azole[9]] were carried out by previously published procedures, as indicated.

1,4-Dimethyl-5-nitro-2-piperidinoimidazole (5).—A soln of 11.5 g (0.054 mole) of 2-bromo-1,4-dimethyl-5-nitroimidazole (4) and 37.5 ml (*ca.* 0.35 mole) of piperidine in 1 l. of abs EtOH was refluxed for 1 hr and the solvent was removed. The residue was dissolved in 200 ml of petr ether (bp 30–60°) and chilled to give **5** (10.5 g), mp 74–76.5°.

2-Amino-1,4-dimethyl-5-nitroimidazole (6).—A soln of **4** (25 g; 0.117 mole) in 80 ml of satd ammoniacal abs EtOH was heated for 16 hr at 75° in a sealed glass tube. The product crystd during the course of the reaction. Filtration of the solid gave 14.9 g of material which was recrystd from $MeNO_2$ to give **6**, mp 220° dec.

2-Acetamido-1,4-dimethyl-5-nitroimidazole (7).—A mixt of **6** (9 g; 0.058 mole) and 60 ml of AcCl was heated in a sealed glass tube at 100° for 6 hr during which time the solid gradually dissolved. Excess AcCl was evapd, and the residue was treated with aq $NaHCO_3$ and extd with $CHCl_3$. Removal of the solvent gave crude **7** (3.5 g), which was crystd from *i*-PrOH to give pure material, mp 165–167.5°.

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(9) R. W. Liggett and H. L. Hoffman, Jr., U. S. Patent 3,030,376 (1962).

Potential Antimalarials. 6. Some 2-Phenyl-6- and -8-quinolinemethanols[1,2] and 8-Phenyl-4-quinolinemethanols

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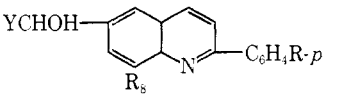
The aliphatic side chain of the 2-aryl-4-quinolinemethanols, 2-ArQCHOHCH$_2$NR$_2$ (Q = quinoline), potent but phototoxic antimalarials, has been placed in the 5,[4] 7,[1] 8,[5] and 3 positions.[6] Testing results for these compds indicate that activity and phototoxicity are for the most part inseparable with the possible exception of 6-chloro-8-(2-dibutylamino-1-hydroxyethyl)-2-(4-chlorophenyl)quinoline, the activity of which was low but the phototoxicity nil.[5] This paper completes the series in which the side chain is placed at the 6 position and, in 2 compds, at the 8 position. All these compds, the syntheses of which are described in the Experimental Section, have a low order of activity (see Tables I and II) and are no longer of interest as antimalarials.

Since the above approach to separation of antimalarial activity and phototoxicity had failed, it seemed feasible to place the aryl group at the 8 position (rather than the 2 position) and still retain blocking of the metabolic degradation of antimalarials without 2-aryl groups[7] on the assumption that degradation is a multi-center process involving the heterocyclic N. The results of testing compds of such a structure are shown in Table III. They indicate that the 8-phenyl-4-quinolinemethanol structure is promising as an antimalarial provided activity can be increased. Modification of the 8-Ph group may produce such an increase.

TABLE I

ACTIVITIES OF 6-QUINOLINEMETHANOLS

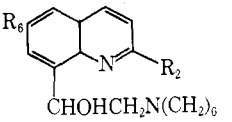


No.	Y	R_8	R	Dose, mg/kg	ΔMST,[b] days
4a[a]	$CH_2N(C_4H_9)_2$	Cl	H	320	7.4
4b	$CH_2N(CH_2)_5$	Cl	H	640	0.8
4c	$CH_2N(CH_2)_6$	Cl	H	640	1.6
9	$CH_2N(CH_2)_6$	CH_3	CH_3	320	1.0
11	$CH_2N(CH_2)_6$	CH_3	H	640	0.1
12	α-C_5H_4N (α-Pyridyl)	CH_3	H	640	0.4

[a] Phototoxic at 50 mg/kg. All activities were supplied by the Walter Reed Army Institute of Research. [b] Increased mean survival time in *P. berghei* test.

TABLE II

ACTIVITIES OF 8-QUINOLINEMETHANOLS[a]

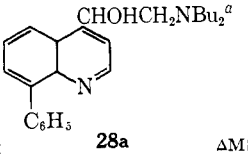


No.	R_2	R_6	Dose, mg/kg	ΔMST, days
16	C_6H_5	CH_3	640	1.2
17[b]	H	C_6H_5	640	0.1
	Quinine		640	7.1

[a] All activities were supplied by the Walter Reed Army Institute of Research. [b] Tested as the dihydrochloride.

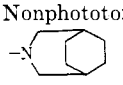
TABLE III

ACTIVITIES OF 8-PHENYL-4-QUINOLINEMETHANOLS



28a

Dose, mg/kg	ΔMST, days
40	0.3
80	2.7
160	4.3
320	6.9
640	2 cures

[a] Nonphototoxic at 50 mg/kg. If the NBu_2 group is replaced by  group, giving **28b**, the ΔMST drops to 0.

Experimental Section[8]

8-Chloro-2-phenyl-6-quinolinemethanols (4a, b, and c). 8-Chloro-6-methyl-2-phenylquinoline (1).—To a stirred, refluxing

(1) Paper 5: L. C. Washburn, T. G. Barbee, Jr., and D. E. Pearson, *J. Med. Chem.*, **13**, 1004 (1970).

(2) Contribution No. 893 to the Army Research Program on Malaria.

(3) Taken in part from the Ph.D. thesis of T. G. B.

(4) E. R. Atkinson and A. J. Puttick, *J. Med. Chem.*, **13**, 537 (1970); I. C. Popoff and C. B. Thanawalla, *ibid.*, **13**, 1002 (1970).

(5) J. S. Gillespie, Jr., S. P. Acharya, R. E. Davis, and B. K. Barman, *ibid.*, **13**, 860 (1970).

(6) R. E. Lutz, C. J. Ohnmacht, Jr., and F. Davis, *ibid.*, **14**, 17 (1971).

(7) A. Burger, "Medicinal Chemistry," Interscience, New York, N. Y., 1960, p 824.

(8) Analyses, by Galbraith Laboratories, Knoxville, Tenn., are within ±0.4% and are recorded with the Editor. Melting points are uncorrected and were taken with A. H. Thomas Uni-Melt apparatus. Nmr spectra of new compounds were compatible with the related structure and are on file with the authors.

soln of 1 mole of 2-chloro-4-toluidine·HCl in 1 l. of EtOH, 1.5 moles of cinnamaldehyde was added dropwise in 24 hr, and the mixt was poured into H_2O and extd with C_6H_6. The C_6H_6 residue was stirred and heated with 500 ml of concd HCl for 30 min and extd with CH_2Cl_2, and the acid layer was made basic with aq NaOH and extd with Et_2O. The Et_2O residue was recrystd from MeOH giving yellow plates, 50 g, 20%, mp 95–95.5°. *Anal.* ($C_{16}H_{12}ClN$) C, H, N.

8-Chloro-2-phenylquinoline-6-carboxaldehyde (**2**) was made by the Sommelet reaction.[9] The intermediate quaternary salt from $(CH_2)_6N_4$ was a granular solid, mp 185–188° dec, gas. The aldehyde **2** was obtd as slightly yellow-colored needles from EtOH, mp 153.5–154°, 46%. *Anal.* ($C_{16}H_{10}ClNO$) C, H, Cl. The thiosemicarbazone of **2** was obtd in the form of yellow, shiny plates, mp 240–241° dec. *Anal.* ($C_{17}H_{13}ClN_4S$) N. It was inactive in the *Plasmodium berghei* test.

8-Chloro-6-epoxyethyl-2-phenylquinoline (**3**).—The epoxide **3** was made from **2** and $(CH_3)_2S{=}CH_2$ as described previously.[1] It was obtd from MeOH as colorless cryst, mp 99–100°, 61.5%. *Anal.* ($C_{16}H_{12}ClNO$) C, H, N.

8-Chloro-6-(2-dibutylamino-1-hydroxyethyl)-2-phenylquinoline (**4a**).—Five g of **3** and 20 ml of $(C_4H_9)_2NH$ were heated at 128° for 6 hr, and the mixt was steam-distd to remove excess amine. The residue was extd into 10% HCl from Et_2O and repptd with NH_4OH. This process was repeated. The free base then was chromatogd on neutral alumina using Et_2O–C_6H_{14} as the eluting solvents. The free base was obtd as a pale yellow oil in 44% yield. *Anal.* ($C_{25}H_{31}ClN_2O$) C, H, Cl, N. The picrate of **4a** had a mp of 180.5–181.5°.

8-Chloro-6-(2-*N*-piperidino-1-hydroxyethyl)-2-phenylquinoline (**4b**) was made from piperidine and **3** as in the prep of **4a** except that the solid free base was recrystd from EtOH giving colorless, small crystals, mp 127–128°, 67%. *Anal.* ($C_{22}H_{23}ClN_2O$) C, H, N.

8-Chloro-6-(2-*N*-homopiperidino-1-hydroxyethyl)-2-phenylquinoline (**4c**) was made from **3** and hexamethyleneimine as in the prep of **4a**. It was recrystd from EtOH (decolorizing C) to give colorless plates, mp 106–107°. 57%. *Anal.* ($C_{23}H_{25}ClN_2O$) C, H, N. The HCl salt melted at 261–263° dec.

6-(2-*N*-Homopiperidino-1-hydroxyethyl)-8-methyl-2-*p*-tolylquinoline (**9**).—The following intermediates led to the preparation of **9**.

6-Bromo-8-methyl-2-(*p*-tolyl)-4-quinolinecarboxylic Acid (**5**).—5-Bromo-7-methylisatin[10] (0.33 mole), *p*-methylacetophenone (0.38 mole), 200 ml of 33% aq KOH, and 400 ml of EtOH were refluxed for 24 hr. The solvent was allowed to evap, and the resulting solid was filtered and washed with C_6H_6 until it was free of a blood-red color. The crude K salt was dissolved with difficulty in hot H_2O, and filtered while hot, and concd HCl was added to the hot, clear filtrate. The acid, **5**, was pptd as a light yellow solid, 52 g, 29%, recrystd from EtOAc, mp 283.5–286°. *Anal.* ($C_{18}H_{14}BrNO_2$) C, H. The same acid was made in 5% yield by the Doebner method.[11]

6-Bromo-8-methyl-2-*p*-tolylquinoline (**6**).—A mixt of **5** (0.056 mole) in 300 ml of $(C_6H_5)_2O$ was refluxed for 24 hr, cooled, dild with 500 ml of Et_2O, and filtered. The filtrate was satd with HCl gas, and the yellow-green salt (9.8 g, 50%) was filtered off and washed with cold Et_2O. The salt was suspended in Et_2O and treated with 15% aq NH_4OH with stirring. The dark brown Et_2O layer was sepd, combined with a second Et_2O wash of the H_2O layer, dried, and evapd. The brown solid was recrystd from EtOH (decolorizing C) to yield 72% of light yellow needles, mp 118.5–120°. *Anal.* ($C_{17}H_{14}BrN$) C, H.

8-Methyl-2-*p*-tolylquinoline-6-carboxaldehyde (**7**) was made from **6** in 74% yield by the method of Wommack, *et al.*,[12] yellow needles, mp 158.5–160.5°, from EtOAc. *Anal.* ($C_{18}H_{15}NO$) C, H.

6-Epoxyethyl-8-methyl-2-*p*-tolylquinoline (**8**).—The epoxide was made from **7** in the same manner as **3**. It was obtd in 99% crude yield and after recryst from EtOH–H_2O (decolorizing C), was a light yellow powder, mp 124.5–127°. *Anal.* ($C_{19}H_{17}NO$) C, H.

9.—The epoxide **8** was treated with hexamethylenimine in the same manner as in **4c**. After recryst from C_6H_{14} (decolorizing C) and a second from MeCN 1.6 g, 49%, of white needles, mp 126–127°, was obtained. *Anal.* ($C_{25}H_{30}N_2O$) C, H, N.

6-(2-*N*-Homopiperidino-1-hydroxyethyl)-8-methyl-2-phenylquinoline (**11**). **6-Epoxyethyl-8-methyl-2-phenylquinoline** (**10**).—The epoxide was made from 8-methyl-2-phenylquinoline-6-carboxaldehyde[12] in the same manner as **3**. It was obtd as a yellow solid which, recrystd from EtOH, gave white tufts, mp 90.5–91.5°, 75% yield. *Anal.* ($C_{18}H_{15}NO$) C, H, N.

11.—The epoxide, **10**, was treated in the same manner as in **4c**, and the free base, after recryst from EtOH (decolorizing C), gave white needles, mp 97–98°, 72%. *Anal.* ($C_{24}H_{28}N_2O$) C, H, N.

2-Arylquinoline-6-α-pyridylmethanols.—These compds were made for the purpose of obtg α-piperidinomethanols by selective reduction of the pyridine ring using the method of Boykin and Lutz.[13] In this series, however, the selective reduction failed because of concomitant reduction of the quinoline ring.

8-Methyl-2-phenylquinoline-6-α-pyrimidylmethanol (**12**).—Under N_2, to a stirred soln of 0.012 mole of C_4H_9Li (22% in C_6H_{14}) in 130 ml of 1:1 Et_2O–THF at −70° was added a soln of 0.012 mole of 6-bromo-8-methyl-2-phenylquinoline in 20 ml of Et_2O–THF (precooled to −70°). The temp rose to −60° as the mixt turned orange. After 45 min, 0.012 mole of 2-pyridinecarboxaldehyde was added. The soln was stirred 3 hr at −70° while a purple color developed which faded to a light orange. It was poured into H_2O and extd with Et_2O, and the ext was washed, dried, and concd. Recryst of the residue from MeOH gave 0.7 g of the original bromoquinoline, and concn of the filtrate to half-vol gave **12** which, recrystd from MeCN, gave white needles, 2.1 g, 52%, mp 143–144.5°. *Anal.* ($C_{22}H_{18}N_2O$) C, H, N.

6-Bromo-2-(*p*-chlorophenyl)-8-methylquinoline (**13**).—*p*-Chlorophenyllithium was prepd by adding 0.022 mole of BuLi to 0.2 mole of *p*-chlorobromobenzene in 500 ml of refluxing Et_2O. Exactly 10 min after completion of addn, 0.02 mole of 6-bromo-8-methylquinoline was added all at once as a ground solid and the dark green soln refluxed 1 hr becoming light yellow-green. EtOH (30 ml) and then 50 ml of $C_6H_5NO_2$ were added, the solution was evapd, and the residue in $C_6H_5NO_2$ was refluxed for 20 min. The soln was steam-distd, and the brown residue was recrystd from CCl_4 (decolorizing C) and then MeCN to give **13** as white tufts, 5 g, 75%, mp 139–139.5°. *Anal.* ($C_{16}H_{11}BrClN$) C, H.

8-Methyl-2-*p*-chlorophenylquinoline-6-α-pyridylmethanol (**14**) was made from **13** as in the synthesis of **12**. The crude solid was recrystd from EtOH to give 3.5 g, 73%, of **14** as tan needles, mp 168–169.5°. *Anal.* ($C_{22}H_{17}ClN_2O$) C, H, N. The methiodide of **14** was obtained as yellow plates, mp 204–207°. *Anal.* ($C_{23}H_{20}ClIN_2O$) C, H, I.

8-Quinolinemethanols. 8-Epoxyethyl-6-methyl-2-phenylquinoline (**15**) was made from 6-methyl-2-phenylquinoline-8-carboxaldehyde[12] and $(CH_3)_2S{=}CH_2$ as previously described.[1] Recryst from EtOH gave 60% of a light yellow, amorphous solid, mp 85–91°, 60%. *Anal.* ($C_{18}H_{15}NO$) C, H, N.

8-(2-*N*-Homopiperidino-1-hydroxyethyl)-6-methyl-2-phenylquinoline (**16**) was made from **15** and hexamethylenimine as in the prepn for **4a**. Two recrystns from EtOH (decolorizing C) gave **16** as a light yellow powder, mp 86.5–87.5°, 54%. *Anal.* ($C_{24}H_{28}N_2O$) C, H, N.

8-(2-*N*-Homopiperidino-1-hydroxyethyl)-6-phenylquinoline Dihydrochloride (**17**).—6-Phenyl-8-quinolinecarboxaldehyde[12] was converted to the crude epoxide with $(CH_3)_2S{=}CH_2$ as previously described.[1] The crude epoxide and a 10-fold excess of hexamethylenimine were heated at 110° for 12 hr, and the base was worked up as described in **4a**. The free base, 3.7 g, 71%, was dissolved in 50 ml of EtOH and mixed with 20 ml of EtOH satd with gaseous HCl. The pptd salt was filtered off and washed with Et_2O to yield **17**, 4.1 g, mp 242–243° dec. *Anal.* ($C_{23}H_{28}Cl_2N_2O$) C, H, N. The overall yield of **17** was 28.6% starting from 4-aminobiphenyl.

New Model Compounds.—Attempts were made to carry out BuLi exchanges with bromoquinoline compds unsubstd in the 2 position. With Br at the 6 position, addn did occur at the 2 position but not with Br at the 3 position.

2-*sec*-Butyl-6-(1-hydroxy-1-cyclohexyl)quinoline (**18**).—6-Bromoquinoline (0.07 mole) in 50 ml of Et_2O was added in 1 hr to

(9) S. J. Angyal, *Org. React.*, **8**, 210 (1954), following directions for prepn of *o*-$IC_6H_4CH{=}O$.

(10) N. P. Buu-Hoi and D. Guettier, *Bull. Soc. Chim. Fr.*, 586 (1946).

(11) R. E. Lutz, *et al.*, *J. Amer. Chem. Soc.*, **68**, 1813 (1946).

(12) J. B. Wommack, Jr., T. G. Barbee, Jr., D. J. Thoennes, M. A. McDonald, and D. E. Pearson, *J. Heterocycl. Chem.*, **6**, 243 (1969).

(13) D. W. Boykin, Jr., A. R. Patel, and R. E. Lutz, *J. Med. Chem.*, **11**, 273 (1968).

0.16 mole of *sec*-BuLi (2 *M* in C_6H_{14}) at −65 to −70° with magnetic stirring. To this red-brown, opaque soln 0.2 mole of cyclohexanone was added, and the mixt was allowed to warm to 25°. The yellow soln was added to cold H_2O satd with NH_4Cl. The residue from the Et_2O ext was steam-distd to remove excess ketone, and the viscous residue was triturated with C_6H_{14} to yield 2.5 g, 12.6%, of **18**, mp 124–126° after recryst from C_6H_{14}. *Anal.* ($C_{19}H_{25}NO$) C, H. This compd was inactive in the *P. berghei* test but capable of partial sporozoite suppression in the *P. gallinaceum Aedes aegypti* test.

3-(1-Hydroxy-1-methyl-4-diethylaminobutyl)quinoline (19).—In a similar manner 3-bromoquinoline (0.07 mole) was added to 0.075 mole of BuLi followed by the addn of 5-diethylamino-2-pentanone (0.08 mole). The product was a viscous yellow oil, 10.9 g. The dipicrate was made, mp 147–148°. *Anal.* ($C_{30}H_{32}N_8O_{15}$) C, H, N. The dipicrate was reconverted to the free base **19** by means of aq NaOH and Et_2O extrn. The free base **19** showed an increased survival time of 0.7 day at 640 mg/kg in the *P. berghei* test. BuLi exchange with 3-bromoquinoline has been carried out previously.[14]

Normal *vs.* Abnormal Addition of Amines to Epoxides.—The epoxide ring may open in 2 different ways to give $QCHOHCH_2NR_2$ (**20**, normal addition) or $QCHNR_2CH_2OH$ (**21**, abnormal). Nmr spectra have been used previously to detect the presence of **20** or **21**.[15] For **9** and **11**, mass spectral analyses, in which the comparison of heights of the signals for the fragments, $CH_2{=}N^+R_2$ from **20** and $QCH{=}N^+R_2$ from **21**, indicate only traces of the abnormal product, **21**.

6-Bromo-8-phenyl-4-quinolinemethanols. 6-Bromo-8-phenyllepidine (22).—5-Bromo-2-aminobiphenyl·HCl[16] (0.46 mole), methyl vinyl ketone (2 moles, with stabilizer), and As_2O_5 (0.152 mole) in 350 ml of EtOH were refluxed for 22 hr and then most of the EtOH was removed by distn. The residue was poured into H_2O, extd with C_6H_6, and the C_6H_6 ext was washed, dried, and concd. The heavy black oil was eluted from Merck alumina with C_6H_6 yielding 61 g, 44%, of an oil which crystd on trituration with C_6H_{14} and cooling to give **22**, pale yellow crystals, mp 63–64°. *Anal.* ($C_{16}H_{12}BrN$) C, H, N.

8-Phenyllepidine–Trinitroresorcinol Adduct (23).—8-Phenyllepidine was made in 40% crude yield from 2-aminobiphenyl in the same manner as **22**. The heavy oil was treated with an equiv amount of trinitroresorcinol in hot EtOH. The crystals which separated were hand-sepd from a small amt of gum and recrystd from MEK giving yellow, brittle rhombics, mp 195–196° dec. *Anal.* ($C_{22}H_{15}N_4O_8$) N. This compd showed a ΔMST of 1.7 days at 640 mg/kg in the *P. berghei* test and was not used in further synthesis.

2,4-Dibromo-6-phenylaniline (24).—$AlCl_3$ (0.16 mole) was dissolved carefully in 100 ml of DMF (heat evolved) followed by addn of *o*-aminobiphenyl·HCl (0.05 mole). To the stirred pasty white complex at 80°, Br_2 (0.12 mole) was added dropwise in 20 min. After 2 hr the mixt was poured into ice and H_2O and decolorized with $NaHSO_3$. Overnight the oil turned to a solid which was filtered, crushed, and washed with 10% HCl and then H_2O to yield 15.5 g of purple-colored solid. After elution from Merck alumina with C_6H_{14}–C_4H_9Cl and recryst from C_6H_{14}, 10 g, 61%, of **3** was obtd as beige-colored needles, mp 51–52°. *Anal.* ($C_{12}H_9Br_2N$) Br. This compd showed a ΔMST of 0.3 day at 640 mg/kg in the *P. berghei* test and was not used in further synthesis.

6-Bromo-8-phenylquinoline-4-carboxaldehyde (25).—Following a modified procedure of Campbell,[17] a soln of SeO_2 (0.075 mole, freshly prepared) in 25 ml of dioxane and 8 ml of H_2O was added during 30 min to a well-stirred soln of **22** (0.075 mole) in 50 ml of dioxane at 75°, and the mixt was held at 90° for 5 hr. The residue from filtration and concn of the filtrate was dissolved in C_6H_6–Et_2O and washed with aq $NaHCO_3$ and the org layer was stirred overnight with aq satd $NaHSO_3$ during which time a $NaHSO_3$, adduct formed. The adduct was filtered, washed with C_6H_6, and treated with 20% aq NaOH, and the resulting aldehyde was extd with C_6H_6. (In other runs, dil acid was used to regenerate the aldehyde.) The residue from the C_6H_6 ext was **25**, 20.5 g, 87.5%, recrystd from 50:50 C_6H_6–C_6H_{14} to give golden-yellow crystals, mp 113–114°. *Anal.* ($C_{16}H_{10}BrNO$) C, H, N. It was inactive in the *P. berghei* test.

4-Acetyl-6-bromo-8-phenylquinoline (26).—The aldehyde **25** was added to excess MeMgBr to give the carbinol in 81% crude yield. The carbinol, 1 g, was oxidized with 25 ml of DMSO and 1 g of P_2O_5 at 60–65° for 12 hr to give 80% of **26**, colorless crystals, mp 109.5–110.5°. *Anal.* ($C_{17}H_{12}BrNO$) C, H, N. This compd showed a ΔMST of 1.2 days at 640 mg/kg in the *P. berghei* test.

6-Bromo-4-epoxyethyl-8-phenylquinoline (27).—The epoxide was made from **25** and $(CH_3)_2S{=}CH_2$ as described previously.[1] It was recrystd from MeOH to give buff-colored crystals, mp 141–142°. *Anal.* ($C_{17}H_{12}BrNO$) C, H.

6-Bromo-4-(2-dibutylamino-1-hydroxyethyl)-8-phenylquinoline (28a) was made from **27** and Bu_2NH as described.[1] The crude oil was extd into 3% aq HCl and regenerated with aq NaOH followed by elution from a silica gel column using 7% EtOAc in C_6H_6 (R_f 0.1; impurity R_f 0.26, 0.58, 0.68). The free base was obtd as a light yellow oil, 58% overall yield from **25**. *Anal.* ($C_{25}H_{31}BrN_2O$) C, H, Br, N. The base failed to form cryst salts with HCl, HBr, H_2SO_4, or $H_2C_2O_4$ but did form a solid dipicrate from EtOH, mp 147–147.5°. *Anal.* ($C_{37}H_{37}BrN_8O_{15}$) C, H, N.

6-Bromo-4-[2-(3-azabicyclo[3.2.2]nonyl)-1-hydroxyethyl]-8-phenylquinoline (28b) was made from **27** and 3-azabicyclo[3.2.2]nonane[18] by refluxing in MeOH for 20 hr, concn, and multiple extrn of the residue with petr ether (bp 30–60°). The white solid remaining, 1.3 g, 78%, mp 161–163° was recrystd from abs EtOH to give white needles, 1 g, mp 163–164°. *Anal.* ($C_{25}H_{27}BrN_2O$) C, H, N.

8-Phenyl-6-quinolinemethanols. 6-(2-Dibutylamino-*N*-oxide-1-hydroxyethyl)-8-phenylquinoline (29).—6-Epoxyethyl-8-phenylquinoline was made in 95% yield from 8-phenylquinoline-6-carboxaldehyde[12] and $(CH_3)_2S{=}CH_2$ as described.[1] The light yellow, viscous oil, the nmr of which was compatible with structure, was heated with Bu_2NH at 115° for 10 hr yielding 86% of a yellow-orange oil. The oil was purified *via* its dipicrate, yellow plates, mp 194.5–195.5°. *Anal.* ($C_{37}H_{38}N_8O_{15}$) C, H. The free base was generated from 2 treatments with Dowex 1-X8 in EtOH (or until supernatant liquid was colorless). The residue from EtOH was dissolved in Et_2O and shaken with aq NaOH. The white solid formed between the layers was filtered off and recrystd from aq EtOH giving 0.2 g, less than 5%, of **29** (unexpectedly) as white needles, mp 108.5–111°. *Anal.* ($C_{25}H_{32}N_2O_2$) C, H. The CH_2NO signals in the nmr were at 2.97–3.0 ppm (and broadened) rather than at 2.7 ppm for CH_2N. Air oxidn (*N*-oxide formation) occurred during generation of the free base from the dipicrate.

8-Phenylquinoline-6-(α-pyridyl)methanol (30).—6-Bromo-8-phenylquinoline (4 mmoles) was added to BuLi (4.4 mmoles) in 100 ml of 1:1 THF–Et_2O at −72°. After 30 min, 20 mmoles of 2-pyridinecarboxaldehyde in 20 ml of THF was added, the soln becoming light yellow. After 90 min stirring and then work-up, the heavy oil was extd from Et_2O into 1% aq HCl. The HCl ext was made basic and extd with Et_2O, and the Et_2O ext concd giving 0.85 g, 68%, of a viscous, orange oil. The dipicrate formed yellow needles, mp 178.5–179°. *Anal.* ($C_{33}H_{22}N_8O_{15}$) C, H, N. Attempts to reduce the pyridine ring in **30** by the method of Boykin and Lutz[13] gave products indicative of quinoline ring reduction as well.

8-Phenylquinoline-6-carboxylic Acid (31).—6-Bromo-8-phenylquinoline (0.025 mole) was added to a stirred soln of BuLi, 0.05 mole in 70 ml of Et_2O, and 40 ml of THF at −70°. After 1 hr the mixt was poured into an Et_2O–Dry Ice mixt with stirring. H_2O was added, and the aq phase was extd with Et_2O and then acidified yielding 5.2 g, 83%, of **31**, mp 256–257.5°, after recryst from AcOH. *Anal.* ($C_{16}H_{11}NO_2$) C, H, N. The Me ester melted at 91–92°. Both **31** and its Me ester had a ΔMST of 0.4 day at 640 mg/kg in the *P. berghei* test.

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