Total Synthesis of 4,5,7a,8-Tetrahydro-1,2-dimethoxyphenanthro[10,1-*bc*]-azepin-6(7*H*)-one: A Photochemical Approach

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The total synthesis of a novel benzazepine, 4,5,7a,8-tetrahydro-1,2-dimethoxyphenanthro[10,1-*bc*]azepin-6(7*H*)-one is described. Of crucial importance to the preparation of this material was a regiospecific Beckmann rearrangement reaction and the development of an aryl-aryl linkage by a photochemically induced coupling. Details of successful and attempted methodology are reported.

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The tremendous variety of pharmacological properties displayed by the benzazepine-class of heterocycles has led to considerable activity devoted to the synthesis of these types of compounds [3]. Derivatives of 1-, 2-, 3-benzazepines have exhibited hypotensive, hypoglycemic, analgesic, tranquilizing, anoxetic bacterial, antidepressant and anticancer activity. Within this group are several naturally occurring alkaloids, including the rhoeadines, indenobenzazepines, isopavines, homoprotoberberines, and cephalotaxines.

As part of a continuing effort to develop new and improved methods for the synthesis of 2-benzazepines related to the homoaporphines, we wish to report herein the total synthesis of 4,5,7a,8-tetrahydro-1,2-dimethoxyphenanthro[10,1-*bc*]azepin-6(7*H*)-one (I). This compound has the skeletal features of a homoaporphine alkaloid but differs in the site of ring enlargement, therefore, this unnatural heterocyclic compound has been termed a B-ring "homoaporphine". Previous synthetic efforts in our laboratory directed toward the preparation of this heterocyclic skeleton have focused on the benzylation of 2-tetralones and a regiospecific Beckmann rearrangement of the corresponding oximes to develop the A-, B-, and D-rings of this system. However, formation of the C-ring by aryl-aryl ring coupling presented a major problem. In our hands, attempts to utilize the Pschorr cyclization procedure was, at best, very capricious. Under the most ideal conditions, this reaction proved to be difficult to reproduce, starting materials were numerous, difficult to make and difficult to purify, and only moderate yields of product were realized.

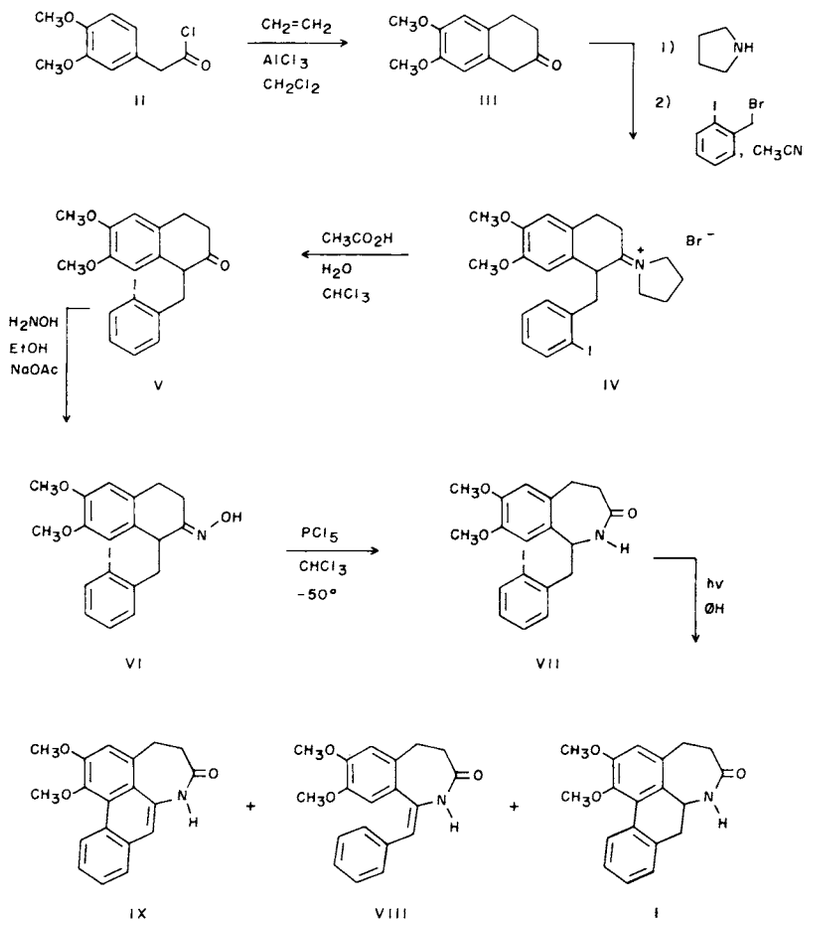
In a previous publication by Berney and Schuh [4], the benazepine moiety of the phenanthro[10,1-*bc*]azepin ring-system described in this paper was constructed using a Schmidt reaction. In turn, the strategic bond linking the A-D rings was prepared by way of a traditional Pschorr closure. Both methods, however, encountered serious difficulties. The Schmidt reaction afforded only moderate to low yields of isomeric mixtures of 2-benzazepin-3-ones and 3-benzazepin-2-ones. Equally troublesome were their attempts to form aryl-aryl linkages using the Pschorr ring closure method. This method led to very low yields of the expected tetracyclic compound while a majority of the product proved to be non-cyclized phenolic or deaminated derivatives.

Attempts in our laboratory to overcome these problems have met with much success. In two preceding papers, we have described the synthetic value of a regiospecific Beckmann rearrangement process which affords only 2-benzazepin-3-ones in excellent yield. Results of our initial studies demonstrated that steric controls were operative both before and during the rearrangement of 1-benzylated-2-tetralone oximes [5]. Consequently, high yields of the desired product were realized. Furthermore, this reaction sequence was effectively put into practice in the synthesis of the first B-ring "homoaporphine" [6]. Yet, as effective as the Beckmann process proved to be, the development of methodology for the construction of the aryl-aryl bond remained a major problem. Consequently, we chose to investigate a photochemical approach to this synthesis.

The successful synthetic scheme for the preparation of I is shown in Scheme I. In this scheme the A & B rings were provided in the form of a tetralone system. The dimethoxy substituents were introduced so as to potentiate possible biological activity of the final product [7]. 3,4-Dimethoxyphenylacetic acid was converted to its acid chloride derivative and then reacted with ethylene in the presence of aluminum chloride in methylene chloride at -5° to produce 6,7-dimethoxy-2-tetralone (III) in 36% yield.

In turn, III was alkylated with *o*-iodobenzyl bromide using an improved enamine reaction developed in this laboratory [8]. In this procedure, crude 2-(*N*-pyrrolidyl)-6,7-dimethoxytetralone was reacted with *o*-iodobenzyl bromide in refluxing dry acetonitrile. Washing of the highly colored crude product with acetone provided the pure iminium salt IV as a high melting stable crystalline material. Purification of IV by this method prior to hydrolysis often eliminated the need for tedious column chromatography in the isolation of the corresponding ketone. In fact, IV could be conveniently stored for long periods before hydrolysis to the ketone V. Mild hydrolysis of IV with aqueous acetic acid/chloroform at room temperature afforded V in 73% isolated yield.

Scheme I



Conversion of V to its oxime VI also required very mild conditions so as to avoid undesirable side-reactions and tar formation. The reaction of V with hydroxylamine in an ethanolic sodium acetate solution furnished VI in excellent yeild. Most importantly, the 200 MHz ^{1}H-nmr of the isolated product revealed that virtually all of the oxime which had formed was of the *E*-configuration(compound VI). Only a small amount of the *Z*-isomer (< 5%) could be detected. These results are in keeping with our previous report [5] that bulky *ortho*-1-benzyl substituents of 2-tetralones favor the *anti* oxime. In turn, these same steric controls dictate the course of the subsequent Beckmann rearrangement and, thus, lead to only the desired 2-benzazepin-3-one VII. Rearrangement of VI was carried out in a chloroform solution of phosphorus pentachloride at -50° to furnish VII in 46% yield.

The photolytic ring-closure of VII was accomplished in a dry degassed benzene solution under a nitrogen atmosphere [9]. The iodolactam was irradiated for 24 hours using a 450 watt Hanovia ultraviolet lamp equipped with a Corex filter. Workup of the reaction mixture and isolation of the product by preparative thin-layer chromatography afforded 42% of the desired cyclized phenanthroazepin-3-one I. A variety of spectroscopic data provided proof of structure for this compound, in particular, 400 MHz ^{1}H-nmr proved most informative. The four-spin AA'BB' system presented by the $-CH_2-CH_2-$ group [10] was displayed as two 7-line patterns, one centered at 2.49 ppm and the other at 3.29 ppm. The multiplicity, spacing, and intensity of the peaks in these patterns matched computer simulated spectra for this system [11]. The diastereotopic protons of the remaining methylene group formed two doublets centered at 3.13 and 3.11 ppm. The methoxyl functions were found at 3.73 and 3.92 ppm. The methine proton was shown at 4.85 ppm as a 6-line pattern due to a coupling between the diastereotopic methylene protons and the NH-proton. The N-H absorption was found as a broad peak at 5.90 ppm. The lone shielded aromatic proton on the dimethoxyaryl moiety was displayed as a sharp singlet at 6.73 ppm. All of the remaining aromatic protons, except one, formed a complex multiplet centered at 7.26 ppm. However, the aromatic proton nearest the methoxyl function was substantially deshielded owing to through-space electric dipole and/or Van der Waals interactions

[12]. The mass spectrum of I gave a molecular ion at m/z value 309 which was also the base peak. Except for the loss of a methyl group, the mass spectrum was virtually free of fragmentations. In addition, the ultraviolet spectrum displayed λ max values which were characteristic of the dimethoxybiphenyl chromophore [13].

The formation of I was accompanied by a nearly equivalent amount (39%) of the photo-cyclized unsaturated lactam IX. Proof of structure for IX was provided by a combination of spectroscopic techniques and chemical reactions. The 200 MHz ^{1}H-nmr of IX showed two three-line patterns for the AA'BB' system centered at 2.89 and 3.45 ppm. With the absence of the CH-CH_2 function, only the lone aromatic proton at C-3(7.07 ppm), the =CH proton from the C-ring (7.14 ppm) and the NH absorption centered at 7.65 ppm remained up-field from the D-ring aromatic protons. (The NH absorption disappeared upon addition to the sample of deuterium oxide containing sodium.) The unusually low field absorption of the lactam proton is a characteristic feature of aromatization in the C-ring since dehydroaporphines display similar deshielding effects for N-CH_3 groups [14]. Protons at C-9, -10, -11 were centered at 7.70 ppm while the proton at C-12 was again heavily deshielded (9.61 ppm) because of steric and electronic effects. The mass spectrum, as was the case with I, provided a molecular ion (m/z 307) which was also the base peak. Further fragmentation was very rare in this molecule and only low-intensity peaks were observed. A high-resolution mass spectrum of this sample provided an excellent elemental analysis. Further verification of the phenanthrene ring-system was obtained through the UV spectrum [15].

In addition, a small amount (14%) of 1-benzylidene-1,2,4,5-tetrahydro-7,8-dimethoxy-3*H*-2-benzazepin-3-one(VIII) was isolated from this mixture. This compound displayed two 3-line patterns for the AA'BB' system centered at 2.65 and 3.47 ppm. The methoxyl groups had absorptions at 3.91 and 4.02 ppm. The NH-proton produced a broad singlet at 5.26 ppm. Protons at C-9 and C-6 appeared as sharp singlets at 7.25 and 7.36 ppm, respectively. The benzylidene proton was found as a sharp singlet at 7.60 ppm among a three-proton aromatic multiplet centered at 7.50-7.90 ppm. One highly deshielded *ortho*-proton was found at 9.65 ppm. Mass spectral and ultraviolet analyses provided further support for this structural assignment.

Because proton-nmr provided somewhat tenuous evidence for the structures of IX and VIII, two oxidation reactions were conducted on compound I. In the first experiment, I was treated with an acetone solution of potassium permanganate [16] while the second reaction involved re-irradiation of I in the presence of a catalytic amount of molecular iodine [17]. Both conditions led to excellent yields of IX, as evidenced by comparison of spectroscopic and tlc data. Furthermore, continued irradiation of IX slowly afforded the benzylidene VIII. It would appear, therefore, that a free-radical ring-closure is involved during the irradiation of VII and its conversion to I. In turn, I undergoes an iodine catalyzed photo-dehydrogenation leading to the formation of IX. Finally, under these conditions IX is capable of slowly undergoing an electrocyclic ring-opening to give VIII [18]. The likelihood that a free-radical ring-closure is involved here was supported further by the observation that the use of any proton-source or protic solvent must be avoided during the reaction. For example, attempts to use the methodology developed by Cava and coworkers [19], namely *t*-butoxide/*t*-butyl alcohol/hv, failed to yield any of the desired product. Likewise, I is the direct precursor to IX since attempts to photo-cyclize compound VIII to compound IX under the same photochemical conditions described here were unsuccessful.

One particular aspect of this photocyclization procedure which merits some comment is the exceptionally high yields which were realized. The combined yield of photocyclized products was 81%. The lactam moiety in this system provides not only a functional group capable of removing the nitrogen non-bonding electron-pair from participating in undesired photochemical [9] reactions but, in addition, induces additional coplanarity in the structure [6]. These effects combine to give an optimal situation for a ring-closure reaction. Unfortunately, it has proven impossible to prevent aromatization of I following its formation under these photolysis conditions. Attempts to capture iodine as it is formed requires a partially aqueous media in which to dissolve sodium thiosulfate [9] and thus drastically reduces the effectiveness of the coupling procedure. Attempts to use acetonitrile/sodium thiosulfate have also been ineffective in preventing formation of IX.

EXPERIMENTAL

Melting points were obtained with a Thomas-Hoover melting point apparatus and are uncorrected. Distillations were performed on Büchi/Brinkman Kugelrohrofen microdistillation oven or a short-path distillation unit and boiling points were uncorrected. Infrared (ir) spectra were determined on a Perkin-Elmer model 457 spectrophotometer and were recorded in reciprocal centimeters. Nuclear magnetic resonance (nmr) spectra were recorded on a Varian XL-200 (200 MHz), Hitachi Perkin-Elmer R20-B (60 MHz), or Bruker WH-400 (400 MHz) spectrometer in parts per million downfield from tetramethylsilane as an internal standard. Mass spectral (ms) analyses were performed on a Hewlett-Packard 5985 system (low resolution) or at the NIH Mass Spectrometry Facility, Massachusetts Institute of Technology (high resolution). Ultraviolet (uv) spectra were taken on a Perkin-Elmer Model 124 recording spectrophotometer. Preparative thin-layer chromatography was carried out using Analabs precoated tlc plates with Anasil-OF (250 microns). Column chromatography was done on Brinkman Instruments silica gel 60 (70-230 mesh) or Brockmann basic alumina I (80-200 mesh). Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn.

o-Iodobenzyl Bromide.

This compound was prepared in 88% yield by the method described by Bradsher et al. [20], mp 57-58° (lit [21] mp 52-53°).

6,7-Dimethoxy-2-tetralone (III).

This compound was prepared by the method of Horn and coworkers using 3,4-dimethoxyphenylacetyl chloride, aluminum chloride, and ethylene [22], mp 86-87° (lit [22] mp 85.5-86°).

1-(*o*-Iodobenzyl)-6,7-dimethoxy-2-tetralone (V).

To a solution of 6,7-dimethoxy-2-tetralone (III) (1.53 g, 7.42 mmoles) and one crystal of *p*-toluenesulfonic acid in dry benzene (25 ml) heated to reflux and under a nitrogen atmosphere was added dropwise a solution of pyrrolidine (1.06 g, 15 mmole) in dry benzene (5 ml). The resulting solution was then refluxed for 3 hours using a Dean-Stark water trap. The solution was cooled and the solvent removed *in vacuo*.

A solution of crude 2-(*N*-pyrrolidyl)-6,7-dimethoxytetralone, prepared above and *o*-iodobenzyl bromide (3.30 g, 11 mmoles) in dry acetonitrile (25 ml) was refluxed for 24 hours under a nitrogen atmosphere. The solution was cooled and the solvent removed under reduced pressure. The crude iminium salt was washed thoroughly with dry acetone (50 ml) and collected by filtration (3.6 g, 87%, mp 214-216°).

The colorless iminium salt was then stirred at room temperature in a mixture of chloroform (5 ml), glacial acetic acid (10 ml), and water (40 ml) for 8 hours. Chloroform (75 ml) was added, the organic layer was washed well with water, and dried with sodium sulfate. The solvent was evaporated and the resulting residue was chromatographed over a column of silica gel using chloroform elution to give a yellow oil which, upon recrystallization, from (ether-pet ether), afforded V as a colorless solid (2.3 g, 73%), mp 84-86°; ir (neat): 1709, 1244, 754 cm^{-1}; ^1H nmr (deuteriochloroform, 200 MHz): δ 2.30-3.27 (m, 2H-3, 2H-4, 4H), 3.33 (dd, benzylic CH_2, 2H, J = 6.4 Hz, J = 5.9 Hz), 3.51 (s, CH_3O-7, 3H), 3.67 (dd, H-1, 1H, J = 9.5 Hz, J = 6.4 Hz), 3.85 (s, CH_3O-6, 3H), 6.00 (s, H-8, 1H), 6.71 (s, H-5, 1H), 6.80-7.30 (m, ArH, 3H), 7.76 (dd, ArH, 1H, J_o = 8.1 Hz, J_m = 1.5 Hz); ms: (70 eV) m/z (relative intensity) 422 (M^+, 11), 205 (100).

Anal. Calcd. for $C_{19}H_{19}IO_3$: C, 54.04; H, 4.53. Found: C, 54.04; H, 4.61.

1-(*o*-Iodobenzyl)-6,7-dimethoxy-2-tetralone Oxime (IV).

Compound V (1.02 g, 2.4 mmoles), hydroxylamine hydrochloride (0.33 g, 4.3 mmoles) and sodium acetate (0.39 g, 4.8 mmoles) were refluxed in a solution of ethanol (4 ml) and water (2 ml) for 2 hours. After cooling, the solution was filtered and the filtrate extracted with chloroform. The combined extracts were washed with water before drying over sodium sulfate. Removal of the solvent left a residue which recrystallized from benzene to afford 0.92 g (87%) of VI as a colorless crystals, mp 185-186°; ir (potassium bromide): 3700-3000, 1600, 1504, 1458, 1220, 1111, 922, 753 cm^{-1}; ^1H nmr (deuteriochloroform, 200 MHz): δ 2.60-3.30 (m, 2H-3, 2H-4, $1CH_2$, 6H), 3.60 (s, CH_3O-7, 3H), 3.74 (t, H-1, 1H, J_{CH} = 8.1 Hz), 3.86 (s, CH_3O-6, 3H), 6.24 (s, H-8, 1H), 6.68 (s, H-5, 1H), 7.0-7.30 (m, ArH, 3H), 7.80 (dd, ArH, 1H, J_o = 4.9 Hz, J_m = 2.0 Hz); ms: (70 eV) m/z (relative intensity) 437 (M^+, 1), 220 (100).

Anal. Calcd. for $C_{19}H_{20}INO_3$: C, 52.18; H, 4.61. Found: C, 51.92; H, 4.52.

1,2,4,5-Tetrahydro-1-(*o*-iodobenzyl)-7,8-dimethoxy-3*H*-2-benzazepin-3-one (VII).

The oxime VI (0.50 g, 1.1 mmoles), prepared above, was suspended in dry chloroform (40 ml) and cooled to −50° using a dry ice-acetone bath. With stirring, phosphorus pentachloride (0.25 g, 1.2 mmoles) was added portionwise over a period of 10 minutes so as to maintain the internal temperature at −35°. The temperature was maintained between −30 and −20° for 4 hours. The reaction mixture was then allowed to come to room temperature and stirring was continued for an additional 2-18 hours until the reaction mixture had changed from a yellow to an orange color and tlc indicated the presence of no starting material. The mixture was poured, with stirring, into water and then extracted with chloroform. The combined extracts were washed with water, 5% sodium hydroxide solution and aqueous sodium chloride solution before drying over sodium sulfate. Removal of the solvent afforded a residue which was chromatographed over basic alumina using 50/50 chloroform-ether to remove colored impurities and then with 70/30 chloroform-ethyl acetate to give 1,2,4,5-tetrahydro-1-(*o*-iodobenzyl)-7,8-dimethoxy-3*H*-2-benzazepin-3-one (VII) as a colorless solid. Recrystallization from chloroform-ether furnished 0.23 g (46%) of VII, mp 205-206°; ir (potassium bromide): 3294, 1640, 1241 cm^{-1}; ^1H nmr (deuteriochloroform, 200 MHz): δ 2.60-2.95 (m, 2H-5, 2H-4, 4H), 3.33 (dd, benzylic CH_2, 2H, J = 8.4 Hz), 3.78 (s, CH_3O-8, 3H), 3.88 (s, CH_3O-7, 3H), 4.71 (6-lines, H-1, 1H), 5.96 (d, NH, 1H, J = 5.4 Hz), 6.63 (s, H-9, 1H), 6.71 (s, H-6, 1H), 6.90-7.40 (m, ArH, 3H), 7.85 (dd, ArH, 1H, J_o = 8.1 Hz, J_m = 1.7 Hz); ms: (70 eV) m/z (relative intensity) 437 (M^+, 1), 220 (100), 177 (42); uv (methanol): λ max 216, 232, 243, 248, 254, 261.

Anal. Calcd. for $C_{19}H_{20}INO_3$: C, 52.19; H, 4.61. Found: C, 52.39; H, 4.64.

Photolysis of 1,2,4,5-Tetrahydro-1-(*o*-iodobenzyl)-7,8-dimethoxy-3*H*-2-benzazepin-3-one (VII).

A solution of VII (0.10 g, 0.23 mmoles) was dissolved in dry degassed benzene (500 ml) and irradiated under a nitrogen atmosphere for 24 hours using a 450 watt Hanovia ultraviolet lamp equipped with a Corex filter. After approximately 24 hours the solution had a noticeable yellow color and the starting material had dissolved. The solution was evaporated to dryness and the yellow residue was subjected to preparative thin-layer chromatography using 95/5 chloroform-methanol elution. The bands at R_f = 0.74, 0.46, and 0.37 were collected. The adsorbent was extracted with chloroform, filtered and evaporated to dryness.

The sample with R_f = 0.37 was recrystallized from benzene-hexane to afford 1-(benzylidene)-1,2,4,5-tetrahydro-7,8-dimethoxy-3*H*-2-benzazepin-3-one (VIII) as colorless crystals (8.6 mg, 14%), mp 166-167°; ir (poassium bromide): 3406, 1660, 1283, 1121 cm^{-1}; ^1H nmr (deuteriochloroform, 200 MHz): δ 2.65 (3-lines, 2H-4, 2H), 3.47 (3-lines, 2H-5, 2H), 3.91 (s, CH_3O-8, 3H), 4.02 (s, CH_3O-7, 3H), 5.26 (bs, NH, 1H), 7.26 (s, H-6, 1H), 7.36 (s, H-9, 1H), 7.60 (s, =CH, 1H), 7.50-7.90 (m, ArH, 3H), 9.65 (m, ArH, 1H); ms: (70 eV) m/z (relative intensity) 309 (M^+, 100), 251 (70), 178 (24), 165 (23); uv (methanol): λ max 213, 233, 250, 256, 308.

Anal. Calcd. for $C_{19}H_{19}NO_3 \cdot 0.1\phi H$: C, 74.21; H, 6.23. Found: C, 74.32; H, 6.58. Calcd. for $C_{19}H_{19}NO_3$: 309.1363, Found: 309.1362.

The sample with R_f = 0.46 was recrystallized from benzene-hexane to yield 26.5 mg (42%) of 4,5,7a,8-tetrahydro-1,2-dimethoxyphenanthro-[10,1-*bc*]azepin-6(7*H*)-one (I) as a colorless solid, mp 193-194° (soften 161°); ir (potassium bromide) 3220, 1660, 1241, 1028 cm^{-1}; ^1H nmr (deuteriochloroform, 400 MHz): δ 2.49 (7-lines of AA'BB', 2H-5, 2H), 3.09 (d, H-8, 1H, J = 5.9 Hz), 3.13 (d, H-8, 1H, J = 5.9 Hz), 3.29 (7-lines of AA'BB', 2H-4, 2H), 3.73 (s, CH_3O-1, 3H), 3.92 (s, CH_3O-2, 3H), 4.85 (6-lines, H-7a, 1H), 5.90 (br s, NH, 1H), 6.73 (s, H-3, 1H), 7.26 (m, ArH, 3H), 8.39 (d, H-12, 1H, J_o = 7.9 Hz); ms: (70 eV) m/z (relative intensity) 309 (M^+, 100), 294 (20), 251 (25); uv (methanol): λ max 218, 233, 271.

Anal. Calcd. for $C_{19}H_{19}NO_3$: C, 73.75; H, 6.19; N, 4.53. Found: C, 73.54; H, 6.20; N, 4.72.

The sample with R_f = 0.74 was recrystallized from benzene-hexane to furnish 24.7 mg (39%) of 4,5-dihydro-1,2-dimethoxyphenanthro[10,1-*bc*]-azepin-6(7*H*)-one (IX) as colorless crystals, mp 215-216°; ir (potassium bromide): 3210, 1670, 1618, 1120 cm^{-1}; ^1H nmr (deuteriochloroform, 200 MHz): δ 2.89 (3-lines, 2H-5, 2H), 3.45 (3-lines, 2H-4, 2H), 3.85 (s, CH_3O-1, 3H), 4.03 (s, CH_3O-2, 3H), 7.07 (s, H-3, 1H), 7.14 (s, H-8, 1H), 7.65 (br s, NH, deuterium exchange, 1H), 7.50-7.80 (m, ArH, 3H), 9.61 (m, H-12, 1H); ms: (70 eV) m/z (relative intensity) 307 (M^+, 100), 292 (21), 264 (17), 220 (12), uv (methanol): λ max 215, 262, 317, 328.

Anal. Calcd. for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 73.92; H, 5.43; N, 4.31. Calcd. for $C_{19}H_{17}NO_3$: 307.1207, Found: 307.1206.

In addition, starting material VII (10 mg) (R_f = 0.53) was recovered from this reaction.

Oxidation of 4,5,7a,8-Tetrahydro-1,2-dimethoxyphenanthro[10,1-*bc*]azepin-6(7*H*)-one (I) Under Photolytic Conditions.

Compound I (7 mg, 0.023 mmole) and a very small crystal of iodine were dissolved in dry degassed benzene (500 ml) before irradiating the

solution for 12 hours using a 450 watt Hanovia ultraviolet lamp equipped with a Corex filter. The solvent was removed *in vacuo* and the residue was chromatographed on a silica gel preparative tlc plate using a chloroform-methanol (95:5) mixture as the developing solvent system. The band with R_f = 0.71 gave 4.0 mg (57%) of IX while the band with R_f = 0.35 afforded 1.0 mg (14%) of the benzylidene VIII.

Oxidation of 4,5,7a,8-Tetrahydro-1,2-dimethoxyphenanthro[10,1-*bc*]azepin-6(7*H*)-one (I) Using Potassium Permanganate.

Compound I (7 mg, 0.023 mmole) was dissolved in dry acetone (2 ml) and with stirring potassium permanganate was added until the purple color persisted. Stirring was continued for 15 minutes longer before isopropyl alcohol was added dropwise to discharge the purple color of the solution. The dark precipitate was removed by filtration through a Celite pad. The acetone was removed to leave the dihydroazepinone IX, spectroscopically identical with previous samples.

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[1] To whom inquiries should be sent.

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