equimolar solution showed 3 vinyl H, 6 allylic H, 1 α-CH, and 4.4 HDO; calcd 4.5 HDO. Correction was made for the HDO in D_2O–NaOD and for the Phe + Ene content.

Attempts to Dry L-DiHPhe·0.75H_2O.—When heated on a hot block under a stream of H_2 gas at 100°, DiHPhe hydrate lost 3.5% in weight, at 120° 4.7–4.8%, and at 155° 6.9% (Micro-Tech). At 100 and 110° in a vacuum it lost 6.8 and 7.04%, respectively (Schwarzkopf); calcd (cor) for DiHPhe·0.75H_2O: 7.1%. The latter procedure was adopted for the determination of water. Heating at 139° with constant evacuation at 0.05 Torr was unreliable, since some material, which contained Phe and DiHPhe, condensed onto the cool portion of the Abderhalden pistol.

Kinetics of Dehydrogenation.—The timed experiment showing the effect of reduced pressure was carried out by placing 100–200 mg of L-DiHPhe·0.75H_2O in a 30-ml crystallizing dish over P_2O_5 in a desiccator (10-cm diameter) that was evacuated to 2 Torr for 2 min, closed, and then allowed to stand at 25°. At the times indicated in Figure 1, several milligrams were removed and dissolved in water for analysis. The desiccator was reevacuated to 2 Torr and allowed to stand, and the process was repeated. For comparison, one sample was kept at 1 atm in a sealed tube and another sample over P_2O_5 in an unevacuated desiccator.

The timed experiment showing the effect of temperature was conducted by heating 2- to 3-mg samples of L-DiHPhe·0.75H_2O in corked 3-ml test tubes in an oil bath heated to 60 or 100 ± 1.5°. At the times indicated in Figure 2, 1 ml of water was added, and the solutions were kept frozen until placed on the amino acid analyzer.

Isolation of L-Phenylalanine as the Dehydrogenation Product.—In batches of 20–30 mg per test tube, 448 mg of L-DiHPhe hydrate were heated for 5 hr in an oil bath at 100°, with approximately 78% conversion to Phe. Each batch was chromatographed on the amino acid analyzer in system 1.[2] Fractions of 1 ml were collected and analyzed with ninhydrin.[17] Phe, eluting at 69–78 ml, separated from DiHPhe, eluting at 87–92 ml. The combined eluate containing 281 mg of Phe was desalted on a column of 150 ml of Dowex 50 W X8 (H^+) resin, 100–200 mesh.[18] Two recrystallizations from 50% ethanol yielded 130 mg of L-Phe, a homogeneous product on the analyzer, $[\alpha]_D$ −33.6° (*c* 0.85, water) [lit.[15] $[\alpha]_D$ −34.5° (*c* 1, water)]. Its nmr spectrum as the carboxylate ion in D_2O was identical with that of commercial L-Phe. At concentrations of 5, 10, and 15 μg/ml in Anderson's asparagine medium[19] supplemented with 1.5 mg of $FeNH_4SO_4 \cdot 6H_2O$/l., it afforded the same growth for *E. coli* 9723f as did L-Phe.

Registry No.—L-1,4-Cyclohexadiene-1-alanine hydrate, 16055-12-2; L-phenylalanine, 63-91-2; L-DiHPhe·HCl, 32507-80-5.

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The Synthesis of Atheroline. A Route to Phenolic Oxoaporphines

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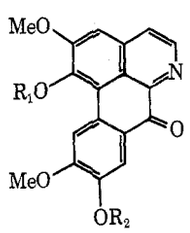
The alkaloid antheroline (II) has been synthesized. This work represents the first synthesis of a phenolic oxoaporphine base.

The yellow alkaloid atheroline occurs in the bark of *Atherosperma moschatum* L.[1] It was at first assigned the phenolic oxoaporphine structure I,[1] but this formulation was later modified to II as a result of direct comparison of *O*-ethylatheroline (IV) with a series of



I, $R_1 = H; R_2 = Me$
II, $R_1 = Me; R_2 = H$
III, $R_1 = Me; R_2 = COMe$
IV, $R_1 = Me; R_2 = Et$

synthetic trimethoxyethoxyoxoaporphines.[2] We now report the first synthesis of atheroline; this represents also the first synthesis of any phenolic oxoaporphine.

1-(5-Benzyloxy-4-methoxy-2-nitrobenzyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (compound V) was prepared starting from 3,4-dimethoxyphenethylamine and 5-benzyloxy-4-methoxy-2-nitrobenzaldehyde[3] (VIII) as described in the literature.[4] Mild oxidation of V with chromic acid in acetic acid afforded the corresponding benzoylisoquinoline (VI) in 53% yield; the aldehyde VIII and the isocarbostyryl[5] IX were obtained as minor products. Dehydrogenation of VI with 10% palladium on charcoal under nitrogen yielded 1-(5-benzyloxy-4-methoxy-2-nitrobenzoyl)-6,7-dimethoxyisoquinoline (VII), mp 168–169°, in 71% yield. The success of this reaction is worthy of note, in view of the survival in the product of both the readily hydrogenolyzed benzyl group and the readily reduced nitro function. A minor proportion of VII (or V) is, in fact, undoubtedly destroyed by acting as the hydrogen acceptor in the dehydrogenation.

A direct one-step conversion of V to VII could also be achieved by heating V with palladium on charcoal in *p*-cymene in the presence of air. In this practical reaction (~50% yield), dehydrogenation of the dihydroisoquinoline system is accompanied by the catalytic oxidation of the activated benzylic methylene group.

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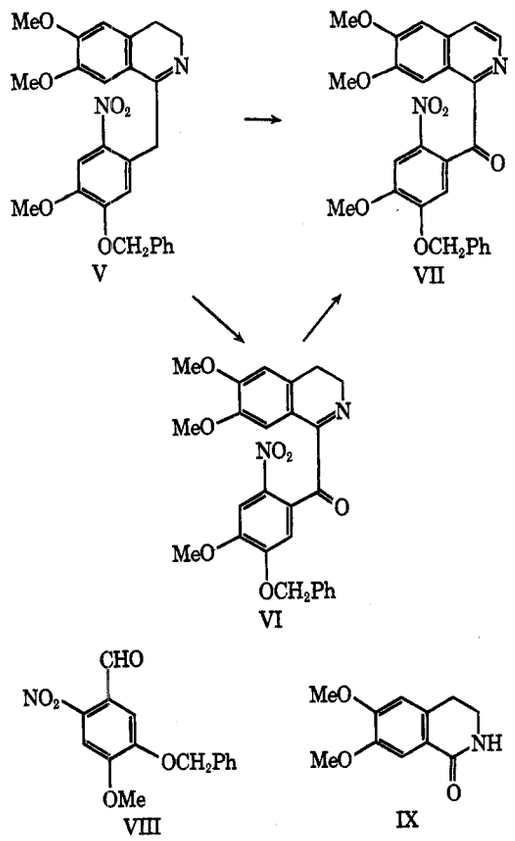
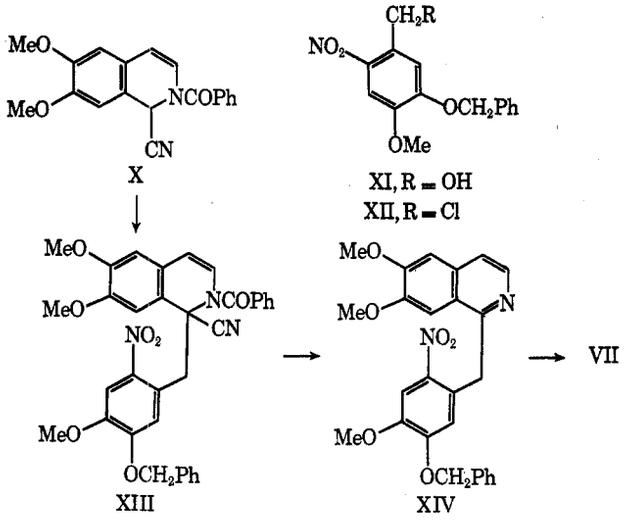
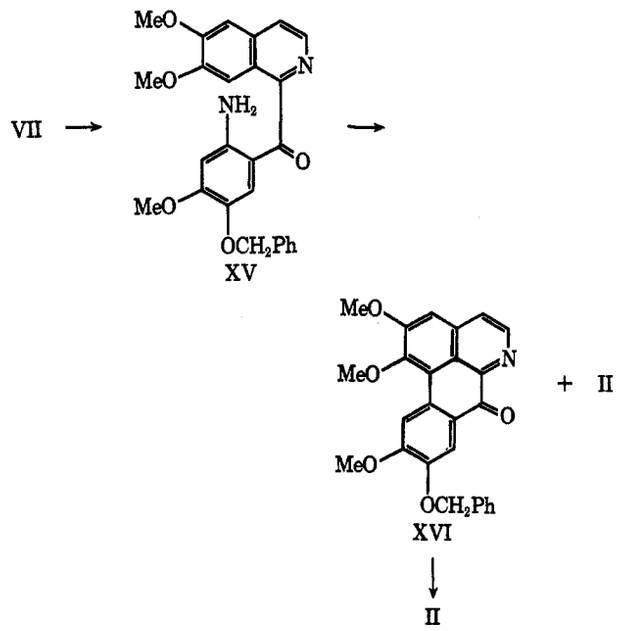


A quite different synthesis of intermediate VII was also carried out in the following manner. Borohydride reduction of aldehyde VIII, followed by treatment of the corresponding benzyl alcohol (XI) with thionyl chloride, afforded the benzyl chloride XII. The Reissert compound X, prepared from 6,7-dimethoxyisoquinoline[6] by reaction with benzoyl chloride and potassium cyanide, was alkylated with halide XII to



give mainly the 1,2-dihydroisoquinoline XIII, mp 176–177°, along with some of the hydrolysis product, 1-(5-benzyloxy-4-methoxy-2-nitrobenzyl)-6,7-dimethoxyisoquinoline (XIV). The nitrile XIII was then hydrolyzed cautiously with Triton B in dimethylformamide[7,8] to give an additional quantity of XIV. Finally, oxidation of XIV with sodium dichromate in acetic acid gave the benzoylisoquinoline VII. Despite careful study, the best yield obtained in this oxidation was rather low (16%), probably due to attack of the benzyl ether function of XIV by the oxidant.

Catalytic hydrogenation of VII in the presence of Raney nickel catalyst, followed by Pschorr cyclization of the resulting keto amine XV, gave not only the desired oxoaporphine, 9-benzyloxy-1,2,10-trimethoxydibenz[*de*,*g*]quinolin-7-one (XVI), mp 228° dec, in 10% yield but also 9-hydroxy-1,2,10-trimethoxydibenz[*de*,*g*]quinolin-7-one (II), mp 252° dec, in 1% yield. The ir spectrum of II showed hydroxyl and carbonyl signals at 2.93 and 6.00 μ, respectively. Its mass spectrum showed a molecular ion peak at *m/e* 337. Furthermore, its uv–visible region spectrum showed absorption bands at 243, 273, 292, 354, 380, and 435 nm which shifted bathochromically in aqueous ethanolic alkali. These spectral properties were in accord with those reported for natural atheroline[1,2] and compatible with structure II.



Catalytic debenzylation of XVI was attempted under a variety of conditions, but II could not be isolated from these reactions. Hydrolysis of XVI in hydrochloric acid and tetrahydrofuran was, however, successful and afforded the desired phenol II in good yield.

As a final proof of identity, II was treated with acetic anhydride to give the corresponding crystalline acetyl derivative III, mp 216–218° dec.[9] The ir spectrum of our synthetic III was superimposable upon that of a sample of *O*-acetylatheroline prepared from the natural base. Furthermore, all of the signals in the nmr spectrum of III were identical within 0.04 ppm with those of *O*-acetylatheroline as reported in the literature.[1,2]

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(9) The melting point (190–195°) recorded for *O*-acetylatheroline in ref 1 is apparently in error. Recrystallization from chloroform–ether–*n*-hexane of an authentic sample of III donated by Professor Bick gave yellow needles, mp 217–219° dec.

In conclusion, the work described above suggests several approaches which should be of general applicability to the synthesis of phenolic oxoaporphines. The one-step oxidation dehydrogenation of V to VII, in particular, may be the prototype of a very useful conversion in oxoaporphine synthesis.

Experimental Section

Analyses were carried out by Midwest Microlab, Inc., Indianapolis, Ind. All melting points are uncorrected. Nmr spectra were measured on a Varian A-60 and a Varian A-100 instrument in $CDCl_3$ using tetramethylsilane as an internal standard unless noted. Mass spectra were measured on a Perkin-Elmer Model 270 instrument. Ultraviolet spectra were measured on a Perkin-Elmer 202 spectrophotometer.

1-(5-Benzyloxy-4-methoxy-2-nitrobenzoyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (VI).—To a stirred solution of 1-(5-benzyloxy-4-methoxy-2-nitrobenzyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (V, 6.0 g) in AcOH (250 ml) was added portionwise chromic acid (4.8 g). After stirring for 1.5 hr at 15–20°, the reaction mixture was poured into ice–water and the precipitate was extracted into $CHCl_3$. Work-up in the usual manner gave a brownish gum (5.6 g), which was chromatographed on silica gel (300 g, $CHCl_3$ eluent). The first fraction yielded 5-benzyloxy-4-methoxy-2-nitrobenzaldehyde (VIII, 690 mg) as yellow prisms, mp 129–131°[3] ($CHCl_3$–ether–*n*-hexane).

The second fraction contained the benzoyl derivative VI (3.2 g), which was recrystallized from $CHCl_3$–*n*-hexane to give yellow needles: mp 148–149°; ir (KBr) 5.85 (CO), 13.45, 14.30 μ (monosubstituted benzene); nmr δ 7.58 (1 H, s, $C_{3'}$ H), 7.84 (1 H, s, $C_{6'}$ H), 7.34 (5 H, s, C_6H_5), 7.12 (1 H, s, C_8 H), 6.65 (1 H, s, C_5 H), 5.20 (2 H, s, OCH_2Ph), 3.92, 3.90, 3.88 (each 3 H, s, 3 OCH_3); mass spectrum *m/e* 476 (M^+).

Anal. Calcd for $C_{26}H_{24}N_2O_7$: C, 65.54; H, 5.08; N, 5.88. Found: C, 65.53; H, 5.03; N, 5.91.

The third fraction gave the isocarbostyryl IX (170 mg) as colorless needles, mp 172–174° (lit.[5] mp 175°).

1-(5-Benzyloxy-4-methoxy-2-nitrobenzoyl)-6,7-dimethoxyisoquinoline (VII).—A mixture of the 3,4-dihydroisoquinoline VI (700 mg), *p*-cymene (200 ml), and 10% Pd/C (800 mg) was heated at 140–145° under N_2 for 4 hr. The catalyst was filtered off, and ether saturated with HCl gas was then added dropwise to the filtrate to afford a yellowish precipitate, which was basified with ammonia and extracted into $CHCl_3$. The usual work-up gave a brownish gum, which crystallized from MeOH to give compound VII (502 mg) as yellow needles: mp 168–169°; ir (KBr) 5.85 (CO), 13.35, 14.30 μ (monosubstituted benzene); nmr δ 8.60, 7.62, 7.18, 7.06 (each 1 H, s, aromatic protons), 8.19, 7.57 (each 1 H, d, J = 6.0 Hz, C_3 and C_4 H), 7.38 (5 H, broad singlet, C_6H_5), 5.22 (2 H, s, OCH_2Ph), 4.10, 4.02, 3.97 (each 3 H, s, 3 OCH_3); λ_{max}^{EtOH} 232 nm (log ϵ 4.42), 349 (3.95); mass spectrum *m/e* 474 (M^+), 91 (tropylium ion).

Anal. Calcd for $C_{26}H_{22}N_2O_7$: C, 65.82; H, 4.67; N, 5.90. Found: C, 65.38; H, 4.84; H, 5.90.

Dehydrogenative Oxidation of V.—A stirred mixture of the 3,4-dihydroisoquinoline V (1.7 g), *p*-cymene (300 ml), and 10% Pd/C (3.5 g) was heated at 140–145° for 4.5 hr. The catalyst was filtered off, and ether saturated with HCl gas was then added to the filtrate to afford a yellowish precipitate, which was basified with ammonia and extracted into $CHCl_3$. The washed extract was evaporated to afford a yellowish gum, which crystallized from MeOH to give yellow needles of 1-(5-benzyloxy-4-methoxy-nitrobenzoyl)-6,7-dimethoxyisoquinoline (VII, 910 mg), mp 169–170°. Its ir spectrum was superimposable on that of the authentic sample.

5-Benzyloxy-4-methoxy-2-nitrobenzyl Alcohol (XI).—To a stirred solution of 5-benzyloxy-4-methoxy-2-nitrobenzaldehyde[3] (VIII, 2.0 g) in MeOH (150 ml) was added portionwise sodium borohydride (0.5 g). The solvent was evaporated and water (200 ml) was added. The yellow precipitate was dissolved in $CHCl_3$ and after washing (H_2O) and removal of the solvent, the resulting residue was crystallized from $CHCl_3$–ether–*n*-hexane to give the benzyl alcohol XI (1.41 g) as yellow needles: mp 132–134°; ir (KBr) 2.75 (OH), 6.60, 7.55 (NO_2), 13.30, 14.40 μ (monosubstituted benzene); nmr δ 7.73 (1 H, s, C_3 H), 7.43 (5, H, broad singlet, C_6H_5), 7.27 (1 H, s, C_6 H), 5.24 (2 H, s, OCH_2Ph), 4.94 (2 H, broad, CH_2OH), 3.94 (3 H, s, OCH_3).

Anal. Calcd for $C_{15}H_{15}NO_5$: C, 62.28; H, 5.23; N, 4.84. Found: C, 61.99; H, 5.40; N, 4.88.

2-Benzoyl-1-cyano-6,7-dimethoxy-1,2-dihydroisoquinoline (X).—To a stirred mixture of 6,7-dimethoxyisoquinoline[6] (3.1 g), CH_2Cl_2 (35 ml), potassium cyanide (4.2 g), and water (10 ml) was added dropwise benzoyl chloride (3 ml) at 0–5°. After stirring for an additional 4 hr, CH_2Cl_2 (50 ml) was added and the organic layer was separated. The washed (H_2O) and dried (Na_2SO_4) solvent was evaporated to afford a gum, which crystallized from EtOH to give the Reissert compound X (1.7 g) as colorless needles: mp 167–168°; ir (KBr) 4.35 (CN), 5.95 (CO), 6.05 μ (C=C); nmr δ 7.57 (5 H, broad singlet, C_6H_5), 6.91 (1 H, s, C_8 H), 6.77 (1 H, s, C_5 H), 6.54 (1 H, s, methylene proton), 6.58 (1 H, d, J = 8.0 Hz, C_4 H), 6.00 (1 H, d, J = 8.0 Hz, C_3 H), 3.90 (6 H, s, 2 OCH_3).

Anal. Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.75. Found: C, 71.27; H, 5.26; N, 8.87.

Alkylation of X with XII.—To a stirred suspension of the benzyl alcohol XI (3.0 g) and sodium acetate (1.2 g) in dry benzene (200 ml) was added dropwise thionyl chloride (6 ml). After stirring for 1 hr at room temperature, the filtered solution was evaporated to give the benzyl chloride XII as a brownish gum. To a solution of chloride XII and the Reissert compound X (3.0 g) in dimethylformamide (100 ml) was added portionwise sodium hydride (50% in mineral oil, 0.9 g) with stirring at 0–5°. After stirring for a further 4 hr at 0–5°, aqueous ammonium chloride was added to the reaction mixture, which was then poured into a large amount of ice–water. The resulting solid was dissolved in $CHCl_3$ and worked up as usual to give a brownish gum (3.7 g). Chromatography on silica ($CHCl_3$ eluent) gave the following compounds. The first fraction afforded 1-(5-benzyloxy-4-methoxy-2-nitrobenzyl)-6,7-dimethoxyisoquinoline (XIV, 0.7 g) as pale yellow needles: mp 254° dec ($CHCl_3$–*n*-hexane); ir (KBr) 6.08 (C=C and C=N), 6.52, 7.42 (NO_2), 13.55, 14.35 μ (monosubstituted benzene); nmr δ 8.28 (1 H, d, J = 6.0 Hz, C_3 H), 8.14, 7.92 (each 1 H, s, aromatic protons), 7.30 (6 H, broad singlet, C_6H_5 and C_4 H), 4.05, 3.96, 3.64 (each 3 H, s, 3 OCH_3); uv λ_{max}^{EtOH} 241 nm (log ϵ 4.54), 315 (sh, 3.57), 329 (3.63), 344 (3.53).

Anal. Calcd for $C_{26}H_{24}N_2O_6$: C, 67.81; H, 5.25; N, 6.08. Found: C, 67.35; H, 5.17; N, 6.15.

The second fraction gave 2-benzoyl-1-(5-benzyloxy-4-methoxy-2-nitrobenzyl)-1-cyano-6,7-dimethoxy-1,2-dihydroisoquinoline (XIII, 1.9 g) as yellow needles: mp 176–177° (EtOH); ir (KBr) 5.85 (CO), 5.97 (C=C), 6.50, 7.48 (NO_2), 13.25, 14.35 μ (monosubstituted benzene); nmr δ 7.38, 7.10 (each 1 H, s, $C_{3'}$ and $C_{6'}$ H), 6.58, 6.53 (each 1 H, s, C_5 and C_8 H), 6.37 (1 H, d, J = 8.0 Hz, C_3 H), 5.68 (1 H, d, J = 8.0 Hz, C_4 H), 5.24, (2 H, s, OCH_2Ph), 3.94 (6 H, s, 2 OCH_3), 3.66 (3 H, s, OCH_3); uv λ_{max}^{EtOH} 228 nm (log ϵ 4.45), 245 (4.42), 313 (4.07).

Anal. Calcd for $C_{34}H_{29}N_3O_7$: C, 69.02; H, 4.94; N, 7.10. Found: C, 69.27; H, 5.21; N, 6.86.

1-(5-Benzyloxy-4-methoxy-2-nitrobenzyl)-6,7-dimethoxyisoquinoline (XIV).—To a stirred solution of XIII (1.0 g) in dimethylformamide (30 ml) was added Triton B (3.0 ml) at room temperature. After stirring for 1 hr, the reaction mixture was poured into ice–water to afford a yellowish precipitate. Work-up as usual gave a brownish gum, which crystallized from MeOH to afford the isoquinoline XIV (205 mg) as pale yellow needles, mp 254° dec.

Oxidation of XIV with Sodium Dichromate.—A mixture of XIV (300 mg), AcOH (15 ml), and sodium dichromate (600 mg) was refluxed for 30 min. The reaction mixture was poured into ice–water to afford a yellowish precipitate, which was filtered and extracted with $CHCl_3$. The usual work-up gave a brownish gum, which was chromatographed on silica ($CHCl_3$ eluent) to give compound VII (51 mg), mp 168–170°.

Hydrogenation of VII and Pschorr Reaction of XV.—The nitrobenzoylisoquinoline VII (500 mg) was dissolved in tetrahydrofuran (100 ml) and hydrogenated in the presence of Raney nickel (W-2) at atmospheric pressure for 20 hr. The catalyst was removed and the solvent was then evaporated to afford a yellow residue, which was dissolved in ether (200 ml). Ether saturated with HCl gas was added to the solution to give the hydrochloride of amine XV (490 mg) as a yellow, amorphous powder. This hydrochloride (480 mg) was dissolved in a mixture of 10% H_2SO_4 (5 ml), MeOH (20 ml), and water (15 ml) and then diazotized with 10% $NaNO_2$ (5 ml) at 0–5°. After stirring for a further 30 min at 0–5°, copper powder (50 mg) was added to the reaction mixture. After heating at 45–50°

for 30 min, the reaction mixture was basified with ammonia and extracted with $CHCl_3$. The extract was washed with 10% NaOH in order to separate the products into nonphenolic and phenolic fractions. Purification of the nonphenolic material by tlc (silica, using 1:1 benzene–acetone as developer) gave 9-benzyloxy-1,2,10-trimethoxydibenz[*de*,*g*]quinolin-7-one (XVI, 47 mg): mp 228° dec ($CHCl_3$–MeOH); ir (KBr) 5.95 (CO), 13.60, 14.45 μ (monosubstituted benzene); nmr δ 8.82 (1 H, d, J = 6.0 Hz, C_5 H), 8.73 (1 H, s, C_{11} H), 8.06 (1 H, s, C_8 H), 7.68 (1 H, d, J = 6.0 Hz, C_4 H), 7.60–7.25 (5 H, m, C_6H_5), 7.12 (1 H, s, C_3 H), 5.30 (2 H, s, OCH_2Ph), 4.07, 4.03, 4.00 (each 3 H, s, 3 OCH_3); uv λ_{max}^{EtOH} 243 nm (log ε 4.04), 272 (4.03), 291 (sh, 3.85), 355 (3.65), 380 (sh, 5.95), 428 (sh, 3.45); mass spectrum m/e 427 (M^+), 336, 91 (tropylium ion).

Anal. Calcd for $C_{26}H_{21}NO_5$: C, 73.05; H, 4.95; N, 3.28. Found: C, 72.55; H, 4.84; N, 3.28.

The aqueous alkaline layer was neutralized with ammonium chloride and then extracted with $CHCl_3$. The extract was dried over sodium sulfate. The usual work-up gave a brownish gum, which was purified by tlc (silica, using 10:1 $CHCl_3$–MeOH as developer) to give 9-hydroxy-1,2,10-trimethoxydibenz[*de*,*g*]-quinolin-7-one (II, 6 mg) as an amorphous powder: mp 252° dec ($CHCl_3$–*n*-hexane); ir (KBr) 2.93 (OH), 6.00 μ (CO); uv λ_{max}^{EtOH} 243 nm (log ε 4.12), 273 (4.11), 292 (3.92), 354 (3.70), 380 (sh), (3.67), 435 (3.55); $\lambda_{max}^{EtOH-NaOH}$ 251 nm (log ε 4.07), 296 (3.99), 324 (3.97), 390 (3.42), 535 (3.30); $\lambda_{max}^{EtOH-HCl}$ 256 nm (log ε 4.08), 286 (4.01), 380 (3.68), 500 (3.17); mass spectrum m/e 337 (M^+).

Hydrolysis of XIX.—A mixture of *O*-benzylatheroline (XVI, 22 mg), tetrahydrofuran (3 ml), and hydrochloric acid (5 ml) was refluxed for 2 hr. The solvent was evaporated to afford a dark purple hydrochloride, which was washed with ether, suspended in $CHCl_3$, and basified with ammonia. The $CHCl_3$ extract was dried (Na_2SO_4) and the solvent was then concentrated to 5 ml. Addition of a small amount of *n*-hexane gave atheroline (II, 11 mg) as an amorphous yellow powder, mp 252° dec.

9-Acetoxy-1,2,10-trimethoxydibenz[*de*,*g*]quinolin-7-one (III).—A mixture of synthetic atheroline (II, 10 mg), tetrahydrofuran (15 ml), acetic anhydride (10 drops), and potassium carbonate (300 mg) was stirred for 20 hr at room temperature. The inorganic salt was filtered off and the solvent was then evaporated to give a gum which was extracted into $CHCl_3$. The extract was washed with 5% $NaHCO_3$ and water and dried (Na_2SO_4), and the solvent was evaporated. Trituration with ether gave crystals which were recrystallized ($CHCl_3$–ether) to give 9-acetoxy-1,2,10-trimethoxydibenz[*de*,*g*]quinolin-7-one (III) (9 mg) as yellow needles: mp 216–218° dec; ir (KBr) 5.54 ($OCOCH_3$), 5.92 μ (CO); nmr ($CDCl_3$) δ 8.82 (1 H, s, C_{11} H), 8.82 (1 H, d, J = 6.0 Hz, C_5 H), 8.20 (1 H, s, C_8 H), 7.68 (1 H, d, J = 6.0 Hz, C_4 H), 7.14 (1 H, s, C_3 H), 4.04 (3 H, s, OCH_3), 4.02 (6 H, s, 2 OCH_3), 2.37 (3 H, s, $OCOCH_3$); nmr (CF_3COOH) δ 9.08 (1 H, s, C_{11} H), 8.73 (1 H, d, J = 6.0 Hz, C_5 H), 8.50 (1 H, d, J = 6.0 Hz, C_4 H), 8.26 (1 H, s, C_8 H), 7.68 (1 H, s, C_3 H), 4.37, 4.31, 4.18 (each 3 H, s, 3 OCH_3), 2.50 ppm (3 s, H, $OCOCH_3$). Its spectral properties (ir, nmr) were identical with those of *O*-acetylatheroline derived from natural atheroline, and a mixture melting point (216–219° dec) showed no depression.[9]

Registry No.—II, 1349-20-8; III, 5140-36-3; VI, 35096-38-9; VII, 35096-39-0; X, 35096-40-3; XI, 35096-42-5; XIII, 35096-41-4; XIV, 35096-43-6; XVI, 35096-44-7.

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Reduction and Hydrolysis of Triethyl α-Phosphonocinnamate and Its Derivatives

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The triethyl ester of α-phosphonocinnamic acid and some of its derivatives can be reduced with sodium borohydride to the corresponding triethyl α-phosphonohydrocinnamates. Hydrolysis of both the unsaturated and the saturated esters in concentrated hydrochloric acid causes dephosphonation and the formation of cinnamic acid and hydrocinnamic acid and their derivatives, respectively.

A number of aromatic aldehydes, **1**, undergo condensation with triethyl phosphonoacetate (**2**) to give triethyl α-phosphonocinnamates (**3**)[2] (Scheme I); however, the chemistry of compounds of type **3** has been examined only cursorily to date. As a part of an attempt to find a convenient general method for the synthesis of β-styryl- (**10**) and β-phenethylphosphonic acids[3] (**11**), we have examined some of the chemical properties of these compounds.

Reduction.—The selective reduction of the carbon–carbon double bond of the phosphonocinnamate esters **3** to give the corresponding phosphonopropionates **4** has been accomplished by treating the unsaturated esters with a 1:1 molar ratio of $NaBH_4$.[4] The results of these reductions are summarized in Table I. Both ethanol and pyridine were used as solvents; it may be deduced from Table I that pyridine is the superior solvent. The reduction reactions were relatively simple to carry out; however, some decomposition occurred during distillation and considerable difficulty was experienced in obtaining analytically pure products. Due to the minor differences in the percentage composition of starting materials and products, more emphasis was placed on nmr data than on elemental analysis. In the case of the unsaturated esters **3**, absorption due to the vinylic hydrogen occurred as a doublet (J = 24 ± 1 cps) at δ 7.52–8.42; in the reduced esters **4**, the absorption in this region disappeared with the emergence of new absorption at δ 2.7–3.3 (multiplet) due to the new methylene and methine hydrogens.

In addition to the compounds listed in Table I, attempts were made to reduce three other compounds: triethyl *p*-methyl-α-phosphonocinnamate, triethyl 3,4-dimethoxy-α-phosphonocinnamate, and the diethyl ester of courmarin-3-phosphonic acid (**15**). Decomposition during distillation of the reduced products was so extensive that reasonable analyses could not be obtained; however, the vinylic proton absorption in the nmr spectra of the crude products was reduced in size or disappeared entirely and the expected absorption appeared in the δ 2.7–3.3 region. Additional evidence for

(1) (a) The authors gratefully acknowledge the support of this work by the National Institutes of Health, U. S. Public Health Service (GM-12480). (b) Part of the work discussed in this article is abstracted from work presented for the M.S. Thesis by P. K. Li.

(2) C. N. Robinson and J. F. Addison, *J. Org. Chem.*, **31**, 4825 (1966).

(3) This problem has now largely been solved by the work of G. H. Jones, E. K. Hamamura, and J. G. Moffatt, *Tetrahedron Lett.*, 5731 (1968).

(4) Reduction procedures were patterned after the work of S. B. Kadin, *J. Org. Chem.*, **31**, 620 (1966).