

TABLE I

No.	Deriv. of quinoline	Yield, %	Mp, °C ^c	Formula ^b	Ultraviolet λ _{max} ^{abs} , mμ (log ε)	KB cell test ED ₅₀ ^d μg/5ml	—Effect ^e — Tumor wt mg/kg	—Toxicity— T/C	—Lethality— mg/kg (killed)	—No.
1	3-[(2-Pyridylmethylene)- amino]-	77	110–111 ^e	C ₁₅ H ₁₁ N ₂	214 (4.5)	29	100	1.3	250	2/3
2	3-[(3-Pyridylmethylene)- amino]-	65	87–88 ^f	C ₁₅ H ₁₁ N ₂	211 (4.6)	>100	100	1.4	250	2/3
3	3-[(4-Pyridylmethylene)- amino]-	70	87–88 ^g	C ₁₅ H ₁₁ N ₂	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	210 (4.7)	28	1500	1.1	1500	0/3
5	4,3'-(Methylidynenitrilo)di-	85	125	C ₁₉ H ₁₃ N ₃	208 (4.7)	2.0 ⁱ	250	0.7	125	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. Minchley 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 were 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 C₆H₆-*i*-PrOH. ⁱ ED₅₀ 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°, [α]_D²⁰ –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°, [α]_D²⁰ –4.0° (c 2, EtOH) (30% over-all).

Anal. Calcd for C₁₅H₂₃I₃N₂O₂: 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°, [α]_D²⁰ +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°, [α]_D²⁰ +3.6 (c 2, EtOH). After further crystallization from 240 ml of EtOH, we obtained 12.2 g of white crystals, mp 167°, [α]_D²⁰ +4.1 (c 2, EtOH) (35%).

Anal. Calcd for C₁₅H₂₃I₃N₂O₂: 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 (H₂O), and crystallized from 40 ml of AcOH; yield 6 g, mp 162–163°, [α]_D²⁰ –5.2 ± 0.1° (c 2, EtOH).

Anal. Calcd for C₁₅H₂₃I₃N₂O₂: 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°, [α]_D²⁰ +5.1 ± 0.1° (c 2, EtOH).

Anal. Calcd for C₁₅H₂₃I₃N₂O₂: C, 23.14; I, 66.68. Found: C, 23.14; I, 66.70.

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