(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	Formula[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.

TABLE I

No.	Deriv of quinoline	Yield, %	Mp, °C[a]	Formula[b]	Ultraviolet $\lambda_{max}^{alcohol}$, mμ (log ε)	KB cell test ED_{50},[c] μg/ml	Effect[d] Tumor wt mg/kg	T/C	Lethality No. mg/kg	Lethality No. Killed
1	3-[(2-Pyridylmethylene)-amino]-	77	110–111[e]	$C_{15}H_{11}N_3$	214 (4.5)	29	100	1.3	250	2/3
2	3-[(3-Pyridylmethylene)-amino]-	65	87–88[f]	$C_{15}H_{11}N_3$	241 (4.6)	>100	100	1.4	250	2/3
3	3-[(4-Pyridylmethylene)-amino]-	70	87–88[g]	$C_{15}H_{11}N_3$	209 (4.5)	33	100	0.8	625	1/2
4	2,3′-(Methylidynenitrilo)di-	90	173–174[h]	$C_{19}H_{13}N_3$	240 (4.7)	28	1500	1.1	(500	0/3
5	4,3′-(Methylidynenitrilo)di-	85	125	$C_{19}H_{13}N_3$	208 (4.7)	2.0[i]	250	0.7	625	1/3
6	2-(N-3-Pyridylformimidoyl)-	56	93–94	$C_{15}H_{11}N_3$	209 (4.6)	29	100	1.1	250	2/3

[a] Corrected for thermometer stem exposure; determined with Thiele tube. [b] Average of two analyses by Galbraith Laboratories. All compounds were analyzed for C and H. Analytical results for these elements were within ±0.4% of the theoretical values. [c] Results of the standard *in vitro* KB tumor cell inhibition tests carried out under sponsorship of the Cancer Chemotherapy National Service Center at Southern Research Institute. [d] We are grateful to Professor Alexander Haddow, Mr. J. E. Everett, and Mr. C. V. Mitchley of the Chester Beatty Research Institute for data on toxicity and activity against the Walker 256 tumor in rats weighing 200–250 g. Each compound was administered as a single intraperitoneal injection in Arachis oil on the day following tumor implantation or on the first day of the toxicity observation. Tumor-bearing animals were sacrificed approximately 8 days later and the average weights of tumors in treated and untreated hosts are reported as the ratio T/C. [e] All compounds are yellow unless otherwise indicated. [f] White. [g] After extracting impurities with isohexane, the crude quinoline, 3-[(4-pyridylmethylene)amino]-, was dissolved in benzene and chromatographed on Florisil. The pure product was obtained by eluting from the column with benzene. [h] Recrystallized from C_6H_6–*i*-PrOH. [i] ED_{50} against H2 cells, 0.66 μg/ml; inactive against L1210 in mice at 400 mg/kg ip.

Optical Resolution of Iodopanoic Acid

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In connection with a study on physicochemical properties of X-ray contrast media the two enantiomers of (±)-α-ethyl-β-(3-amino-2,4,6-triiodophenyl)propionic acid (iodopanoic acid) were prepared. Optical resolution was carried out by Marckwald's technique,[1] operating in EtOH solution with (−)- and (+)-α-phenethylamine.

Experimental Section

(±)-α-Ethyl-β-(3-amino-2,4,6-triiodophenyl)propionic acid (57.1 g, 0.1 mole) and 12.1 g (0.1 mole) of (−)-α-phenylethylamine were dissolved in 700 ml of boiling 95% EtOH. After decoloration with active charcoal, the solution was kept overnight at room temperature. The (−)-α-phenylethylamine salt was filtered off (29 g), mp 162–163°, $[\alpha]^{20}D$ −4.0° (*c* 2, EtOH). The mother liquor was used for recovery of the optical isomer. Recrystallization from EtOH gave 10.5 g of crystals, mp 167°, $[\alpha]^{20}D$ −4.0° (*c* 2, EtOH) (30% over-all).

(1) W. Marckwald, *Chem. Ber.*, **29**, 43 (1896).

Anal. Calcd for $C_{19}H_{20}I_3N_2O_2$: C, 32.97; H, 3.25; I, 55.01. Found: C, 33.00; H, 3.29; I, 54.95.

The mother liquor containing the (−)-α-phenethylamine salt was evaporated to dryness. The residue was stirred with 500 ml of 4% NaOH solution and (−)-α-phenethylamine was extracted with four 50-ml portions of ether. After acidification with HCl, 29 g of (+)-α-ethyl-β-(3-amino-2,4,6-triiodophenyl)-propionic acid, mp 75–110°, $[\alpha]^{20}D$ +3.1 (*c* 2, EtOH), was obtained. This acid (28.6 g, 0.05 mole) and 6.05 g (0.05 mole) of (+)-α-phenethylamine were dissolved in 600 ml of boiling EtOH and the solution was allowed to crystallize at room temperature overnight. This gave 17 g of salt, mp 166–167, $[\alpha]^{20}D$ +3.6 (*c* 2, EtOH). After further crystallization from 240 ml of EtOH, we obtained 12.2 g of white crystals, mp 167°, $[\alpha]^{20}D$ +4.1 (*c* 2, EtOH) (35%).

Anal. Calcd for $C_{19}H_{20}I_3N_2O_2$: C, 32.97; H, 3.35; I, 55.01. Found: C, 32.88; H, 3.49; I, 54.75.

(−)-α-Ethyl-β-(3-amino-2,4,6-triiodophenyl)propionic Acid. — The (−)-α-phenethylamine salt (8.2 g) was dissolved in 280 ml of 7% NaOH solution and extracted with three 50-ml portions of ether. The water solution was acidified with HCl, and the acid was filtered, washed (H_2O), and crystallized from 40 ml of AcOH: yield 6 g, mp 162–163°, $[\alpha]^{20}D$ −5.2 ± 0.1° (*c* 2, EtOH).

Anal. Calcd for $C_{11}H_{12}I_3NO_2$: C, 23.14; I, 66.68. Found: C, 23.15; I, 66.80.

(+)-α-Ethyl-β-(3-amino-2,4,6-triiodophenyl)propionic acid was obtained in the same way as the (−) form, operating on the other enantiomeric salt. From 10 g of salt was obtained 6.9 g of (+) acid, mp 162°, $[\alpha]^{20}D$ +5.1 ± 0.1° (*c* 2, EtOH).

Anal. Calcd for $C_{11}H_{12}I_3NO_2$: C, 23.14; I, 66.68. Found: C, 23.14; I, 66.70.