excess of dissolved ozone. The reaction was assumed to be complete and oxygen was passed through the mixture for 5 min to remove excess ozone. The solution became colorless. Methanol (25 ml) was then added and the mixture was left to stand at room temperature for 1 hr. Work-up involved the addition of 50 ml of water followed by solvent removal to give a yellow oil (750 mg, 70%).[24] This yellow oil exhibited no C≡N stretching band in the ir, and the NMR spectrum exhibited an intense aldehydic proton resonance. The NMR spectrum indicated the presence of some impurities which were removed by distillation of the oil at 150° (2 mm) in a molecular still. The distillate solidified to give a white compound (550 mg, mp 74–76°, 52%, 2,4-DNP derivative mp 232–234°). Ozonolysis of the isomers **8b** and **8c** gave the same aldehyde in comparable yields: mass spectrum *m/e* (rel intensity) 214 (15), 182 (66), 138 (15), 127 (65), 126 (100), 124 (42), 94 (83), 92 (97), 81 (55), 80 (34); ir 2800 (CH aldehyde), 1707 cm^{-1} (C=O aldehyde); uv 205 nm (log ϵ 3.60), 215 (3.55, broad), 267 (3.20, broad); NMR δ 3.98, 4.04 (carboxylic CH_3); 10.65 ppm (CHO). Anal. Calcd for $C_8H_7NO_6$: C, 45.08; H, 3.31; N, 6.57. Found: C, 45.18; H, 3.26; N, 6.45.

Acknowledgments. We wish to thank Dr. G. A. Webb and the University of Surrey, England, for 100-MHz ^1H NMR spectra, mass spectra, and computing facilities. We greatly appreciate the use of Professor F. A. L. Anet's ^{13}C and ^1H NMR equipment at UCLA and we should like to acknowledge the assistance of Dr. F. H. Köhler at Technischen Universität München in taking some ^{13}C NMR spectra.

Registry No.—**6**, 273-09-6; **8a**, 56086-88-5; **8b**, 56086-89-6; **8c**, 56086-90-9; **9**, 56086-91-0; **9** 2,4-DNPH, 56086-92-1; **10**, 7710-44-3; **11**, 300-87-8; **12**, 95-21-6; **13**, 573-34-2; **14**, 1557-59-1; DAD, 762-42-5.

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Photochemical Synthesis of 6,7-Dihydro-5*H*-dibenz[*c,e*]azepine and 5,6,7,8-Tetrahydrodibenz[*c,e*]azocine Derivatives[1]

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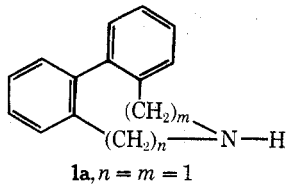
Photolysis of several substituted 2-iododibenzylamine hydrochlorides in aqueous solution provided convenient syntheses of the corresponding 6,7-dihydro-5*H*-dibenz[*c,e*]azepines in useful yields. Thus, irradiation of amines **2**, **3**, **4**, and **5** gave dibenzazepines **1a**, **10**, **11**, and **12** in 57, 44, 32, and 27% yield, respectively. However, irradiation of **6** yielded only biphenyl **14** together with a small amount of dibenzoxepine **15**. The formation of **14** and **15** was rationalized as originating from a photoassisted hydrolysis of the desired product **13**. Likewise, photolysis of three *N*-(2-halogenobenzyl)-β-phenethylamine hydrochlorides provided convenient syntheses of the corresponding 5,6,7,8-tetrahydrodibenz[*c,e*]azocines. Thus, irradiation of amines **7** and **8** gave dibenzazocines **1b** and **16** in 33% yield, while irradiation of **9** yielded the corresponding cyclic product in 22% yield. ^1H NMR examination of the dibenzazocines confirmed that they existed in a skewed biphenyl conformation, and that inversion of the system by rotation through the planar biphenyl was hindered.

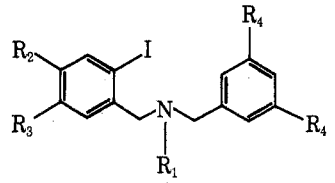
The physiological activities manifested by certain compounds containing either the bridged biphenyl system **1a**,[3–5] **1b**,[4] or **1c**[5,6] continue to stimulate interest in the development of general synthetic routes to these ring systems. The reported synthesis of substituted biphenyls by the photolysis of aryl iodides in benzene[8] prompted us to investigate a photochemical route to the bridged biphenyl systems **1a** and **1b**. During the course of our investigation an extension of the original reaction was employed for effecting intramolecular arylations leading to phenanthrenes,[9] and later to the synthesis of aporphines.[10]



1a, $n = m = 1$
b, $n = 1; m = 2$
c, $n = m = 2$

The results of our investigation demonstrate that photochemically induced intramolecular arylation may be employed not only in the formation of six-membered rings but also for constructing some seven- and eight-membered cycles. In this paper, we summarize the synthesis of several 6,7-dihydro-5*H*-dibenz[*c,e*]azepine (**1a**) derivatives and provide further details on the synthesis of the 5,6,7,8-tetrahydrodibenz[*c,e*]azocine (**1b**) ring system.

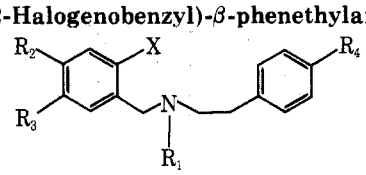
Table I
Substituted 2-Iododibenzylamines



Compd	Method	R_1	R_2	R_3	R_4	Yield, %[a]	HCl mp, °C
2	1	H	H	H	H	95	153–155
3	1	Me	H	H	H	88	190.5–192.5
4	2	H	H	NO_2	H	62	216–218
5	2	H	H	NO_2	OMe	52	253–255
6	2	H	H	H	OMe	94	180–182

[a] For the steps depicted in eq 1 or 2.

Table II
***N*-(2-Halogenobenzyl)-β-phenethylamines**



Compd	X	R_1	R_2	R_3	R_4	Yield, %	HCl mp, °C
7	I	H	H	H	H	82	145
8	I	Me	H	H	H	89	168–170
9	Br	H	OCH_2O		OH	77	226–228

Results and Discussion

Aryl Halides. The preparation of the substituted 2-iododibenzylamines used in this study was readily accomplished by one of two alternate methods: (1) nucleophilic displacement on a 2-iodobenzyl bromide by a substituted benzylamine (eq 1), or (2) condensation of a substituted 2-

$$ArCH_2Br \xrightarrow{Ar'CH_2NHR} ArCH_2NRCH_2Ar' + HBr \quad (1)$$

iodobenzaldehyde with a substituted benzylamine and subsequent reduction of the resultant Schiff base with borohydride (eq 2). The choice between method 1 and method 2

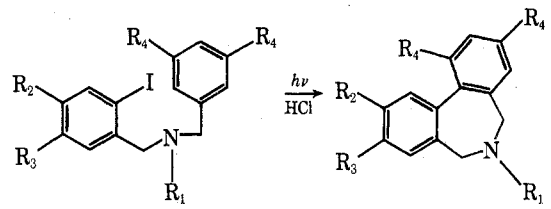
$$ArCHO \xrightarrow{Ar'CH_2NH_2} ArCH{=}NCH_2Ar' \xrightarrow{BH_4^-} ArCH_2NHCH_2Ar' \quad (2)$$

was generally dictated by the available starting materials. The structures of the 2-iododibenzylamines employed in this study are summarized in Table I.

The *N*-(2-iodobenzyl)-β-phenethylamines used in this study were also prepared by the displacement method. The aryl bromide was synthesized by the second method.[11] The *N*-(2-halogeno)-β-phenethylamines prepared are summarized in Table II.

Photolysis Conditions. The photolysis of 2-iododibenzylamine (**2**) was studied in some detail in order to establish the optimum reaction conditions. Irradiation of **2** in hexane solution with light of wavelength >280 nm from a medium-pressure mercury lamp afforded dibenzylamine as the only identifiable product.[12] From this result it appeared that water, a very poor hydrogen atom donor, would be a better choice of solvent.[13] Accordingly, irradiation of a dilute aqueous solution of **2**, as the hydrochloride, gave, after 196 hr, dibenzazepine **1a** in 57% yield together with 13% of the starting material.[1a] Characterization of **1a** was established by comparison with an authentic sample.[14]

Table III
Photolysis of Substituted 2-Iododibenzylamines



Compd	Irradiation time, hr	Starting material, %	Dibenzazepine, %	Other products, %
2	196	13	**1a**, 57	
3	96	10[a]	**10**, 44	Chloro compd, 5[a] Dehalogenated compd, <1
4	192	8	**11**, 32	
5	480	26	**12**, 27	
6	192	0	**13**, 0	**14**, 22; **15**, <5

[a] GC yield.

We found that optimum yields of **1a** were obtained when the longer wavelength regions of the ultraviolet spectrum were used to effect photolysis. The synthesis of **1a** using light of wavelengths <280 nm gave a low recovery of basic material, suggesting that photolytic cleavage of the benzylic carbon–nitrogen bond occurred on irradiation at shorter wavelengths.

As a result of the above observations, the standard photolysis procedure used for the aryl iodides was the irradiation of the amine hydrochlorides in water under a nitrogen atmosphere and with a mercury lamp fitted with a Pyrex filter. As noted below, a variation in the procedure was possible with aryl bromide **9**. The progress of the photolysis reactions was monitored by either gas chromatography (GC) or thin layer chromatography (TLC).

Photolysis of Substituted 2-Iododibenzylamines. Having established the apparently optimum conditions for the photochemical synthesis of the 6,7-dihydro-5*H*-dibenz[*c*,*e*]azepine ring system, we turned our attention to the effect of various substituents on the reaction. The subsequent photolysis experiments are summarized in Table III.

A logical first variation was the use of tertiary amine **3** instead of the secondary amine.[15] Accordingly, we found that irradiation of **3** afforded a 44% yield of 6-methyl-6,7-dihydro-5*H*-dibenz[*c*,*e*]azepine (**10**). In addition, the reaction mixture contained starting material (10%), *N*-methyl-2-chlorodibenzylamine (5%),[16] and a trace of *N*-methyldibenzylamine (<1%).

Identification of **10** was facilitated by the agreement of the melting point of its hydrobromide salt with the reported value.[3a] The mass spectral fragmentation pattern of this compound was also of diagnostic value. It showed strong M^+ and M − 1 peaks together with minor ions resulting from cleavage of the heteroatom bridge. This fragmentation behavior was also characteristic of the mass spectra of the other dibenzazepines prepared during this study. Final confirmation of the structure of **10** was obtained by its independent synthesis from **1a** by reductive methylation.

Photolysis of the aryl-substituted amines **4** and **5** afforded, respectively, 3-nitro-6,7-dihydro-5*H*-dibenz[*c*,*e*]azepine (**11**) and 1,3-dimethoxy-9-nitro-6,7-dihydro-5*H*-dibenz[*c*,*e*]azepine (**12**). Although the yields of **11** and **12** were considerably lower than that of **1a**, the photolysis pro-

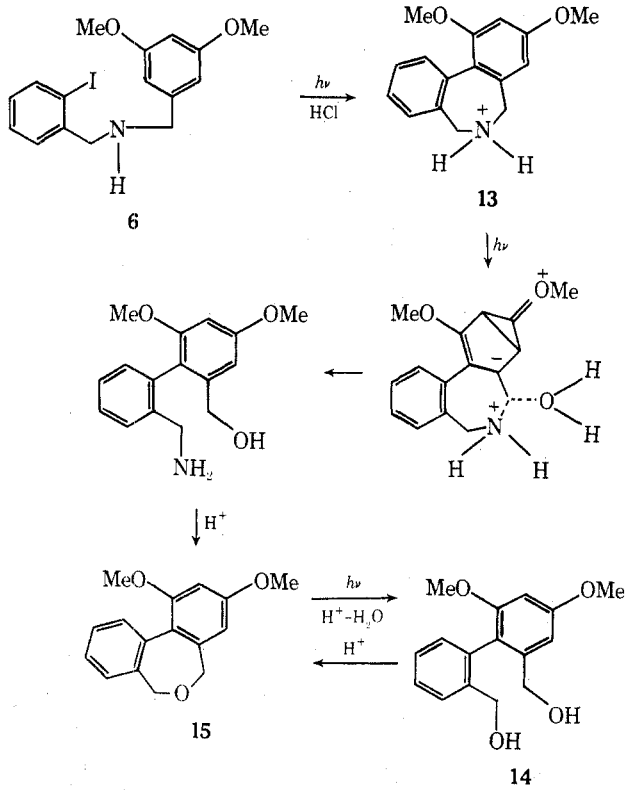
cedure nevertheless was superior to alternative methods of synthesis. The slow rate of the latter reaction may have been due to the intense absorptions of **12** in the long-wavelength ultraviolet region, thus decreasing the energy available to effect homolysis of the carbon–iodine bond.

In addition to the mass spectral evidence, characterization of compound **11** was provided by its uv spectrum, which showed a strong maximum at 300 nm (log ϵ 4.13), consistent with the presence of the 4-nitrobiphenyl chromophore.

The ^{1}H NMR spectrum of **12** was especially useful in assigning its structure. The occurrence of a clearly defined ABX pattern at low field was indicative of the substitution pattern on the nitro-substituted aromatic ring and the appearance of two nonequivalent methoxyl resonances at δ 3.83 and 3.80 was in full accord with the dibenzazepine structure. A variable-temperature ^{1}H NMR study resulted in a sharpening of the benzylic methylenes[17] from a broad diffuse multiplet at 25° to two singlets at 100°. This result implied that dibenzazepine **12** existed in a preferred skewed biphenyl conformation in which the benzylic hydrogens were diastereotopic and that conformational interchange to the equivalent skewed form was slow at 25°.[18]

A limitation of the photolysis reaction for the general synthesis of aryl-substituted dibenzazepines was demonstrated in the case of 3′,5′-dimethoxy-2-iododibenzylamine (**6**). Irradiation of **6** yielded 2,2′-bis(hydroxymethyl)-4,6-dimethoxybiphenyl (**14**) as the major product together with a very small amount of 1,3-dimethoxy-5,7-dihydrodibenz[*c*,*e*]oxepine (**15**). The molecular formulae of **14** and **15** were established by high-resolution mass spectrometry, and the fragmentation pattern of **14** below the M − 18 peak was essentially identical with that of **15**. The ^{1}H NMR and ir spectra of **14** and **15** were likewise confirmatory of the structures. Treatment of **14** with *p*-toluenesulfonic acid in refluxing benzene effected its conversion to **15**, thereby establishing the relationship between the two compounds.

Scheme I
Photolysis of 3′,5′-Dimethoxy-2-iodobenzylamine (6)



In previous studies Zimmerman and Sandel[20] had shown that electron-donating groups have the ability to stabilize a negative charge at a meta position in a benzene ring in the first photoexcited state. Thus, the formation of **14** and **15** may be rationalized as having occurred through a photoassisted hydrolysis of the desired dibenzazepine **13** (cf. Scheme I) with charge stabilization of the transition state provided by the first excited state of the *m*-dimethoxy aryl system. Additional driving force for hydrolytic cleavage was undoubtedly provided by the relief of strain attendant upon opening of the seven-membered ring. However, it appeared that strain relief alone was not sufficient to promote the hydrolytic cleavage, since the other dibenzazepines were stable to the photolysis conditions. Furthermore, the presence of the nitro group in **11** appeared to counteract the facilitating effect on the hydrolysis, since no neutral cleavage product was detected in this reaction.

In summary, photolysis of several substituted 2-iododibenzylamine hydrochlorides in aqueous solution provided convenient syntheses of the corresponding dibenzazepines in synthetically useful yields. The chief limitations of the method were the long reaction times required and the possibility of competing hydrolysis reactions in the presence of aryl oxygen substituents meta to the bridging carbons.

Photolysis of *N*-(2-Iodobenzyl)-β-phenethylamines. We previously reported that irradiation of **7** for 113 hr afforded a 25% yield of 5,6,7,8-tetrahydrodibenz[*c*,*e*]azocine (**1b**) together with *N*-benzyl-β-phenethylamine (10%).[1a] However, further examination of the reaction mixture indicated the presence of other unidentified bases. In subsequent experiments, the structures of these bases were elucidated by spectral examination and confirmed by unambiguous syntheses. Thus, the products obtained from the irradiation of **7** for 222 hr are shown in Scheme II and the yield data for the experiment are summarized in Table IV. These data were obtained by GC examination of the reaction mixture.

A similar mixture resulted from the irradiation of the tertiary amine **8** for 144 hr (Scheme II and Table IV). In

Scheme II
Photolysis of *N*-(2-Iodobenzyl)-β-phenethylamine (7) and Its *N*-Methyl Derivative (8)

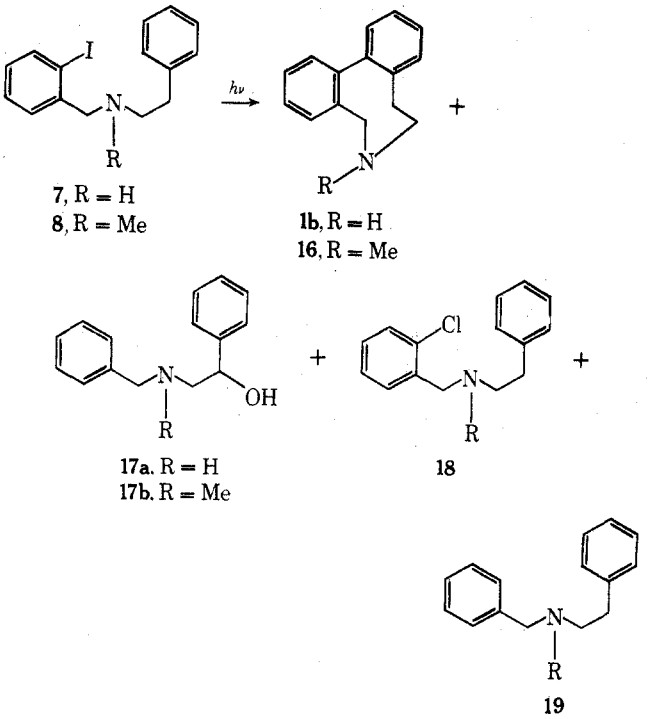


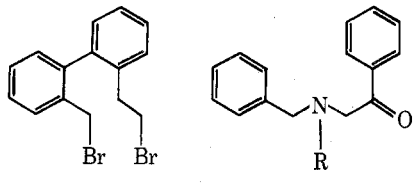
Table IV
Yield Data for the Photolysis of 7 and 8

Component	Yield, % a (R = H)	b (R = Me)
7 or 8	15 (7)	28 (8)
Dibenzazocine	33 (1b)	33[a] (16)
17	15	12[a]
18	8	5
19	13.5	6

[a] Isolated yield.

this case, the 6-methyl-5,6,7,8-tetrahydrodibenz[c,e]azocine (16) and the ethanolamine derivative 17b were isolated from the reaction mixture. The remainder of the yield data for the experiment was derived from GC analysis.

The structure of dibenzazocine 1b was verified by an unambiguous synthesis from dibromide 20.[1a] Compound 20



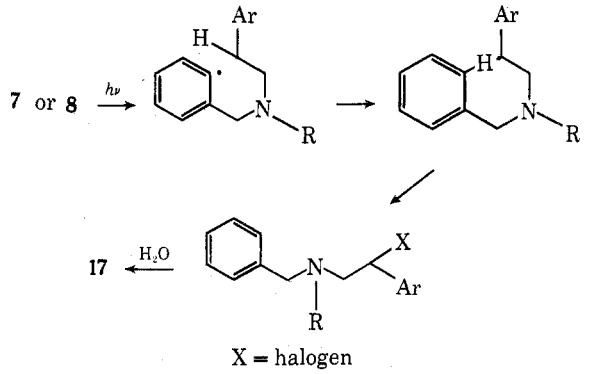
20 21

was prepared in seven steps from 2,2′-diphenic acid using procedures reported by Ahmed and Hall.[21] Careful methylation of 1b with methyl iodide gave 16.

The ethanolamine derivatives 17a and 17b were prepared independently by reaction of α-bromoacetophenone with the appropriate benzylamine followed by borohydride reduction of the intermediate ketones 21. The chlorinated and dehalogenated photolysis products were likewise prepared by standard procedures.

The photolysis of 7 and 8 presumably involved the initial formation of an aryl radical by the homolysis of the carbon–iodine bond.[8] The isolation of 17 provided some evidence that this pathway was indeed followed. The most logical mechanism for the formation of 17 is depicted in Scheme III and involves the formation of a benzyl radical from the initial aryl radical via hydrogen transfer. An alternative, the production of 17 from dehalogenated compound 19, seems unlikely in the absence of any ethanolamine byproducts corresponding to 1b or 16.

Scheme III
Radical Mechanism for the Formation of Ethanolamine Derivative 17



X = halogen

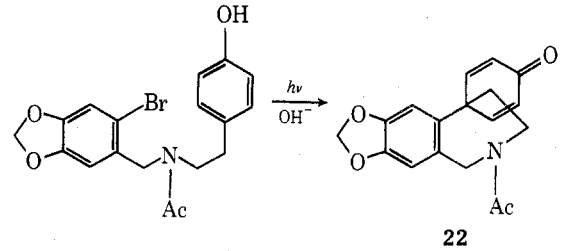
The synthesis of 1b and 16 demonstrated that the photolysis procedure used to prepare some dibenzazepine derivatives could also be applied to the synthesis of some simple dibenzazocines. Once again, the long reaction times were a drawback to the method.

Table V
Chemical Shifts and Geminal Coupling Constants for the Dibenzazocine $ArCH_2N$ Protons

Compd	δ values, ppm	J_{gem}, Hz
1b	3.10, 3.83	15.0
16	3.14, 3.49	13.5
23	3.02, 5.22	14.0
24	3.07, 5.25	14.0

Photolysis of *N*-(2-Bromobenzyl)-β-phenethylamines. During the course of our investigation Omura and Matsuura[22] reported that the irradiation of *p*-bromophenol in a basic medium gave, among other products, 2,4′-dihydroxybiphenyl and 4,4′-dihydroxybiphenyl. At the same time, Kametani and coworkers[23] summarized the synthesis of several aporphines and morphinandienones by irradiation of the appropriate phenolic bromoisoquinolines under similar conditions. In a later paper, this same group reported the photochemical synthesis of the crinine ring system in 5% yield by irradiation of 4′-hydroxy-*N*-(2-bromopiperonyl)-β-phenethylamine (9). No other photoproducts were reported.

In our hands attempts to reproduce this result were unsuccessful. However, irradiation of the *N*-acetyl derivative of 9 in an alkaline solution did afford a 2% yield of the dienone 22 as the only isolable product.



22

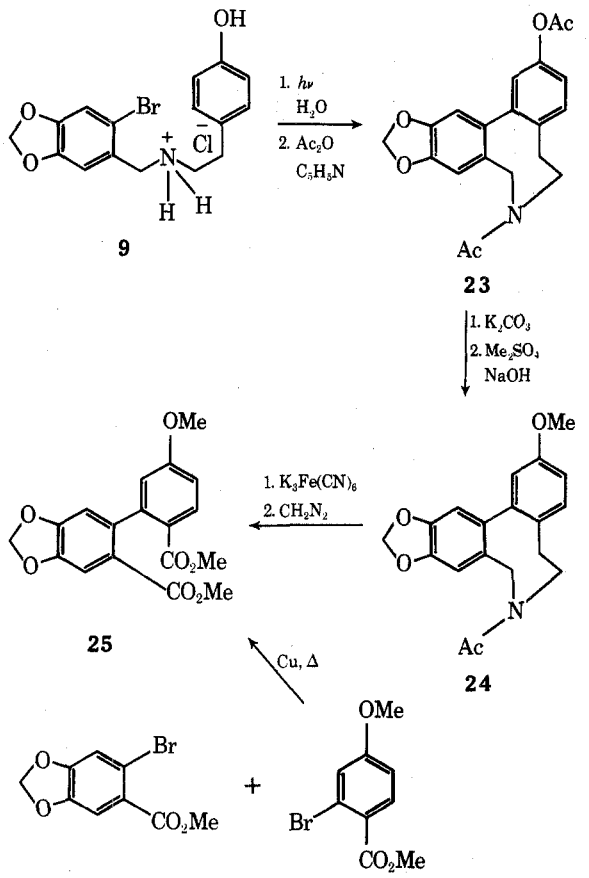
In contrast to these results, we found that irradiation of the hydrochloride of 9 in water for 10 hr followed by acetylation of the total product gave a 22% yield of 6,11-diacetoxy-2,3-methylenedioxy-5,6,7,8-tetrahydrodibenz[c,e]azocine (23) together with starting material *O,N*-diacetate (57%, Scheme IV).[24] Moreover, use of a Corex filter shortened the reaction time to 2 hr without decreasing the product yield. In both cases, the reaction times were substantially shorter than those encountered in the aryl iodide photolysis and the desired product was formed in a synthetically useful yield.

The structure of 23 was confirmed by the stepwise degradation outlined in Scheme IV. Previous experience in our laboratory[25] suggested that intermediate 24 could be further degraded using excess potassium hexacyanoferrate(III) in a strongly basic medium. The two-step procedure afforded the 2,2′-diphenic ester 25 in low yield. The structure of 25 was subsequently verified by an Ullmann synthesis.

The synthesis of 23 suggested that photolysis of other *N*-(2-bromobenzyl)-β-phenethylamines might be the preferred method for preparing various substituted 5,6,7,8-tetrahydrodibenz[c,e]azocines. The generality of this reaction is presently under investigation.

^{1}H NMR Data on the Dibenzazocines. ^{1}H NMR examination of the dibenzazocines prepared in this study showed that the bridge protons of each compound exhibited geminal coupling. In particular, the $ArCH_2N$ protons in this series appeared in the spectra as easily recognized doublets which are summarized in Table V. In view of the large chemical shift difference between the two diastereotopic protons of the $ArCH_2N$ group in compounds 23 and

Scheme IV
Formation and Stepwise Degradation of 6,11-Diacetoxy-2,3-methylenedioxy-5,6,7,8-tetrahydrodibenz[c,e]azocine (23)



24, the assignment was verified by both double resonance and homonuclear INDOR decoupling experiments. The nonequivalence of the bridge protons indicated that the eight-membered ring existed predominantly in one conformation at room temperature, and that inversion of the system by partial rotation of the skewed biphenyl was hindered.

The magnitude of the chemical shift difference (ca. 2.2 ppm) between the diastereotopic hydrogens of the $ArCH_2N$ group in 23 and 24 is a consequence of the geometry of the preferred conformation. Examination of models indicates that such a result is best accounted for if these compounds adopt a distorted half-tub conformation similar to that suggested by Mislow and coworkers[19] for the analogous carbocyclic system. It is in this conformation that one of the hydrogens of the benzylic aminomethyl group experiences deshielding from the more proximate aromatic ring and the amide carbonyl[26] while its diasteotopic partner is placed in a position to experience shielding from the more distant aromatic ring. As a consequence of the skewed biphenyl conformation, the methylenedioxy protons of 23 and 24 were also expected to be in slightly different environments with respect to the bridge atoms. In accordance with our expectations, we found that these protons appeared as two narrow doublets with a geminal coupling of 1.2 Hz.[27,28]

Experimental Section

Melting points were determined on a Thomas-Hoover Unimelt apparatus. ^1H NMR spectra were recorded on the following spectrometers: Varian A-60, Bruker HF-X 90, and Jeol MH-100. Chemical shifts are reported in parts per million downfield from Me_4Si as an internal standard. Ir spectra were obtained on a Perkin-Elmer 137 or 621 spectrometer and uv spectra were run on a Beckman DB-G spectrometer. Mass spectra were run on the AEI MS-902 mass spectrometer at the Research Triangle Institute, Research Triangle Park, N.C. Gas chromatographic analyses were carried out on a F & M Model 402 instrument equipped with a flame ionization detector. Elemental analyses were performed by Janssen Pharmaceutica, Beerse, Belgium, Galbraith Laboratories, Inc., Knoxville, Tenn., and M-H-W Laboratories, Garden City, Mich.

2-Iodo-5-nitrobenzaldehyde. 2-Acetamidobenzaldehyde[29] was nitrated and hydrolyzed to 2-amino-5-nitrobenzaldehyde by the procedure of Cohn and Springer.[30] This product (33.2 g, 0.2 mol) was added to 20% H_2SO_4 (400 ml) cooled below 10°. The mixture was cooled and maintained at 0° while $NaNO_2$ (13.8 g, 0.2 mol) in water (200 ml) was added slowly with vigorous stirring. Thirty minutes after the addition was complete the mixture was filtered rapidly into an iced flask and the filtrate was added to a solution of KI (200 g) in water (250 ml). The resulting mixture was heated on a steam bath for 30 min, cooled in ice, and filtered. The residue was dissolved in $CHCl_3$ and the solution was washed successively with water, aqueous Na_2CO_3, aqueous $Na_2S_2O_3$, and water, and then dried ($MgSO_4$). Evaporation of the solvent left a solid residue which yielded 28.0 g (51.3%) of yellow needles after chromatography on alumina with C_6H_6 and recrystallization from EtOH. An analytical sample, recrystallized from C_6H_6–hexane as yellow flakes, had mp 111–112°; ir (Nujol) 1685 cm^{-1}; ^1H NMR (Me_2CO-d_6) δ 8.33 (dd, 1, J = 2.5, 9 Hz), 8.54 (dd, 1, J = 0.75, 9 Hz), 8.66 (dd, 1, J = 0.75, 2.5 Hz), 10.26 (s, 1). Anal. Calcd for $C_7H_4INO_3$: C, 30.35; H, 1.46; N, 5.05. Found: C, 30.11; H, 1.35; N, 5.07.

3,5-Dimethoxybenzylamine. To a stirred refluxing suspension of $LiAlH_4$ (3.5 g, 0.09 mol) in dry THF (75 ml) was added dropwise a solution of 3,5-dimethoxybenzonitrile (10.0 g, 0.06 mol) in THF (50 ml). One hour after addition was complete, the reaction mixture was cooled and a solution of water (5 ml) in THF (25 ml) was added slowly. The mixture was filtered and the residue was washed with Et_2O. The combined filtrate and wash were evaporated and the residual oil was dissolved in MeOH (50 ml) and treated with concentrated HCl (6 ml). Addition of Et_2O precipitated 10.5 g (84.3%) of the hydrochloride, mp 205–207°. (Although 3,5-dimethoxybenzylamine had been previously reported,[31] its hydrochloride salt had not been reported.)

Substituted 2-Iododibenzylamines. A representative procedure for each different method of synthesis is provided.

2-Iododibenzylamine (2). 2-Iodobenzyl bromide[32] (2.0 g, 6.7 mmol) in DME (25 ml) was added to a threefold quantity of benzylamine in DME (10 ml) and the resulting mixture was stirred for 2.5 hr at room temperature. Afterwards, the solvent was evaporated and the residue was washed with aqueous Na_2CO_3 and with water. The residual yellow oil was then dissolved in Et_2O and the hydrochloride generated with anhydrous HCl gas. Two recrystallizations from EtOH–Et_2O afforded 2.3 g (95%) of white microneedles, mp 153–155°. The free base vacuum distilled as a pale yellow oil: bp 154–156° (0.4 mm); ^1H NMR ($CDCl_3$) δ 1.48 (broad s, 1), 3.67 (s, 2), 3.70 (s, 2), 6.65–7.53 (m, 8), 7.70 (dd, 1, J = 7.0, 1.2 Hz). Anal. Calcd for $C_{14}H_{15}ClIN$: C, 46.73; H, 4.17; N, 3.89. Found: C; 47.04; H, 4.21; N, 4.04.

***N*-Methyl-2-iododibenzylamine (3).** The tertiary amine was prepared and isolated by the same method described for 2. Anal. Calcd for $C_{15}H_{17}ClIN$: C, 48.21; H, 4.59; N, 3.75. Found: C, 48.38; H, 4.66; N, 3.80.

2-Iodo-5-nitrodibenzylamine (4). A solution of 2-iodo-5-nitrobenzaldehyde (1.0 g, 3.6 mmol) and benzylamine (0.4 g, 3.7 mmol) in MeOH (75 ml) was stirred at room temperature for 4 hr. The solvent was then removed, the solid residue (1.31 g) was dissolved in warm MeOH (100 ml), and KBH_4 (500 mg) was added to the still warm solution (about 40°). The solution was allowed to cool to room temperature and, after 1 hr, additional KBH_4 (500 mg) was added. After stirring overnight, the solvent was removed in vacuo and the residue was treated with water (25 ml) and extracted with Et_2O. Addition of concentrated HCl to the Et_2O gave 935 mg (62.3%) of the amine hydrochloride as pale yellow flakes: mp 216–218° dec; ^1H NMR ($CDCl_3$, amine) δ 1.91 (s, 1), 3.90 (s, 2), and 3.91 (s, 2, overlapping), 7.40 (s, 5), 7.82 (dd, 1, J = 2.5, 8.2 Hz), 8.08 (d, 1, J = 8.2 Hz), 8.38 (d, 1, J = 2.5 Hz). Anal. Calcd for $C_{14}H_{14}ClIN_2O_2$: C, 41.55; H, 3.49; N, 6.92. Found: C, 41.22; H, 3.37; N, 6.88.

3′,5′-Dimethoxy-2-iodo-5-nitrodibenzylamine (5). The alcohol insoluble Schiff base derived from 2-iodo-5-nitrobenzaldehyde and 3,5-dimethoxybenzylamine was reduced in DME using $Zn(BH_4)_2$.[33] The product was isolated as the hydrochloride salt, mp 243–245° dec. Anal. Calcd for $C_{16}H_{18}ClIN_2O_4$: C, 41.35; H, 3.91; N, 6.03. Found: C, 41.11; H, 3.91; N, 6.04.

3',5'-Dimethoxy-2-iododibenzylamine (6). The synthesis and isolation of **6** was carried out by the same method described for **4**. The hydrochloride salt crystallized from MeOH–Et_2O, mp 176–178°. Anal. Calcd for $C_{16}H_{19}ClINO_2$: C, 45.79; H, 4.57; N, 3.34. Found: C, 46.02; H, 4.71; N, 3.47.

***N*-(2-Iodobenzyl)-β-phenethylamine (7).** A mixture of 2-iodobenzyl bromide[32] (5.0 g, 17 mmol) and β-phenethylamine (3.5 ml) in DME (30 ml) was stirred at room temperature for 45 min. The mixture was then poured into dilute Na_2CO_3 (250 ml) and the resulting suspension was extracted with several portions of Et_2O. The combined Et_2O extracts were washed with water, dried (Na_2SO_4), and evaporated. The residual oil was dissolved in ethanolic HCl and crystallized by addition of Et_2O and cooling. The hydrochloride was recrystallized from Me_2CO as white plates: 5.14 g (81.9%); mp 145°; ^1H NMR (CCl_4, amine) δ 1.90 (s, 1), 2.70 (s, 4), 3.73 (s, 2), 6.67–7.57 (m, 8), 7.72 (d, 1, J = 8.0 Hz). Anal. Calcd for $C_{15}H_{17}ClIN$: C, 48.21; H, 4.59; N, 3.75. Found: C, 48.44; H, 4.75; N, 3.77.

***N*-Methyl-*N*-(2-iodobenzyl)-β-phenethylamine (8).** The synthesis and isolation of **8** was analogous to that described for **7**. The hydrochloride salt was crystallized from Me_2CO, mp 168–170°. Anal. Calcd for $C_{16}H_{19}ClIN$: C, 49.56; H, 4.95; N, 3.61. Found: C, 49.85; H, 4.89; N, 3.74.

4'-Hydroxy-*N*-(2-bromopiperonyl)-β-phenethylamine (9). A mixture of 2-bromopiperonal[34] (2.29 g, 0.01 mol), tyramine hydrochloride (1.735 g, 0.01 mol), and anhydrous K_2CO_3 (4.14 g, 0.03 mol) in MeOH (450 ml) was refluxed for 2.5 hr and then cooled to 0°. In one batch KBH_4 (3.24 g, 0.06 mol) was added and the resulting mixture was stirred for 2.5 hr at room temperature. Solid CO_2 was then added in small portions until pH 8. The MeOH was removed, the residue was partitioned between H_2O (60 ml) and $CHCl_3$ (100 ml), and the aqueous phase was extracted with additional $CHCl_3$ (three times). After drying (Na_2SO_4), the combined $CHCl_3$ extracts were evaporated and the residual solid was dissolved in hot methanolic HCl. Concentration and cooling gave 2.99 g (77.3%) of the hydrochloride, mp 227–228.5° dec. An analytical sample recrystallized from MeOH gave plates, mp 226–228° dec (lit.[11] mp 234–236°). Anal. Calcd for $C_{16}H_{17}BrClNO_3$: C, 49.70; H, 4.43; N, 3.62. Found: C, 49.52; H, 4.44; N, 3.45.

The amine was regenerated with K_2CO_3 and crystallized as white needles, mp 139–141°, from C_6H_6–hexane. Anal. Calcd for $C_{16}H_{16}BrNO_3$: C, 54.87; H, 4.60; N, 4.00. Found: C, 54.63; H, 4.47; N, 4.02.

The *O,N*-diacetate of **9** was prepared by acetylation in C_5H_5N–Ac_2O (2:1). Recrystallization from C_6H_6–hexane afforded needles: mp 133–133.5°; ir ($CHCl_3$) 1754, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.04 and 2.08 (two s, 3 total, NAc), 2.27 (s, 3, OAc), 2.77–2.98 and 3.30–3.69 (m, 2 each, $ArCH_2CH_2N$), 4.38 and 4.73 (two s, 2 total, $ArCH_2N$), 5.97 (s, 2), 6.63–7.33 (m, 6). Anal. Calcd for $C_{20}H_{20}BrNO_5$: C, 55.31; H, 4.64; N, 3.33. Found: C, 55.26, H, 4.43; N, 3.11.

Photolysis Apparatus. The apparatus used in the photolysis experiments contained an outer glass vessel in which the solution to be irradiated was placed. Fitting inside this vessel was a water-cooled quartz well containing a type L 450-W medium-pressure mercury vapor lamp manufactured by Englehard Hanovia, Inc. When in use the Pyrex or Corex filter sleeve was inserted around the lamp within the quartz well. Inlet and outlet ports on the outer vessel provided a means of purging the solution continuously with nitrogen.

GC analysis of the photolysis reactions was done using a glass column (8 ft × 0.1 in. i.d.) packed with 4% SE-30 on Aeropak 30. TLC analyses were carried out on microscope slides coated with a 4:1 mixture of silica gel H and silica gel HF_{254} (Brinkmann).

Photochemical Synthesis of 6,7-Dihydro-5*H*-dibenz[*c,e*]azepines. A. Irradiation of 2. Using the standard conditions discussed in the text, a solution of **2** (1.24 g, 3.8 mmol) in 2% HCl (425 ml) was irradiated for 196 hr. The yellow solution was washed with Et_2O (2 × 75 ml), made basic with aqueous Na_2CO_3, and reextracted with Et_2O (3 × 100 ml). Evaporation of the second Et_2O extract gave a yellow oil. When a solution of the oil in fresh Et_2O was treated with anhydrous HCl gas, an off-white solid precipitated. Two recrystallizations from EtOH–Et_2O gave 108 mg of white needles identified as 6,7-dihydro-5*H*-dibenz[*c,e*]azepine (**1a**) hydrochloride by ir comparison with an authentic sample.[14] The mother liquors were combined, basified, and extracted with Et_2O. The residual oil from evaporation of the Et_2O was subsequently chromatographed on alumina. Elution with C_6H_6 yielded 165 mg (13%) of slightly impure **2** while further elution with C_6H_6–$CHCl_3$ (3:1) and $CHCl_3$ gave 177 and 159 mg, respectively, of **1a**. The total yield of the product, as the amine, was thus 428 mg (57%). The amine formed white needles from C_6H_6–hexane: mp 50°; ir (film) 749 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.08 (s, 1), 3.53 (s, 4), 7.08–7.50 (m, 8). The hydrochloride formed white needles from EtOH–Et_2O: mp 292° dec (lit.[3a] mp 288° dec); uv (95% EtOH) 247 nm (log ε 4.18). Anal. Calcd for $C_{14}H_{14}NCl$: C, 72.55; H, 6.10; N, 6.05. Found: C, 72.73; H, 6.18; N, 6.21.

B. Irradiation of 3. The irradiation of **3** (1.01 g, 3.0 mmol) was carried out by the same procedure described for **2**. On alumina chromatography, elution with C_6H_6 removed all of the product mixture components except the major one. The yields of the minor components reported in the text were estimated from the GC and column chromatography data. Further elution of the column with a C_6H_6–$CHCl_3$ gradient yielded 276 mg (44%) of **10** as a yellow oil: ^1H NMR (CCl_4) δ 2.42 (s, 3), 3.32 (s, 4, bridge methylene), 7.17–7.50 (m, 8); mass spectrum *m/e* (rel intensity) 209 (M^+, 65.6), 208 (M − 1, 100). The hydrobromide salt formed nodules from EtOH–Et_2O, mp 225–227° (lit.[3a] mp 223–225°). The hydroperchlorate salt precipitated from an aqueous solution of the hydrobromide on addition of 35% $HClO_4$, and gave white prisms, mp 193–195°, from EtOH–Et_2O. Anal. Calcd for $C_{15}H_{16}ClNO_4$: C, 58.16; H, 5.22; N, 4.52. Found: C, 57.91; H, 5.35; N, 4.53.

Methylation of compound **1a** using modified Clarke–Eschweiler conditions[35] afforded a product whose spectral and chromatographic properties were identical with those of the sample obtained from the photolysis reaction.

C. Irradiation of 4. The hydrochloride salt (1.21 g, 3.0 mmol) of **4** was irradiated in water (435 ml) and the resulting cyclic product **11** was purified as the hydrochloride salt: mp 320–321° dec; uv (95% EtOH) 300 nm (log ε 4.13); ir (Nujol) 1335 cm^{-1}; ^1H NMR (CCl_4, amine) δ 2.13 (s, 1), 3.60 (s, 2), and 3.66 (s, 2, overlapping, bridge methylene), 7.33–7.83 (m, 5), 8.17–8.33 (overlapping s, 2); mass spectrum *m/e* (rel intensity) 240 (M^+, 89.5), 239 (M − 1, 100), 193 (47.5), 165 (73.5). Anal. Calcd for $C_{14}H_{13}ClN_2O_2$: C, 60.76; H, 4.74; N, 10.12. Found: C, 60.96; H, 4.79; N, 9.89.

D. Irradiation of 5. The experiment was carried out in the same manner described above for **4** using the hydrochloride salt (1.39 g, 3.0 mmol) of **5**. The oily product, **12**, was converted to the hydrochloride, mp 281–282° dec, after recrystallization from EtOH as yellow needles: uv (95% EtOH) 348 nm (log ε 4.00), 236 (4.08); ^1H NMR (CCl_4, amine) δ 2.08 (s, 1), 3.00–3.80 (m, 4, bridge methylene), 3.80 (s, 3), 3.83 (s, 3), 6.48 (overlapping d, 2), 7.67 (d, 1, J = 9 Hz), 8.03–8.23 (overlapping d, 2); mass spectrum *m/e* (rel intensity) 300 (M^+, 100), 299 (M − 1, 53.2), 271 (73.5), 269 (78.2). Anal. Calcd for $C_{16}H_{17}ClN_2O_4$: C, 57.05; H, 5.10; N, 8.32. Found: C, 56.95; H, 5.09; N, 8.10.

E. Irradiation of 6. An aqueous solution of the hydrochloride salt (900 mg, 2.1 mmol) of **6** was irradiated under the usual conditions for 192 hr. Following an acid–base extraction, the major product was shown by GC to be in the nonbasic fraction. Subsequent chromatography of this fraction on alumina gave 130 mg (22.4%) of diol **14** as a brown oil which was shown to be essentially pure by GC and ^1H NMR. A portion of the oil was sublimed at 150° (0.2 mm) to get a waxy solid which recrystallized as white prisms, mp 72.5–74.5°, from C_6H_6–hexane: uv (95% EtOH) 282 nm (log ε 3.52); ir (Nujol) 3500–3100 cm^{-1} (hydrogen-bonded hydroxyl); ^1H NMR (CCl_4) δ 3.51 (s, 3), 3.67 (s, 3), 3.90–4.20 (m, 6, methylene and hydroxyl), 6.33 (d, 1, J = 2 Hz), 6.55 (d, 1, J = 2 Hz), 6.70–7.40 (m, 4); mass spectrum *m/e* (rel intensity) 274 (M^+, 92.5), 256 (M − 18, 100), 44 (62.9). Anal. Calcd for $C_{16}H_{18}O_4$: 274.1205. Found: 274.1208.

A small amount of a second component was noted by GC in the mother liquors from the crystallization of **14**. This component, dibenzoxepine **15**, was isolated from a separate reaction in low yield (<5%) as a solid which recrystallized as white prisms from C_6H_6–hexane: mp 137–138.5°; uv (95% EtOH) 261 nm (log ε 4.14), 287 (3.95), 293 (3.92); ^1H NMR (CCl_4) δ 4.80 (s, 3), 4.83 (s, 3), 4.00–4.40 (m, 4, bridge methylene), 6.54 (s, 2), 7.20–7.70 (m, 4); mass spectrum *m/e* (rel intensity) 256 (M^+, 100). Anal. Calcd for $C_{16}H_{16}O_3$: 256.1099. Found: 256.1124.

A solution of the diol **14** (39.4 mg) in C_6H_6 (10 ml) containing a catalytic amount of *p*-toluenesulfonic acid was refluxed overnight in an apparatus fitted with a Dean-Stark trap. Preparative chromatography of the resulting residue on a silica gel plate afforded a white solid (17.2 mg), mp 137–138°, which proved identical in its chromatographic and spectral properties with compound **15** obtained from the photolysis experiment.

5,6,7,8-Tetrahydrodibenz[*c,e*]azocine (1b). A. From Irradia-

tion of 7. A solution of **7** (3.37 g, 10 mmol) in 2% HCl (435 ml) was irradiated for 222 hr. Afterwards, the reaction mixture was subjected to an acid–base extraction and the basic fraction was passed through a short alumina clean-up column to get 2.14 g of a mixture of bases (cf. Scheme II). The components of the mixture were identified by comparison of the GC retention times with those of authentic samples prepared by unambiguous methods (vide infra). In addition, small samples of **17a** and **18a** were isolated by preparative GC and were found to have spectral properties identical with those of the reference compounds.

The basic mixture obtained from a 113-hr photolysis of **7** was chromatographed on alumina to get **19a** (10%), a mixture of the other as then unidentified bases, and **1b** (25%).[1a] The cyclic product was purified as the hydrochloride salt, which crystallized from EtOH as needles: mp 321–323° dec; uv (95% EtOH) 231 nm (log ϵ 4.15), 276 (2.89). The free base was regenerated with aqueous Na_2CO_3 and crystallized from hexane as prisms: mp 119–120°; ^1H NMR (CCl_4) δ 2.10–3.20 (m, 5, $ArCH_2CH_2NH$), 3.10 and 3.83 (d, 1 each, J = 15.0 Hz, $ArCH_2N$), 6.95–7.38 (m, 8). Anal. Calcd for $C_{15}H_{15}N$: C, 86.07; H, 7.24; N, 6.69. Found: C, 85.77; H, 7.28; N, 6.64.

B. From Dibromide 20.[21] Overnight treatment of a C_6H_6 solution of **20** with excess benzylamine at 50° afforded, in low yield, 6-benzyl-5,6,7,8-tetrahydrodibenz[c,e]azocine: ^1H NMR (CCl_4) δ 2.55 (s, 2), 2.30–4.00 (m, 6, bridge methylene), 6.90–7.50 (m, 13). The product was isolated by acid–base extraction and preparative chromatography on a silica gel plate. The hydroperchlorate salt crystallized from EtOH–Et_2O as white prisms, mp 227–229°. Anal. Calcd for $C_{22}H_{22}ClNO_4$: C, 66.07; H, 5.56; N, 3.50. Found: C, 65.83; H, 5.64; N, 3.40.

Catalytic debenzylation was effected over 10% Pd/C at atmospheric pressure and in the presence of a few drops of concentrated HCl. Hydrogen uptake was 98% complete after 45 min. The catalyst was removed by filtration and the solvent was evaporated to get a white, solid residue. Recrystallization from EtOH–Et_2O gave an 86% yield of amine hydrochloride that was identical with the photochemically produced material.

2-Benzylamino-1-phenylethanol (17a). α-Bromoacetophenone (500 mg, 2.7 mmol) and benzylamine (600 mg, 5.6 mmol) were condensed in DME to get ketone **21a** (R = H). A solution of the product in Et_2O was treated with HCl gas and the resulting amorphous solid, 130 mg, was dissolved in MeOH. The solution was cooled in ice and treated with KBH_4 (70 mg), added in small portions over 45 min. Following addition, the mixture was kept cold for 90 min and then allowed to stand overnight at room temperature. Water was added and the mixture was extracted with Et_2O. Evaporation of the Et_2O gave **17a** as a pale yellow oil which solidified on standing. The product sublimed readily over a steam bath at 2 mm to yield white crystals: mp 100–102°; ir (Nujol) 3250 cm^{-1}; ^1H NMR (CCl_4, amine) δ 2.50–3.00 (m, 4), 3.71 (s, 2), 4.60 (broad s, 1), 7.20 (broad s, 10); mass spectrum m/e (rel intensity) 227 (M^+, 8), 120 (100), 91 (84.5). Anal. Calcd for $C_{15}H_{17}NO$: C, 79.25; H, 7.55; N, 6.16. Found: C, 79.40; H, 7.42; N, 6.09.

***N*-(2-Chlorobenzyl)-β-phenethylamine (18a).** The amine was produced in 88.9% yield by the in situ $NaBH_4$ reduction of the Schiff base formed from β-phenethylamine (1.0 g) and excess 2-chlorobenzaldehyde in EtOH. The hydroperchlorate salt formed white needles, mp 198–200°, from EtOH. Anal. Calcd for $C_{15}H_{17}Cl_2NO_4$: C, 52.03; H, 4.96; N, 4.05. Found: C, 52.33; H, 4.94; N, 4.12.

6-Methyl-5,6,7,8-tetrahydrodibenz[c,e]azocine (16). A. From Irradiation of 8. The photolysis experiment was carried out in the same manner as described for the irradiation of **7**. The requisite reference compounds were prepared using the methods described for the corresponding secondary amines. Following the GC analysis, the basic mixture was chromatographed on alumina to get, in pure form, **17b** (12%) and **16** (33%): ^1H NMR (CCl_4) δ 2.00–2.90 (m, 4, $ArCH_2CH_2N$), 2.33 (s, 3, NMe), 3.14 and 3.49 (d, 1 each, J = 13.5 Hz, $ArCH_2N$), 7.00–7.30 (m, 8); mass spectrum m/e (rel intensity) 223 (M^+, 93), 222 (M − 1, 52), 208 (54), 180 (66), 179 (100), 178 (68), 155 (64). The hydroperchlorate salt crystallized from EtOH as white rods, mp 185–186°. Anal. Calcd for $C_{16}H_{18}ClNO_4$: C, 59.35; H, 5.61; N, 4.32. Found: C, 59.34; H, 5.62; N, 4.33.

B. From Dibenzazocine 1b. Treatment of **1b** with MeI in Et_2O gave a crystalline precipitate which was dissolved in dilute Na_2CO_3 and extracted with Et_2O. The Et_2O extract was dried ($MgSO_4$) and evaporated. The residual oil was treated with ethanolic HCl and some unreacted **1b** was recovered by crystallization of the hydrochloride salt. The mother liquor residue was then dissolved in dilute hydrochloric acid and treated with 35% $HClO_4$ to get the hydroperchlorate salt of **16** that was identical with the above photochemically produced material.

6,11-Diacetoxy-2,3-methylenedioxy-5,6,7,8-tetrahydrodibenz[c,e]azocine (23). The hydrochloride salt (400 mg, 1.034 mmol) of **9** was dissolved in water (700 ml) and the solution was divided into two batches. Each was irradiated for 2 hr under the usual conditions except that the Corex filter was used. Afterwards, the mixtures were adjusted to pH 2 with 6 *N* HCl and extracted once with Et_2O (175 ml). The Et_2O extracts were discarded. The mixtures were then adjusted to pH 7–8 with 10% NaOH and extracted with $CHCl_3$ (2 × 200 ml). The combined $CHCl_3$ extracts were dried (Na_2SO_4) and evaporated to get 182.0 mg of basic residue. Acetylation of this residue in C_5H_5N–Ac_2O (2:1 by volume) overnight afforded 243.0 mg of an *O,N*-diacetate mixture.

Preparative chromatography of the mixture on a silica gel plate gave 68.7 mg (15%) of the starting material *O,N*-diacetate and 75.7 mg (21%) of **23** as a white foam. Bulb-to-bulb distillation of the foam gave a clear, pale yellow glass: bp 140° (0.003 mm); uv (MeOH) 222 nm (log ϵ 4.28), 259 (3.84), 290 (3.67); ir ($CHCl_3$) 1755, 1628, 1499 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.13 (s, 3, NAc), 2.30 (s, 3, OAc), 2.34–5.00 (m, 4, $ArCH_2CH_2N$), 3.02 and 5.22 (d, 1 each, J = 14.0 Hz, $ArCH_2N$), 5.95 (two narrow d, 2, J = 1.2 Hz, OCH_2O), 6.73 and 7.37 (s, 1 each), 6.99–7.33 (m, 3); mass spectrum m/e (rel intensity) 353 (M^+, 100). Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.94; H, 5.17; N, 3.76.

6-Acetyl-11-methoxy-2,3-methylenedioxy-5,6,7,8-tetrahydrodibenz[c,e]azocine (24). Compound **23** (27.3 mg, 0.077 mmol) and K_2CO_3 (10.7 mg, 0.077 mmol) were stirred at room temperature in MeOH for 25 min. The reaction was quenched by addition of small pieces of Dry Ice (to pH 7–8). Preparative chromatography then gave 18.1 mg (75%) of the intermediate phenol as a white solid. Recrystallization from MeOH yielded needles: mp 275–277°; ir (KBr) 1608, 1500 cm^{-1}. Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.25; H, 5.19; N, 4.40.

A solution of the phenol (28.6 mg, 0.092 mmol) in refluxing 95% EtOH (4 ml) was treated, under nitrogen, with 10% NaOH and Me_2SO_4, both added dropwise, after the procedure of Uyas and Shah.[36] When the reaction was complete by TLC, the mixture was cooled, adjusted to pH 7, diluted with water, and extracted with $CHCl_3$ (three times). Evaporation of the dried (Na_2SO_4) extracts gave 32.4 mg (108%) of **24** as a solid. Recrystallization from C_6H_6 afforded a solid: mp 187.5–188.5°; ir ($CHCl_3$) 1625, 1604, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.12 (s, 3, NAc), 2.30–4.43 (m, 4, $ArCH_2CH_2N$), 3.82 (s, 3, OMe), 3.07 and 5.25 (d, 1 each, J = 14.0 Hz, $ArCH_2N$), 5.98 (two narrow d, 2, J = 1.2 Hz, OCH_2O), 6.76 and 7.43 (s, 1 each, 1-H and 4-H), 6.80 (d, 1, J = 2.7 Hz, 12-H), 6.90 (dd, 1, J = 2.7, 8.0 Hz, 10-H), 7.11 (d, 1, J = 8.0 Hz, 9-H); mass spectrum m/e (rel intensity) 325 (M^+, 100). Anal. Calcd for $C_{19}H_{19}NO_4$: 325.1314. Found: 325.1313.

2,2′-Dicarbomethoxy-4,5-methylenedioxy-5′-methoxybiphenyl (25). A. From the Degradation of 24. A mixture of **24** (53 mg, 0.163 mmol), KOH (4.4 g), and $K_3Fe(CN)_6$ (25 g) in water (100 ml) was heated on a steam bath with occasional swirling for 71 hr. Additional KOH (4.4 g) and $K_3Fe(CN)_6$ (25 g) were added every 24 hr. Afterwards, the mixture was cooled and filtered, and the separated yellow solid was washed with cold water. The combined filtrate and washings were acidified with 50% H_2SO_4 and reheated on a steam bath for 24 hr. Upon cooling a very dark blue solid precipitated. Both the solid and the dark blue aqueous phase were continuously extracted with $CHCl_3$ for 38 hr. The combined $CHCl_3$ extracts were dried (Na_2SO_4) and evaporated to get 370.4 mg of yellow oil.

A solution of the oil and CH_2N_2 in CH_2Cl_2 was stored in a freezer for 18 hr. Afterwards, the solvent and excess CH_2N_2 were evaporated and the resulting residue was subjected to three preparative chromatographs to get 6.2 mg (11%) of **25** as a solid. Although the material still contained some traces of impurity by TLC and GC, the R_f, retention time, and spectral properties were identical with those of the unambiguously prepared sample. Anal. Calcd for $C_{18}H_{16}O_7$: 344.0896. Found: 344.0900.

B. From the Ullmann Synthesis. A mixture of methyl 2-bromopiperonylate[37] (375 mg, 1.45 mmol), methyl 2-bromo-4-methoxybenzoate[38] (375 mg, 1.53 mmol), and copper powder (200 mg, 3.15 mmol) was heated under nitrogen in a Woods metal bath at 225° for 4 hr. After cooling the mixture was dissolved in $CHCl_3$, filtered, and twice subjected to preparative chromatography to get 313.8

mg of yellow oil. GC analysis showed this to be a mixture of three components. Subsequent purification by preparative GC using a 10 ft × 0.25 in. 20% SE-30 column at 250–260° then gave 29.3 mg (6%) of **25** as a yellow-white solid. Sublimation at 125° (0.9 mm) yielded an analytically pure white solid: ir ($CHCl_3$) 1718 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.59 (s, 3), 3.65 (s, 3), 3.84 (s, 3), 6.08 (s, 2), 6.67 and 7.54 (s, 1 each), 6.70 (d, 1, J = 2–3 Hz), 6.94 (dd, 1, J = 2–3, 9.0 Hz), 8.05 (d, 1, J = 9.0 Hz). Anal. Calcd for $C_{18}H_{16}O_7$: C, 62.79; H, 4.68. Found: C, 62.77; H, 4.75.

Irradiation of *N*-Acetyl-4′-hydroxy-*N*-(2-bromopiperonyl)-β-phenethylamine in Alkaline Solution. A solution of the *N*-acetyl derivative of **9** (200 mg, 0.509 mmol) and NaOH (200 mg) in deionized H_2O–EtOH (3:2, 425 ml) was irradiated for 5 hr under standard conditions. Afterwards the reaction mixture was concentrated by in vacuo removal of the EtOH, and the aqueous phase was treated with an excess of solid NH_4Cl and extracted with $CHCl_3$ (twice). Evaporation of the dried (Na_2SO_4) $CHCl_3$ extracts yielded 149.8 mg of brown residue. Purification by preparative TLC (5% Me_2CO in $CHCl_3$, three developments) afforded eight components. Comparative TLC on the major component, weighing 74.5 mg, established that it was unreacted starting material (37.2% recovery).

Examination of the remaining components by ir revealed one, weighing 15.3 mg, which had the dienone bands expected for **22**. Further purification via preparative TLC (20% Me_2CO in $CHCl_3$) yielded 5.8 mg of **22** as a white residue. This material appeared pure by TLC but was impure by high-pressure liquid chromatography. Final purification of **22** was accomplished on two 2 ft × 0.125 in. stainless steel alumina (40 μm) columns with a $CHCl_3$–hexane (1:1) solvent system to give 2.2 mg of **22** as a white residue: uv (MeOH) 216 nm (log ε 4.28), 227.5 (4.20), 285 (3.51), 320 (313); ir ($CHCl_3$) 1663 (CO), 1635 (amide), 1627 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) 2.06 δ (s, 3, NAc), 4.51 (s, 2, $ArCH_2N$), 5.89 (s, 2, OCH_2O), 6.22 (d, 2, J = 10.0 Hz, αα′), 6.51 and 6.58 (s, 1 each, Ar), 6.68 (d, 2, J = 10.0 Hz, ββ′). Anal. Calcd for $C_{18}H_{17}NO_4$: 311.1158. Found: 311.1151.

Registry No.—**1a,** 6672-69-1; **1a** HCl, 32372-86-4; **1b,** 6196-54-9; **1b** HCl, 6196-36-7; **2,** 56008-40-3; **2** HCl, 56008-41-4; **3** HCl, 56087-02-6; **4** HCl, 56008-42-5; **5** HCl, 56008-43-6; **6** HCl, 56008-44-7; **7** HCl, 56008-45-8; **8** HCl, 56008-46-9; **9,** 34315-37-2; **9** HCl, 38715-00-3; **9** *N*-acetate, 56008-47-0; **9** diacetate, 56008-48-1; **10,** 35232-96-3; **10** $HClO_4$, 56008-49-3; **11** HCl, 56008-50-5; **12** HCl, 56008-51-6; **14,** 56008-52-7; **15,** 56008-53-8; **16,** 6188-86-9; **16** $HClO_4$, 56008-54-9; **17a,** 27159-30-4; **18a** $HClO_4$, 56008-55-0; **20,** 21851-83-2; **21a,** 50606-93-4; **22,** 56008-56-1; **23,** 56008-57-2; **24,** 56008-58-3; **25,** 56008-59-4; 2-iodo-5-nitrobenzaldehyde, 56008-60-7; 2-amino-5-nitrobenzaldehyde, 56008-61-8; 3,5-dimethoxybenzylamine, 56008-62-9; 3,5-dimethoxybenzonitrile, 19179-31-8; 2-iodobenzyl bromide, 40400-13-3; benzylamine, 100-46-9; β-phenethylamine, 64-04-0; 2-bromopiperonal, 56008-63-0; tyramine hydrochloride, 60-19-5; 6-benzyl-5,6,7,8-tetrahydrodibenz[*c,e*]azocine, 6188-49-4; 6-benzyl-5,6,7,8-tetrahydrodibenz[*c,e*]azocinehydroperchlorate, 56008-64-1; 2-chlorobenzaldehyde, 89-98-5; 6-acetyl-11-hydroxy-2:3-methylenedioxy-5,6,7,8-tetrahydrodibenz-[*c,e*]azocine, 56008-65-2; 2-bromopiperonylate, 56008-66-3; 2-bromo-4-methoxybenzoate, 17100-65-1.

References and Notes

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(12) Presumably, the dibenzylamine was formed by hydrogen atom abstraction from the solvent by the aryl radical produced by the homolysis of the carbon–iodine bond.[8]

(13) In their preliminary communication Kupchan and Kanojia[10a] also reported that amines were best irradiated as the hydrochlorides in water rather than as the free bases.

(14) We are indebted to Dr. W. E. Scott, Hoffmann-La Roche, Nutley, N.J., for providing an authentic sample of **1a** for comparison.

(15) Kupchan and Kanojia[10a] showed that secondary and tertiary amines could both be used in the synthesis of the aporphine system.

(16) The formation of this compound through halogen interchange with the solvent was suggested by a brief study of the effect of concentrated hydrochloric acid on the photolysis reaction. Thus, irradiation of 2-iododibenzylamine hydrochloride in water gave no halogen exchange. Repetition of the photolysis in 2% hydrochloric acid afforded a small amount of 2-chlorodibenzylamine (GC identification). However, when the solvent was concentrated hydrochloric acid, very little cyclization could be detected and the major products were 2-chlorodibenzylamine and dibenzylamine.

(17) Comparable effects on the benzylic methylene signals were observed in the ^1H NMR spectra of the benzazepines **1a, 10,** and **11.**

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