$CH_3C_6H_4$	52	275 dec	$C_{18}H_{14}Br_2N_2OS$
m-ClC_6H_4	42	255 dec	$C_{17}H_{11}Br_2ClN_2OS$
p-ClC_6H_4	53	236 dec	$C_{17}H_{11}Br_2ClN_2OS$
p-$OCH_3C_6H_4$	54	215	$C_{18}H_{14}Br_2N_2O_2S$
p-$OC_2H_5C_6H_4$	60	157	$C_{19}H_{16}Br_2N_2O_2S$
CH_3	45	282 dec	$C_{12}H_{10}Br_2N_2OS$
C_2H_5	68	115	$C_{13}H_{12}Br_2N_2OS$
n-C_4H_9	40	199	$C_{15}H_{16}Br_2N_2OS$
$C_6H_5CH_2$	65	135	$C_{18}H_{14}Br_2N_2OS$

[a] See Table I, footnote *a*.

Similarly, various 6,8-dibromo-2-mercapto-3-aryl- (or alkyl-) 4-quinazolones were prepared from the corresponding aryl (or alkyl) isothiocyanates and 3,5-dibromoanthranilic acid (see Table I).

6,8-Dibromo-2-ethylthio-3-phenyl-4-quinazolone.—To a solution of NaOH (5.00 g) in 85 ml of 50% EtOH–H_2O, 6,8-dibromo-2-mercapto-3-phenyl-4-quinazolone (7.50 g) was added. The solution was stirred, filtered, and treated with EtI (4.00 ml). After being stirred for another hour, the crystalline product was washed (H_2O, EtOH). Long needles were obtained on crystallization from EtOH, mp 230°.

Similarly, various 6,8-dibromo-S-substituted-2-mercapto-3-aryl- (or alkyl-) 4-quinazolones have been prepared (see Tables II–V).

TABLE V

6,8-DIBROMO-2-ISOPROPYLTHIO-3-ARYL- (OR ALKYL-) 4-QUINAZOLONES

R	% yield	Mp, °C	Formula[a]
C_6H_5	65	248 dec	$C_{17}H_{14}Br_2N_2OS$
o-$CH_3C_6H_4$	57	273 dec	$C_{18}H_{16}Br_2N_2OS$
m-$CH_3C_6H_4$	50	268 dec	$C_{18}H_{16}Br_2N_2OS$
p-$CH_3C_6H_4$	60	265 dec	$C_{18}H_{16}Br_2N_2OS$
m-ClC_6H_4	40	263 dec	$C_{17}H_{13}Br_2ClN_2OS$
p-ClC_6H_4	38	222 dec	$C_{17}H_{13}Br_2ClN_2OS$
o-$OCH_3C_6H_4$	30	262 dec	$C_{18}H_{16}Br_2N_2O_2S$
p-$OCH_3C_6H_4$	55	266 dec	$C_{18}H_{16}Br_2N_2O_2S$
p-$OC_2H_5C_6H_4$	41	98	$C_{19}H_{18}Br_2N_2O_2S$
CH_3	45	264 dec	$C_{12}H_{12}Br_2N_2OS$
C_2H_5	35	258 dec	$C_{13}H_{14}Br_2N_2OS$
n-C_4H_9	32	255 dec	$C_{15}H_{18}Br_2N_2OS$
$C_6H_5CH_2$	54	275 dec	$C_{18}H_{16}Br_2N_2OS$

[a] See Table I, footnote *a*.

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Schiff Bases Containing Quinoline Rings[1]

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Schiff bases listed in Table I were prepared by heating equal molar quantities (0.03 mole) of aldehyde and amine in a hot oil bath at 130° for 1 hr. After cooling each mixture, the product was extracted with hot isohexane[2] and separated in crystal form upon cooling. One of the compounds showed activity against tumor cells *in vitro*. None of them was effective against Walker 256 tumors in rats (see Table I on the following page).

(1) This investigation was supported by Public Health Service Research Grants No. CA-03717-08-9 from the National Cancer Institute.

(2) A mixture of isomeric branched hexanes.