$[\alpha]_D$ −109°; RD (*c* 0.001, dioxane) $[\phi]_{600}$ −60°, $[\phi]_{366}$ ±0°, $[\phi]_{316}$ +2880°, $[\phi]_{312}$ +2700°, $[\phi]_{306}$ +3060°, $[\phi]_{298}$ +690°, $[\phi]_{294}$ ±0°, $[\phi]_{260}$ −8230°, $[\phi]_{246}$ −8090°, $[\phi]_{210}$ −11,430°; ν_{max} 1730, 1720 cm^{-1}; nmr 0.66 (s, 18 H), 1.02 (s, 19 H), 2.00 (s, 3-acetoxy H), 2.28 (d, J_{HF} = 2.3 Hz, 21 H), 5.37 ppm (ill-resolved m, 6 H); mass spectrum *m/e* 456 (M^+), 396, 381.

Anal. Calcd for $C_{25}H_{32}O_3F_4$: C, 65.77; H, 7.07. Found: C, 66.07; H, 7.07.

3β-Acetoxy-16β,17β-tetrafluoroethylene-17α-pregn-5-en-20-one (**17**, 690 mg) had mp 147–148° (from ethanol–methylene chloride); $[\alpha]_D$ −76°; RD (*c* 0.001, dioxane) $[\phi]_{600}$ −410°, $[\phi]_{305}$ −3660°, $[\phi]_{299.5}$ −3470°, $[\phi]_{295}$ −3470°, $[\phi]_{270}$ −1740°, $[\phi]_{213}$ −16,810°, ν_{max} 1740, 1715 cm^{-1}; nmr 1.02 (s, 19 H), 1.14 (d, J_{HF} = 3.5 Hz, 18 H), 2.01 (s, 3-acetoxy H), 2.26 (d, J_{HF} = 3.0 Hz, 21 H), 5.36 ppm (ill-resolved m, 6 H); mass spectrum *m/e* 456 (M^+), 396, 381.

Anal. Calcd for $C_{25}H_{32}O_3F_4$: C, 65.77; H, 7.07. Found: C, 65.92; H, 6.62.

Photochemical Addition of *cis*- and *trans*-Dichloroethylene to 3β-Acetoxypregna-5,16-dien-20-one (**1**).—A solution of **1** (20.0 g) and *cis*-dichloroethylene (40.7 g) in 1.5 l. of tetrahydrofuran was irradiated for 2.5 hr. The solvents were evaporated to dryness and a benzene solution of the residue was chromatographed on 800 g of silica gel to yield the following compounds.

17α-Chloro-3β-acetoxypregn-5-en-20-one (**20**, 250 mg) had mp 141–142°; $[\alpha]_D$ −85° (lit.[14] mp 147–149°, $[\alpha]_D$ −84.9°); RD (*c* 0.001, methanol) $[\phi]_{600}$ −170°, $[\phi]_{400}$ −590°, $[\phi]_{350}$ −820°, $[\phi]_{320}$ −1030°, $[\phi]_{290}$ −2290°, $[\phi]_{270}$ −2370°, $[\phi]_{250}$ −3190°, $[\phi]_{216}$ −9060°, $[\phi]_{209}$ −10,210°; ν_{max} 1735, 1715 cm^{-1}; nmr (100 Mc), 0.75 (s, 18 H), 1.03 (s, 19 H), 2.04 (s, 3-acetoxy H), 2.33 (s, 21 H), 5.4 ppm (ill-resolved m, 6 H).

Anal. Calcd for $C_{23}H_{33}O_3Cl$: C, 70.30; H, 8.46; Cl, 9.02. Found: C, 70.36; H, 8.35; Cl, 9.15.

3β-Acetoxy-16α,17α-(16′ξ,17′-*endo*-dichloro)ethylenepregn-5-en-20-one (**19**, 6.1 g) had mp 214–215° (from methanol–methylene chloride); $[\alpha]_D$ −80°, RD (*c* 0.001, dioxane) $[\phi]_{600}$ −340°, $[\phi]_{450}$ −710°, $[\phi]_{306}$ −3840°, $[\phi]_{278}$ ± 0°, $[\phi]_{270}$ + 380°, $[\phi]_{252}$ ± 0°, $[\phi]_{235}$ −1980°, $[\phi]_{213}$ −3930°, CD (*c*, 0.001 in dioxane) $[\Theta]_{322}$ ± 0°, $[\Theta]_{284-289}$ −3370°, $[\Theta]_{260}$ −1450°; ν_{max} 1730, 1710, 1665, 1240 cm^{-1}; nmr (100 Mc) in benzene-d_6 0.36 (s, 18 H), 0.79 (s, 19 H), 3.28 (broad t, 16 H), 3.80 (pair of d, $J_{16,16'}$ = 4.5 Hz, $J_{16',17'}$ = 6.0 Hz, 16′ H), 4.34 (pair of d, $J_{16,17'}$ = 1.5 Hz, $J_{16',17'}$ = 6.0 Hz, 17′ H), 5.27 ppm (ill-resolved m, 6 H).

Anal. Calcd for $C_{25}H_{34}O_3Cl_2$: C, 66.22; H, 7.55; O, 10.59; Cl, 15.64. Found: C, 66.61; H, 7.51; O, 9.83; Cl, 15.62.

3β-Acetoxy-16α,17α-(16′ξ,17′-*exo*-dichloro)ethylenepregn-5-en-20-one (**18**, 4.0 g) had mp 172–173° (from methanol–methylene chloride); $[\alpha]_D$ −16°; CD (*c* 0.0007, dioxane) $[\Theta]_{338}$ ±0°, $[\Theta]_{304-308}$ +8120°, $[\Theta]_{294-297}$ +10,430°, $[\Theta]_{287-291}$ +10,130°, $[\Theta]_{260}$ +2500°; ν_{max} 1730, 1710, 1670, 1260 cm^{-1}; nmr (100 Mc) in benzene-d_6 0.35 (s, 18 H), 0.81 (s, 19 H), 1.80 (s, 3-acetoxy H), 2.01 (s, 21 H), 3.49 (t, $J_{16,16'}$ = 9.5 Hz, 16 H), 4.26 (d, $J_{16',17'}$ = 7.5 Hz, 17′ H), 4.42 (pair of d, $J_{16,16'}$ = 9.5 Hz, $J_{16',17'}$ = 7.5 Hz, 16′ H) 5.28 ppm (ill-resolved m, 6 H).

Anal. Calcd for $C_{25}H_{34}O_3Cl_2$: C, 66.22; H, 7.55. Found: C, 66.38; H, 7.60.

The same products were isolated when **1** was photolysed under the same conditions in the presence of *trans*-dichloroethylene.

Photochemical Addition of Hexafluoroacetone to 3β-Acetoxypregna-5,16-dien-20-one (**1**).—A solution of **1** (2.5 g) in 140 ml of dioxane was irradiated for 1 hr at 15–20° using a Corex apparatus while bubbling a stream of anhydrous hexafluoroacetone through the solution. The solvent was evaporated and a solution of the residue dissolved in benzene–ethyl acetate (99:1) was adsorbed on a column of 100 g of silica gel. Elution with benzene–ethyl acetate (97:3) furnished 250 mg of the oxetane **21**: mp 212–217° (from ethanol–methylene chloride); $[\alpha]_D$ −72°; RD (*c* 0.001, dioxane) $[\phi]_{600}$ −160°, $[\phi]_{398}$ ±0°, $[\phi]_{321}$ +5230°, $[\phi]_{314}$ +4920°, $[\phi]_{311}$ +4920°, $[\phi]_{300}$ +520°, $[\phi]_{297}$ ±0°, $[\phi]_{291}$ −4550°, $[\phi]_{284}$ −8000°, $[\phi]_{268}$ −10,100°, $[\phi]_{242}$ −9050°; ν_{max} 1735 cm^{-1}; nmr 0.60 (s, 18 H), 1.04 (s, 19 H), 2.00 (s, 3-acetoxy H), 2.18 (s, 21 H), 5.42 ppm (ill-resolved m, 6 H); mass spectrum *m/e* 462 (M^+ − 60), 419 (M^+ − 103).

Anal. Calcd for $C_{26}H_{32}O_4F_6$: C, 59.77; H, 6.17; F, 21.82. Found: C, 60.04; H, 6.36; F, 21.74.

Registry No.—**1**, 1778-02-5; **2**, 10030-06-5; **3**, 7769-14-4; **4**, 21876-65-3; **5a**, 21876-66-4; **5b**, 21876-67-5; **6**, 21876-68-6; **8**, 21876-69-7; **10a**, 21876-70-0; **10b**, 21876-71-1; **11**, 21876-72-2; **12**, 21876-73-3; **13**, 21876-74-4; **14**, 21876-75-5; **15**, 21876-76-6; **16**, 7769-17-7; **17**, 7769-18-8; **18**, 21876-79-9; **19**, 21876-80-2; **20**, 21876-81-3; **21**, 21927-70-8; 3β-acetoxy-16α,17α-ethylenepregn-5-en-20-one-21-d_3, 21876-82-4; (20*S*)-3β-acetoxy-18,20-cyclo-16α,17α-ethylenepregn-5-en-20-ol-21-d_3, 21876-84-6; 3α,4α-dihydroxy-16α,17α-(17′-methylene)ethylene-5α-pregnan-20-one, 21876-85-7.

Structure of Mesuagin.[1] A New 4-Phenylcoumarin

D. P. CHAKRABORTY AND D. CHATTERJI

Bose Institute, Calcutta 9, India

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Mesuagin, $C_{24}H_{22}O_5$, a new 4-phenylcoumarin isolated from the seed oil of *Mesua ferrea* L., is shown to be 5-hydroxy-6-isobutyryl-8,8-dimethyl-4-phenyl-2H,8H-benzo[2,2-*b*:3,4-*b*′]dipyran-2-one.

In a previous communication[2] we reported the structure of mesuol (I), a bitter antibiotic constituent from the seed oil of *Mesua ferrea* L. (family *Guttiferae*). The present paper relates to the structure of a new 4-phenylcoumarin named mesuagin (II) and the isolation of mammeigin[3] (III) from the same source. The seed oil of *M. ferrea* L. on chromatography over silica gel furnished a mixture, a yellow crystalline product which melted at 125–127°. It was a mixture of II and III, from which the constituents could only be separated by thin layer chromatography using benzene–ethyl acetate–diethylamine (7:2:1) as the developing solvent and silica gel G as an adsorbent. As some samples of II, even though found homogeneous by tlc, were found to be contaminated with III when examined mass spectrometrically, the homogeneity by both the methods was the criterion of a pure specimen of II.

Mesuagin (II), mp 152–153°, was obtained as pale yellow needles from hexane. Analytical results and molecular weight determination (M^+ 390) by mass spectrum established the molecular formula of mesuagin as $C_{24}H_{22}O_5$. The ir spectrum of II (KBr) showed bands at 3400 (chelated hydroxyl), 1739 (δ-lactone), and 709 cm^{-1} (monosubstituted benzene nucleus). Its uv spectrum showed the presence of an acyl substituent at the 6 position[4] of the coumarin nucleus, which was

(1) Presented at the 56th session of Indian Science Congress, Bombay, India, Jan 1969. Taken in part from the Ph.D. thesis of D. Chatterji, University of Calcutta, 1968.

(2) D. P. Chakraborty and B. C. Das, *Tetrahedron Lett.*, 5727 (1966).

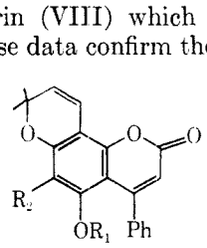
(3) R. A. Finnegan and W. H. Mueller, *J. Org. Chem.*, **30**, 2342 (1965).

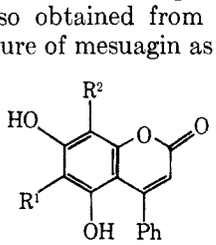
(4) L. Crombie, D. E. Games, and A. McCormick, *J. Chem. Soc.*, 2553 (1967).

probably chelated as the ir spectrum of II showed no bands for the acyl function in the carbonyl region.

The nmr spectrum of II like some 4-phenylcoumarins showed signals at δ 5.97 (for the ethylenic proton at 3 position) and δ 7.33 for five aromatic protons with concomitant absence of the signal at δ 7.98 for the proton at 4 position. The sharp singlet at δ 1.58 for six protons and the doublets of one proton each at δ 5.62 and 6.88 (J = 10 cps/sec) reveal the presence of a 2,2-dimethyl-Δ^3-pyran ring. The high intensity mass spectral peak of II at M − 15 also supports this conclusion. The signals at δ 1.25 (J = 10 cps/sec) for six protons together with the multiplet for a deshielded methine proton at δ 3.73 like that in mesuol (I) (3.75) suggest the presence of an isobutyryl chain in II. The abundant mass spectral peak at M − 43 shows the loss of a propyl radical from the isobutyryl chain. The hydroxyl resonance of mesuagin (II) at δ 14.63 like those of mammeigin[4] (III) (14.75) and isomesuol[2] (IV) (14.70) suggests the presence of the hydroxyl function at position 5 chelated to the acyl function at 6. The additional ir spectral peak for a carbonyl function (ν_{max}^{Nujol} 1709 cm^{-1}) of mesuagin monomethyl ether (V), $C_{25}H_{24}O_5$, mp 129–130°, also supports this conclusion. It gave a colorless crystalline monoacetate (VI), $C_{26}H_{24}O_6$, mp 166–167°.

On alkaline degradation (40% aqueous KOH) II furnished acetone, acetophenone, isobutyric acid, and 5,7-dihydroxy-4-phenylcoumarin (VII). The formation of acetophenone and VII shows that II is built on a 5,7-dihydroxy-4-phenylcoumarin skeleton. Acetone and isobutyric acid are contributions arising from the 2,2-dimethyl-Δ^3-pyran ring and isobutyryl residue, respectively. The sharp six-proton singlet at δ 1.58 support the fusion of the pyran ring in II at 7,8 position rather than at 5,6 position in which case the *gem*-dimethyl group would be shielded by the phenyl ring at 4 position, as has been found to be the case in callophyllolide and inophyllolide[5] (δ 0.94, 0.90, and 0.96, respectively). To confirm the position of the 2,2-dimethyl-Δ^3-pyran moiety, II was deacylated with acetic acid and sulfuric acid[6] to a new 4-phenylcoumarin (VIII) which was also obtained from III. All these data confirm the structure of mesuagin as II.





II, R_1 = H; R_2 = CO·CH(CH$_3$)$_2$ I, R_1 = CO·CH(CH$_3$)$_2$;
III, R_1 = H; R_2 = CO·CH$_2$·CH(CH$_3$)$_2$ R_2 = CH$_2$CH = C(CH$_3$)$_2$
V, R_1 = CH$_3$; R_2 = CO·CH(CH$_3$)$_2$ IV, R_1 = CH$_2$·CH = C(CH$_3$)$_2$;
VI, R_1 = CO·CH$_3$; R_2 = CO·CH(CH$_3$)$_2$ R_2 = CO·CH(CH$_3$)$_2$
VIII, R_1, R_2 = H VII, R_1, R_2 = H

The occurrence of mesuagin (II) in a plant elaborating mesuol (I) is biogenetically rational. Mesuagin is slightly antibacterial against *Staphyllococcus aureus*.

Experimental Section

Melting points were determined on a Kofler block and are uncorrected. Petroleum ether had bp 60–80° unless otherwise mentioned. For tlc Merck silica gel G was used. Ultraviolet spectra (95% ethanol as solvent) were recorded on a Beckman DU spectrophotometer.

Isolation of Mesuagin (II) and Mammeigin (III).—The brown oil (70 g) obtained by removal of the solvent from the ethereal extract of the seeds (120 g) of *Mesua ferrea* L. was dissolved in petroleum ether and chromatographed over a column (70 × 6 cm) of silica gel (2 kg). The chromatogram was developed using successively, petroleum ether and petroleum ether–benzene mixture as eluents. Fractions of 500 ml were taken.

From the fractions 23–32, of the petroleum ether–benzene (1:1) eluent, a yellow solid was obtained which on crystallization from hexane melted at 125–127° and was found to be apparently homogeneous by tlc in several solvent systems. Mass spectral measurements, however, showed it to be a mixture of compounds of mass 390 and 404. The constituents of the mixture was resolved on a tlc plate using the solvent system benzene–ethyl acetate–diethylamine (7:2:1). This method was utilized in a preparative scale.

Mesuagin (II).—The yellow spot of R_f 0.51 was scraped from the plate and was dissolved in chloroform. A pale yellow crystalline compound was obtained on removal of the solvent which melted at 152–153° on crystallization from hexane: yield 100 mg; like 6-acylcoumarins it gave an olive green color with ethanolic ferric chloride solution; uv 235 mμ (log ϵ 4.31), 285–86 (4.40), 362 (3.79); ir (KBr) 3400 (broad), 1739, 1653, 1613, 1378, and 709 cm^{-1}; nmr (CDCl$_3$) δ 5.97 (s, 1 H), 7.33 (m, 5 H), 1.58 (s, 6 H), 5.62, 6.88 (d, 1 H for each), 1.25 (d, 6 H), 3.73 (m, 1 H), and 14.63 (s, 1 H).

Anal. Calcd for $C_{24}H_{22}O_5$: C, 73.83; H, 5.68. Found: C, 73.68; H, 5.84; M$^+$ 390.

Mammeigin (III).—The yellow spot of R_f 0.67 was worked up as before and the yellow compound on crystallization from hexane melted at 149–150° (lit.[3] mp 144–146°): yield 400 mg; the compound gave an olive green color with ethanolic ferric chloride solution; ir (KBr) 3400 (broad), 1740, 1639, 1613, 1380, and 706 cm^{-1}; M$^+$ 404.

An authentic specimen of mammeigin[7] was identical with the above sample (III) in all respects (mixture melting point, tlc, and ir).

O-Methylmesuagin (V).—Mesuagin (15 mg) in methanol (10 ml) on treatment with excess diazomethane at 5° and storing for 10 days furnished a yellow oil giving a negative ferric chloride reaction. The oily residue crystallizes from aqueous methanol and recrystallized from hexane as colorless crystals: mp 129–130° (10 mg); uv 232 mμ (log ϵ 4.64), 285 (4.37) (4.19); ir (Nujol) 1742, 1709, 1590, 1380, and 700 cm^{-1}.

Anal. Calcd for $C_{25}H_{24}O_5$: C, 74.24; H, 5.98; OMe, 7.67. Found: C, 73.95; H, 6.03; OMe; 7.60.

Mesuagin Acetate (VI).—The solution of II (15 mg) in pyridine (3 ml) and acetic anhydride (3 ml) was warmed on a water bath for 3 hr. The reaction mixture was poured into crushed ice when a solid separated. It was then crystallized from a mixture of benzene–petroleum ether (40–60°) and colorless needles, mp 166–167°, were obtained (14 mg): uv 235 mμ (log ϵ 4.60), 285 (4.20), 335 (3.98); ir (Nujol) 1770, 1739, 1695, 1642, 1587, and 704 cm^{-1}.

Anal. Calcd for $C_{26}H_{24}O_6$: C, 72.21; H, 5.59. Found: C, 72.07; H, 5.65.

Alkaline Hydrolysis of II.—Mesuagin (25 mg) was placed in a Claisen flask (25 ml) with 40% aqueous caustic potash solution (10 ml) and the resulting orange–red solution was distilled for 10 min keeping the volume constant at intervals. All the distillates were trapped in a 50-ml round bottom flask containing a solution of 2,4-dinitrophenyl hydrazine (20 ml, 0.1%) in sulfuric acid (10%, w/v, 15 ml). An orange red precipitate was obtained. It was then extracted with carbon tetrachloride (E. Merck grade) and chromatographed over Brockmann's alumina.

Acetone.—From the petroleum ether eluent yellow crystals were obtained which were identical with 2,4-dinitrophenylhydrazone of acetone (mp 125–126°, mmp 125–126°).

Acetophenone.—The benzene eluent gave brick red crystals, mp 242–243° alone or admixed with the 2,4-dinitrophenylhydrazone of acetophenone.

Isobutyric Acid.—The aqueous solution remaining after removal of the steam volatile compounds was diluted and acidified

(5) S. K. Nigam, C. R. Mitra, G. Kunesch, B. C. Das, and J. Polonsky, *Tetrahedron Lett.*, 2633 (1967).

(6) K. Hata, *J. Pharm. Soc.*, **76**, 666 (1956).

(7) The authors are indebted to Professor R. A. Finnegan, State University of New York at Buffalo, Buffalo, N. Y., for a gift of an authentic specimen of mammeigin.

with 10% hydrochloric acid and extracted with ether. From the bicarbonate extract of the ethereal solution, an oily acidic substance with the characteristic odor of a fatty acid was isolated. The oily substance was identified as isobutyric acid by glpc.

5,7-Dihydroxy-4-phenylcoumarin (VII).—The ethereal layer left after washing with bicarbonate was washed and dried. The oil obtained after removal of the solvent, was crystallized from aqueous alcohol as colorless needles: mp 234–235° (lit.[8] mp 235–237°); uv 260 mμ (log ε 4.07), 340 (4.01); ir (KBr) 3200, 1681, 1626, 1556, and 704 cm^{-1}. Owing to paucity of the material, the analysis of this compound was not possible.

The above degraded product was identical with that of synthetic specimen of 5,7-dihydroxy-4-phenylcoumarin[9] in all respects (mixture melting point, uv, ir, and tlc).

Deacylation of II.—To a solution of II (25 mg) in glacial acetic acid (5 ml) was added concentrated sulphuric acid (2 ml) and the mixture was kept on a water bath for 1 hr. After the reaction was over the mixture was poured into crushed ice (50 g). The precipitate was filtered and crystallized from ethyl acetate as pale yellow needles: mp 244–245° (12 mg); uv 283 mμ (log ε 4.33); ir (Nujol) 3125, 1703, 1617, 1370, and 698 cm^{-1}. A similar deacylation reaction using mammeigin (III) as a substrate was carried out. The reaction product after working up in the above way gave the compound identical with VIII.

Anal. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 74.63; H, 4.87.

(8) J. Polonsky, *Bull. Soc. Chim., Fr.*, 541 (1955).

(9) Synthetic specimen prepared in our laboratory by Pechmann condensation of phloroglucinol and benzoyl ethylacetate using acetic acid and bronotrifluoride dietherate complex as the condensing agent.

Registry No.—II, 21721-08-4; III, 2289-11-4; V, 21721-10-8; VI, 21721-11-9.

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The Chemistry of Aporphines. IV. Synthesis of Aporphines *via* Reissert Alkylation, Photochemical Cyclization, and the Pschorr Cyclization Route[1a]

J. L. NEUMEYER,[1b] K. H. OH, K. K. WEINHARDT, AND B. R. NEUSTADT

Arthur D. Little, Inc., Cambridge, Massachusetts 02140

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Nitrobenzyl- (**4b**) and iodobenzylisoquinoline (**4a**) derivatives have been synthesized by the condensation of Reissert compounds (**1**) with nitrobenzyl (**2b**) and iodobenzyl chlorides (**2a**). Subsequent reduction and Pschorr cyclization of the nitrobenzylisoquinoline resulted in a facile route to the synthesis of aporphines (**4b** → **5b** → **6c** → **7**). Photochemical cyclization of 1-(2-iodobenzyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (**6a** → **7**) also resulted in the isolation of aporphine, but in considerably lower yields.

Aporphine and the naturally occurring aporphine alkaloids have a long and interesting chemical history. One of the shortcomings in this field of chemistry is due in large measure to the fact that the methods generally used for the synthesis are very poor in yields. Toward this end we have investigated promising new approaches to the synthesis of the aporphine ring system, which can be similarly applied to the synthesis of the related aporphine alkaloids.

In a preliminary communication[2] from our laboratories we have reported the synthesis of aporphine (**7**) by the generation of 1-(*o*-nitrobenzyl)isoquinoline (**4b**) by the reaction of a Reissert compound **1a** with *o*-nitrobenzyl chloride (**2b**) with subsequent reduction and Pschorr cyclization (**5b** → **6c** → **7**). In this report we wish to further expand the utility of the Reissert alkylation procedure for the generation of 1-(2-iodobenzyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (**6a**), an aporphine precursor which when subjected to photolysis effects cyclization to the aporphine **7**. The advantages and experimental details of the two methods will be discussed.

The reaction of Reissert compounds with aldehydes or alkyl halides has proved a valuable method for the synthesis of a number of benzylisoquinoline alkaloids.[3] Alkylation of a Reissert compound with *o*-nitrobenzaldehyde has yielded *o*-nitrophenyl-1-isoquinolylmethyl benzoate, but the attempted base hydrolysis to *o*-nitrophenyl-1-isoquinolylmethanol failed to yield the desired product.[4] We have attributed this failure to the vigorous basic hydrolysis conditions used, which by analogy to similar systems studied in our laboratories[5] probably yields the anthranil **8**.

The generation of 1-cyano-1-(2-nitrobenzyl)-2-benzoyl-1,2-dihydroisoquinoline (**3b**) from **1a** and **2b** in 80% yield and further careful hydrolysis has yielded the desired benzylisoquinoline **4b** in 73% yield. The details of the conversion of **3b** → **4b** → **5b** → **6c** → **7** in excellent yields are described in the Experimental Section of this paper. The limiting step in this sequence of reactions was still the Pschorr cyclization step, since yields of better than 50% could not be obtained.

In our previous study[1] we discussed the borohydride reduction products of a number of nitrobenzylisoquinolinium salts and the unusual carbon–carbon cleavage which occurred when these salts were subjected to a borohydride reduction. It thus became necessary to resort to a catalytic reduction (Adams catalyst) for the conversion of **5b** → **6c**. As expected, the reduction of **5a** → **6a** with sodium or preferably potassium borohydride proceeded smoothly.

Condensation of **2a** (prepared in two steps by the diborane reduction of *o*-iodobenzoic acid to the alcohol followed by conversion into the chloride **2a** with thionyl chloride) with the Reissert compound (**1**, R′ =

(1) (a) Paper III: J. L. Neumeyer, M. McCarthy, K. K. Weinhardt, and P. L. Levins, *J. Org. Chem.*, **33**, 2890 (1968). (b) To whom inquiries should be addressed: The Department of Medicinal Chemistry, School of Pharmacy, Northeastern University, Boston, Mass. 02115

(2) J. L. Neumeyer, B. R. Neustadt, and J. W. Weintraub, *Tetrahedron Lett.*, 3107 (1967).

(3) F. D. Popp, *Advan. Heterocycl. Chem.*, **9**, 1 (1968).

(4) H. W. Gibson and F. D. Popp, *J. Chem. Soc., C*, 1860 (1966).

(5) C. B. Boyce and J. L. Neumeyer, unpublished results.