Enamide Photochemistry. Synthesis of Protoberberine Iodides from 1-Benzylidene-3,4-dihydro-2(1*H*)-isoquinoline Carboxaldehydes

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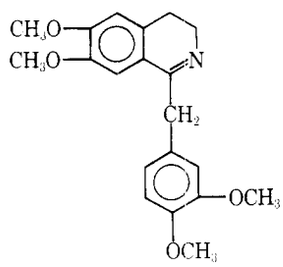
The syntheses of substituted 1-benzylidene-3,4-dihydro-2(1*H*)-isoquinoline carboxaldehydes from 1-benzyl-3,4-dihydroisoquinolines and mixed formic–acetic anhydride is described. The predominant and often exclusive isomer possesses the *Z* configuration, although the *E* isomer has been isolated in some instances. Irradiation in the presence of hydriodic acid forms protoberberine iodides in good yield. The photocyclization is regiospecific forming 10,11-disubstituted protoberberines from 3′,4′-disubstituted benzylidene enamides. The enamide **12**, monosubstituted in an ortho position of the benzylidene group, was synthesized to test for the elimination of an *o*-methoxy group to form oxyprotoberberine **20** in a nonoxidative photocyclization. Irradiation gave exclusive cyclization at the unsubstituted position to form 2,3,9,12-tetramethoxyprotoberberine iodide (**19**) and there was no evidence for the occurrence of nonoxidative photocyclizations.

The synthesis of the tetracyclic berbine ring system has been accomplished in a wide variety of ways.[1] Photochemically, this has been done by irradiation of 1-methylene-2-aroyltetrahydroisoquinolines to form 8-oxoberbines,[2] as well as by photoacylation of 1-benzylideneisoquinoline carbamates to prepare oxyprotoberberines.[3] These oxidized compounds are readily reduced to berbines. Both the naturally occurring berbines, as well as modified derivatives, have shown hypotensive activity,[4] and the recent use of tetrahydropalmatine as an antipsychotic[5] has increased interest in these compounds. A common method used to prepare derivatives of these compounds has been reduction of protoberberine salts.[1] We have been interested in extending the uses of enamides, and had previously accomplished the photocyclization of 2-acetyl-1-benzylideneisoquinoline enamides to 8-methylprotoberberines.[6] As a result of this we have studied the photochemistry of 2-formyl-1-benzylideneisoquinoline enamides to form protoberberine alkaloids and their subsequent reduction to berbines.

Results and Discussion

Enamides. The only report in the literature on the preparation of 2-formyl-1-benzylidene isoquinolines is that reported by Baxter and Swan on the reaction of 3,4-dihydropapaverine (1) with acetic anhydride and formic acid in the presence of sodium acetate to yield **2**.[7] The structure shown is that shown



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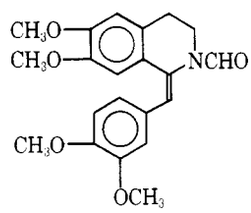

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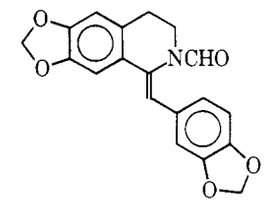
in the original article. We have prepared a series of these enamides using essentially the same reaction conditions, except that we have used preformed mixed acetic–formic anhydride (Table I).[8] The initial procedure called for warming on a steam bath for 1 h and standing overnight. When this procedure was followed, omitting the warming, only one isomer was obtained. However, it was subsequently found that the reaction with mixed formic–acetic anhydride was virtually instantaneous and the reaction mixture could be worked up immediately after mixing. When this was done a mixture of *E* and *Z* isomers was obtained. These could be separated by crystallzation (**3** and **4**) or by low-pressure liquid chromatography (**7** and **8**, **10** and **11**). These isomers could be differentiated on the basis of both NMR and UV spectra. For example, in the isomeric pair **7** and **8**, the formyl proton in the *E* isomer **8** appears at δ 8.67 while a model shows that in the *Z* isomer **7**, the formyl proton is shielded by the benzylidene



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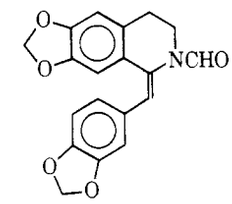

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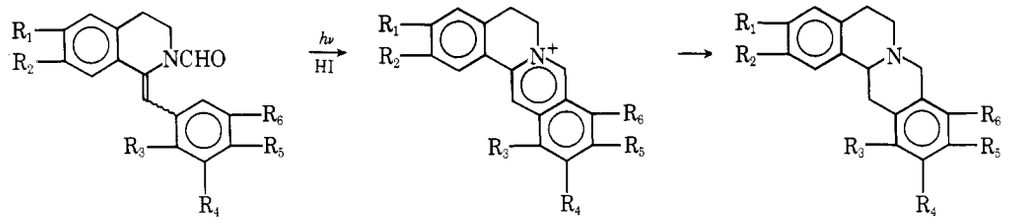
phenyl ring and appears at δ 8.13.[9] Additionally, the C-8 isoquinoline proton and the C-7 methoxyl group are known to be shielded by the phenyl ring of a 1-benzyl substituent when, because of steric factors, the benzyl group adopts a conformation similar to the *E* isomer.[10] In the *Z* isomer **7**, the C-8 proton resonates at δ 6.60 while in the *E* isomer **8** shielding by the 1-benzylidene group shifts the C-8 proton to δ 6.48. Acylation of dihydroisoquinolines to benzylidene enamides forms molecules with the stilbene chromophore.[9,11] In the stilbenes, the trans isomer is known to absorb at lower energy with a higher intensity than *cis*-stilbene.[12] Then the *Z* isomer **7**, equivalent to the *trans*-stilbene chromophore, should absorb at lower energy and with a greater intensity than the *E* isomer **8**. This is indeed the case with λ_{max} for **7** at 337 nm (ϵ 21 500) and **8** at 298 nm (ϵ 13 500) and the ultraviolet spectral assignments are in agreement with the NMR assignments.

Where only one isomer was isolated, these were all assigned the *Z* configuration because of a shielded formyl proton between δ 8.08 and 8.22 and a UV maximum between 328 and 335 nm. On this basis the *E* configuration of **2** should be revised to the *Z* configuration **5**. It was also found that heating the *E* isomers **3** and **11** in an Abderhalden drying pistol over refluxing toluene, in vacuo, caused rapid isomerization to the *Z* isomers **4** and **10**. The formation of the *E* isomers may be the result of kinetic deprotonation of the iminium intermediate. The *Z* isomers are thermodynamically more stable and may be formed directly or through isomerization of the less stable *E* isomers.

Photochemistry. The enamides were all irradiated in a mixture of dioxane and *tert*-butyl alcohol, as there was no evidence for hydrolysis of the enamides by hydriodic acid in this solvent combination.[13] The enamides were irradiated either as the *Z* isomer or as a mixture of the *E* and *Z* isomers when they occurred as such. As the irradiation progressed, a bright yellow precipitate of the protoberberine iodide formed in the irradiation well and the product could be isolated by

Table I. Formation of Protoberberines from Formyl Enamides



Enamide	Con-fign	R_1	R_2	R_3	R_4	R_5	R_6	Protoberberine[a] (yield, %)	Berbine[a] (yield, %)
3	*E*	H	H	H	H	H	H		
4	*Z*	H	H	H	H	H	H	13[b] (45)	22 (76)
5	*Z*	OCH_3	OCH_3	H	OCH_3	OCH_3	H	14 (75)	23 (78)
6	*Z*	OCH_3	OCH_3	H	OCH_2O		H	15 (100)	24 (100)
7	*Z*	OCH_2O		H	OCH_2O		H	16[b] (79)	25 (98)
8	*E*	OCH_2O		H	OCH_2O		H		
9	*Z*	OCH_3	OCH_3	H	OCH_3	OCH_3	OCH_3	17 (75)	26 (81)
10	*Z*	OCH_2O		H	OCH_3	OCH_3	OCH_3	18[b] (55)	27 (72)
11	*E*	OCH_2O		H	OCH_3	OCH_3	OCH_3		
12	*Z*	OCH_3	OCH_3	OCH_3	H	H	OCH_3	19 (98)	28 (66)

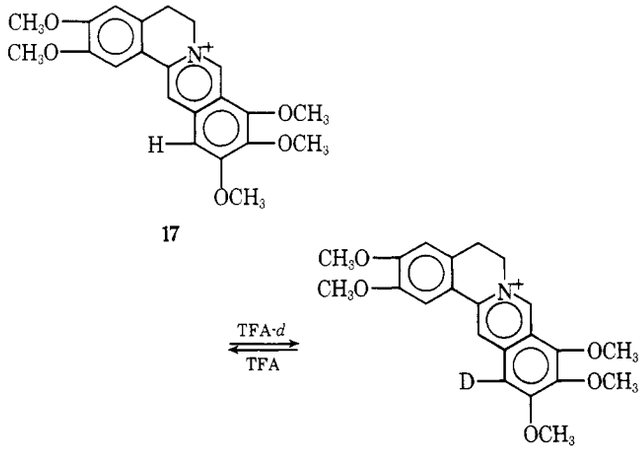
[a] References to known compounds are collected in the Experimental Section. [b] *E*–*Z* mixtures were used for the irradiations.

simple filtration. The exception was protoberberine iodide (**13**), which has a slight solubility in the irradiation solution. The yields of the protoberberine iodides are collected in Table I. The photoproducts were characterized by the absence of a carbonyl absorption in the infrared and their very characteristic ultraviolet spectra.[14] With the synthesis of protoberberine iodide (**13**), all of the parent members of the berbine family of alkaloids have now been synthesized by irradiation of the appropriate enamides. The oxyprotoberberine[3] and 8-oxoberbine[2b] thus formed have all been reduced to berbine.[15] It should also be noted that the yield of protoberberine **13** via photocyclization of enamides **3** and **4** is substantially better than the reported thermal cyclization of 1-benzyl-3,4-dihydroisoquinoline.[16]

When substituents are present in the 3′,4′ positions of the benzylidene group, **5, 6,** and **7,** cyclization can occur in two different positions to form either 9,10- or 10,11-substituted protoberberines, or a mixture of both. These isomeric protoberberine iodides can be differentiated on the basis of their ultraviolet spectra.[14] When the tetramethoxyenamide **5** was irradiated, a 75% yield of a single photoproduct **14** was obtained. Its UV spectrum indicated 10,11 substitution and this was confirmed by the NMR spectrum in trifluoroacetic acid-*d*.[17] The C-8 and C-13 protons resonated at δ 9.27 and 8.54, respectively, while the remaining four aromatic protons occurred as four sharp singlets between δ 7.10 and 7.72. In a similar manner, protoberberines **15** and **16** were shown to have 10,11 substitution.[19] Exclusive formation of 10,11 substitution also occurred in the formation of the 8-methylprotoberberines.[6] Additionally, reduction of **14** gave the naturally occurring xylopinine[18] which was identical with an authentic sample.[2a]

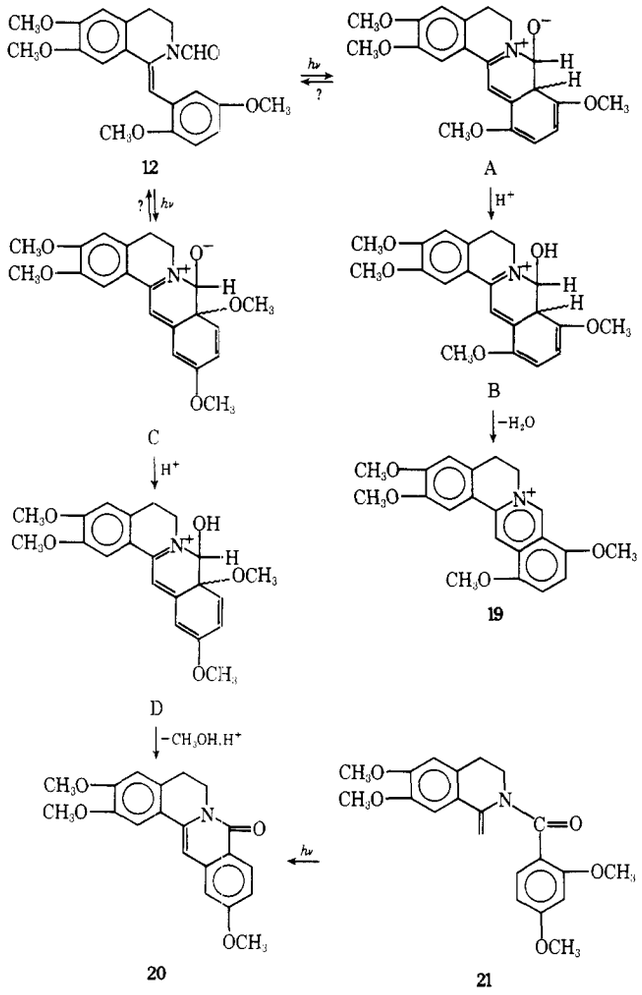
The 3′,4′,5′-trimethoxy substitution in the benzylidene moiety of enamides **9** and **10** was introduced to determine whether photocyclization could result in introduction of a methoxyl substituent at C-9 to reflect the commoner oxygenation pattern in protoberberines. The trimethoxy substitution, being symmetrical, can only result in one isomer, that which possesses 9,10,11 substitution. When the irradiations were performed, the protoberberines were isolated in good yield. Thus it appears that there is either a steric or an electronic effect which results in the exclusive formation of the 10,11-oxygenation pattern from 3′,4′-disubstituted benzylidene enamides. The same exclusivity has been found in photocyclization of 2-aroyl-1-methyleneisoquinoline enamides.[2a]

The NMR spectra of these protoberberines showed an interesting exchange phenomenon. When the pentamethoxyprotoberberine **17** was dissolved in trifluoroacetic acid-*d* and the NMR spectrum recorded, the C-8 and C-13 protons appeared at δ 9.37 and 8.42, respectively. However, instead of the expected three additional aromatic protons corresponding to C-1,4,12 on rings A and D, only two were observed as sharp singlets at δ 7.04 and 7.65. When the solvent was evaporated and replaced by trifluoroacetic acid, an additional sharp one-proton singlet appeared at δ 7.31. Apparently, the ortho-para methoxyl substitution, relative to C-12, renders C-12 of the D ring sufficiently basic to undergo electrophilic attack and subsequent exchange by the deuterated trifluoroacetic acid.[20] This exchange is specific for C-12 in 9,10,11-trisubstituted protoberberines since no exchange was observed in 10,11-disubstituted protoberberines.



The final enamide studied, **12,** possessed 2′,5′-dimethoxy substitution in the benzylidene group. This enamide was synthesized and irradiated to determine whether methanol could be expelled in a nonoxidative photocyclization analogous to the ortho-substituted 2-aroyl-1-methyleneisoquinoline enamides.[21] If the probable mechanism for formation of the protoberberines from the formyl enamides is considered (Scheme I), then irradiation of **12** can cause cyclization via a 6π-electrocyclic ring closure[6] at either of the ortho positions of the benzylidene group. If cyclization occurs at the unsubstituted ortho position, then an intermediate A is formed which is protonated to form B and which loses water to gen-

Scheme I. Photocyclization Possibilities of Enamide 12



erate the 2,3,9,12-tetramethoxyprotoberberine **19.** On the other hand, if cyclization occurs at *o*-methoxyl position, then an intermediate C is formed. Protonation of this intermediate forms D which can rearomatize by elimination of methanol and tautomerization to form the oxyprotoberberine **20.** A sample of the oxyprotoberberine was synthesized from the enamide **21** by a nonoxidative photocyclization.[21] When **12** was irradiated under standard conditions a 98% yield of protoberberine iodide was obtained. This was identified as **19** by its characteristic UV spectrum and by its NMR which showed the C-8 and -9 protons as singlets at δ 9.59 and 8.86. Additionally, the C-10 and -11 protons appeared as two one-proton doublets at δ 7.48 and 7.17 with a coupling constant of J = 9 Hz, thereby confirming the oxygenation pattern in ring D. Although the yield of protoberberine **19** precluded any appreciable amount of oxyprotoberberine **20** being formed, the irradiation solution was concentrated, freed from hydriodic acid, and examined by gas chromatography. Comparison with an authentic sample of **20,** prepared from **21,** showed that there was no oxyprotoberberine formed. A similar experiment, in which aliquots were taken during the irradiation, also indicated the absence of **20.** It was concluded that in the 2-formyl-1-benzylidene enamides, the expulsion of *o*-methoxyl groups does not occur. A possible explanation is that if C is formed, an energy-wasting reversal to **12** occurs which is much faster than the elimination to **20.** Also reversal of intermediate A, besides the general *E–Z* photoequilibrium,[9] could account for the inefficient formation of the protoberberines.

In a review article, Sammes postulated the protonation of the enamide and subsequent excitation to generate B which loses water to form the protoberberine salt.[22] Although plausible, there is no evidence for the formation of a protonated species. The UV spectrum of **5,** for example, was the same before and after the addition of hydriodic acid. Even if this postulate is correct it would not affect the previous mechanistic discussion; it would only eliminate intermediates A and C and proceed directly from protonated **12** to B and D.

The reduction of the protoberberines to berbines with sodium borohydride was also accomplished; the compounds and yields are collected in Table I.

Experimental Section

General. Melting points were taken on a Thomas-Hoover Unimelt capillary apparatus and are uncorrected. Infrared spectra were run in KBr, and ultraviolet and visible spectra were run in methanol. A Varian Associates A-60 or T-60 NMR spectrometer was used to record the spectra of all compounds other than the protoberberine salts. These spectra were all run in deuteriochloroform using tetramethylsilane as an internal standard. The protoberberine iodides were run on a Varian Associates EM-390 90-MHz spectrometer using either trifluoroacetic acid or trifluoroacetic acid-*d* as solvent with tetramethylsilane as an internal standard. Microanalyses were determined by Searle Laboratories Microanalytical Department under the supervision of Mr. E. Zielinski. GLC analyses were run on a Perkin-Elmer 900 gas chromatograph.

(*E*)- and (*Z*)-1-Benzylidene-3,4-dihydro-2(1*H*)-isoquinoline Carboxaldehyde (3, 4). A solution of 10.0 g of 1-benzyl-3,4-dihydroisoquinoline hydrochloride (Aldrich-Bader) in 250 mL of water was neutralized with 10 mL of 50% sodium hydroxide solution and extracted with three 125-mL portions of chloroform. The chloroform extracts were combined, dried with sodium sulfate, and evaporated. The residual oil was flame distilled at 160 °C (~1 mm) to yield 5.90 g of 1-benzyl-3,4-dihydroisoquinoline. The isoquinoline was mixed with 10 g of anhydrous sodium acetate and 50 mL of mixed formic–acetic anhydride[23] at room temperature and stirred for 2 h. The homogeneous solution was poured into excess methanol to destroy residual anhydride and then diluted with distilled water. The compounds oiled out but quickly solidified and were filtered. The solids were triturated with 30 mL of methanol to give 3 g of an *E–Z* mixture. Upon standing overnight, the mother liquors deposited 220 mg of pure *E* isomer **3:** mp 97–108 °C; IR 1680, 1670, 1650 cm^{-1}; UV 230 nm (ϵ 20 000), 261.5 (min, 8000), 287 (10 750); NMR δ 8.72 (s, 1 H, formyl H), 6.83–7.42 (m, 9 H), 6.50 (s, 1 H, benzylidene H), 3.78 (t, 2 H), 2.97 (t, 2 H).

Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.07; N, 5.62. Found: C, 82.11; H, 5.77; N, 5.43.

The *E* isomer is rather unstable, isomerizing readily to the *Z* isomer. Drying in vacuo over refluxing toluene rapidly caused this isomerization. This probably accounts for the wide range in the melting point.

Concentration of the mother liquors gave, in two successive crops, 2.20 g of the *Z* isomer **4:** mp 101–103 °C; IR 1675 cm^{-1}; UV 228 nm (min, ϵ 16 500), 240 (17 750), 270 (min, 9500), 307 (17 000); NMR δ 8.17 (s, 1 H, formyl H), 7.83 (m, 1 H), 7.17–7.67 (m, 7 H), 7.02 (s, 1 H), 4.03 (t, 2 H), 2.98 (t, 2 H).

Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.07; N, 5.62. Found: C, 81.52; H, 6.10; N, 5.47.

(*Z*)-1-(3′,4′-Dimethoxybenzylidene)-3,4-dihydro-6,7-dimethoxy-2(1*H*)-isoquinoline Carboxaldehyde (5). This compound was prepared from dihydropapaverine according to the published procedure,[7] excepting that mixed formic–acetic anhydride was preformed and added to the dihydroisoquinoline–sodium acetate mixture and the mixture was not warmed. Compound **5** exhibits mp 168–169 °C (lit.[7] 168 °C); IR 1655 cm^{-1}; UV 223 nm (ϵ 31 000), 258 (min, 11 000), 268 (11 500), 299 (sh, 14 000), 333 (23 000); NMR δ 8.18 (s, 1 H, formyl H), 7.23 (s, 1 H), 6.97 (s, 2 H), 6.92 (s, 1 H), 6.78 (s, 1 H), 6.63 (s, 1 H), 4.03 (t, 2 H, partially obscured by the methoxyl resonances), 3.98 (s, 3 H), 3.92 and 3.90 (s, 9 H), 2.92 (t, 2 H).

(*Z*)-1-(3′,4′-Methylenedioxybenzylidene)-3,4-dihydro-6,7-dimethoxy-2(1*H*)-isoquinoline Carboxaldehyde (6). The compound was prepared from 10 g (27.7 mmol) of 1-(3′,4′-methylenedioxybenzyl)-3,4-dihydro-6,7-dimethoxyisoquinoline hydrochloride,[24] 10 g of sodium acetate, and 75 mL of mixed formic–acetic anhydride at 0 °C. After standing for 18 h, 50 mL of methanol was added and then the mixture poured into 700 mL of water. The light tan solid was filtered to yield 7.35 g (20.8 mmol, 75%) of **6:** mp 194–196 °C (methylene chloride–ethyl acetate); IR 1675, 1645, 1615, 1520 cm^{-1}; UV 223 nm (ϵ 33 000), 257 (min, 10 000), 269 (10 500), 294 (sh, 12 500), 333 (22 250); NMR δ 8.16 (s, 1 H, formyl H), 7.18 (s, 1 H), 6.78–6.92 (m,

3 H), 6.73 (s, 1 H), 6.61 (s, 1 H), 5.93 (s, 2 H, methylenedioxy H), 3.95 (t, 2 H), 3.93 (s, 3 H), 3.87 (s, 3 H), 2.86 (t, 2 H).

Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.65; H, 5.39; N, 4.12.

(*E*)- and (*Z*)-1-(3′,4′-Methylenedioxybenzylidene)-3,4-dihydro-6,7-methylenedioxy-2(1*H*)-isoquinoline Carboxaldehyde (8, 7). Homopiperonylamine hydrochloride (5.0 g, 25 mmol), 2.1 g (25 mmol) of sodium bicarbonate, and 5 g (27.8 mmol) of homopiperonylic acid in 150 mL of xylene were refluxed for 3.5 h using a modified Dean-Stark trap as a water separator. The refluxing solution was filtered from the sodium chloride and after cooling 6.6 g (20.2 mmol, 81%) of *N*-homopiperonylhomopiperonamide was filtered.[25] The 6.6 g of amide was cyclized to 1-(3′,4′-methylenedioxybenzyl)-3,4-dihydro-6,7-methylenedioxyisoquinoline using phosphorus oxychloride in toluene.[26] Three grams (9.7 mmol) of the dihydroisoquinoline and 5 g of sodium acetate were added to 50 mL of mixed formic–acetic anhydride and after 10 min poured into 50 mL of pyridine and 850 mL of water. The compounds oiled, but quickly crystallized and were filtered to 2.80 g (8.3 mmol, 86%) of a mixture of isomers (TLC, 1:1-ethyl acetate–benzene on silica). The mixture, 1.43 g, was separated by low-pressure chromatography on alumina. Elution with ethyl acetate–benzene (8:92) gave 431 mg of the *Z* isomer **7** in fractions 25–45: mp 160–162 °C (ether–ethyl acetate); IR 1670, 1640 cm^{-1}; UV 222 nm (ϵ 33 000), 258 (min, 8000), 295 (sh, 12 000), 337 (21 500); NMR δ 8.13 (s, 1 H, formyl H), 7.18 (s, 1 H), 6.75–6.92 (m, 3 H), 6.68 (s, 1 H), 6.60 (s, 1 H), 5.97 (s, 4 H, methylenedioxy H), 3.95 (t, 2 H), 2.83 (t, 2 H).

Anal. Calcd for $C_{19}H_{15}NO_5$: C, 67.65; H, 4.67; N, 4.25. Found: C, 67.72; H, 4.67; N, 4.25.

Fractions 65–85 gave 151 mg of the *E* isomer **8**: mp 206–208 °C (ether–ethyl acetate); IR 1670, 1645 cm^{-1}; UV 222 nm (ϵ 31 000), 245 (sh, 13 750), 263 (min, 8750), 298 (13 500), 321 (sh, 11 250); NMR δ 8.67 (s, 1 H, formyl H), 6.58–6.83 (m, 5 H), 6.48 (s, 1 H), 5.95 (s, 2 H, methylenedioxy H), 5.90 (s, 2 H, methylenedioxy H), 3.72 (t, 2 H), 2.83 (t, 2 H).

Anal. Calcd for $C_{19}H_{15}NO_5$: C, 67.65; H, 4.48; N, 4.15. Found: C, 67.70; H, 4.67; N, 4.06

(*Z*)-1-(3′,4′,5′-Trimethoxybenzylidene)-3,4-dihydro-6,7-dimethoxy-2(1*H*)-isoquinolinecarboxaldehyde (9). This compound was prepared from 4.0 g (9.8 mmol) of 1-(3′,4,5′-trimethoxybenzyl)-3,4-dihydro-6,7-dimethoxyisoquinoline[27] and 4 g of potassium acetate in 30 mL of mixed formic–acetic anhydride for 3 h. The reaction mixture was poured into 50 mL of pyridine in 500 mL of water and extracted with chloroform. The extract was washed twice with water. The organics were dried with sodium sulfate and evaporated. Crystallization from ethyl acetate–ether gave 3.0 g (7.5 mmol, 77%) of **9**: mp 171–172 °C; IR 1700, 1675, 1520 cm^{-1}; UV 222 nm (ϵ 32 000), 262 (min, 10 000), 305 (sh, 15 000), 335 (23 000); NMR δ 8.22 (s, 1 H, formyl H), 7.25 (s, 1 H), 6.75 (s, 1 H), 6.67 (s, 3 H), 4.03 (t, 2 H), 3.97 (s, 3 H), 3.92 (s, 3 H), 3.87 (s, 9 H), 2.90 (t, 2 H).

Anal. Calcd for $C_{22}H_{25}No_6$: C, 66.15; H, 6.31; N, 3.51. Found: C, 65.81; H, 6.37; N, 3.84.

(*E*)- and (*Z*)-1-(3′,4′,5′-Trimethoxybenzylidene)-3,4-dihydro-6,7-methylenedioxy-2(1*H*)-isoquinoline Carboxaldehyde (11,10). 1-(3′,4′,5′-Trimethoxybenzyl)-3,4-dihydro-6,7-methylenedioxyisoquinoline[28] (1.0 g, 2.8 mmol) was reacted with 17.5 mL of mixed formic–acetic anhydride and 5 g of sodium acetate for 0.5 h. Workup as above gave 1.0 g (2.6 mmol, 93%) of a mixture of *E* and *Z* isomers. The mixture (400 mg) was separated by low-pressure liquid chromatography on Woelm silica. Elution with ethyl acetate–benzene (15:85) gave the *Z* isomer **10**: mp 194–196 °C (ethyl acetate–ether); IR 1680, 1585, 1515, 1510 cm^{-1}; UV 220 nm (end, ϵ 34 000), 247 (sh, 13 500), 263 (min, 8500), 300 (sh, 13 000), 334 (20 500); NMR δ 8.17 (s, 1 H, formyl H), 7.20 (s, 1 H), 6.67 (s, 1 H), 6.62 (s, 3 H), 5.97 (s, 2 H, methylenedioxy H), 3.97 (t, 2 H), 3.85 (s, 6 H), 3.83 (s, 3 H), 2.86 (t, 2 H).

Anal. Calcd for $C_{21}H_{21}NO_6$: C, 65.78; H, 5.52; N, 3.65. Found: C, 65.59; H, 5.32; N, 3.72.

Continued elution with ethyl acetate–benzene (1:4) gave 80 mg of the *E* isomer **11**: mp 180–184 °C (ether); IR 1680, 1590, 1515 cm^{-1}; UV 200 nm (end, ϵ 31 000), 246 (sh, 14 000), 263 (min, 8250), 295 (sh, 12 250), 326 (14 250); NMR δ 8.70 (s, 1 H, formyl H), 7.27 (s, 1 H), 6.75 (s, 1 H), 6.47 (s, 1 H), 6.33 (s, 1 H), 5.88 (s, 2 H, methylenedioxy H), 3.97 (t, 2 H), 3.85 (s, 6 H), 3.75 (s, 3 H), 2.86 (t, 2 H).

Anal. Calcd for $C_{21}H_{21}NO_6$: C, 65.78; H, 5.52; N, 3.65. Found: C, 65.69; H, 5.52; N, 3.58.

(*Z*)-1-(2′,5′-Dimethoxybenzylidene)-3,4-dihydro-6,7-dimethoxy-2(1*H*)-isoquinoline Carboxaldehyde (12). *N*-(3,4-Dimethoxyphenylethyl)-2,5-dimethoxyphenylacetamide was prepared from 2,5-dimethoxylphenylacetic acid and 3,4-dimethoxyphenylethylamine,[25] mp 105–107 °C (ethanol).

Anal. Calcd for $C_{20}H_{25}NO_5$: C, 66.83; H, 7.01; N, 3.90. Found: C, 66.56; H, 7.16; N, 3.89.

The amide was converted to 1-(2′,5′-dimethoxybenzyl)-3,4-dihydro-6,7-dimethoxyisoquinoline,[26] which was not characterized but used directly to prepare the enamide **12**. A mixture of 5.0 g (14.7 mmol) of dihydroisoquinoline and 10 g of sodium acetate was reacted with 50 mL of mixed formic–acetic anhydride analogous to **5** to yield 4.9 g (13.3 mmol, 90%) of **12**: mp 138–141 °C (ethyl acetate–ether); IR 2850, 1670, 1615, 1525, 1505 cm^{-1}; UV 220 nm (end, ϵ 39 000), 256 (min, 10 000), 285 (sh, 12 500), 328 (15 500); NMR δ 8.08 (s, 1 H, formyl H), 7.28 (s, 1 H), 6.75–7.00 (m, 4 H), 6.63 (s, 1 H), 4.00 (t, 2 H, obscured by methoxyls), 3.95 (s, 3 H), 3.90 (s, 3 H), 3.83 (s, 3 H), 3.75 (s, 3 H), 2.88 (t, 2 H).

Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.31; H, 6.67; N, 3.78.

General Irradiation Conditions. A solution of the formyl enamide in either 300 or 560 mL, depending on the irradiation well volume of a 2:1 mixture of dioxane–*tert*-butyl alcohol, was irradiated with a 450-W medium-pressure mercury arc, using a Pyrex filter. A hefty stream of nitrogen was bubbled through the irradiation mixture to prevent the protoberberine iodide from adhering to the wall of the irradiation well. The irradiations' progress was followed by thin layer chromatography and generally lasted 20–48 h.

Protoberberine Iodide (13). A solution of 1.0 g (4.02 mmol) of the *E*–*Z* mixture of **3** and **4** in 375 mL of solvent and 2 mL of 47% hydriodic acid was irradiated for 22 h. A bright yellow, flocculent precipitate of **13** was present which was filtered to 163 mg. Dioxane (40 mL) was added to the reaction mixture to replace lost solvent and irradiation was continued for an additional 22 h. A further 301 mg of **13** was collected and TLC indicated a substantial amount of **13** present in solution as well as starting material. An equal volume of chloroform was added to the irradiation mixture and this was washed with 75 mL of 20% sodium chloride solution and 10 mL of saturated sodium sulfite. The dark red organic solution immediately turned bright yellow. The colorless aqueous portion was separated and discarded while the organics were dried with sodium sulfate. When the solvent volume had been reduced to approximately 50 mL it was mostly dioxane and *tert*-butyl alcohol and a further 179 mg of **13** crystallized (643 mg, 1.79 mmol, 45%). After filtration of the protoberberine iodide, the mother liquors were evaporated and crystallization from methanol gave 400 mg (40%) of pure *Z*-**4**. The TLC of the mother liquor indicated a mixture of *E*-**3** and *Z*-**4**. 5,6-Dihydrodibenzo[*a*,*q*]quinolizinium iodide (**13**) could be recrystallized from water: mp ~225 °C dec (lit.[16] 232 °C dec); IR no carbonyl; UV 225 nm (ϵ 26 500), 238 (min, 14 250), 260 (32 250), 265 (33 500), 287 (min, 7000), 302 (9250), 306.5 (min, 9000), 314 (11 000), 329 (min, 2000), 365 (5500); NMR (trifluoroacetic acid) δ 9.58 (s, 1 H), 8.75 (s, 1 H), 7.83–8.42 (m, 5 H), 7.42–7.75 (m, 3H), 5.03 (t, 2 H), 3.47 (t, 2 H).

2,3,10,11-Tetramethoxyprotoberberine Iodide (14). A solution of 1.0 g (2.7 mmol) of **5** in 550 mL of solvent and 2 mL of 47% hydriodic acid was irradiated in a Pyrex vessel using eight 3500-Å lamps in a Rayonet preparative photoreactor. After 24 h of irradiation, a substantial precipitate of product had formed which was filtered and dried to 500 mg. Irradiation for a further 16 h gave an additional 450 mg of product, total 950 mg (2.0 mmol, 75%). An analytical sample was obtained by suspending the product in dilute sodium bisulfite and extracting with several portions of chloroform until the aqueous phase was colorless. Drying with sodium and evaporation to a small volume of chloroform caused **14** (5,6-dihydro-2,3,10,11-tetramethoxydibenzo[*a*,*g*]quinolizinium iodide) to crystallize: mp 245 °C dec (lit.[29] 250–255 °C); IR showed no carbonyl; UV 222 nm (26 500), 240 (sh, 20 000), 249 (min, 13 500), 265 (20 000), 287 (42 000), 310 (sh 27 500), 331 (min, 17 500), 339 (18 500), 380 (6500); NMR (trifluoroacetic acid-*d*) δ 9.27 (s, 1 H), 8.54 (s, 1 H), 7.72 (s, 1 H), 7.68 (s, 1 H), 7.63 (s, 1 H), 7.10 (s, 1 H), 4.93 (t, 2 H), 4.26 (s, 3 H), 4.22 (s, 3 H), 4.16 (s, 3 H), 4.09 (s, 3 H), 3.40 (t, 2 H).

2,3-Dimethoxy-10,11-methylenedioxyprotoberberine Iodide (15). A solution of 1.02 g (2.9 mmol) of **6** in 330 mL of solvent and 1.5 mL of 47% hydriodic acid was irradiated for 18 h. Filtration of the light yellow-orange precipitate gave 1.34 g (2.9 mmol, 100%) of 5,6-dihydro-2,3-dimethoxybenzo[*a*]-1,3-benzodioxolo[5,6-*g*]quinolizinium iodide (pseudoepiberberine): mp >300 °C (lit.[24] 303 °C dec); IR 1645 (weak), 1610, 1515 cm^{-1}; UV 220 nm (ϵ 29 500), 238 (22 500), 247 (min, 16 000), 263 (22 000), 269 (min, 20 500), 288 (39 000), 311 (sh, 26 500), 331 (min, 17 500), 339 (19 000), 362 (sh, 10 000), 390 (sh, 5250); NMR (trifluoroacetic acid-*d*) δ 9.08 (s, 1 H), 8.43 (s, 1 H), 7.68 (s, 1 H), 7.48 (s, 1 H), 7.10 (s, 1 H), 6.33 (s, 2 H), 4.88 (t, 2 H), 4.15 (s, 3 H), 4.09 (s, 3 H), 3.38 (t, 2 H).

2,3,10,11-Dimethylenedioxyprotoberberine (Isocoptisine, 16). A mixture of *E* and *Z* isomers (**7** and **8**), 880 mg (2.6 mmol), in 375 mL

of solvent and 2 mL of 47% hydriodic acid was irradiated for 4 h. The irradiation was interrupted and 406 mg of bright yellow salt was collected. The filtered solution was irradiated for a further 16 h and again filtered to yield a further 513 mg of bright yellow 5,6-dihydro-1,3-benzodioxolo[5,6-*a*][1,3]benzodioxolo[5,6-*g*]quinolizinium iodide (**16**, 20 mmol, 79%): mp >300 °C (lit.[25] >300 °C); UV 222 nm (ε 33 000), 238 (sh, 24 500), 247 (min, 17 000), 264 (26 000), 271 (min, 23 500), 286 (31 500), 304 (min, 18 000), 314 (20 000), 329 (min, 16 000), 341 (19 000), 362 (sh, 12 000), 388 (sh, 4500); NMR (trifluoroacetic acid) δ 9.04 (s, 1 H), 8.28 (s, 1 H), 7.48 (s, 1 H), 7.43 (s, 1 H), 7.39 (s, 1 H), 6.76 (s, 1 H), 6.28 (s, 2 H), 6.10 (s, 2 H), 4.83 (t, 2 H), 3.28 (t, 2 H).

2,3,9,10,11-Pentamethoxyprotoberberine Iodide (17). A solution of 1.00 g (2.51 mmol) of **9** in 300 mL of solvent and 1.5 mL of 47% hydriodic acid was irradiated for 4 h when a yellow precipitate had formed. The precipitate was filtered and dried to 150 mg. The solution was irradiated for a further 16 h and more of the protoberberine salt crystallized on the walls of the irradiation well. This was filtered to an additional 350 mg. TLC of the filtered solution indicated only the presence of starting enamide. An additional 1 mL of hydriodic acid was added and irradiation continued for an additional 6 h to yield another 250 mg. The solution was then poured into 20% sodium chloride solution and 10 mL of saturated sodium sulfite solution. The bright yellow solution was evaporated to a small volume, water added, and the solution placed in a continuous extractor. The yellow aqueous phase was extracted continuously until colorless. The bright yellow chloroform solution was evaporated and the residue triturated with refluxing ethyl acetate to yield a final 200 mg (total 950 mg, 1.87 mmol, 75%) of 5,6-dihydro-2,3,9,10,11-pentamethoxydibenzo[*a*,*g*]quinolinizium iodide (**17**): mp >300 °C: UV 220 nm (end, 26 000), 243 (sh, 18 500), 253 (min, 13 250), 268 (sh, 24 500), 277 (sh, 31 000), 287 (40 000), 312 (21 500), 342 (16 500), 369 (min, 7500), 388 (9000); NMR (trifluoroacetic acid) δ 9.37 (s, 1 H), 8.42 (s, 1 H), 7.65 (s, 1 H), 7.31 (s, 1 H), 7.04 (s, 1 H), 4.90 (t, 2 H), 4.38 (s, 3 H), 4.23 (s, 3 H), 4.19 (s, 3 H), 4.16 (s, 3 H), 4.10 (s, 3 H), 3.37 (t, 2 H).

Anal. Calcd for $C_{22}H_{24}NO_5I$: C, 51.87; H, 4.75; N, 2.75. Found: C, 51.73; H, 4.75; N, 3.06.

9,10,11-Trimethoxy-2,3-methylenedioxyprotoberberine Iodide (18). A mixture of the *E*- and *Z* enamides (**11** and **10**), 0.55 g (1.44 mmol), was dissolved in 365 mL of solvent and 2 mL of 47% hydriodic acid and irradiated for 19 h. The bright yellow precipitate was filtered and dried to 263 mg. Irradiation was continued for an additional 8 h to yield another 125 mg (total 388 mg, 0.79 mmol, 55%) of 5,6-dihydro-9,10-11-trimethoxybenzo[*g*]-1,3-benzodioxolo[5,6-*a*]quinolizinium iodide (**18**): mp >300 °C; UV 223 nm (ε 29 500), 238 (sh, 21 000), 251 (min, 13 500), 269 (sh, 26 000), 277 (sh, 30 500), 285.5 (35 500), 302 (min, 16 000), 316 (18 000), 337 (14 000), 344 (14 500), 366 (min, 7000), 384 (8000); NMR (trifluoroacetic acid) δ 9.28 (s, 1 H), 8.27 (s, 1 H), 7.48 (s, 1 H), 7.24 (s, 1 H), 6.90 (s, 1 H), 6.10 (s, 2 H), 4.83 (t, 2 H), 4.37 (s, 3 H), 4.23 (s, 3 H), 4.18 (s, 3 H), 3.28 (t, 2 H).

Anal. Calcd for $C_{21}H_{20}NO_5I$: C, 51.13; H, 4.09; N, 2.84. Found: C, 50.83; H, 4.01; N, 2.53.

2-(2′,4′-Dimethoxybenzoyl)-3,4-dihydro-6,7-dimethoxy-1-methylene-2(1*H*)-isoquinoline (21). 3,4-Dihydro-6,7-dimethoxy-1-methylisoquinoline[30] (7.90 g) in 200 mL of dry toluene and 30 mL of pyridine was stirred magnetically under nitrogen. Then 8 g of 2,4-dimethoxybenzoyl chloride (Aldrich) was added and the mixture heated to 65 °C for 2 h. The solution was washed with water three times and dried with sodium sulfate. The solvent was removed on a rotary evaporator and the residue crystallized from ether to yield 10.0 g of enamide: mp 148–151 °C; IR 1625, 1585, 1520 cm^{-1}; UV 245 nm (min, ε 13 500), 263 (19 500), 291 (sh, 9500), 303 (sh, 8500), 316 (sh, 6000); NMR δ 6.17–7.33 (m, 5 H), 5.17 (broad s, 1 H), 4.53 (broad s, 1 H), 4.08 (t, 2 H), 3.90 (s, 3 H), 3.86 (s, 3 H), 3.80 (s, 3 H), 3.39 (s, 3 H), 2.90 (t, 2 H).

Anal. Calcd for $C_{21}H_{23}NO_5$: C, 69.23; H, 5.24; N, 3.83. Found: C, 69.23; H, 5.38; N, 3.77.

2,3,11-Trimethoxy-8-oxyprotoberberine (20). A solution of 1.0 g of **21** in 195 ml of ethyl acetate was irradiated, under argon, with a 450-W mercury arc (Pyrex filter) for 3 h when TLC indicated consumption of starting material. The solvent was evaporated and chromatography on E. Merck silica thick layer plates to yield 315 mg (35%) of 5,6-dihydro-2,3,11-trimethoxy-8*H*-dibenzo[*a*,*g*]quinolizin-8-one: mp 151–152 °C (acetone–water); IR 1655, 1620, 1520 cm^{-1}; UV 227 nm (ε 24 000), 234 (21 500), 239 (22 500), 250 (sh, 24 500), 258 (27 000), 277 (sh, 12 500), 288 (min, 5500), 329 (21 500), 340 (22 250), 355 (15 500); NMR δ 8.33 (d, *J* = 8.5 Hz, 1 H), 6.67–7.33 (m, 5 H), 4.33 (t, 2 H), 3.98 (s, 3 H), 3.93 (s, 3 H), 3.90 (s, 3 H), 2.88 (t, 2 H).

Anal. Calcd for $C_{20}H_{19}NO_4$: C, 72.06; H, 4.54; N, 4.20. Found: C, 71.83; H, 4.41; N, 4.09.

Irradiation of the *o*-Methoxy-Substituted Formyl Enamide 12. A solution of 1.00 g (2.71 mmol) of **12** in 360 mL of solvent and 2 mL of 47% hydriodic acid was irradiated for 6.5 h and then filtered from the precipitated protoberberine iodide (300 mg). The internal temperature of irradiation solution was 14 °C. Further irradiation for 30 h gave an additional 970 mg (total 1270 mg, 2.65 mmol, 98%) in three crops of 5,6-dihydro-2,3,9,12-tetramethoxydibenzo[*a*,*g*]quinolizinium iodide (**19**): mp 246–254.5 °C dec (water containing a few crystals of sodium bisulfite); IR (1645, 1615, 1530, 1515 cm^{-1}; UV 242 nm (min, ε 21 500), 251.5 (25 500), 274 (min, 12 000), 288 (14 250), 303 (min, 8000), 330 (sh, 13 500), 352 (15 500), 393 (min, 6750), 426 (10 250); NMR (trifluoroacetic acid-*d*) δ 9.59 (s, 1 H), 8.86 (s, 1 H), 7.69 (s, 1 H), 7.48 (d, *J* = 9 Hz, 1 H), 7.17 (d, *J* = 9 Hz, 1 H), 7.05 (s, 1 H), 4.97 (t, *J* = 6 Hz, 2 H), 4.17 (s, 6 H), 4.09 (s, 3 H), 4.08 (s, 3 H), 3.38 (t, *J* = 6 Hz, 2 H).

Anal. Calcd for $C_{21}H_{22}NO_4I$: C, 52.62; H, 4.63; N, 2.92. Found: C, 52.70; H, 4.70; N, 2.88.

TLC examination of the mother liquor indicated the absence of any oxyprotoberberine **20**. Nevertheless, the solvent was evaporated to an oily residue, dissolved in ether, and extracted with dilute sodium sulfite solution. The solvent was removed and investigated by GLC. On a 6-ft 1.5% OV-17 column at 285 °C, the oxyprotoberberine had a retention time of 5.3 min. There were no peaks beyond 2.8 min in the GLC of the irradiation residue.

Control Experiments. A solution of 1.00 g of **5** in 300 mL of solvent and 1.5 mL of 47% hydriodic acid was stored at room temperature in the dark. At varying periods, aliquots were removed and diluted to 1 mg % and monitored by UV. When the experiment was terminated at 100 h, there had been no change in the ultraviolet spectrum, nor in the peak intensities. An equal volume of chloroform was added and the solution was washed with 100 mL of 20% sodium chloride solution and 25 mL of 10% sodium carbonate solution. The organics were dried with sodium sulfate and evaporated and the residue was crystallized from ethyl acetate–ether to return 883 mg of starting enamide.

General Procedure for Reduction of Protoberberines to Tetrahydroprotoberberines. An amount of protoberberine iodide was stirred magnetically in a 100-fold excess of either methanol or ethanol (w/v). To this suspension was added an equal weight of sodium borohydride in small portions, because of foaming. The bright yellow color was discharged immediately. The resultant solution was poured into water and extracted with methylene chloride. The solvent was dried and removed and the residue crystallized from an appropriate solvent.

Where the spectral characteristics of known tetrahydroprotoberberines are not known or generally available, they have been included.

Berbine 22. 13 (236 mg, 0.66 mmol) was reduced to yield 117 mg (0.50 mmol, 76%) of 5,6,13,13a-tetrahydro-6*H*-dibenzo[*a*,*g*]quinolizine (**22**): mp 82–84 °C (methanol–water) (lit.[16] 85 °C); UV 252.5 nm (sh, ε 550), 259 (sh, 750), 266 (925), 271 (min, 550), 273 (950); NMR δ 7.00–7.33 (m, 8 H), 2.5–4.17 (m, 9 H).

2,3,10,11-Tetramethoxyberbine (Xylopinine, 23). 14 (784 mg, 1.64 mmol) was reduced to yield 458 mg (1.28 mmol, 78%) of 5,6,13,13a-tetrahydro-2,3,10,11-tetramethoxy-6*H*-dibenzo[*a*,*g*]quinolizine (**23**), mp 182–183 °C (lit.[31] 182–183 °C).

2,3-Dimethoxy-10,11-methylenedioxyberbine (24). 15 (250 mg, 0.54 mmol) was reduced to yield 186 mg (0.54 mmol, 100%) of 5,6,13,13a-tetrahydro-2,3-dimethoxy-6*H*-benzo[*a*][1,3]benzodioxolo[5,6-*g*]quinolizine (**24**): mp 159–160 °C (lit.[32] 160–161 °C).

2,3,10,11-Bis(methylenedioxy)berbine (25). 16 (270 mg, 0.60 mmol) was reduced to yield 190 mg (0.59 mmol, 98%) of 5,6,13,13a-tetrahydro-6*H*-1,3-benzodioxolo[5,6-*g*]-1,3-benzodioxolo[5,6-*a*]-quinolizine (**25**): mp 212–214 °C (lit.[25] 214 °C); NMR δ 6.75 (s, 1 H), 6.69 (s, 1 H), 6.62 (s, 1 H), 6.57 (s, 1 H), 5.93 (s, 2 H), 5.91 (s, 2 H), 2.33–4.08 (m, 9 H).

2,3,9,10,11-Pentamethoxyberbine (26). 17 (566 mg, 1.11 mmol) was reduced to yield 5,6,13,13a-tetrahydro-2,3,9,10,11-pentamethoxy-6*H*-dibenzo[*a*,*g*]quinolizine (**26**): mp 136–138 °C (lit.[33] 132–134, 138–1 °C); NMR δ 6.77 (s, 1 H), 6.65 (s, 3 H), 6.52 (s, 3 H), 4.16 (d, *J* = 15 Hz, C-8H), 3.93, 3.90, 3.88, 3.86 (s, 15 H), 2.5–3.7 (m, 8 H).

9,10,11-Trimethoxy-2,3-methylenedioxyberbine (27). 18 (138 mg, 0.28 mmol) was reduced to yield 74 mg (0.20 mmol, 72%) of 5,8,13,13a-tetrahydro-9,10,11-trimethoxy-6*H*-benzo[*g*]-1,3-benzodioxolo[5,6-*a*]quinolizine: mp 147–148 °C (lit.[34] 135–136 °C); ir 1505, 1490 cm^{-1}; UV 229 nm (sh, ε 15 000), 255 (min, 750), 285 (5500), 294 (5000); NMR δ 6.73 (s, 1 H), 6.60 (s, 1 H), 6.48 (s, 1 H), 5.92 (s, 2 H), 4.12 (d, *J* = 16 Hz, 1 H), 3.92 (s, 3 H), 3.85 (s, 6 H), 2.5–3.7 (m, 8 H).

2,3,9,12-Tetramethoxyberbine (28). 19 (502 mg, 1.05 mmol) was reduced to yield 243 mg (0.69 mmol, 66%) of 5,8,13,13a-tetrahydro-2,3,9,12-tetramethoxy-6*H*-dibenzo[*a*,*g*]quinolizine (**28**): mp 142–144

°C (methanol–water); IR 1530, 1520, 1490 cm^{-1}; UV 220 nm (end, ϵ 17 000), 229 (sh, 13 750), 252 (min, 750), 281 (sh, 7000), 285 (7750), 291 (sh, 7250); NMR δ 6.81 (s, 1 H), 6.65 (s, 2 H), 6.62 (s, 1 H), 4.2 (d, J = 16 Hz, 1 H, C-8H), 3.90 (s, 3 H), 3.78 (s, 3 H), 3.63 (s, 6 H), 2.50–3.83 (m, 8 H).

Anal. Calcd for $C_{21}H_{25}NO_4$: C, 70.96; H, 7.09; N, 3.94. Found: C, 71.04; H, 7.03; N, 3.79.

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Registry No.—**3,** 61348-93-4; **4,** 61348-94-5; **5,** 61348-95-6; **6,** 61348-96-7; **7,** 61348-97-8; **8,** 61348-98-9; **9,** 61348-99-0; **10,** 61349-00-6; **11,** 61349-01-7; **12,** 61349-02-8; **13,** 19716-68-8; **14,** 10211-02-6; **15,** 61349-03-9; **16,** 36295-41-7; **17,** 61349-04-0; **18,** 61349-05-1; **19,** 61349-06-2; **20,** 61349-07-3; **21,** 61349-08-4; **22,** 483-49-8; **25,** 7259-08-7; **26,** 16724-64-4; **27,** 61349-09-5; **28,** 61349-10-8; 1-benzyl-3,4-dihydroisoquinoline, 24853-83-6; dihydropapaverine, 6957-27-3; 1-(3′,4′-methylenedioxybenzyl)-3,4-dihydro-6,7-dimethoxyisoquinoline HCl, 42971-28-8; 1-(3′,4′-methylenedioxybenzyl)-3,4-dihydro-6,7-methylenedioxyisoquinoline, 36295-45-1; 1-(3′,4′,5′-trimethoxybenzyl)-3,4-dihydro-6,7-dimethoxyisoquinoline, 61349-11-9; 1-(3′,4′,5′-trimethoxybenzyl)-3,4-dihydro-6,7-methylenedioxyisoquinoline, 61349-12-0; *N*-(3,4-dimethoxyphenylethyl)-2,5-dimethoxyphenylacetamide, 61349-13-1; 1-(2′,5′-dimethoxybenzyl)-3,4-dihydro-6,7-dimethoxyisoquinoline, 52050-48-3; 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline, 4721-98-6; 2,4-dimethoxybenzoyl chloride, 39828-35-8.

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Stilbenelike Photocyclizations of 1-Phenylvinyl-2-pyridones. Preparation of 4*H*-Benzo[*a*]quinolizin-4-ones[1]

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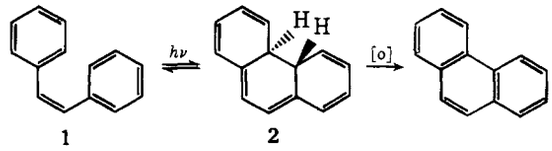
The photochemistry of 1-(2-phenylvinyl)-2-pyridone (**9**) and 1-(2,2-diphenylvinyl)-2-pyridone (**10**) has been investigated. Direct irradiation of **9** in a variety of solvents causes cis–trans photoisomerization exclusively. However, when irradiations are conducted on solutions of **9** containing hydrochloric acid with or without added iodine or oxygen, photocyclization occurs yielding 4*H*-benzo[*a*]quinolizin-4-one (**11**). Similarly, **10** is transformed to 4*H*-benzo[*a*]-7-phenylquinolizin-4-one by irradiation in solutions containing hydrochloric acid and no added oxidant. The mechanisms and regioselectivities of these reactions are discussed and compared to related observations from the photochemistry of acylaminostyrenes and aroylenamides.

Conjugated polyenes containing the hexatriene chromophore typically undergo photochemical electrocyclization reactions leading to products having the cyclohexadiene structural unit.[3] Characteristic of this reaction type are the facile conversions of *cis*-stilbenes (**1**) to dihydrophenanthrenes (**2**), which under oxidative conditions are transformed to phenanthrenes.[4] The striking synthetic potential of this general reaction has been repeatedly demonstrated and a large



1 **2**

number of examples of its use in the synthesis of alkaloids[5] and heterocyclic compounds[6] have been presented.