Enamide Photochemistry. Formation of Oxyprotoberberines by the Elimination of Ortho Substituents in 2-Aroyl-1-methylene-1,2,3,4-tetrahydroisoquinolines[1]

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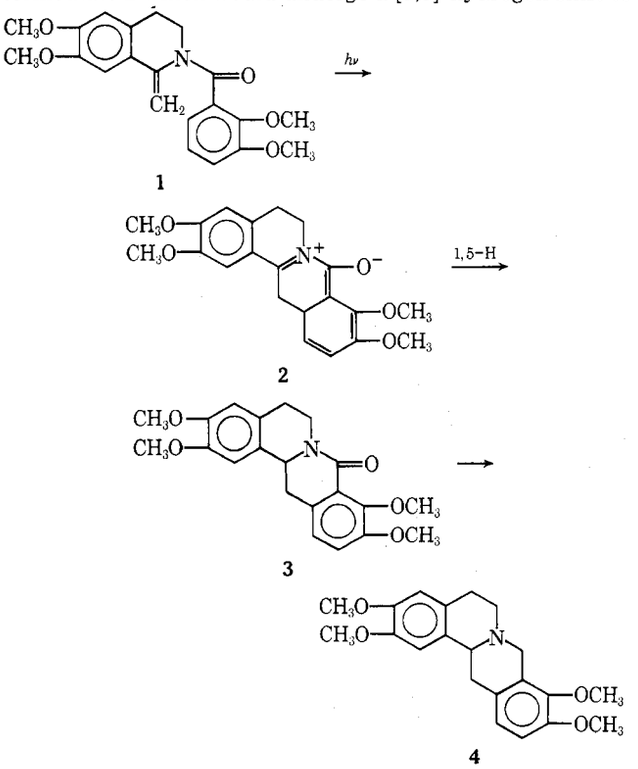
The synthesis of ortho-substituted 2-aroyl-1-methylene or ethylidene enamides was accomplished and their photochemistry investigated. Irradiation of these enamides results in an azatriene–azacyclohexadiene cyclization followed by elimination of an ortho substituent to form oxyprotoberberines in good yield. A wide variety of ortho substituents has been found to be capable of elimination: methoxyl, acetoxyl, nitro, halo, and thiomethyl. Polysubstitution does not seem to affect the reaction, since D-ring substituted oxyprotoberberines can also be formed. The reaction has been extended to form 13-methyloxyprotoberberines. Nonoxidative photocyclization was used to form phenanthridones from 2-methoxybenzanilides, but not all benzanilides react.

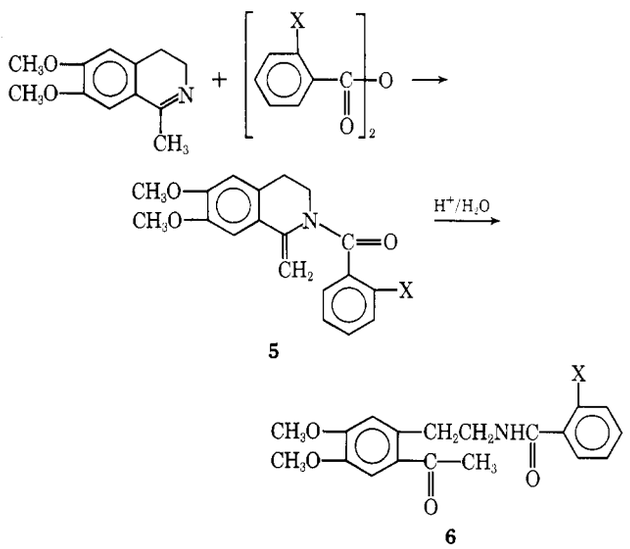
Previous studies on the photochemistry of enamides has shown this chemical grouping to be reactive photochemically and capable of undergoing synthetically useful reactions. Simple enamides undergo a facile [1,3]-acyl shift to give vinylogous amides in high yield.[2] When the enamide has been included as part of an isoquinoline ring system, irradiation has given rise to a variety of isoquinoline alkaloids.[3] Among the alkaloid nuclei synthesized photochemically are dehydroaporphines and aporphines,[4] oxyprotoberberines,[5] protoberberines, and tetrahydroprotoberberines,[6] benzophenanthridines,[7] and 8-oxoberbines.[8] In order to extend the usefulness of enamide photochemistry in the synthesis of isoquinoline alkaloids, the synthesis of 2-aroyl-1-methylene-1,2,3,4-tetrahydroisoquinolines and a study of their photochemistry were undertaken.

Results and Discussion

Based on analogy with the photocyclization and photoacylation reactions of enamides,[5,6] it was postulated that synthesis of enamide 1 and irradiation would lead to an intermediate **2** which would undergo a [1,5]-hydrogen shift to generate the 8-oxoberbine **3**. Reduction of the 8-oxoberbine **3** would then give the tetrahydroprotoberberine alkaloids with the natural oxygenation pattern **4**.[9]

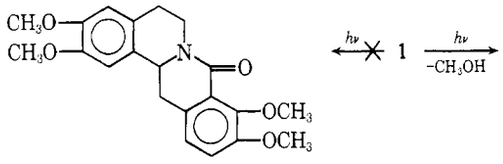


Initial attempts at synthesizing the enamides by a 1-*N,N*-diethylaminopropyne coupling reaction of equimolar amounts of acid and imine were unsuccessful, giving only low yields and several by-products. The best method found was to preform the acid anhydride in benzene using the ynamine,[10] adding the dihydroisoquinoline and refluxing. Work-up by aqueous and bicarbonate extraction gave the enamides **5** as nicely crystalline compounds. The enamides **5** are stable in the absence of acid; however the presence of acid causes hydrolysis to the acetylamide **6**.[11] The 1-methylene enamides **5** have two characteristically low-field exomethylene resonances in the nmr. In the eight methylene enamides studied, the first resonance occurs between δ 5.13 and 5.33, and the second between δ 4.54 and 4.80, presumably due to shielding by the aroyl group.



The first enamide studied was the tetramethoxy **1**. Irradiation of **1** in benzene with a medium pressure mercury lamp gave a clean conversion into a single highly fluorescent compound **7**, which was isolated in 85% yield. The compound isolated was not the expected **3**, but rather the oxyprotoberberine **7**. The nmr spectrum of **7** shows the absence of the low-field resonances attributable to the exomethylene protons. There is a low-field resonance at δ 8.02 for an aromatic proton ortho to a carbonyl, as part of a total of six aromatic protons. Most significant was the pres-

ence of only three of the initial four methoxy groups. The mass spectrum confirmed the loss of methanol with a parent peak at *m/e* 337 (97.1%). Other significant peaks were the loss of a methoxyl methyl group [*m/e* 322 (100%)] and a further loss of two hydrogens [*m/e* 320 (18.9%)]. The uv spectrum of **7** was characteristic of oxyprotoberberines.[5] On the basis of the physical evidence, **7** was assigned the 2,3,12-trimethoxy-8-oxyprotoberberine structure indicated.



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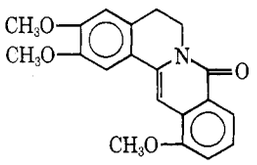

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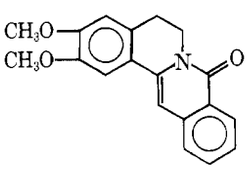
To test the generality of this photoelimination, a series of ortho aroyl-substituted enamides **5** was synthesized and irradiated. The 2-fluoro derivative **5a** (X = F) was irradiated in degassed *tert*-butyl alcohol in a Rayonet photoreactor with 3000 Å lamps to yield 2,3-dimethoxy-8-oxyprotoberberine **8** in 85% yield. The structural elucidation proceeded as for **7**. Additionally, an authentic sample of **8** was prepared by the intramolecular photoacylation of the carbamate **9**.[12] The irradiation of **9**, in ethanol, gave **8** as the major product, in addition to significant amounts of *N*-carbethoxy-6,7-dehydronornuciferine (**10**), and the hydrate **11**.



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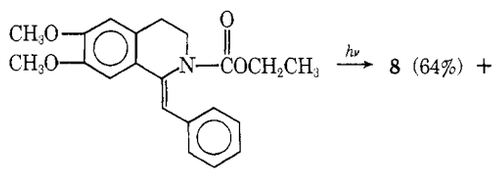

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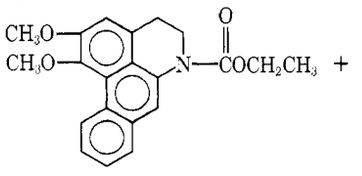

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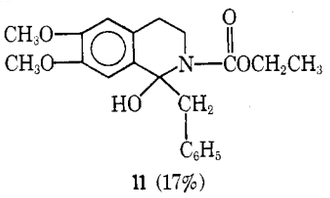


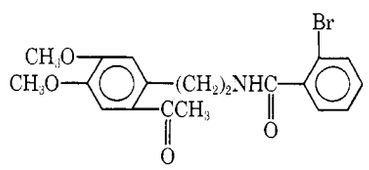
11 (17%)

The results for the enamides studied are collected in Table I. All of the enamides **5a–f** cyclized smoothly to the oxyprotoberberine **8**, without side products, except **5b** and **5c**.[13] In these enamides, photocyclization and elimination generate hydrogen chloride and hydrogen bromide, respectively. These strong mineral acids catalyze the addition of trace amounts of water to the enamide double bond to form the amides **6**. This amide was fully characterized for X = Br, **12**, as this type of compound had previously been prepared in the *N*-acyl series.[11] The amide **12** can exist in the open form **12a** or the closed form **12b**. The ir spectrum shows an acetophenone carbonyl at 1660 cm^{-1} and a secondary amide at 3280, 1640, and 1610 cm^{-1}, while the nmr spectrum shows only a single methyl resonance at δ 2.33. On this basis, the amide is better represented in the open form **12a**. On the other hand, in the double bond hydration of **9**, the ring remains closed in **11** as evidenced by the absence of ketone absorptions other than the carbamate carbonyl (1710 cm^{-1}) in the ir spectrum, and the presence of a hydroxyl absorption at 3340 cm^{-1}. Again, the nmr spectrum showed the presence of only one isomer.

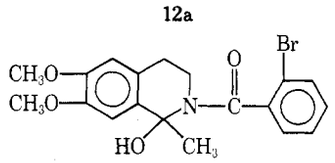
Table I
The Elimination of Ortho Substituents to Form Oxyprotoberberines[a]

Enamide	Product (% yield)	Remarks
1 (49619-28-5)	**7** (85) (52050-41-6)	
5a (X = F) (52050-38-1)	**8** (85) (32255-47-3)	
5b (X = Cl) (49619-29-6)	**8** (50)	
5c (X = Br) (49619-30-9)	**8** (50)	38% **12** (52050-42-7)
5d (X = O_2CCH_3) (49619-27-4)	**8** (76)	
5e (X = SCH_3) (52050-39-2)	**8** (55)	
5f (X = NO_2) (49619-31-0)	**8** (17)	20% **5f** recovered
13 (49619-32-1)	**14** (85) (10211-78-6)	
15 (52050-40-5)	**16** (69) (26665-00-9)	

[a] Registry no. are in parentheses beneath compounds.



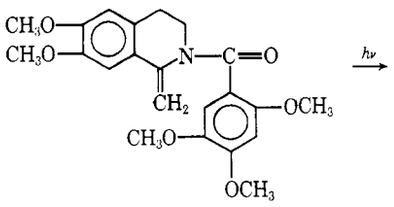
12a



12b

Polymethoxyl substitution was investigated to determine whether photoelimination could be of use in the synthesis of polyoxygenated oxyprotoberberines. The pentamethoxy enamide **13** was synthesized and then irradiated in *tert*-butyl alcohol where it was smoothly converted in 85% yield to the known tetramethoxyoxyprotoberberine **14**.[14] Based on this limited sample (**1** and **13**), it appears that polyfunctionality does not have much of an effect on the reaction nor on its rate compared with monosubstituted enamides.

The presence of a C-13 methyl group is a fairly common feature in the berbine alkaloids.[9] In order to extend the enamide photoelimination to prepare C-13 methyl oxyprotoberberines, it was necessary to synthesize 1-ethylidene enamides. The ethylidene enamide **15** was conveniently



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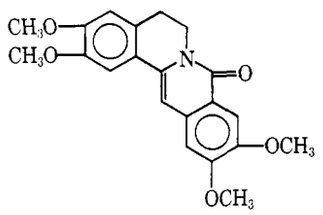

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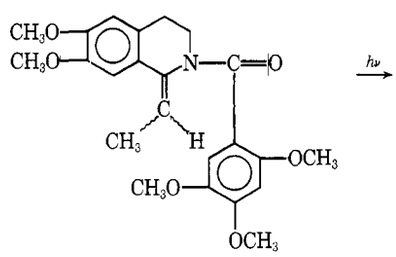
prepared from 1-ethyl-3,4-dihydro-6,7-dimethoxyisoquinoline and the anhydride of arasonic acid. Enamide **15**, as prepared, exists as a mixture of ethylidene isomers, which is indicated by the appearance of two pairs of doublets in the nmr for the ethylidene methyl resonance at δ 1.70 and 1.41 in a ratio of 2:1. Irradiation of this mixture in *tert*-butyl alcohol for 12 hr gave the 13-methyloxyprotoberberine **16** in 69% yield. The oxyprotoberberine **16** showed the



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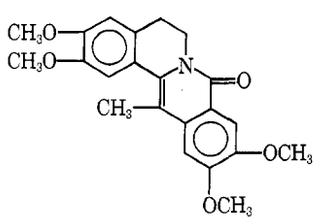

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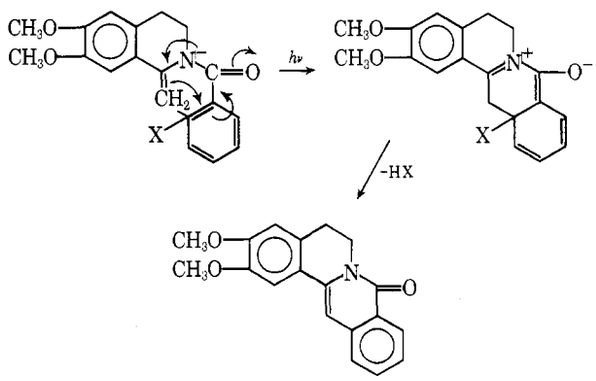
same physical properties as the C-13 unsubstituted compounds and the nmr spectrum showed the C-13 methyl resonance as a singlet at δ 2.64.

A plausible mechanism for the photoelimination reaction of the enamides proceeds from viewing the enamide as an aza analog of a hexatriene. Irradiation then gives the aza analog of a hexatriene–cyclohexadiene interconversion.[15] This is borne out in the enamide photoacylation reactions,[5] protoberberine synthesis,[6] and other nonoxidative cyclizations.[1,7,16] Then irradiation of the aroyl enamides (**4**) would cause the azacyclohexadiene formation at the ortho substituent according to Scheme I. Elimination of HX and electron redistribution generates the oxyprotoberberine. There is not much analogy in the literature for the elimination of ortho substituents in photocyclizations. The loss of halogen[17] and methoxyl[18] groups from diphenyl ethers to form dibenzofurans has been observed. The photolysis of ortho haloaromatic systems has been systematically exploited.[19] The problem arises for the *o*-chloro and *o*-bromo enamides of whether the photocyclization is as depicted in Scheme I or whether a simple homolysis or heterolysis of the carbon–halogen bond occurs. There is, at present, no way to decide between these alternatives. Photofragmentation is clearly unlikely in the remainder of the cases studied as, for example, with fluorine substitution, the energy of the carbon–fluorine bond is above that available to the molecule from the wavelength of the absorbed light and would be unlikely to fragment.[20] In the other enamides, *e.g.*, **1, 5d, 5e, 13,** photofragmentation would lead to phenoxy or thiophenoxy radicals and reactions characteristic of these, which is clearly not in accord with the observed facts.[21] For these reasons, we prefer the mechanism of cyclization followed by elimination of the elements of HX as outlined in Scheme I. The reaction appears to be very general. All the enamides, where X is a suitable leaving group, photocyclized and aromatized without side products in good to excellent yields.

Scheme I



Several other fully aromatic enamides were studied to see whether the photoelimination would occur in the fully aromatic systems. It is known that photolysis of *o*-bromo and *o*-iodo anilides gives acceptable yields of phenanthridones.[22] The reaction has been postulated to proceed through a radical mechanism.[23] It was of interest to see whether the reaction could proceed through a cyclized intermediate with elimination of a suitable leaving group. With this in mind, the benzanilide **17** was synthesized and irradiated.[24,25] Irradiation of **17** either at 3000 or 2537 Å gave no detectable phenanthridone **18**, starting material being recovered.[26] Equivalent results were obtained with 2-acetoxybenzanilide **19**.[27] However, when the trimethoxybenzanilide **20** was irradiated, a slow conversion to the phenanthridone **21** took place in 55% yield. The mass spectrum of **21** confirmed the loss of methanol and **21** possesses the typical phenanthridone uv spectrum.[5] The results of the benzanilide irradiations are collected in Table II.

Irradiation of the *N*-methyl derivative **22** also gave a smooth conversion to the *N*-methylphenanthridone **23**. The nmr spectrum of **23** indicated the loss of a methoxyl methyl group. The C-1 and C-10 protons in **23** appear as a low-field multiplet and singlet at δ 8.13 and 7.91, respectively, indicating distortion of the protons from coplanarity. A similar situation exists in phenanthrene.[28] The mass spectrum of **23** indicated the loss of methanol with a parent at *m/e* 269 (100%). The uv spectrum was essentially the same as **21**.

The tetramethoxybenzanilide **24** was also studied and irradiation at 2537 and 3000 Å, as well as acetone sensitization, gave no indication of reaction and **24** was recovered.

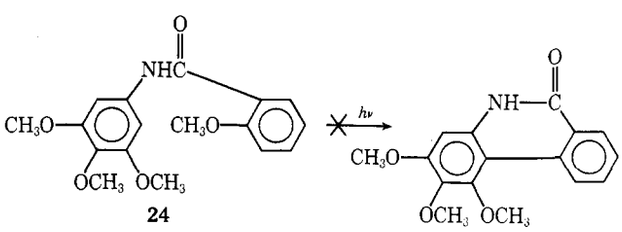


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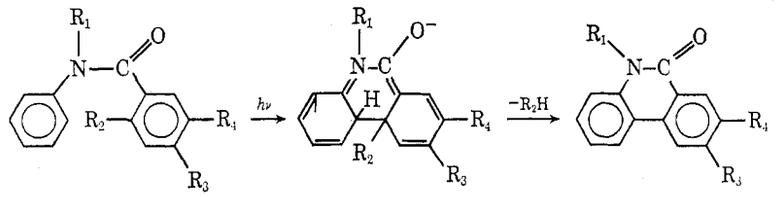
Table II
The Elimination of Ortho Substituents to Form Phenanthridones[a]

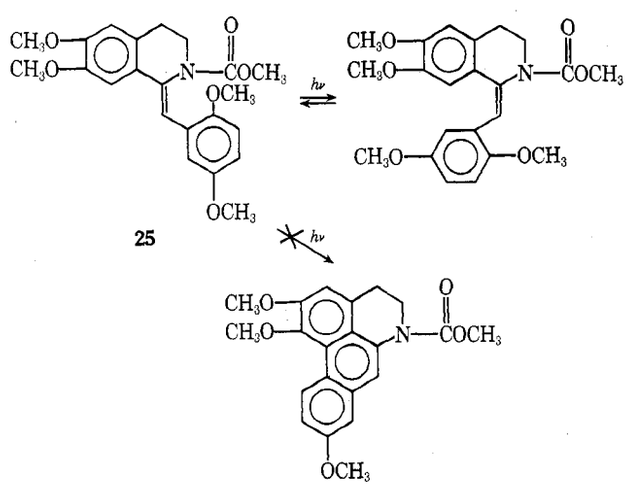


Benzanilide	R_1	R_2	R_3	R_4	Phenanthridone	Yield, %
17 (6833-21-2)	H	OCH_3	H	H	**18**	0
19 (6005-59-0)	H	O_2CCH_3	H	H	**18**	0
20 (50879-52-2)	H	OCH_3	OCH_3	OCH_3	**21** (50879-53-3)	55
22 (52050-43-8)	CH_3	OCH_3	OCH_3	OCH_3	**23** (52050-44-9)	41

[a] Registry no. in parentheses beneath compounds.

From a consideration of the results with the benzanilides, it can be seen that ortho substituents can be eliminated in a nonoxidative cyclization. However, the reaction does not appear to be as general as in the isoquinoline enamides, and no clear trends can be gleaned from this limited sample.

The final system studied was the benzylidene enamide **25**, with the aim of producing dehydroaporphine carbamates **26** under nonoxidative conditions. This had previously been observed to occur with *o*-chloro, bromo-, and iodo substituents.[4b,c,e,29]



25 **26**

The elimination of ortho substituents in the stilbene–phenanthrene conversion is uncommon but known: chloro, bromo, iodo, methyl, carboxyl, and methoxyl having been reported.[30] It was felt that the combination of the stilbene and enamide systems would offer a greater chance of success for forming dehydroaporphines. However, irradiation of **25** gave only a cis/trans isomeric mixture under varying conditions.[4d]

From a consideration of the above results, it appears that cyclization and elimination in a 6π-electron enamide array can occur. When one of the enamide double bonds is not part of an aromatic system, as in the methyleneisoquinolines, cyclization and elimination is especially facile. However, when both double bonds are aromatic, as in the benzanilides, cyclization and elimination can occur but the reaction is not facile and appears to be dependent on substitution pattern.[30a]

Experimental Section

Melting points were taken on a Thomas-Hoover Uni-melt capillary apparatus and are uncorrected. Infrared spectra were run in KBr unless otherwise noted, and ultraviolet and visible spectra were run in methanol unless otherwise indicated. A Varian Associates A-60, T-60, or HA-100 spectrometer was used to record nmr spectra. All spectra were run in deuteriochloroform with tetramethylsilane as an internal standard, unless otherwise indicated. Mass spectra were run on either an A.E.I. MS-9 or MS-30. Microanalyses were performed by the Searle Laboratories Microanalytical Department, Mr. E. Zielinski, Director.

3,4-Dihydro-6,7-dimethoxy-1-methylisoquinoline.[31] *N*-Acetylhomoveratrylamine (50 g) in refluxing toluene was stirred magnetically, and 40 ml of phosphorus oxychloride was slowly added. After the initial exothermic reaction, the mixture was refluxed a further 0.5 hr and allowed to cool while stirring was continued. Usually 80 g of dihydroisoquinoline salt crystallized. Treatment of 15 g of dihydroisoquinoline salt with aqueous base and chloroform extraction yielded approximately 9 g of free base.

2-(2,3-Dimethoxybenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline (1). 2,3-Dimethoxybenzoic acid (17 g, 0.094 mol) (Aldrich) was suspended in 300 ml of benzene and brought to reflux and 25 ml of solvent removed (Dean-Stark trap). The suspension was cooled to room temperature and 6 g (8 ml, 0.054 mol) of 1-*N*,*N*-diethylaminopropyne (Fluka) was added. The suspension immediately dissolved to give a reddish solution of the benzoic anhydride. Dihydroisoquinoline salt (18 g) was added to 25 g of sodium hydroxide in 500 ml of water, and the resulting solution of free base was extracted with chloroform (2 × 250 ml) and the chloroform extract dried (sodium sulfate). Removal of the chloroform gave approximately 11 g of crystalline free base. The dihydroisoquinoline was taken up in 50 ml of pyridine and added to the anhydride solution in benzene. The resulting mixture was refluxed 1 hr and allowed to stand overnight. The solution was poured into 1 l. of water and washed further with water (2 × 1 l.). The benzene solution was dried with sodium sulfate and evaporated to a syrup. The syrup was dissolved in ether, and stirred magnetically, whereupon 14.5 g (0.039 mol, 73%) of the enamide, **1**, mp 120–122°, crystallized as a white solid: λ_{max} 200 nm (ϵ 37,000), 244 (min, 12,000), 264 (16,000), 306 (7000), 316 (6000); γ_{max} 1650, 1615, 1585, 1520 cm^{-1}; nmr δ 6.61 (m, 5 H), 5.30 (broad s, 1 H), 4.80 (very broad s, 1 H), 4.03 (t, 2 H), 3.88 (s, 3 H), 3.85 (s, 6 H), 3.78 (s, 3 H), 2.92 (t, 2 H).

Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 67.95; H, 6.27; N, 3.89.

2-(2-Fluorobenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline (5a). *o*-Fluorobenzoic acid (Aldrich), 18.5 g (0.13 mol), 6.8 g of 1-*N*,*N*-diethylaminopropyne (0.06 mol), and 9 g of dihydroisoquinoline treated as above gave 8.1 g (0.021 mol, 41%) of the enamide **5a** as a white crystalline solid: mp 112–115° (ethyl acetate–petroleum ether); λ_{max} 220 nm (ϵ 29,500), 230 (sh, 23,000), 243 (min, 11,000), 262 (17,000), 287 (min, 6000), 304 (7500), 314 (sh, 6000); γ_{max} 1640, 1625, 1520 cm^{-1}; nmr δ 6.96 (s, 1 H), 6.61 (s, 1 H), 7.0–7.5 (m, 4 H), 5.26 (broad s, 1 H), 4.54 (broad s, 1 H), 4.08 (t, 2 H), 3.87 (s, 3 H), 3.85 (s, 3 H), 2.92 (t, 2 H).

Anal. Calcd for $C_{19}H_{18}FNO_3$: C, 69.71; H, 5.54; N, 4.28. Found: C, 69.50; H, 5.65; N, 4.31.

2-(2-Chlorobenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline (5b). *o*-Chlorobenzoic acid (Aldrich), 21 g (0.132 mol), 6.8 g (0.061 mol) of 1-*N*,*N*-diethylaminopropyne, and 9 g (0.044 mol) of dihydroisoquinoline were treated as above to yield 6.45 g (0.019 mol, 43%) of enamide **5b** as a white crystalline solid: mp 143–144° (ethyl acetate–ether); λ_{max} 229 nm (sh, ϵ 29,500), 245 (min, 10,000), 265 (14,200), 289.5 (min, 5000), 305 (7000), 317 (sh, 5500); γ_{max} 1650, 1635, 1615, 1605, 1520 cm^{-1}; nmr δ 7.29 (m, 4 H), 6.98 (s, 1 H), 6.63 (s, 1 H), 5.32 (broad s, 1 H), 4.67 (broad s, 1 H), 4.09 (t, 2 H), 3.86 (s, 3 H), 3.83 (s, 3 H), 2.95 (t, 2 H).

Anal. Calcd for $C_{19}H_{18}ClNO_3$: C, 66.37; H, 5.28; N, 4.07. Found: C, 66.66; H, 5.24; N, 3.92.

2-(2-Bromobenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline (5c). 5c was prepared from 26.5 g (0.132 mol) of *o*-bromobenzoic acid, 0.061 mol of 1-*N*,*N*-diethylaminopropyne, and 9 g of (0.044 mol) of dihydroisoquinoline as detailed above. Crystallization from ether gave 11.5 g (0.030 mol, 68%) of the enamide **5c:** mp 146–147°; λ_{max} 220 nm (ϵ 35,000), 230 (sh, 26,000), 245 (min, 11,000), 264 (14,500), 289 (min, 4500), 305 (7000), 315 (sh, 6500); γ_{max} 1650, 1635, 1615, 1520 cm^{-1}; nmr, δ 7.52 (m, 1 H), 7.27 (m, 3 H), 6.97 (s, 1 H), 6.63 (s, 1 H), 5.33 (broad s, 1 H), 4.67 (broad s, 1 H), 4.14 (t, 2 H), 3.90 (s, 3 H), 3.87 (s, 3 H), 2.95 (t, 2 H).

Anal. Calcd for $C_{19}H_{18}BrNO_3$: C, 58.77; H, 4.67; N, 3.61. Found: C, 58.70; H, 4.65; N, 3.57.

2-(2-Acetoxybenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline (5d). 5d was synthesized from 23.8 g (0.132 mol) of acetylsalicylic acid, 10 g of 1-*N*,*N*-diethylaminopropyne, and 12 g (0.059 mol) of dihydroisoquinoline as detailed above. Crystallization from 150 ml of ether gave 15.7 g (0.043 mol, 73%) of enamide **5d:** mp 108–110°; λ_{max} 220 nm (ϵ 30,000), 231 (sh, 23,000), 244 (min, 11,000), 263 (16,000), 289 (min, 5500), 304 (7000), 314 (sh, 7000); γ_{max} 1770, 1647, 1635 (sh), 1610, 1515 cm^{-1}; nmr δ 7.30 (m, 4 H), 6.97 (s, 1 H), 6.63 (s, 1 H), 5.26 (d, $J \simeq 1.5$ Hz, 1 H), 4.57 (d, $J \simeq 1.5$ Hz, 1 H), 4.12 (t, 2 H), 3.86 (s, 6 H), 2.94 (t, 2 H), 1.72 (s, 3 H).

Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.42; H, 5.84; N, 3.80.

2-(2,4,5-Trimethoxybenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline (13). 13 was synthesized from 2,4,5-trimethoxybenzoic acid (Aldrich), 28 g (0.132 mol), 0.061 mol of 1-*N*,*N*-diethylaminopropyne, and 9 g (0.44 mol) of dihydroisoquinoline as above. Crystallization from ethyl acetate–ether gave 12.7 g (0.032 mol, 73%) of enamide **13:** mp 222–225°; λ_{max} 230 nm (sh, ϵ 31,000), 247 (min, 14,000), 263 (16,500), 284 (min, 9000), 304 (12,500), 316 (sh, 9000); γ_{max} 1630, 1615, 1510 cm^{-1}; nmr, δ 6.97 (s, 1 H), 6.87 (s, 1 H), 6.63 (s, 1 H), 6.37 (s, 1 H), 5.13 (d, $J \simeq 1$ Hz, 1 H), 4.72 (d, $J \simeq 1$ Hz, 1 H), 4.06 (broad s, 2 H), 3.90 (s, 3 H), 3.86 (s, 6 H), 3.64 (s, 3 H), 3.37 (s, 3 H), 3.07 (t, 2 H).

Anal. Calcd for $C_{22}H_{25}NO_6$: C, 66.15; H, 6.31; N, 3.51. Found: C, 66.05; H, 6.41; N, 3.55.

2-(2-Methylthiobenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline (5e). 2-Methylthiobenzoic acid was prepared from *o*-mercaptobenzoic acid (Eastman Kodak) and dimethyl sulfate, according to the literature.[32] The enamide was prepared from 2-methylthiobenzoic acid (16.8 g, 0.10 mol), 5.55 g of 1-*N*,*N*-diethylaminopropyne (0.05 mol), and 9 g (0.044 mol) of dihydroisoquinoline. Work-up as detailed above gave 6.3 g of **5e** (0.018 mol, 41%): mp 117–118°; λ_{max} 220 nm (ϵ 34,000), 242 (min, 14,000), 260 (17,500), 290 (min, 6000), 304 (7500), 314 (sh, 6000); nmr δ 7.22 (m, 4 H), 6.98 (s, 1 H), 6.63 (s, 1 H), 5.27 (d, $J \simeq 1.5$ Hz, 1 H), 4.77 (d, $J \simeq 1.5$ Hz, 1 H), 4.08 (t, 2 H), 3.91 (s, 3 H), 3.86 (s, 3 H), 2.94 (t, 2 H), 2.42 (s, 3 H).

Anal. Calcd for $C_{20}H_{21}NO_3S$: C, 67.58; H, 5.96; N, 3.94; S, 9.02. Found: C, 67.62; H, 6.08; N, 3.89; S, 9.40.

2-(2-Nitrobenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline (5f). 5f was synthesized from 22 g (0.132 mol) of *o*-nitrobenzoic acid (Aldrich), 6.8 g (0.061 mol) of 1-*N*,*N*-diethylaminopropyne, and 10.6 g dihydroisoquinoline (0.052 mol) as above. The mixture was refluxed 1 hr and allowed to stand overnight. Methanol (50 ml) was added and a violent reaction ensued. The solvent was removed at vacuum aspirator pressure to give a black gummy mass. The gum was taken up in 500 ml of methylene chloride and washed with water (2 × 1 l.) and 5% potassium carbonate (500 ml). The solution was dried with sodium sulfate, treated with activated carbon, and filtered to give a light orange solution. The solution was evaporated and the residue crystallized from methylene chloride–ethyl acetate to give 13.85 g (0.039 mol, 75%) of bright yellow plates of the enamide **5f:** mp 189–190°; λ_{max} 230 nm (sh, ϵ 25,500), 243 (min, 14,000), 264 (18,000), 290 (min, 7000), 305 (8500), 316 (7000); γ_{max} 1635, 1625 (sh), 1610, 1575, 1520 cm^{-1}; nmr δ 8.10 (m, 1 H), 7.44 (m, 3 H), 7.03 (s, 1 H), 6.63 (s, 1 H), 5.23 (m, 1 H), 4.57 (s, 1 H), 4.14 (m, 2 H), 3.88 (s, 3 H), 3.84 (s, 3 H), 2.98 (t, 2 H).

Anal. Calcd for $C_{19}H_{18}N_2O_5$: C, 64.40; H, 5.12; N, 7.91. Found: C, 64.68; H, 5.24; N, 7.89.

2-(2,4,5-Trimethoxybenzoyl)-1-ethylidene-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (15). 15 was prepared from 2,4,5-trimethoxybenzoic acid, 16.5 g (0.080 mol), 4.3 g of 1-*N*,*N*-diethylaminopropyne, and 1-ethyl-3,4-dihydro-6,7-dimethoxyisoquinoline (0.039 mol) (prepared from *N*-propionoylhomoveratrylamine as detailed for *N*-acetylhomoveratrylamine) to give 5.7 g of enamide 15 (0.015 mol, 38%): mp 131–133°: λ_{max} 244 nm (min, ϵ 16,000), 258 (18,000), 282 (min, 9000), 300 (12,500); γ_{max} 1620, 1520 cm^{-1}; nmr δ 6.30–7.00 (m, 4 H), 5.0–5.7 (very broad multiplet, 1 H), 3.3–4.2 (m, 17 H), 2.90 (t, 2 H), 1.70 (d, $J \simeq 8$ Hz, 2 H), and 1.41 (d, $J \simeq 8$ Hz, 1 H). The ethylidene methyl resonances at δ 1.70 and 1.41 indicated a mixture of ethylidene isomers in the ratio of approximately 2:1.

Anal. Calcd for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.58; N, 3.39. Found: C, 67.06; H, 6.37; N, 3.45.

Irradiation of 2-(2,3-Dimethoxybenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline (1). The enamide 1 (1.0 g) was dissolved in 200 ml of dry benzene and irradiated, under nitrogen, through Pyrex, with a 450-W medium pressure mercury arc (Hanovia 679A). After 4.5 hr, tlc examination indicated consumption of starting material and formation of a single highly fluorescent compound. The solvent was removed and the residue crystallized from methanol to give 775 mg of 2,3,12-trimethoxy-8-oxyprotoberberine (7): mp 219–220°; λ_{max} 220 nm (ϵ 38,000), 238 (min, 16,500), 248 (18,500), 253 (18,000), 267 (sh, 10,500), 285 (min, 7000), 304 (sh, 11,000), 316 (sh, 15,000), 330 (21,000), 340 (20,000), 361 (25,000), 388 (20,000); γ_{max} 1650, 1615, 1600 cm^{-1}; nmr δ 8.02 (d, $J \simeq 8$ Hz, 1 H), 6.9–7.4 (m, 4 H), 6.72 (s, 1 H), 4.37 (t, 2 H), 3.95 (s, 6 H), 3.90 (s, 3 H), 2.91 (t, 2 H).

Anal. Calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.14; H, 5.65; N, 4.11.

Irradiation of 2-(2-Fluorobenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline. The enamide **5a** (1.0 g) was dissolved in 600 ml of *tert*-butyl alcohol in a quartz vessel and degassed by three freeze–thaw cycles in a Dry Ice–isopropyl alcohol bath. The degassed solution was irradiated for 2 hr in a Rayonet Preparative Photoreactor (Southern New England Ultraviolet Model RPR-208).[33] Removal of the solvent on a rotary evaporator gave 830 mg of 2,3-dimethoxy-8-oxyprotoberberine (8), mp 181–182° (methanol). The mother liquor indicated the presence of a small amount of starting material as the only other compound. The oxyprotoberberine 8 exhibits: λ_{max} 220 nm (ϵ 35,000), 226 (31,000), 240 (sh, 18,000), 256 (12,000), 283 (min, 6000), 304 (sh, 11,000), 317 (sh, 16,000), 331 (20,000), 350 (sh, 14,500), 368 (8000); γ_{max} 1650, 1615, 1600, 1520 cm^{-1}; nmr δ 8.52 (d, $J \simeq 8$ Hz, 1 H), 7.26–7.84 (m, 4 H), 6.94 (s, 1 H), 6.82 (s, 1 H), 4.38 (t, 2 H), 4.02 (s, 3 H), 3.95 (s, 3 H), 2.94 (t, 2 H).

Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.28; H, 5.78; N, 4.34.

Irradiation of 2-(2-Bromobenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline. The enamide **5c** (1.0 g) was irradiated as indicated for the 2-fluoro enamide. Removal of the majority of the solvent on a rotary evaporator and addition of methanol gave 400 mg of *N*-2-bromobenzoyl-2-acetyl-4,5-dimethoxyphenylethylamine (12): mp 158–160°; λ_{max} 228 nm (ϵ 15,500), 250 (min, 2500), 273 (5500), 302 (3000); γ_{max} 3280, 1660, 1640, 1610 cm^{-1}; nmr δ 7.34 (m, 3 H), 7.25 (s, 1 H), 6.89 (s, 1 H), 3.97 (s, 3 H), 3.94 (s, 3 H), 3.70 (t, 2 H), 3.15 (t, 2 H), 2.23 (s, 3 H).

Anal. Calcd for $C_{19}H_{20}BrNO_4 \cdot H_2O$: C, 51.67; H, 5.02; N, 3.17. Found: C, 51.21; H, 5.18; N, 3.45.

The yellow mother liquor was evaporated and the residue was dry column chromatographed on 150 g of E. Merck silica, deactivated with 12 ml of water. The dry column was developed with 12:88 ethyl acetate–benzene to give 400 mg of the oxyprotoberberine 8.

1-Benzyl-3,4-dihydro-6,7-dimethoxyisoquinoline. This was prepared from *N*-[2-(3,4-dimethoxyphenyl)ethyl]phenylacetamide[34] according to the method of Tschesche, *et al.*[35]

1-Benzylidene-2-carbethoxy-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (9).[12] 1-Benzyl-3,4-dihydro-6,7-dimethoxyisoquinoline (13.4 g, 0.061 mol) was dissolved in 250 ml of dry benzene and 10 ml of Hünig's base (*N*,*N*-diisopropylethylamine) and

to this solution was added 10 ml of ethyl chlorocarbonate in 25 ml of benzene. The mixture was allowed to stand overnight and filtered from a precipitate, and the solution was evaporated to an oil. The oil was crystallized (2×) from methanol to give 8.28 g (0.023 mol, 38%) of **9**: mp 122–124°; mol wt 353 (mass spectrum, calcd 353); λ (EtOH) 229 nm (ε 20,000), 302 (sh, 20,000), 322 (22,000); γ_{max} ($CHCl_3$) 1680, 1250 cm^{-1}; nmr δ 7.1–7.7 (m, 6 H), 6.77 (s, 1 H), 6.57 (s, 1 H), 3.6–4.2 (m, 4 H), 3.90 (s, 3 H), 3.83 (s, 3 H), 2.87 (t, 2 H), 0.77 (t, 3 H).

Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.54; H, 6.63; N, 4.25.

Irradiation of 1-Benzylidene-2-carbethoxy-6,7-dimethoxyisoquinoline (9). A solution of **9** (1.00 g) in 150 ml of absolute ethanol was irradiated through a Vycor filter, with a 450-W mercury arc for 120 hr. Dry nitrogen was passed through the solution for 0.5 hr prior to the irradiation and during the irradiation. Evaporation of solvent gave 1.36 g of residue which was chromatographed on 40 g of Florisil. Elution with benzene gave 0.20 g of *N*-carbethoxy-6a,7-dehydronornuciferine: mp 131–132°; mol wt 351.1471 (mass spectrum, calcd 351.1440); λ (EtOH) 249 nm (ε 48,700), 259 (47,500), 308 (12,200), 320 (12,200), 352 (1900), 370 (1900); γ ($CHCl_3$) 1670, 1240 cm^{-1}; nmr δ 9.41–9.74 (m, 1 H), 6.7–7.0 (m, 4 H), 6.97 (s, 1 H), 4.24 (q, 2 H), 4.00 (t, 2 H), 3.89 (s, 3 H), 3.84 (s, 3 H), 2.07 (t, 2 H), 1.27 (t, 3 H).

Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 71.87; H, 6.15; N, 3.98.

Continued elution with methylene chloride containing 0.25% methanol gave 0.55 g of **8.** Elution with methanol–chloroform (1:99) gave 0.19 g of 1-benzyl-2-carbethoxy-1,2,3,4-tetrahydro-1-hydroxy-6,7-dimethoxyisoquinoline (**11**) as a noncrystalline oil: mol wt 371.1730 (mass spectrum, calcd 371.1733); λ (EtOH) 227 nm (ε 17,500), 275 (6600), 303 (8000); γ_{max} (CCl_4) 3340, 1710, 1250 cm^{-1}; nmr δ 7.22 (s, 6 H), 6.72 (s, 1 H), 5.20–5.50 (-OH, 1 H), 4.14 (s, 2 H), 4.04 (q, 2 H), 3.84 (s, 3 H), 3.81 (s, 3 H), 3.31 (t, 2 H), 2.93 (t, 2 H), 1.16 (t, 3 H).

Irradiation of 2-(2,4,5-Trimethoxybenzoyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-methyleneisoquinoline. The enamide **13** (2.0 g) was prepared for irradiation and irradiated for 3.5 hr as described for the 2-fluoro enamide above. Removal of the *tert*-butyl alcohol solvent at the aspirator gave a residue which upon crystallization from ether gave 1.5 g of 2,3,11,12-tetramethoxy-8-oxyprotoberberine (**14**): mp 187–188°; λ_{max} 220 nm (ε 28,000), 227 (31,000), 245 (min, 18,500), 262 (24,000), 286 (min, 5000), 306 (sh, 11,500), 318 (sh, 15,500), 332 (18,500), 346 (sh, 17,500), 362 (10,500); γ_{max} 1650, 1615, 1600, 1515 cm^{-1}; nmr δ 7.80 (s, 1 H), 7.20 (s, 1 H), 6.94 (s, 1 H), 6.80 (s, 1 H), 6.72 (s, 1 H), 4.37 (t, 2 H), 3.94 (s, 9 H), 3.88 (s, 3 H), 2.91 (t, 2 H).

Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.48; H, 6.02; N, 4.02.

Irradiation of 2-(2,4,5-Trimethoxybenzoyl)-1-ethylidene-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline. The enamide **15** (1.0 g) was irradiated in ethyl acetate for 12 hr as described above for the 2,3-dimethoxybenzoyl enamide **1**. The solvent was reduced to small volume and diluted with petroleum ether, whereupon 516 mg of 2,3,10,11-tetramethoxy-13-methyl-8-oxyprotoberberine (**16**), mp 213–215°, crystallized: λ_{max} 230 nm (ε 35,000), 244 (min, 20,000), 262 (28,000), 286 (min, 5500), 328 (24,000), 360 (sh, 10,500); γ_{max} 1645, 1615, 1595, 1515 cm^{-1}; nmr δ 7.94 (s, 1 H), 7.16 (s, 1 H), 7.11 (s, 1 H), 6.83 (s, 1 H), 4.30 (t, 2 H), 4.06 (s, 6 H), 3.98 (s, 3 H), 3.95 (s, 3 H), 2.87 (t, 2 H), 2.64 (s, 3 H).

Anal. Calcd for $C_{22}H_{23}NO_5$: C, 69.27; H, 6.08; N, 3.67. Found: C, 68.97; H, 6.21; N, 3.91.

The residue for the crystallization was found to contain appreciable oxyprotoberberine and was submitted to dry column chromatography on 150 g of CC-7 silica, deactivated with 12 ml of water, and developed with 4:96 ethanol–benzene to yield an additional 120 mg of oxyprotoberberine **16.**

2-Methoxybenzanilide (17). **17** was prepared from aniline and *o*-methoxybenzoyl chloride (Kodak).[24]

Irradiation of 2-Methoxybenzanilide (17). A solution of **17** (1.0 g) in 200 ml of methanol in a quartz vessel was irradiated in a Rayonet photoreactor with 3000 Å lamps for 18 hr. No reaction was detected. The same solution was then irradiated for 20 hr with 2537 Å lamps and starting material was recovered.

2-Acetoxybenzanilide (19). **19** was prepared from salicyloyl chloride and aniline according to the literature.[26]

Irradiation of 2-Acetoxybenzanilide (19). A solution of 250 mg of **19** in 190 ml of ethyl acetate was irradiated under nitrogen with a 450-W mercury lamp (Pyrex filter) for 21 hr. There was no indication of reaction by tlc and starting material was recovered.

2,4,5-Trimethoxybenzanilide (20). **20** was prepared from 2,4,5-trimethoxybenzoyl chloride (53.7 mmol) and 5.0 g (53.7 mmol) of aniline in 10 ml of pyridine and 50 ml of chloroform at 0°. After standing for 0.5 hr, the solution was extracted with water, dilute hydrochloric acid, and dilute sodium carbonate. The chloroform solution was dried with sodium sulfate and the solvent removed. The residue was crystallized from methanol–water: mp 151–152°; λ_{max} 222 nm (ε 25,500), 240 (min, 12,000), 270 (16,500), 293 (min, 11,000), 311 (14,500); γ_{max} 3360, 1650, 1610, 1600 cm^{-1}; nmr δ 7.0–7.8 (m, 6 H), 6.50 (s, 1 H), 3.98 (s, 3 H), 3.91 δ (s, 6 H).

Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.96; N, 4.88. Found: C, 67.14; H, 5.97; N, 5.01.

Irradiation of 2,4,5-Trimethoxybenzanilide (20). A solution of 500 mg of **20** in 190 ml of ethyl acetate was irradiated under nitrogen, through Pyrex, with a 450-W medium pressure mercury lamp. After 20 hr of irradiation a substantial precipitate had formed. The ethyl acetate was removed and the residue combined with the precipitate and the whole recrystallized from hot dimethylformamide to give 245 mg of **21,** 8,9-dimethoxyphenanthridone: mp 300–302°; mol wt 255 [mass spectrum (100%), calcd 255]; λ_{max} 225 nm (ε 22,000), 245 (sh, 43,000), 250 (46,000), 261 (min, 18,000), 264 (20,000), 280 (9500), 287 (min, 8500), 293 (9000), 299 (min, 8000), 305 (9000), 315 (min, 6500), 320 (8000), 328 (min, 5000), 335 (8000); γ_{max} 3180, 3120, 3040, 1660, 1610, 1520, 1510 cm^{-1}; nmr (saturated sol in dimethylformamide) δ 7.2–8.2 (m, 7 H), 4.11 (s, 3 H), 3.98 (s, 3 H).

Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.79; H, 5.21; N, 5.58.

***N*-Methyl-2,4,5-trimethoxybenzanilide (22).** 2,4,5-Trimethoxybenzoyl chloride (11.6 g, 53.7 mmol) in 25 ml of chloroform was added to a solution of 4.9 g (46.8 mmol) of *N*-methylaniline in 10 ml of pyridine and 25 ml of chloroform at 0°. After standing for 0.5 hr, the chloroform solution was washed with distilled water, dilute hydrochloric acid, and dilute sodium bicarbonate. The chloroform layer was dried with sodium sulfate and the solvent removed. Crystallization from methanol–water gave 10.2 g (33 mmol, 71%) of **22:** mp 137–139°; λ_{max} 227 nm (ε 31,000), 275 (min, 8500), 297 (12,500); γ_{max} 1640, 1620, 1600, 1520, 1500 cm^{-1}; nmr δ 7.11 (s, 5 H), 6.80 (s, 1 H), 6.25 (s, 1 H), 3.78 (s, 3 H), 3.73 (s, 3 H), 3.55 (s, 3 H), 3.44 (s, 3 H).

Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.64; H, 6.30; N, 4.88.

Irradiation of *N*-Methyl-2,4,5-trimethoxybenzanilide (22). A solution of 150 mg of **22** in 190 ml of ethyl acetate was irradiated, under nitrogen, through Pyrex, with a 450-W medium pressure mercury arc for 12 hr. The ethyl acetate solution was concentrated to a small volume whereupon 56 mg of 8,9-dimethoxy-5-methylphenanthridone (**23**), mp 219–220°, crystallized. Removal of the ethyl acetate and crystallization from methanol–water gave back starting benzanilide.

8,9-Dimethoxy-5-methylphenanthridone (**23**) shows: mol wt 269 [mass spectrum (100%), calcd 269]; λ_{max} 222 nm (ε 20,000), 246 (sh, 48,000), 252 (50,000), 264 (20,000), 276 (min, 9500), 281 (10,000), 286 (min, 9500), 293 (10,500), 301 (min, 9000), 305 (9500), 316 (min, 6500), 321 (8000), 329 (min, 5000), 336 (8000); γ_{max} 1650, 1620, 1595, 1530 cm^{-1}; nmr δ 8.13 (m, 1 H), 7.91 (s, 1 H), 7.58 (s, 1 H), 7.15–7.55 (m, 3 H), 4.08 (s, 3 H), 4.03 (s, 3 H), 3.82 (s, 3 H).

Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61. Found: C, 71.57; H, 5.40.

2,3′,4′,5′-Tetramethoxybenzanilide (24). 3,4,5-Trimethoxyaniline (Aldrich) (5 g) was dissolved in pyridine and cooled in an ice bath. To this solution was added 6 g of 2-methoxybenzoyl chloride (Eastman Kodak) in 25 ml of methylene chloride and the resulting mixture stirred for 1 hr. The mixture was dissolved in 300 ml of methylene chloride and extracted with 5% potassium carbonate and dilute hydrochloric acid and washed with water. The methylene chloride solution was dried with sodium sulfate, and solvent removed at the aspirator. Crystallization from methanol gave 6.8 g of amide **24:** mp 110–115°; γ 3340, 1655, 1610, 1550, 1515 cm^{-1}.

Anal. Calcd for $C_{17}H_{19}O_5N$: C, 64.34; H, 6.04; N, 4.41. Found: C, 64.52; H, 5.96; N, 4.31.

Irradiation of 2,3′,4′,5′-Tetramethoxybenzanilide (24). (a) The amide (1.0 g) was dissolved in 350 ml of *tert*-butyl alcohol and irradiated, through Pyrex and under nitrogen, with a 450-W medium pressure mercury arc for 6.5 hr. Upon removal of solvent starting material was recovered. (b) The amide (1.0 g) was dissolved in 450 ml of *tert*-butyl alcohol and irradiated in a quartz vessel in the Rayonet photoreactor with 2537 Å lamps for 28 hr. Removal of solvent gave back starting material. (c) The amide (1.0 g) was dis-

solved in 500 ml of acetone and irradiated with 3000 Å lamps, under argon, for 48 hr. Evaporation of acetone gave back starting material.

1-(2,5-Dimethoxybenzylidene)-2-carbomethoxy-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (25). 1-(2,5-Dimethoxybenzyl)-3,4-dihydro-6,7-dimethoxyisoquinoline (15 g, 0.044 mol) was added to a preformed solution of 10 ml of methyl chloroformate in 25 ml of pyridine and 100 ml of benzene. The mixture was brought to reflux under nitrogen for 1 hr. The solution was cooled and washed three times with water. Removal of solvent and crystallization from ether gave 10.8 g (0.027 mol, 61%) of the benzylidene carbamate **25**: mp 144–145°; λ_{max} 256 nm (min, ϵ 7500), 295 (s, 13,000), 327 (16,000); γ_{max} 1705, 1605, 1520 cm^{-1}; nmr δ 7.28 (s, 1 H), 7.05 (s, 2 H), 6.82 (s, 2 H), 6.63 (s, 1 H), 4.02 (t, 2 H, obscured by $-OCH_3$'s), 3.95 (s, 3 H), 3.89 (s, 3 H), 3.85 (s, 3 H), 3.75 (s, 3 H), 3.34 (broad s, 3 H), 2.92 (t, 2 H).

Anal. Calcd for $C_{22}H_{25}NO_6$: C, 66.15; H, 6.31; N, 3.51. Found: C, 66.28; H, 6.10; N, 3.50.

Irradiation of 1-(2,5-Dimethoxybenzylidene)-2-carbomethoxy-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (25). (a) The carbamate (1.0 g) was dissolved in 250 ml of benzene and irradiated, under nitrogen, with a 450-W medium pressure mercury arc (Pyrex) for 2.5 hr. Removal of solvent and crystallization from ether gave back a cis/trans mixture of the starting carbamate. (b) The carbamate (1.0 g) was dissolved in 200 ml of ethanol and irradiated as above for 8 hr. Removal of solvent gave back a cis/trans mixture of the starting carbamate. The evidence for a cis/trans mixture is the absence of either phenanthrene or oxyprotoberberine bands in the uv, and the appearance of the ester methyl group as two broad singlets at δ 3.33 and 3.38 in the ratio of 1:2. There were also eight methoxyl signals instead of the initial four.

Registry No.—**9,** 22185-92-8; **10,** 13555-30-1; **11,** 52050-45-0; **24,** 52050-46-1; **25,** 52050-47-2; 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline, 4721-98-6; *N*-acetylhomoveratrylamine, 6275-29-2; 2,3-dimethoxybenzoic acid, 1521-38-6; 1-diethylaminopropyne, 4231-35-0; *o*-fluorobenzoic acid, 445-29-4; *o*-chlorobenzoic acid, 118-91-2; *o*-bromobenzoic acid, 88-65-3; acetylsalicylic acid, 50-78-2; 2,4,5-trimethoxybenzoic acid, 490-64-2; 2-(methylthio)benzoic acid, 3724-10-5; *o*-nitrobenzoic acid, 552-16-9; 1-ethyl-3,4-dihydro-6,7-dimethoxyisoquinoline, 51665-55-5; 1-benzyl-3,4-dihydro-6,7-dimethoxyisoquinoline, 4876-00-0; *N*-[2-(3,4-dimethoxyphenyl)ethyl]phenylacetamide, 4876-02-2; ethyl chlorocarbonate, 541-41-3; 3,4,5-trimethoxyaniline, 24313-88-0; 2-methoxybenzoyl chloride, 21615,34-9; 1-(2,5-dimethoxybenzyl)-3,4-dihydro-6,7-dimethoxyisoquinoline, 52050-48-3; methyl chloroformate, 79-22-1.

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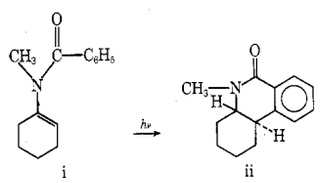

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