Synthetic Quinine Analogs. V. Quinolinemethanols Related to Desvinylquinine (1)

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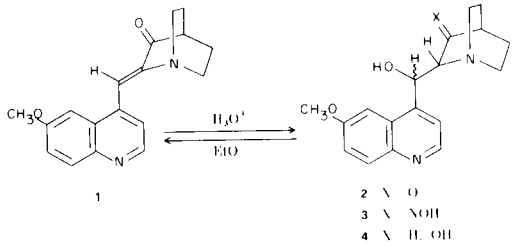
Received June 10, 1971

Aldol condensation of quinolinecarboxaldehydes with 3-quinuclidinone followed by acid-catalyzed hydration of the resulting α,β-unsaturated ketones provides a short and versatile synthesis of desvinylquinine derivatives. A novel rearrangement of 2-(9-phenanthrylmethylene)-3-quinuclidinyl carbinols leading to dibenzoindole derivatives is described.

The emergence of drug-resistant strains of malaria which do respond to quinine chemotherapy has renewed interest in synthetic antimalarials of the quinolinemethanol class (2). Past synthetic work in the quinine area has followed two basic approaches. On the one hand the complete quinine molecule has been taken up as a synthetic objective (3) and on the other, advantage has been taken of the structural and stereochemical simplifications entailed in deletion of the vinyl side-chain (4). Concomitant with the development of a new stereospecific route to the complete skeleton (1), we have utilized this second approach in developing a short and viable synthetic sequence leading to quinolinemethanols related to desvinylquinine.

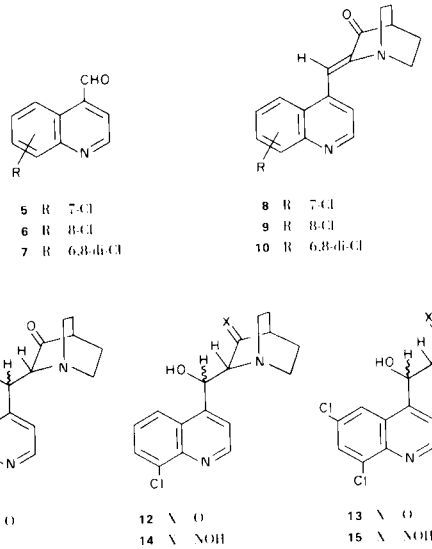
As previously described (5), the quinine ring system, which bears the trivial name rubane (6), is readily generated by a simplet aldol condensation of 6-methoxyquinoline-4-carboxaldehyde with 3-quinuclidinone to give compound **1**.



1

2 X = O
3 X = NOH
4 X = H, OH

A method for introducing the desired hydroxyl group at the 9-position of the rubane skeleton was discovered with the observation that exposure to aqueous sulfuric acid, the conditions used to equilibrate compound **1** with its geometrical isomer (5), also effected hydration of the double bond. Thus the quinolinemethanol **2** was easily obtained by a simple two-step synthesis in high yield. The product is readily crystallized and shows a single spot on thin layer chromatography but is nevertheless a mixture of both possible racemates. This was evident from the broad melting range (86-140°) and the doubling of the methoxyl and C_9 proton nmr signals. Compound **2** is in fact an intermediate in the aldol condensation leading to compound **1**, suggesting that it is readily dehydrated under basic conditions. Since the observed absence of antimalarial activity (7) in this quinolinemethanol may be a result of *in vivo* dehydration, the compound was converted to the corresponding oxime and also reduced to the corresponding 1,3-diol. The oxime **3** was obtained as a single racemate (m.p. 142-145°) of unknown relative



5 R = 7-Cl
6 R = 8-Cl
7 R = 6,8-di-Cl

8 R = 7-Cl
9 R = 8-Cl
10 R = 6,8-di-Cl

11 X = O

12 X = O
14 X = NOH

13 X = O
15 X = NOH

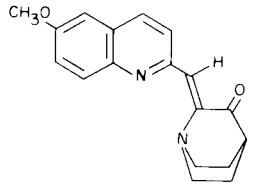
stereochemistry. The crude diol **4** crystallized directly even though a mixture of four racemates was expected.

This condensation-hydration sequence offers an ex-

tremely simple route to quinolinemethanols which is limited only be the availability of substituted quinoline carboxaldehydes. We have used this procedure for the synthesis of the chlorinated analogs **11-13** two of which were also converted to their oximes.

The corresponding chlorolepidines could not be satisfactorily oxidized to the necessary aldehydes with selenium dioxide under normal conditions (refluxing dioxane or xylene) (8). However, this oxidation proceeds smoothly when boiling bromobenzene is used as the reaction medium (9) and the aldehydes **5-7** were readily obtained by this procedure.

One of the earliest counter-measures to the enzymic oxidation of quinine to a carbostyril (10) was the introduction of a phenyl substituent at the 2-position of the quinoline ring (11). The resulting enhancement of antimalarial activity has been shown to be general throughout the quinolinemethanol class but of limited applicability because of phototoxic side-reactions (12). Since moving the entire aminoalcohol side-chain from the 4- to the 2-position offers an alternative method of blocking the 2-position, we applied our two-step method to the synthesis of quinolinemethanol **17**.



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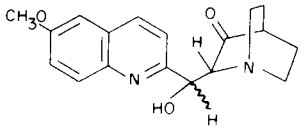

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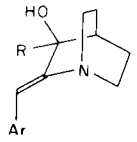
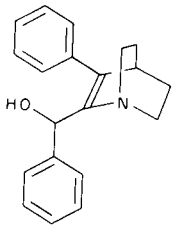
The trans geometry of the double bond in condensation products **8-10** can be inferred from the proven geometry of compound **1** but the extrapolation of this result to compound **16** is hardly valid. The proximity of the quinoline nitrogen provided a unique proof of the trans geometry in this case. In the trans isomer the two nitrogen atoms are ideally situated for chelate formation as was demonstrated by the preparation of cobalt, nickel, and copper dichloride complexes (13).

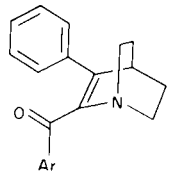
Phenanthrenemethanols are another class of compounds of current interest in malaria chemotherapy (14). We anticipated a convenient synthesis of phenanthrenemethanols based on the facile rearrangement of alcohol **18** to **19** discovered during work on a related project (15).



18 Ar R C_6H_5
21 Ar 9-phenanthryl, R C_6H_5
22 Ar 9-phenanthryl, R CH_3
23 Ar 9-anthryl, R C_6H_5

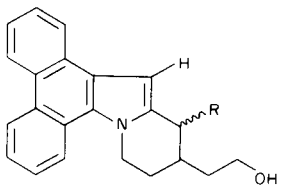


19

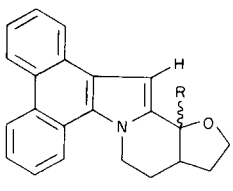


20 Ar C_6H_5
24 Ar 9-anthryl

This rearrangement can be effected either in one step with 10% hydrochloric acid or in two steps using glacial acetic acid followed by hydrolysis of an intermediate acetate. Only the latter procedure gave a clean rearrangement product from alcohol **21**. The structure of alcohol **19** was based largely on the fact that manganese dioxide oxidation yields the ketone **20**. Similar treatment of the rearrangement product from alcohol **21** also results in oxidation but the product, although two mass units lighter, shows no carbonyl absorption in its infrared spectrum and is inert to sodium borohydride, even in refluxing diglyme. In addition, it shows a one proton singlet at 6.79 ppm (which, unlike the signals for the vinyl protons of alcohols **21** and **22**, is not split by a C_{10} phenanthrene proton (16). These data preclude a ketone analogous to **20**. The rearrangement product itself is definitely isomeric (analysis and molecular weight) with alcohol **21**, but unlike **21** is insoluble in 10% hydrochloric acid, *i.e.* the nitrogen is no longer basic. The intermediate acetate shows a two proton triplet (J = 7 cps) at 4.05 ppm which shifts to 3.62 ppm on hydrolysis. Further evidence for a primary alcohol is found in the triplet at 4.38 ppm (J = 5 cps) which appears in the nmr spectrum when recorded in DMSO (17). Of the various structures for the rearranged alcohol which are mechanistically feasible, only the dibenzoindole derivative **25** is consistent with the spectroscopic and chemical properties. The manganese dioxide oxidation product is accordingly formulated as **26**.



25 R C_6H_5
27 R CH_3



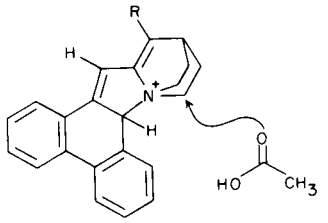
26 R C_6H_5
28 R CH_3

Confirmatory evidence for these structure assignments was obtained by carrying out the same rearrangement with the methyl carbinol **22**. The rearrangement product **27** shows a *doublet* methyl signal (J = 7 cps) at 1.26 ppm

and a doublet (J ≅ 1.2 cps) (18) at 6.76 ppm for the proton at the 3-position of indole. The manganese dioxide oxidation product shows 3H and 1H singlets at 1.71 and 6.93 ppm as required by structure **28**. None of the data reveals the relative stereochemistry of groups on the piperidine ring although all compounds appear to be stereochemically homogeneous. Compounds **25-28** all have virtually identical uv spectra as expected.

The occurrence of this rearrangement is apparently a consequence of the olefinic nature of the C_9-C_{10} phenanthrene bond (19). In the analogous series of anthracene derivatives, the rearrangement step follows the same course observed initially with the transformation **18** → **19**. This was established by treating alcohol **23**, prepared from 2-(9-anthrylmethylene)-3-quinuclidinone (15), sequentially (and without characterization of intermediates) with boiling acetic acid, methanolic potassium hydroxide and manganese dioxide in methylene chloride. This reaction sequence leads to the ketone **24** (ν max = 1660 cm^{-1}).

The quaternary salt **29** is implicated as the principal intermediate in the rearrangement pathway leading to the dibenzoindole derivatives.



29

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were measured as Nujol mulls on a Perkin-Elmer Infracord Model 137. Strong bands or those characteristic of the functional groups present are listed. Mass spectra were recorded on an Atlas CH-5 mass spectrometer. Nmr spectra (ppm) were measured on a Varian A-60A instrument using solvents indicated and tetramethylsilane as an internal standard. Analyses were carried out by Galbraith Laboratories, Inc., Knoxville, Tennessee, and Geller Laboratories, Saddle River, New Jersey.

6′-Methoxy-7-oxo-9-rubanol (2).

Compound **1** (1.57 g.) was dissolved in 6*N* sulfuric acid (50 ml.) and the solution kept at room temperature for 11 days. It was diluted with water, neutralized with aqueous sodium bicarbonate solution and extracted with methylene chloride. The residue from the dried extract was chromatographed on silica gel (92 g.). Starting material and its double bond isomer (5) were eluted with 1% methanol in chloroform (0.68 g., 43% recovered) and the product was eluted with 50% methanol in chloroform. Crystallization from ethanol in the cold afforded, after filtering and washing with ether, 1.02 g. (53%) of colorless crystals of the mono-ethanol solvate, m.p. 86-140° (two epimers) which showed but one spot on tlc; ir bands at 3100, 1730, 1620, 1600, 1510, 1245, 1225, 1120, 1080 and 1040 cm^{-1}; nmr (deuteriochloroform, ethanol free sample) 1.5-3.7 (multiplets, 9H, quinuclidine H), 3.43 (doublet, 1H, H_8) 3.78 and 3.82 (two singlets, 3H, methoxyl), 5.60 and 5.85 (two doublets, 1H, H_9), and 7.2-8.7 ppm (multiplets, 5H, aromatic).

Anal. Calcd. for $C_{20}H_{26}N_2O_4$ (of ethanol solvate): C, 67.02; H, 7.31; N, 7.82. Found: C, 66.83; H, 7.20; N, 7.78.

6′-Methoxy-7-oximino-9-rubanol (3).

A solution of compound **2** (500 mg.) and hydroxylamine hydrochloride (500 mg.) in ethanol (10 ml.) was boiled for 5 minutes then diluted with water and made basic with aqueous sodium carbonate solution. The resulting mixture was chilled and the product filtered out and washed with water giving 520 mg. (99%) of colorless crystals. Recrystallization from ethanol gave thick needles of the ethanol solvate, m.p. 142-145°; ir bands at 3200, 3080, 1620, 1590, 1505, 1240, 1085, 1030, and 948 cm^{-1}.

Anal. Calcd. for $C_{20}H_{27}N_3O_4$ (of ethanol solvate): C, 64.32; H, 7.29; N, 11.25. Found: C, 64.31; H, 7.25; N, 11.15.

6′-Methoxy-7,9-rubanediol (4).

A mixture of compound **2** (400 mg.) in absolute ethanol (10 ml.) was treated with sodium borohydride (100 mg.) and the solution kept at room temperature for 10 minutes. Cold water (10 ml.) was added and the solution reduced to about 1/3 volume by evaporation under reduced pressure causing crystallization of the product. This mixture was chilled, filtered, and the product washed with water and air dried giving 304 mg. (87%) of colorless crystals, m.p. 213-215°; ir bands at 3100, 1630, 1600, and 1510 cm^{-1}, and molecular weight 314 (mass spectrum).

7-Chloroquinoline-4-carboxaldehyde (5).

A mixture of 7-chlorolepidine (20) (3.0 g.) and selenium dioxide (3.0 g.) in bromobenzene (40 ml.) was stirred and heated under reflux for 18 hours. The selenium was filtered off and washed with methylene chloride and the filtrate was evaporated to dryness under vacuum. The residue was taken up in methylene chloride, filtered through Celite and again evaporated to dryness giving 2.06 g. (64%) of crystalline aldehyde. Recrystallization from ethanol gave colorless crystals, m.p. 107-108° (lit. (20) m.p. 112-113°); ir bands at 1700, 1600, 1585, 1495, 1040, 897, and 718 cm^{-1}; nmr (deuteriochloroform), 7.60 (quartet, 1H, H_6, $J_{6,8}$ = 2.5 cps and $J_{5,6}$ = 9 cps), 7.74 (doublet, 1H, H_3, $J_{2,3}$ = 4 cps), 8.17 (doublet, 1H, H_8), 8.93 (doublet, 1H, H_5), 9.17 (doublet, 1H, H_2) and 10.43 (singlet, 1H, aldehydic).

Anal. Calcd. for $C_{10}H_6ClNO$: C, 62.68; H, 3.15; Cl, 18.50; N, 7.31. Found: C, 62.50; H, 3.23; Cl, 18.51; N 7.39.

7′-Chloro-7-oxo-8-rubene (8).

The condensation of aldehyde **5** with 3-quinuclidinone was carried out by the method described (5) for compound **1**. The product was obtained in 77% yield as yellow crystals from ethanol with m.p. 168-170°; ir bands at 1710, 1625, 1575, 1495, 1235, 1095, 823, and 720 cm^{-1}; nmr (deuteriochloroform), 2.05 (triplet of doublets, 4H, $J_{2,3}$ = 8 and $J_{3,4}$ = 3 cps), 2.71 (quintuplet, 1H, $J_{3,4}$ = 3 cps), 3.10 (multiplet 4H), 7.65 (singlet, 1H, vinyl), and 7.3-9.0 ppm (multiplets, 5H, aromatic).

Anal. Calcd. for $C_{17}H_{15}ClN_2O$: C, 68.34; H, 5.06; Cl, 11.88; N, 9.37. Found: C, 68.61; H, 5.00; Cl, 11.74; N, 9.36.

7′-Chloro-7-oxo-9-rubanol (11).

The crude hydration product (6 days) from 500 mg. of compound **8** was taken up in ether. The product (224 mg., 42%)

crystallized out directly. Recrystallization from methylene chloride/ether gave colorless crystals, m.p. 172-177°; ir bands at 3500, 1715, 1605, 1595, 1495, 1115, 990, 850, and 715 cm^{-1}; nmr (deuteriochloroform), 1.7-3.3 (multiplets, 9H, quinuclidine H), 3.57 (doublet, 1H, H_8), $J_{8,9}$ = 7.5 cps), 5.73 (doublet, 1H, H_9), and 7.3-9.0 ppm (multiplets, 5H, aromatic). This product is evidently a single racemate.

Anal. Calcd. for $C_{17}H_{17}ClN_2O_2$: C, 64.45; H, 5.41; Cl, 11.19; N, 8.84. Found: C, 64.70; H, 5.33; Cl, 11.30; N, 8.83.

8-Chloroquinoline-4-carboxaldehyde (**6**).

The oxidation of 8-chlorolepidine (21) with selenium dioxide in boiling bromobenzene (4 hours), as described above for the 7-chloro isomer, afforded the aldehyde in 58% yield. Recrystallization from benzene afforded colorless crystals, m.p. 170-171°. An ir band at 1695 cm^{-1} and the molecular weight of 191 (mass spectrum) confirm the expected structure.

8′-Chloro-7-oxo-8-rubene (**9**).

The aldehyde **6** was condensed with 3-quinuclidinone using the procedure described previously (5) except that the reaction mixture was heated under reflux for 45 minutes. It was obtained in 84% yield and crystallized from methylene chloride/ethanol as yellow needles, m.p. 172-173°; ir bands at 1705 and 1625 cm^{-1}; nmr (deuteriochloroform), 2.10 (triplet of doublets, 4H), 2.72 (quintuplet, 1H), 3.10 (multiplet, 4H), 7.68 (singlet, 1H, vinyl), 7.3-8.3 multiplets, 4H, aromatic), and 9.18 ppm (doublet, 1H, quinoline H_2).

Anal. Calcd. for $C_{17}H_{15}ClN_2O$: C, 68.34; H, 5.06; Cl, 11.88; N, 9.37. Found: C, 68.21; H, 5.22; Cl, 12.04; N, 9.40.

8′-Chloro-7-oxo-9-rubanol (**12**).

The crude hydration product (29 days) from 3.00 g. of compound **9** was fractionally recrystallized from methylene chloride/ether giving 2.165 g. (68%) of aldol **12** as colorless crystals with m.p. 101-108° and ir bands at 3200, 1725 and 1595 cm^{-1}.

Anal. Calcd. for $C_{17}H_{17}ClN_2O_2$: C, 64.45; H, 5.41; Cl, 11.19; N, 8.84. Found: C, 64.67; H, 5.48; Cl, 11.38; N, 8.79.

8′-Chloro-7-oximino-9-rubanol (**14**).

A mixture of the aldol **12** (1.0 g.) and hydroxylamine hydrochloride (0.5 g.) in ethanol (10 ml.) was kept overnight during which time 700 mg. (62%) of the oxime hydrochloride crystallized out, m.p. 216-218°. The free base recrystallized from ethanol in colorless crystals with m.p. 208-210° dec. and ir bands at 3200 and 1595 cm^{-1}.

Anal. Calcd. for $C_{17}H_{18}ClN_3O_2$: C, 61.54; H, 5.47; Cl, 10.69; N, 12.66. Found: C, 61.38; H, 5.77; Cl, 10.60; N, 12.58.

6,8-Dichlorolepidine.

This compound was prepared in 46% yield from 2,4-dichloroaniline and methyl vinyl ketone using the procedure of Campbell and Schaffner (21). It was purified by sublimation and recrystallization from methylene chloride/ether giving colorless crystals, m.p. 131-133°; nmr (deuteriochloroform), 2.54 (singlet, 3H, methyl, slightly coupled to H_3), 7.20 (doublet, 1H, H_3), 7.70 (AB quartet, 2H, $J_{5,7} \cong 4$ cps), and 8.75 ppm (doublet, 1H, H_2, $J_{2,3}$ = 4 cps); molecular weight 211 (mass spectrum).

6,8-Dichloroquinoline-4-carboxaldehyde (**7**).

The oxidation of 6,8-dichlorolepidine with selenium dioxide in boiling bromobenzene (2 hours), as described above for the 7-chloro isomer, afforded the aldehyde in 62% yield. It was purified by vacuum sublimation giving yellowish-white crystals, m.p. 133-139°. An ir band at 1700 cm^{-1}, a 1H singlet in the nmr spectrum (deuteriochloroform) at 10.37 ppm, and the molecular weight of 225 (mass spectrum) confirm the expected structure.

6′,8′-Dichloro-7-oxo-8-rubene (**10**).

The aldehyde **7** was condensed with 3-quinuclidinone using the procedure described previously (5). The reaction mixture was heated for 15 minutes. The product, obtained as yellow crystals in 92% yield had m.p. 190-191°; ir bands at 1705, 1620, 1595, 1575, and 1550 cm^{-1}; nmr (deuteriochloroform), 2.10 (triplet of doublets, 4H), 2.73 (quintuplet, 1H), 3.10 (multiplet, 4H), 7.57 (singlet, 1H, vinyl), and 1H doublet at 7.80, 8.02, 8.22, and 9.03 ppm ($J_{2,3}$ = 4.5 cps and $J_{5,6}$ = 2 cps).

Anal. Calcd. for $C_{17}H_{14}Cl_2N_2O$: C, 61.27; H, 4.23; Cl, 21.28; N, 8.41. Found: C, 61.01; H, 4.23; Cl, 21.11; N, 8.40.

6′,8′-Dichloro-7-oxo-9-rubanol (**13**).

The crude hydration product (23 days) from 3.00 g. of compound **10** was fractionally recrystallized from methylene chloride/ether giving 1.36 g. (43%) of the aldol **13** as a colorless crystalline hydrate with m.p. 107-110° and ir bands at 3200, 1730, and 1595 cm^{-1}.

Anal. Calcd. for $C_{17}H_{18}Cl_2N_2O_3$ (of monohydrate): C, 55.30; H, 4.91; Cl, 19.20; N, 7.59. Found: C, 56.40; H, 4.90; Cl, 19.39; N, 7.32.

The unhydrated ketone **10** was recovered quantitatively from the mother liquor.

6′,8′-Dichloro-7-oximino-9-rubanol (**15**).

A mixture of the aldol **13** (1.8 g.) and hydroxylamine hydrochloride (1.0 g.) in methanol (25 ml.) was kept at room temperature overnight. The oxime hydrochloride separated as a white powder, 1.70 g., 82% yield. The free base was recrystallized from ethanol giving colorless crystals of a mono-ethanol solvate with m.p. 147-152° and ir bands at 3200 and 1595 cm^{-1}.

Anal. Calcd. for $C_{19}H_{23}Cl_2N_3O_3$ (of ethanol solvate); C, 55.35; H, 5.62; Cl, 17.20; N, 10.19. Found: C, 55.50; H, 5.52; Cl, 17.03; N, 10.27.

2-(6′-Methoxy-2′-quinolylhydroxymethyl)-3-quinuclidinone (**17**).

The crude hydration product (21 days) from 1.0 g. of the α,β unsaturated ketone **16** (13) was taken up in ethanol and on cooling 0.80 g. (76%) of the colorless aldol was obtained in three crops. A recrystallized sample had m.p. 150-154°; ir bands at 3050, 2650, 1725, 1630, and 1600 cm^{-1}; and an nmr (deuteriochloroform) spectrum consisting of a series of multiplets at 2.0 (4H), 2.4 (1H), 2.9 (4H), 3.7 (1H), 3.91 (singlet, 3H), 5.25 (1H), 7.2 (3H), and 8.0 ppm (2H). The product may contain both racemates.

Anal. Calcd. for $C_{18}H_{20}N_2O_3$: C, 69.21; H, 6.45; N, 8.97. Found: C, 68.38; H, 6.43; N, 8.59.

2-(9-Phenanthrylmethylene)-3-hydroxy-3-phenylquinuclidine (**21**).

A stirred solution of 2-(9-phenanthrylmethylene)-3-quinuclidinone (15) (10 g.) in 500 ml. of 1:1 ether/benzene was treated with a 1.9 *M* solution of phenyllithium in ether/benzene until a blue color persisted (27 ml.). The solution was then poured into water and the organic layer separated and combined with a methylene chloride extract of the aqueous layer. The solid residue from the dried organic layer after evaporation was triturated with cyclohexane, filtered and washed with cyclohexane giving 10.55 g. (84%) of colorless crystals, m.p. 224-227°. A sample recrystallized from methylene chloride/cyclohexane had m.p. 225-

226°; ir bands at 3300, 1670 (w), and 1590 cm^{-1} (w); nmr (deuteriochloroform), 1.1-3.3 (multiplets, 9H, quinuclidine H), 6.90 (doublet, 1H, vinyl H, J < 1 cps), and 7.2-8.8 (multiplets, 14H, aromatic H); and molecular weight 391 (mass spectrum).

Anal. Calcd. for $C_{28}H_{25}NO$: C, 85.90; H, 6.44; N, 3.58. Found: C, 85.99; H, 6.36; N, 3.51.

2-(9-Phenanthrylmethylene)-3-hydroxy-3-methylquinuclidine (**22**).

This was prepared by adding 2 *M* methyl lithium in ether to a benzene solution of the ketone. The product crystallized from ether as colorless crystals in 50% yield. A second crop showed a strong ir band at 1720 cm^{-1} suggesting that some conjugate addition also occurred.

The main product crystallizes from methylene chloride in fine colorless needles with m.p. 142-143°; ir bands at 3250, 1680 (w), and 1600 cm^{-1} (w); nmr (deuteriochloroform), 1.65 (singlet, methyl H); 1.3-3.2 (multiplets, quinuclidine H), 6.93 (doublet, vinyl H, J < 1 cps), and 7.3-8.8 (multiplets, aromatic H); and molecular weight 329 (mass spectrum).

Anal. Calcd. for $C_{23}H_{23}NO$: C, 83.85; H, 7.04; N, 4.25. Found: C, 83.81; H, 7.02; N, 4.36.

6,7,8,9-Tetrahydro-8-(β-hydroxyethyl)-9-phenylpyrido[1,2-*a*]-dibenz[*e*,*g*]indole (**25**).

A solution of the tertiary alcohol **21** (8.0 g.) in glacial acetic acid was heated under reflux for 3 hours then kept overnight. Most of the acetic acid was evaporated off under reduced pressure and the residue was diluted with water, made basic with aqueous sodium carbonate solution, and extracted four times with methylene/chloride (severe emulsion formation complicates workup). The residue from the extracts after drying and evaporation was crystallized from ether giving 3.53 g. (40%) of the acetate of **25** as colorless crystals with ir bands at 1740, 1610, and 1240 cm^{-1} and an nmr (deuteriochloroform) singlet at 1.98 ppm.

Hydrolysis of the acetate (3.53 g.) was accomplished by heating it with potassium hydroxide (3 g.) in methanol (100 ml.) under reflux for 1 hour. The resulting solution was poured into water and extracted with methylene chloride. The residue from the dried extract after evaporation was crystallized from benzene giving 3.02 g. (95%) of fluffy white needles with m.p. 207-212°; ir bands at 3250 and 1605 cm^{-1} (w); nmr (deuteriochloroform), 1.0-2.5 (multiplets, 5H), 3.62 (triplet, 2H), 3.8 and 4.8 (multiplets, 3H), 6.36 (doublet, 1H, J ≅ 1.2 cps), and 7.2-8.9 (ppm multiplets, aromatic H); and molecular weight 391 (mass spectrum). The product gave a positive Ehrlich's test.

Anal. Calcd. for $C_{28}H_{25}NO$: C, 85.90; H, 6.44; N, 3.58. Found: C, 85.85; H, 6.34; N, 3.56.

6,7,8,9-Tetrahydro-8-(β-hydroxyethyl)-9-methylpyrido[1,2-*a*]-dibenz[*e*,*g*]indole (**27**).

Rearrangement of tertiary alcohol **22** (1.43 g.) using the same procedure (4 days reflux) afforded the acetate of **27** as a yellow syrup with ir bands at 1735, 1610 (w), and 1235 cm^{-1}. Hydrolysis was effected by exposure to potassium hydroxide in methanol/ether for 1½ hours at room temperature. The workup procedure described for compound **25** gave a syrup which crystallized from ethanol giving 883 mg. (59%) of colorless crystals with m.p. 69-71°; ir bands at 3300, and 1610 cm^{-1}, nmr (deuteriochloroform), 1.26 (doublet, methyl H), 1.1-4.6 (multiplets), 6.77 (doublet, 1H, J ≅ 1.2 cps), and 7.3-8.8 ppm (multiplets, aromatic 8H), and molecular weight 329 (mass spectrum). The product gave a positive Ehrlich's test.

Anal. Calcd. for $C_{23}H_{23}NO$: C, 83.85; H, 7.04; N, 4.25. Found: C, 82.72; H, 7.05; N, 4.28.

Manganese Dioxide Oxidation of Compound **25**, Preparation of Compound **26**.

A solution of compound **25** (50 mg.) in methylene chloride (5 ml.) was stirred with active manganese dioxide (500 mg.) for 3 days. The mixture was filtered through Celite, the filtrate evaporated and the residue triturated with ether, filtered and washed giving 35 mg. of crude solid. Recrystallization from ethanol gave colorless crystals with m.p. 183-187°; weak ir bands at 1620 and 1520 cm^{-1}, nmr (deuteriochloroform) includes a singlet (1H) at 6.79 ppm and molecular weight 389 (mass spectrum). The product shows a single spot on tlc.

Manganese Dioxide Oxidation of Compound **27**, Preparation of **28**.

Compound **27** (50 mg.) was oxidized in the manner described for **25** with active manganese dioxide. The crude product shows no carbonyl absorption in its ir spectrum. Following chromatography on alumina and recrystallization from methylene chloride/ethanol, 11 mg. of colorless crystals were obtained with m.p. 119-123°; weak ir bands at 1620 and 1520 cm^{-1}; nmr (deuteriochloroform) 1.71 (singlet, methyl), 1.5-4.4 (multiplets), 6.94 (singlet, 1H), and 7.1-8.2 ppm (multiplets, aromatic H); and molecular weight 327 (mass spectrum).

2-(9-Anthroyl)-3-phenyl-2-quinuclidinene (**24**).

A solution of 2-(9-anthrylmethylene)-3-quinuclidinone (15) (0.58 g.) in benzene (20 ml.)/THF (10 ml.) solvent mixture was treated gradually with 3 ml. of 1 *M* phenyllithium in 1:1 ether-benzene. The reaction was quenched with water and the organic layer dried and evaporated to a pale yellow solid (ir ν max = 3350 cm^{-1}). This crude, tertiary alcohol (**23**) was taken up in glacial acetic acid (10 ml.) and heated under reflux for 2 hours. This solution was then poured into water, neutralized with sodium carbonate solution and extracted with methylene chloride. The residue from the extraction was triturated with ether, filtered and washed with ether giving 370 mg. of recovered alcohol **23**. The residue from the filtrate and washings contained an acetate (ir ν max = 1740 cm^{-1}). This material was hydrolyzed with methanolic potassium hydroxide as described for compound **27** using ether as co-solvent. The dark, gummy product from the hydrolysis reaction showed mainly one spot on tlc (ir ν max at 3350 cm^{-1}). It was taken up in methylene chloride (10 ml.) and stirred with active manganese dioxide (1 g.) for 3 days. After filtration through Celite, the solvent was evaporated and the yellow, solid residue recrystallized from methylene chloride/ethanol giving 121 mg. of yellow needles with m.p. 260°; ir bands at 1660, 1630, 1600, 1580, and 1560 cm^{-1}; nmr (deuteriochloroform), 1.75 (multiplet, 4H), 2.90 (multiplet, 5H), 6.52 (broad singlet, 5H, phenyl), 7.30, 7.8 (multiplets, 8H) and 8.05 ppm (singlet, 1H); and molecular weight 389 (mass spectrum).

Anal. Calcd. for $C_{28}H_{23}NO$: C, 86.34; H, 5.95; N, 3.60. Found: C, 86.22; H, 5.74; N, 3.59.

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