Photochemistry of Structurally-Modified Morphine Alkaloids

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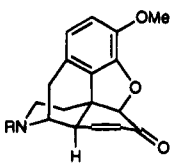
Abstract: *N*-Carbomethoxynorcodeinone (**1b**) was found to be unreactive to photolysis in benzene solution, but irradiation (366 nm) in the presence of methanol, water, ethanol, or *n*-propyl alcohol gave the rearranged and solvent-incorporated phenols **13a-d**. Under comparable photolysis conditions, *N*-carbomethoxynordihydrocodeinone (**33**) did not photorearrange at 366 or >300 nm. Spirocyclopropane **15b** is proposed to be an intermediate in this photorearrangement; addition of ROH to **15b** occurs by nucleophilic attack with inversion of configuration at the cyclopropane carbon atom most able to stabilize a positive charge. In the absence of a suitable nucleophile (benzene or *t*-BuOH solutions) **15b** reverts to **1b**. Irradiation of the C(5)-methyl-substituted codeinone derivative **17a** in methanol solution did not result in solvent incorporation, but rather gave the benzopyran **21a** in quantitative yield by way of the intermediate dienone **20a**. The carbamate **17b** gave separable mixtures of **20b** and **21b**; dienone **20b** was converted to benzopyran **21b** in quantitative yield by treatment with diethylamine in CH_2Cl_2. Additional examples of this tandem photorearrangement-hydrogen atom transfer-intramolecular conjugate addition are described; *e.g.*, **22** → **24** and **25** → **26**. Photolysis of **1b** in the presence of acetic acid gives a mixture of the solvent-incorporated phenol **27** and 8,9-dihydro-2-methoxy-7-carbomethoxydibenz[*d,f*]azonine-1,13-diol (**28**). The less nucleophilic oxalic acid provides a route to **28** free of solvent-incorporated products analogous to **27**. The facial specific photoadditions of THF to enones **13b** and **1b** to give **30** and **31** occur by hydrogen atom transfer from C(2) of THF to the photosubstrate followed by radical coupling at the β-position of the enone. The molecular structure and novel crystal packing arrangement of the monohydrate of **30** were determined by an X-ray diffraction study. Enones **1b** and **17b** also undergo SET-type photoreductions in the presence of triethylamine (TEA) to give α-thebainone derivatives **32a** and **32b**. A mechanism is proposed to account for photoproduct distributions when irradiations are carried out in the presence of varying amounts of both methanol and TEA. It was found that codeine is as effective as TEA in promoting the photoreduction of **1b** to the α-thebainone derivative **32a**. Opportunities for the utilization of the photochemistry of modified morphine alkaloids for approaches to opiate receptor photoaffinity labeling and the provision of new substrates for opiate receptor affinity studies are briefly discussed.

Prior to our decision to investigate the photoreactivity of codeinone (**1a**) and *N*-carbomethoxynorcodeinone (**1b**), very little was known about the behavior of the morphine alkaloids toward exposure to ultraviolet irradiation.[1,2] Indeed, it had been reported that codeinone (**1a**), dihydrocodeinone, and 14-hydroxycodeinone are all photostable.[1b]

We began this investigation because it appeared that the discovery of photoreactivity for the morphine alkaloids might offer a new approach to opiate receptor photoaffinity labeling.[3] While the development of photoaffinity reagents remains a long-term goal, it is clear that the complex photochemistry of **1b** and analogues is of mechanistic and synthetic value. We have reported some of the photochemistry of **1b** in two preliminary communications;[4] in this paper we describe in detail the photochemistry of **1b** and analogues under a wide range of reaction conditions.



1a, R = Me
b, R = CO_2Me

Background

A 2-carbonyl-substituted benzodihydrofuran ring is the key reaction unit in the photochemical studies to be described in this paper.[5] Several years ago we reported that the photorearrangement of 2-carbomethoxybenzodihydrofuran (**2**) to phenol **4** most likely involves the intermediacy of spiro[cyclopropane-2′,4′-cyclohexadien-1′-one] **3**.[6] Flash photolysis studies with **2** (and tetradeuterated **2**)[7] provided evidence for the 2,4-cyclohexadien-1-one chromophore in **3** as well as activation parameters and a deuterium isotope effect for the abnormal Claisen rearrangement **3** → **4**.[8] Irradiation of optically active **2** resulted in retention of enantiomeric purity in the photoproduct

⊗ Abstract published in *Advance ACS Abstracts*, October 15, 1994.

(1) For reports of photochemistry of 7,14-cyclodihydrocodeinone, 14-methyl-C-nordihydrocodeinone and related derivatives, see: (a) Bos, M.; Fleischhacker, W. *Liebigs Ann. Chem.* **1981**, 1994. (b) Bos, M.; Fleischhacker, W. *Liebigs Ann. Chem.* **1981**, 2002. (c) Bos, M.; Fleischhacker, W. *Liebigs Ann. Chem.* **1982**, 112.

(2) For photorearrangements of thebaine, see: Theuns, H. G.; La Vos, G. F.; ten Noever de Brauw, M. C.; Salemink, C. A. *Tetrahedron Lett.* **1984**, *25*, 4161.

(3) Simon, E. J.; Fan, L.-Q.; Hiller, J. M.; Seyed-Mozaffari, A.; Schultz, A. G.; Archer, S. *Life Sci.* **1993**, *53*, 1173.

(4) (a) Schultz, A. G.; Green, N. J.; Archer, S.; Tham, F. S. *J. Am. Chem. Soc.* **1991**, *113*, 6280. (b) Schultz, A. G.; Graves, D. M.; Jacobson, R. R.; Tham, F. S. *Tetrahedron Lett.* **1991**, *32*, 7499.

(5) For pioneering work on the photochemical and thermal rearrangements of benzodihydrofurans see: Schmid, E.; Frater, Gy.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1972**, *55*, 1625.

(6) Schultz, A. G.; Napier, J. J.; Lee, R. *J. Org. Chem.* **1979**, *44*, 663.

(7) Wisniewski, K. Ph.D. Thesis, Rensselaer Polytechnic Institute, 1985.

(8) (a) Marvell, E. N.; Anderson, D. R.; Ong, J. *J. Org. Chem.* **1962**, *27*, 1109. (b) Hansen, H.-J. In *Mechanisms of Molecular Migrations*; Thyagarajan, B. S., Ed.; Wiley: New York, 1971; Vol. 3, p 177.

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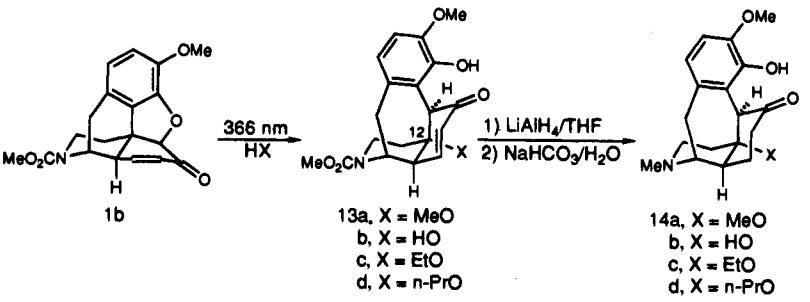
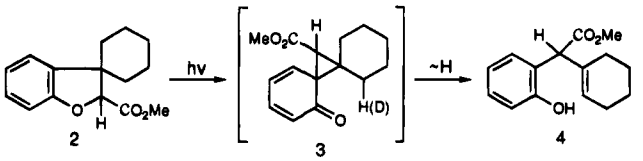
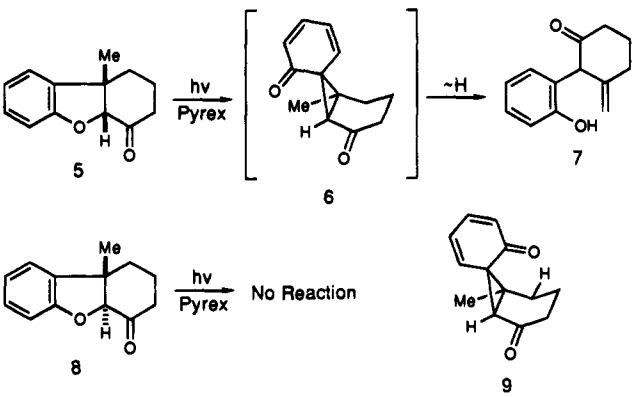
Scheme 1



4, suggesting that the intermediate spirocyclopropane **3** is formed by a concerted 1,3-rearrangement from **2** rather than by the intermediacy of a long-lived biradical. The stereoselectivity of the photorearrangements of 4′-methyl-substituted benzodihydrofuran 2-carboxylic esters also has been reported.[9a]



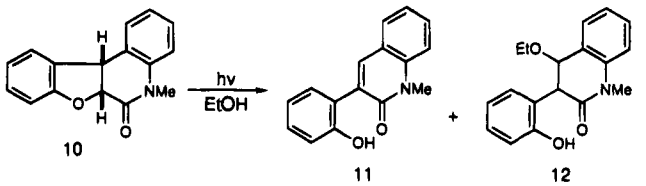
The photorearrangement of cis fused 2-ketobenzodihydrofuran **5** in benzene or methanol solution gives phenol **7** in ~85% isolated yield.[9b] Under the same photoreaction conditions, the considerably more strained trans fused epimer **8** remains unchanged.



It has been proposed that spiro[cyclopropane-2′,4′-cyclohexadien-1′-one] **6** is an intermediate in the rearrangement of **5** to **7**.[9b] Abnormal Claisen rearrangement of **6** involving intramolecular transfer of a γ-hydrogen atom from the methyl substituent to the cyclohexadienone carbonyl oxygen atom would give phenol **7**. The exclusive formation of **7** with no endocyclic olefin detected suggests high stereoselectivity for the benzodihydrofuran photorearrangement[9a] to give only **6** and not the stereoisomeric spiro[cyclopropane-2′,4′-cyclohexadien-1′-one] **9**, although it could be argued that formation of **9** is reversible (*vide infra*) and hydrogen transfer in **9** is slower than in **6**.

Flash photolysis studies with cis fused **5** provided evidence (λ_{max} ~ 320 nm; A_{10} = 0.060) for the intermediate 2,4-cyclohexadien-1-one **6**.[7] Similar photoexcitation of trans fused **8** did not produce an observable transient species. The failure of **8** to undergo photorearrangement may be a result of conformational requirements for the 1,3-rearrangement. The cyclohexanone ring in **8** is very rigid with the dihydrofuran oxygen atom constrained to occupy an equatorial conformation nearly coplanar with the ketone carbonyl group. The photoreactive cis fused isomer **5** is more flexible and can readily adopt a conformation in which the dihydrofuran oxygen atom is perpendicular to the plane of the carbonyl group. It also has been noted that 1,3-rearrangement in **8** with retention of configuration at the migrating carbon atom would produce a diastereomer of **6** with a strained *trans*-bicyclo[4.1.0]heptane ring system.[9b]

Kanaoka and San-nohe have reported the photochemistry of cis fused dihydrobenzofuroquinolone **10**.[10] It was found that photolysis of **10** in ethanol solution gave, among other products, the phenolic olefin **11** and the ethanol incorporated photorearrangement product **12**. A spirocyclopropane analogous to **6** was proposed to be an intermediate in the formation of both **11** and **12**; as with **8**, the corresponding trans fused isomer of **10** failed to undergo the photorearrangement. It is noteworthy that a methyl ether analogous to **12** was not obtained from photolysis of **5** in methanol solution.



Results and Discussion

N-Carbomethoxynorcodeinone (**1b**) was found to be stable to extended periods of irradiation in benzene solution. However, irradiation (366 nm) of **1b** in methanol (0.02 M, 20 h) gave the rearranged methyl ether **13a** in 90% isolated yield (Scheme 1). The structure of **13a** could not be determined with certainty from NMR spectra. Reduction of **13a** with $LiAlH_4$ in THF followed by hydrolysis with $NaHCO_3$ solution gave the crystalline saturated keto amine **14a** in 90% isolated yield. An X-ray diffraction study[4a] provided the structure shown as **14a**; thus, the photorearrangement of **1b** to **13a** involves cleavage of the dihydrofuran ring with overall 1,2-migration of the aryl nucleus and addition of methanol.[11]

Compound **14a** contains a phenolic hydroxyl group and a tertiary amine, structural units common to morphine and other opiate alkaloids. Preliminary opiate receptor affinity studies with **14a** encouraged us to attempt to prepare derivatives in which the substituent at C(12) was varied.[12] Irradiation of **1b** in THF–H_2O solution gave alcohol **13b** in 80% yield, while irradiations in the presence of ethanol and *n*-propyl alcohol gave

(9) (a) Schultz, A. G.; Napier, J. J.; Sundararaman, P. *J. Am. Chem. Soc.* **1984**, *106*, 3590. (b) Schultz, A. G.; Ranganathan, R.; Kulkarni, Y. S. *Tetrahedron Lett.* **1982**, *23*, 4527.

(10) Kanaoka, Y.; San-nohe, K. *Tetrahedron Lett.* **1980**, *21*, 3893.

(11) It has been reported that 7,14-cyclodihydrocodeinone undergoes solvolytic opening of the ether bridge without migration of the aryl nucleus to give a series of 5-alkoxy-4-hydroxy-3-methoxy-17-methyl-7,14-cyclomorphinan-6-ones; see ref 1a.

(12) Details of the opiate receptor binding studies will be reported elsewhere.

Table 1. Relative Rates of Addition of ROH to the Reactive Intermediate Generated from Photolysis of **1b**

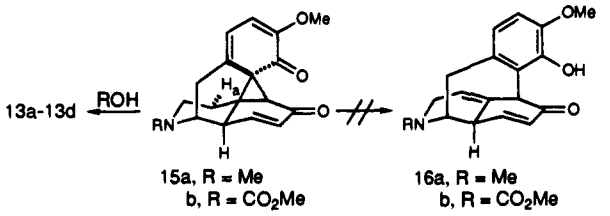
solvents (equimolar mixtures)	relative rates	solvents (equimolar mixtures)	relative rates
H_2O vs MeOH	1.0	H_2O vs EtOH	1.9
EtOH vs MeOH	0.34	*n*-PrOH vs EtOH	1.0
n-PrOH vs MeOH	0.74	H_2O vs *n*-PrOH	2.6
t-BuOH vs MeOH	0.00		

ethyl ether **13c** (98%) and *n*-propyl ether **13d** (95%). Photolysis of **1b** in *tert*-butyl alcohol or a 1:1 mixture of *tert*-butyl alcohol and hexane gave only recovered starting material. Reductions of **13b–d** provided the expected keto amines **14b–d**.

Relative reaction rates for the photoconversions of **1b** to **13a–d** were obtained by photolysis of **1b** in equimolar mixtures of ROH and R'OH (Table 1). These data reflect the relative reactivities of the intermediate generated by photorearrangement of **1b** toward these hydroxylic solvents. There is little difference in reactivity between water and the primary alcohols, but photolysis in a mixture of *t*-BuOH and MeOH resulted only in formation of the methyl ether **13a**.

As the reader will soon appreciate, it has been difficult to unify the diverse photochemical reactivities of **1b** and analogues by a single mechanistic hypothesis. We begin by utilization of what is almost certainly an overly simplistic mechanistic construct based on the known photochemistry of benzodihydrofurans. Subsequent studies provided refinements and an alternative mechanistic proposal is presented at the end of this paper.

The photoreactivity of **1b** in hydroxylic solvents is consistent with an initial photorearrangement to the spirocyclopropane **15b**; solvolysis of **15b** would give **13a–d**. Addition of ROH to **15b** appears to occur by nucleophilic attack with inversion of configuration at the cyclopropane carbon atom most able to stabilize a positive charge. This kind of regioselectivity was observed for the photoconversion of **11** to **12**, but the stereoselectivity for this process was not reported.[10] The absence of reactivity with the sterically demanding *t*-BuOH suggests that the photorearrangement of **1b** to **15b** is reversible and that there is a substantial component of S_N2 character to the conversion of **15b** to **13a–d**.



15a, R = Me
b, R = CO_2Me

16a, R = Me
b, R = CO_2Me

If **15b** is an intermediate in the photoconversion of **1b** to **13a–d**, then why are products analogous to **4** not formed when the photolysis of **1b** is carried out in benzene (or *t*-BuOH)? Abnormal Claisen rearrangement[8] of **15b** would give olefin **16b** by a transfer of H_a to the dienone carbonyl group. Molecular modeling of **15b** (MM2 via MacroModel, Version 3.0) provided a lowest energy conformation in which the pseudoequatorial H_a was found to be 2.42 Å from the dienone oxygen atom. For comparison, intermediate **3** was minimized to give a lowest energy chair conformation for the spirocyclohexyl ring in which the closest γ-hydrogen atom to the dienone carbonyl group is equatorial, 2.33 Å from the oxygen atom. This arrangement nicely approximates the planar C—C—C—C=O (with H somewhat elevated) transition state structure assumed to be optimal for the abnormal Claisen rearrangement.[13a] An even closer H—O disposition could be located (2.29 Å), but this structure suffered from a twist boat conformation for the cyclohexane ring, 4 kcal/mol higher energy than the chair.

Along with a somewhat less favorable proximity of H_a to the dienone carbonyl group in **15b**, it should also be noted that the product of hydrogen atom transfer **16b** would have substantial ring strain because of the bridgehead double bond. The strain energy in **16b** might result in a high activation energy for the abnormal Claisen rearrangement of **15b**; instead, **15b** reverts to **1b** or undergoes nucleophilic attack by water and small to moderately large alcohols to give the relatively strain-free series **13a–d**.

The reversion of **15b** to **1b** might occur by a photochemical pathway. During flash photolysis studies of **2**, it was discovered that dienone **3** photobleaches to a degree that is dependent on the intensity of the analyzing light beam. It was not possible to determine the products (**2** and/or **4**) of photobleaching of **3**; however, analogous photobleaching was found to occur with structurally modified benzodihydrofurans that are incapable of product formation.[7,9b]

Codeinone (**1a**) has been reported to be photostable,[13b] and we have found that **1a** does not rearrange on attempted photolysis (366 nm) in benzene or methanol solutions. It seemed possible that both **1a** and **1b** undergo reversible photorearrangement to spirocyclopropanes **15a** and **15b**, but **15a** might be unreactive toward hydroxylic solvents; as with **15b**, abnormal Claisen rearrangement of **15a** to **16a** should be disfavored.

To examine the effect on photoreactivity of the tertiary amine group in **1a**, the C(5)-methyl-substituted codeinone analogues **17a** and **17b** were prepared from thebaine via the procedure of Gates and co-workers.[14] Irradiation (366 nm) of **17a** in methanol solution gave benzopyran **21a** in 87% isolated yield (quantitative yield based on an inspection of the ^1H NMR spectrum of the crude photolysis mixture). Irradiations in benzene solution gave variable mixtures of dienone **20a** and pyran **21a**; chromatography of these mixtures resulted in conversion of **20a** to benzopyran **21a** (Scheme 2).

Irradiation of carbamate **17b** in benzene solution gave dienone **20b** as the exclusive reaction product. In methanol, **17b** gave a mixture of dienone **20b** and benzopyran **21b** which could be separated by flash chromatography on silica gel. Dienone **20b** was converted to benzopyran **21b** in quantitative yield by treatment with diethylamine in CH_2Cl_2.

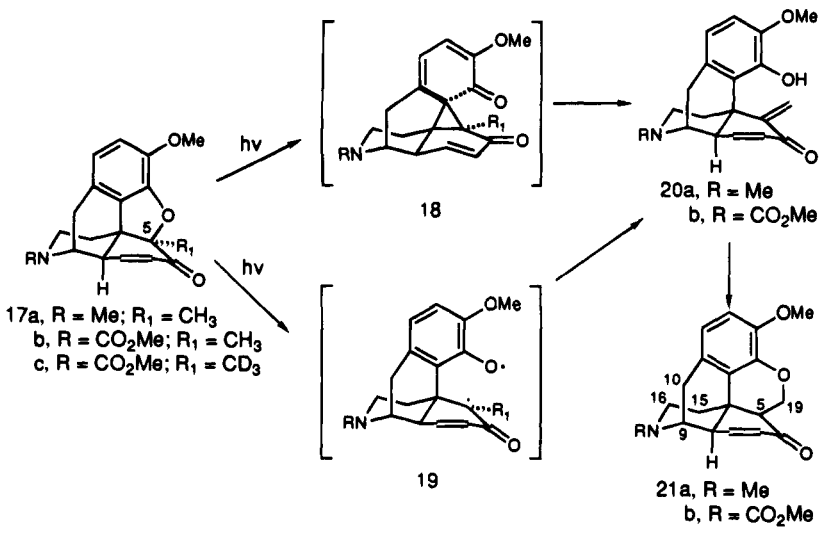
These data are consistent with mechanisms for photorearrangement of **17a** and **17b** that involve spirocyclopropane **18** and/or biradical **19**. Abnormal Claisen rearrangement of **18a** and **18b** would provide the phenolic dienones **20a** and **20b**; amine-catalyzed intramolecular conjugate addition would give benzopyrans **21a** and **21b**. Alternatively, biradicals **19a** and **19b** would be expected to provide **20a** and **20b** by hydrogen atom transfer.

It might be argued that the striking contrast in photoreactivities of codeinone (**1a**) and the C(5)-methyl-substituted analogue **17a** is a consequence of the stabilizing effect of the C(5) methyl group on the putative biradical **19a**. The absence of products of solvolytic rearrangement when **17b** is irradiated in methanol (cf., **1b** → **13a**) also might be viewed as an indication of a change in reaction mechanism with C(5) substitution. However, fast rates of hydrogen atom transfers

(13) (a) Houk, K. N.; Li, Y.; Evanseck, J. D. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 682. (b) Tschany, P. Diplomarbeit, Univ. Wien 1979.

(14) (a) Boden, R. M.; Gates, M.; Ho, S. P.; Sundararaman, P. *J. Org. Chem.* **1982**, *47*, 1347. (b) Gates, M.; Boden, R. M.; Sundararaman, P. *J. Org. Chem.* **1989**, *54*, 972.

Scheme 2[a]



[a] The numbering system for morphinan is shown.

in spirocyclopropanes **18a** and **18b** would be expected in light of (1) the proximity (2.38 Å) of a suitably oriented hydrogen atom on the C(5) methyl group to the dienone oxygen atom and (2) the absence of significant ring strain in the product of abnormal Claisen rearrangement. As a point of reference, it should be recalled that photolysis of benzodihydrofuran **5** in methanol gave only the phenolic olefin **7**. Thus, solvolytic rearrangement of **18b** would not be expected to be competitive with the abnormal Claisen rearrangement to **20b**.

An attempt has been made to distinguish between the spirocyclopropane and biradical pathways for rearrangement of **17b** to **20b**. Flash photolysis studies of **17b** and the C(5)-deuteriomethyl analogue **17c** have been carried out by Professor Matt Platz at the Ohio State University. Although the preliminary observations are complicated and do not allow conclusions to be made, they do show that the transient spectroscopy is very different from that of benzodihydrofuran **2**.

Benzodihydrofuran **2** gives an easily observed, long-lived transient ($t_{1/2}$ ~1 s at 21 °C) with λ_{max} at 320 nm that has been assigned to the intermediate spirocyclopropane **3**. A $\Delta S^{\ddagger}$ of -4 ± 4 eu is indicative of the need for little molecular reorganization to reach the transition state for the abnormal Claisen rearrangement. The thermal rearrangement of the transient has a substantial isotope effect, $k_H/k_D = 4.5$.[7]

Codeinone derivatives **17b** and **17c** give weak transients with λ_{max} at 400 nm in benzene solution.[15a] The transients do not react with oxygen, and there is a small but reproducible isotope effect of k_H/k_D of 1.08 on the lifetime (~8 μs) of the transient generated from **17b**.

The proximity of the C(5) methyl substituent in **17** to the enone carbonyl group was suggestive of yet another possible mechanism for formation of **20**. Givens and co-workers have shown that carvone undergoes a reversible β-hydrogen atom transfer from the C(2) methyl substituent to the enone oxygen atom.[15b] This process was discovered by irradiation of carvone in the presence of triethylamine and deuterated solvents such as CH_3OD, but not CD_3OH, suggesting that D^+/H^+ exchange occurs between solvent and the intermediate 1,3-biradical.

Reversible β-hydrogen atom transfer in **17** would generate a 1,3-biradical that might be expected to undergo C–O bond fragmentation to give a 1,6-biradical with an intervening *exo*-methylene group. Disproportionation of this 1,6-biradical would give **20**.

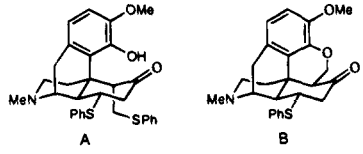
We have been unable to find evidence for the carvone-type mechanism operating in the photochemistry of **17a**. Irradiation of **17a** in CH_3OD taken to 36% conversion revealed no deuterium incorporation in the remaining **17a** (^1H and ^2H NMR spectroscopy; ~1% estimated minimum level of detection). The photoproduct **21a** had ~75% incorporation of deuterium at the C(5) methine, but no deuterium beyond natural abundance at the C(19) methylene group. These data are consistent with the proposed hydrogen transfer from the C(5) methyl substituent in **18a** or **19a** to give **20a**. Intramolecular conjugate addition of the phenol (presumably by amine-base catalysis) would be expected to result in substantial deuterium incorporation at C(5) in **21a**.

It was found that 5-methylmorphinone (**22**) cleanly photorearranges to benzodihydropyran **24** (Scheme 3). In analogy with the photoreactivity of **17a** it is assumed that dienone **23** is an intermediate in the conversion of **22** to **24**. Receptor binding studies with **22** revealed high affinity and selectivity for the μ receptor; consequently, preliminary photoaffinity labeling studies were carried out. It was thought that the intermediate dienone **23** might be capable of reacting with nucleophiles at the receptor (sulfhydryl groups for example),[16] but detectible levels of covalent binding to the receptor have not been observed.

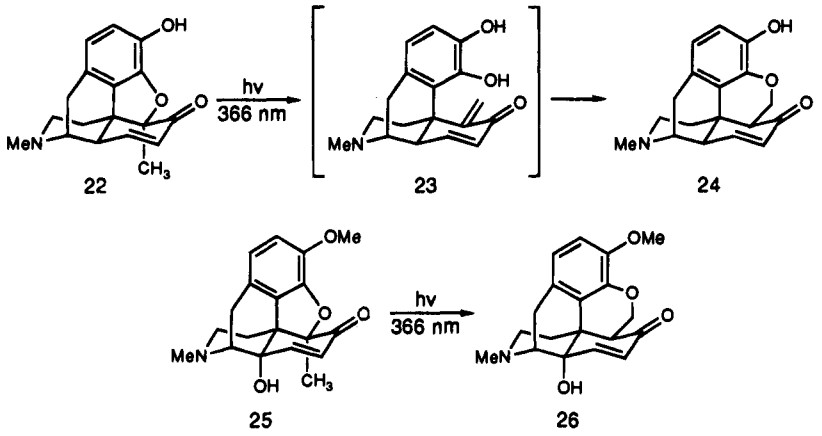
Photochemical studies also have been carried out with 14-hydroxy-5-methylcodeinone **25**. Irradiation of **25** in methanol solution gave the benzopyran **26** in 82% isolated yield. Although a more detailed study of substituent effects is

(15) (a) For a study of the flash photolysis of *N*-(chloroacetyl)tyramines, in which a strong band at 325 nm was assigned to an intermediate 2,4-cyclohexadienone and weak bands at 370–400 nm were assigned to a transient phenoxy radical, see: Iwakuma, T.; Hirao, K.-I.; Yonemitsu, O. *J. Am. Chem. Soc.* **1974**, *96*, 2570. (b) Givens, R. S.; Singh, R.; Xue, J.; Park, Y.-H. *Tetrahedron Lett.* **1990**, *31*, 6793.

(16) In preliminary studies of the chemical reactivity of **20a** it was found that approximately equivalent amounts of **A** and **B** were obtained from treatment of **20a** with excess PhSH in CH_2Cl_2. With regard to possible photoaffinity labeling studies, it is significant that **A** and **B** also were obtained from photolysis of **17a** in CH_2Cl_2–PhSH; the conjugate adduct of PhSH and **20a** is photostable under these conditions.

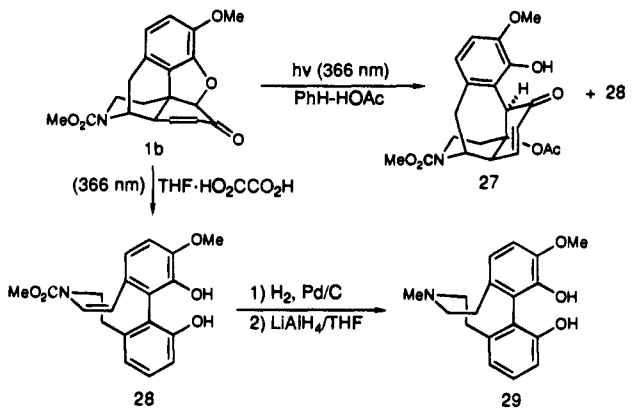


Scheme 3



necessary, it appears that this benzodihydrofuran to benzopyran photorearrangement will have substantial generality for the preparation of skeletally-modified morphine derivatives.[12]

Irradiation of **1b** in benzene–acetic acid (2:1) followed by chromatography of the photoreaction mixture on silica gel provided the acetic acid-incorporated phenol **27** (20%) and 8,9-dihydro-2-methoxy-7-carbomethoxydibenz[*d,f*]azonine-1,13-diol (**28**) isolated in 38% yield.[4b] Control experiments demonstrated that **27** does not convert to **28** in benzene–acetic acid solution either in the dark or when irradiated with light of ~366 nm. It was found that solvent-incorporated products were avoided and that **28** could be generated in high yield by photorearrangement of **1b** in THF in the presence of 5 equiv of anhydrous oxalic acid; **28** was converted to **29** as shown.

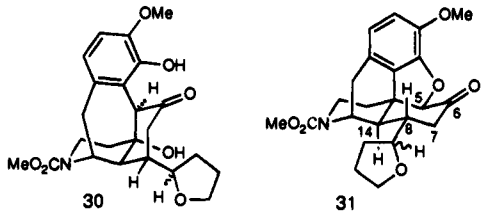


The structure of **27** was assigned on the basis of spectroscopic comparisons with the series **13a–d**, while the structure of **28** was determined by an X-ray diffraction study.[4b] In the solid-state, the twist angle defined by the biaryl residue in **28** is ~85° and the *N*-carbomethoxy group is nearly coplanar with and antiperiplanar to N(7)–C(6) of the enamine unit. Dihydroxydibenzazonine **28** exists as a 55:45 mixture of carbamate rotational isomers in $CDCl_3$ solution as determined by ^1H NMR spectroscopy at ambient temperature.

Chiral biaryl **28** is configurationally stable to heating to 200 °C for periods of at least 5–10 min; additional heating leads to destruction of **28**. A mechanistic hypothesis for the conversion of **1b** to **28** was presented in the preliminary communication.[4b]

Prolonged irradiation of **1b** in THF–H_2O solutions gave not only **13b** but also the THF-incorporated alcohol **30** as the major component of a 5:1 mixture of diastereoisomers. Control experiments demonstrated that **30** and its C(2′) diastereomer are formed by a secondary photoreaction (57% isolated yield) involving addition of THF to **13b**. The diastereomers were separated by column chromatography on silica gel, and crystals of **30** (monohydrate) suitable for X-ray characterization were obtained from ethyl acetate by the isothermal distillation technique with hexane. The photoaddition of THF to **13b** could also be induced by photolysis of **13b** in the presence of the triplet-state-sensitizer benzophenone.

The molecular structure of **30** is shown in Figure 1. The packing of molecules in the crystal is such that a molecule of water provides hydrogen bonding to the oxygen atoms of a THF residue and the carbamate carbonyl group of a molecule of **30**. The C(12) hydroxyl group of a second molecule of **30** is hydrogen bonded to this water molecule and the C(4) phenolic hydroxyl group of a third molecule of **30** also is hydrogen bonded to this same water molecule.



The photoaddition of THF to enone **1b** to give **31** was observed in certain photoreaction mixtures obtained from photolysis of **1b** in THF or THF with oxalic acid. NMR studies (see Experimental Section) indicated that the photoproduct was stereoisomerically pure at C(8) but a 1:1 mixture of diastereomers at the THF residue.

Photoadditions of THF to an olefinic bond, although not previously reported for enones,[17a] have been observed for an α-(acylamino)-α,β-unsaturated ester[17b] and a 1-alkyl-4,6-diarylpyrimidin-2(1*H*)-one.[17c] The photoaddition of THF to enones **1b** and **13b** may be related to the photoreduction of enones, which, depending on the substrate and hydrogen transfer agent, are initiated by a hydrogen atom transfer to the carbonyl oxygen, the α-carbon, or the β-carbon atom of the photoexcited enone.

Irradiation of testosterone acetate in ether gives a pinacol and a mixture of diastereomeric carbonyl addition products that are produced by initial hydrogen abstraction from the α-methylene position of ether by the triplet n → π* state of the enone.[18] By contrast, photolysis of steroidal enones and related octalones

(17) (a) For an excellent review of the photochemistry of enones, see: Schuster, D. I. In *The Chemistry of Enones*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1989; Part 2, pp 623–756. (b) Naito, T.; Ninomiya, I. *Heterocycles* **1988**, *27*, 1325. (c) Nishio, T.; Omote, Y. *J. Chem. Soc. Perkin Trans. 1* **1988**, 957.

(18) Nann, B.; Gravel, D.; Schorta, R.; Wehrli, H.; Schaffner, K.; Jeger, O. *Helv. Chim. Acta* **1963**, *46*, 2473.

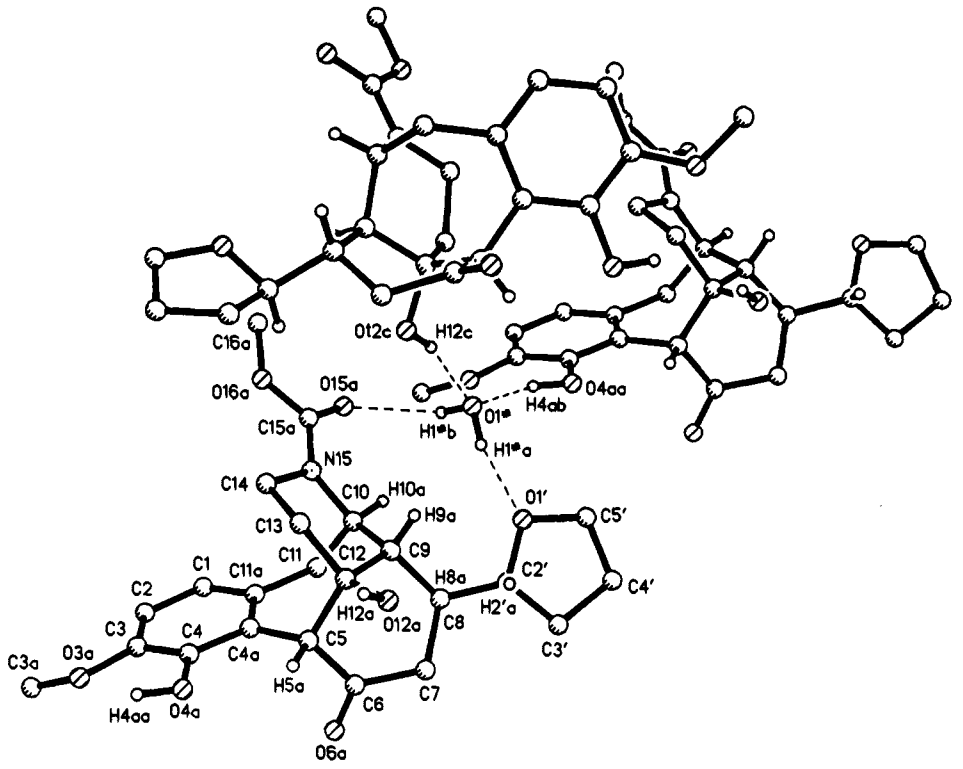


Figure 1. Molecular structure of **30** (monohydrate) showing how three molecules of **30** interact with one water molecule.

in toluene solution give saturated ketones and toluene adducts with an α-benzyl group.[19] These photoreactions are best explained by initial hydrogen atom transfer from toluene to the β-carbon atom of the triplet $\pi \rightarrow \pi^*$ state of the enone.

It has been reported that taxinines which contain an α,β-unsaturated chromophore and certain α,β-unsaturated γ-(dimethoxymethyl) cyclohexenones undergo a photocyclization involving the intramolecular transfer of a hydrogen atom to the α-carbon and ring closure at the β-position.[20] Photolysis of an α,β-unsaturated ketone with a tertiary hydrogen atom on a side-chain equidistant from the α- and β-carbon atoms of the enone resulted in intramolecular hydrogen transfer only to the β position.[21]

The photoaddition of THF to **1b** and **13b** also is related to the well-studied photosensitized addition of secondary alcohols,[22] methanol, carboxaldehydes, and acetals[23] to enones. Evidence has been presented in the case of methanol addition to show that the important photochemical event is hydrogen abstraction by the photoexcited sensitizer to give $\dot{C}H_2OH$ and that energy transfer to the enone is not a factor.[23b]

The possibility that the photoaddition of THF occurs by single electron transfer (SET), a process analogous to the photoaddition of tertiary amines to enones,[24] also was considered. We are not aware of examples of SET photochemistry that occur by direct transfer of an n-electron from an ether oxygen atom to an excited state of an enone although electron transfer from ethers[25a] and (trimethylsilyl)methyl ethers[25b] to photoexcited iminium salts has been reported. Operation of an SET mechanism for the formation of **30** and **31** appears improbable because oxidation potentials of aliphatic ethers are high (≥2.5 V vs Ag/AgCl)[25c] in relation to the expected electron affinities of the excited states of enones **1b** and **13b**.

A reasonable mechanism for photoconversion of **1b** to **31** and **13b** to **30** would involve transfer of a hydrogen atom from C(2) of THF to either the carbonyl oxygen atom or the α-position of the excited state of the enone followed by radical coupling at the β-position of the enone. The facial specificity for this enone photoaddition is of potential medicinal interest considering the spatial relationship of photoproducts **30** and **31** to the superpotent oripavines and related analgetics.

The electron transfer (SET) photochemistry of amines and conjugated enones is well-documented.[24] The effect of a tertiary amine on the photochemistry of carbamates **1b** and **17b** has been studied to provide some insight to the surprising photochemical stability of codeinone (**1a**). Irradiation of carbamate **1b** in benzene−methanol (5:1) with 1 equivalent of triethylamine (TEA) resulted in little if any inhibition of the rate of the photoreaction compared to a control experiment without TEA. The photosolvolysis product **13a** was isolated in 90% yield; however, inspection of the NMR spectrum of the photoreaction mixture indicated that trace amounts of *N*-carbomethoxynor-α-thebainone **32a** had formed. When 5 equiv of TEA were added, it was found that **32a** and **13a** had formed in a ratio of 1.5:1 (^{1}H NMR spectroscopy). Irradiation of **1b** with 5 equiv

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(20) (a) Kobayashi, T.; Kurono, M.; Sato, H.; Nakanishi, K. *J. Am. Chem. Soc.* **1972**, *94*, 2863−2865. (b) Gloor, J.; Schaffner, K.; Jeger, O. *Helv. Chim. Acta* **1971**, *54*, 1864−1869. (c) Gloor, J.; Schaffner, K. *Helv. Chim. Acta* **1974**, *57*, 1815−1845. (d) Bernardinelli, G.; Gerdil, R. *Helv. Chim. Acta* **1974**, *57*, 1846−1850. (e) Karvas, M.; Marti, F.; Wehrli, H.; Schaffner, K.; Jeger, O. *Helv. Chim. Acta* **1974**, *57*, 1851−1859.

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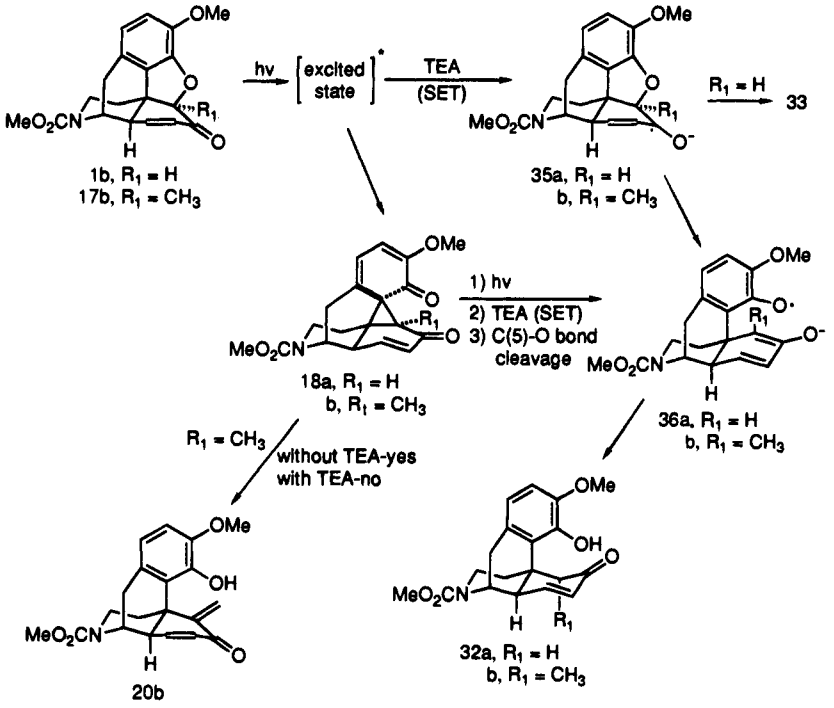
(22) (a) Schenck, G. O.; Koltzenburg, G.; Grossmann, H. *Angew. Chem.* **1957**, *69*, 177. (b) Dulou, R.; Vilkas, M.; Pfau, M. *C. R. Acad. Sci.* **1959**, *249*, 429.

(23) (a) Fraser-Reid, B. *Acc. Chem. Res.* **1975**, *8*, 192; **1985**, *18*, 347. (b) Benko, Z.; Fraser-Reid, B.; Mariano, P. S.; Beckwith, A. L. J. *J. Org. Chem.* **1988**, *53*, 2066.

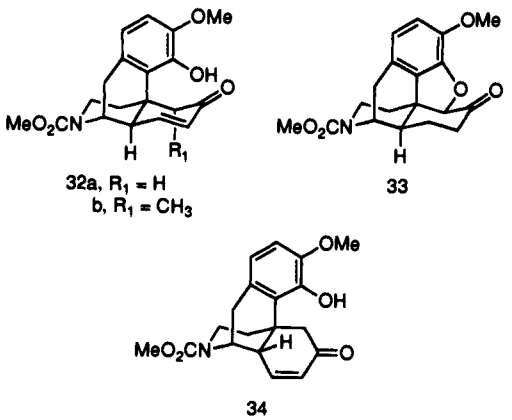
(24) (a) For the electron-transfer photochemistry of cyclohexenone in the presence of triethylamine, see: Schuster, D. I.; Insogna, A. M. *J. Org. Chem.* **1991**, *56*, 1879 and references cited therein. (b) For electron-transfer initiated photocyclizations of aminocyclohexenones, see: Xu, W.; Mariano, P. S. *J. Am. Chem. Soc.* **1991**, *113*, 1431 and references cited therein.

(25) (a) Mariano, P. S.; Stavinoha, J.; Bay, E. *Tetrahedron* **1981**, *37*, 3385. (b) Brumfield, M. A.; Quillen, S. L.; Yoon, U. C.; Mariano, P. S. *J. Am. Chem. Soc.* **1984**, *106*, 6855. (c) Sundholm, G. *Acta Chem. Scand.* **1971**, *25*, 3188.

Scheme 4



of TEA in benzene without methanol provided the α-thebainone derivative **32a** in 58% isolated yield, starting material **1b** (25%), and *N*-carbomethoxydihydronorcodeinone **33** in 4% yield.



The configuration at C(14) of **32a** was established by direct spectroscopic comparison of **32a** to the C(14) epimer **34**, obtained from β-thebainone[26] and $ClCO_2Me/NaHCO_3$ in $CHCl_3$. The formation of the α-thebainone derivative **32a** from photolysis of **1b** in the presence of TEA is related to the reductive opening of the oxide bridge in thebaine from treatment with alkali metals followed by hydrolysis of the dienol ether unit to give a mixture of both α- and β-thebainone.[27,28]

Irradiation of the 5-methyl-substituted carbamate **17b** in a mixture of benzene, methanol, and TEA (5:1:1) gave the 5-methyl-*N*-carbomethoxynor-α-thebainone **32b** in 61% isolated yield. The configuration of **32b** at C(5) was determined by a two-dimensional NOE experiment which gave positive enhancements of the signals from the C(14) proton and the C(5) methyl group. Remarkably, the reductive opening of the oxide bridge in **17b** under the indicated photolysis conditions occurs to the complete exclusion of the formation of dienone **20b**.

Possible mechanisms for the reductive ring opening reactions of **1b** and **17b** are shown in Scheme 4. Single electron transfer from TEA to the excited states of enones **1b** and **17b** would give radical anions **35a** and **35b**; C(5)−O bond cleavage in **35a** and **35b** would produce **36a** and **36b**.[29a] Alternatively, SET might occur between TEA and photoexcited **18a** and **18b** to give **36a** and **36b** after C(5)−O bond cleavage. The remaining steps to generate **32a** and **32b** or the dihydrocodeinone derivative **33** would follow well-established pathways involving proton and hydrogen atom transfers from the radical cation of TEA.[24]

Future mechanistic studies will examine the possibility that the absence of photoreactivity of codeinone (**1a**) may be the result of reversible (nonproductive) SET between the amine and excited enone groups in **1a**.[29b] In this regard, it has been shown that the tertiary amine in codeine is as effective as TEA in promoting the photoreduction of **1b** to give the α-thebainone derivative **32a**.

Consideration of an Alternative Photoreaction Mechanism. It is possible that much of the photochemistry of **1b** and analogues occurs by way of an internal electron transfer process involving the electron rich aryl nucleus and the excited enone chromophore. The photoconversion of **1b** to **13a−d** is at the very least schematically related to the photosensitized transacetalization of aryl glycosides and other phenol derived acetals.[30] The nucleophilic photosubstitution reactions have been proposed to occur via radical cation intermediates generated by electron transfer from the aryl ether to the excited sensitizer.

A mechanism for photorearrangement of **1b** that involves internal electron transfer is shown in Scheme 5. Single electron

(26) We thank Professor Marshall D. Gates for a sample of the perchloric acid salt of β-thebainone.

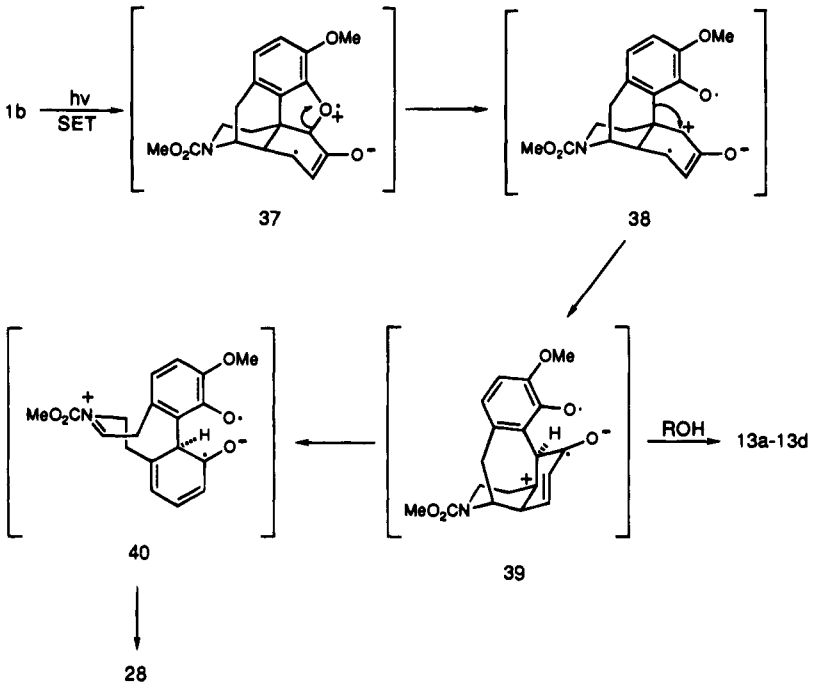
(27) (a) Freund, M. and Holthof, C. *Ber.* **1899**, *32*, 168. (b) Bentley, K. W.; Robinson, R. *Experientia* **1950**, *6*, 353.

(28) The conversion of β- to α-thebainone can be carried out in acetic acid at 100 °C; see: (a) Gates, M.; Helg, R. *J. Am. Chem. Soc.* **1953**, *75*, 379. (b) Tius, M. A.; Kerr, M. A. *J. Am. Chem. Soc.* **1992**, *114*, 5959.

(29) (a) Cossy, J.; Aclinou, P.; Bellosta, V.; Furet, N.; Baranne-Lafont, J.; Sparfel, D.; Souchaud, C. *Tetrahedron Lett.* **1991**, *32*, 1315. (b) For examples of reversible photoredox reactions involving tertiary amines, see: Gan, H.; Whitten, D. G. *J. Am. Chem. Soc.* **1993**, *115*, 8031.

(30) (a) Timpa, J. D.; Griffin, G. W. *Carbohydrate Res.* **1984**, *131*, 185. (b) Hashimoto, S.; Kurimoto, I.; Fujii, Y.; Noyori, R. *J. Am. Chem. Soc.* **1985**, *107*, 1427.

Scheme 5



transfer from the aryl ether in **1b** to the excited enone chromophore would give the radical cation radical anion **37**. Heterolytic cleavage of the dihydrofuran ring in **37** would generate a species that might be best represented as the C(5) carbocation **38**. A 1,2-migration of the aryl nucleus would give **39**. Addition of a hydroxylic solvent to **39** along with a back electron transfer would give **13a–d**. In the absence of a suitable nucleophile, **39** might fragment as indicated to give **40**. Proton and hydrogen atom transfers would convert **40** to the dibenzazonine-1,13-diol **28**.

What evidence is there to support the electron transfer mechanism? Very little at present. The unexpected differences in flash photolysis of **1b** compared to **2** and **5** may be a reflection of fundamental differences in reaction mechanisms for photorearrangement. It may be significant that *N*-carbomethoxynordihydrocodeinone (**33**) which lacks an enone chromophore fails to undergo photorearrangement reactions characteristic of **1b** (see Experimental Section), whereas other 2-carbonyl-substituted benzodihydrofurans are photoreactive; *e.g.*, **2** and **5**. Ring constraints on conformational mobility (cf., reactivity of **5** vs **8**) may operate in **33** to attenuate the photoreactivity expected of a benzodihydrofuran. The excited enone chromophore in **1b** may provide an alternative electron transfer pathway to enable photoreactivity. Finally, it should be clear that the electron transfer mechanism can be modified to encompass the photoreactivity described for analogues of **1b**.

Experimental Section

***N*-Carbomethoxynorcodeinone (1b).** To a stirred mixture of codeine·H_2O (20.0 g, 63.0 mmol) and $NaHCO_3$ (79.4 g, 0.945 mol) in $CHCl_3$ (1.0 L) was added methyl chloroformate (101 g, 1.07 mol, 82.8 mL). The reaction mixture was refluxed for 21 h. After cooling to room temperature the reaction mixture was filtered and the solvent removed under reduced pressure to provide *N*-carbomethoxynorcodeine as a colorless oil.[31] The carbamate was dissolved in CH_2Cl_2 (1.2 L) and pyridinium dichromate (94.8 g, 0.252 mol) was added at room temperature.[32] The resulting slurry was stirred at room temperature for 21 h and filtered through a short column of silica gel and anhydrous $MgSO_4$ (CH_2Cl_2/EtOAc, 3:1). The eluant was then washed with 10% HCl (2 × 250 mL). The organic phase was dried over anhydrous $MgSO_4$ and filtered and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 2% MeOH/CH_2Cl_2) gave **1b** (20.5 g, 95% from codeine, mixture of carbamate rotational isomers) as a white foam, mp 88–90 °C; ^{1}H NMR ($CDCl_3$) δ 6.70–6.56 (m, 3 H), 6.08 (dd, 1 H, J = 2.8 Hz, J = 10.3 Hz), 5.05–4.78 (m, 1 H), 4.66 (s, 1 H), 4.18–3.80 (m, 1 H), 3.81 (s, 3 H), 3.70 (m, 3 H), 3.01 (m, 1 H), 2.77 (m, 3 H), 1.92 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 193.9, 155.8, 147.1, 146.8, 142.7, 133.1, 133.0, 127.8, 124.6, 120.4, 115.0, 87.6, 56.6, 52.7, 50.6, 50.3, 43.3, 40.1, 37.9, 33.3, 33.1, 29.2, 28.9; IR (film) 3020, 2960, 1680, 1605 cm^{-1}; $[\alpha]^{27}_D$ −251° (*c* 2.64, $CHCl_3$); UV (benzene) γ (ϵ) 366 nm (53), 295 (870), UV (MeOH) λ (ϵ) 366 nm (69), 280 (1500); CIMS, *m/z* (relative intensity) 342 (M^+ + 1, 100), 102 (5). Anal. Calcd for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61. Found: C, 66.69; H, 5.46.

General Procedure for Photolysis. Preparative photoreactions were carried out in a standard Pyrex immersion reaction vessel except that the outer wall of the immersion well was made of uranyl glass. The light source was a medium pressure 450 W Hanovia mercury arc lamp. All solvents were deoxygenated prior to use by displacement with N_2 (20 min). The reactor was immersed in a water bath which had been placed on top of a magnetic stirrer; N_2 was bubbled through the solution during irradiation. For small-scale reactions, solutions in Pyrex test tubes (sealed with rubber septa covered parafilm) were strapped to the side of the immersion well with rubber bands. The immersion well, without the external reaction vessel, was immersed in the water bath.

10,12-(Aminoethano)-15-carbomethoxy-3,12-dimethoxy-4-hydroxybenzobicyclo[4.3.1]dec-7-en-6-one (13a). *N*-Carbomethoxynorcodeinone (**1b**) (2.0 g, 5.9 mmol) was dissolved in deoxygenated MeOH (390 mL) and irradiated for 21 h. Evaporation of the solvent *in vacuo* and flash chromatography on silica gel ($CHCl_3$/MeOH; 20:1) provided **13a** as a white foam (1.97 g, 90%): ^{1}H NMR ($CDCl_3$) δ 6.93 (dd, 1 H, J = 9.3 Hz, J = 4.2 Hz), 6.64 (d, 1 H, J = 10.2 Hz), 6.52–6.46 (dd, 1 H, J = 9.3 Hz, J = 2.6 Hz), 6.48–6.45 (d, 1 H, J = 10.2 Hz), 6.05 (s, 1 H, exchangeable with D_2O), 4.94 (s, 1 H), 4.77 and 4.71 (m, 1 H, rotational isomers), 3.88 (s, 1 H), 3.77 and 3.70 (s, 3 H, rotational isomers), 3.32 (d, 1 H, J = 15.2 Hz), 3.26 (s, 3 H), 3.08–2.65 (m, 2 H), overlapping 2.98 (t, 1 H, J = 4.7 Hz), 2.3–2.1 (m, 1 H), 2.0–1.7 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 196, 156, 146, 144, 133, 121, 120, 109, 56, 52, 51, 50, 48, 45, 40, 31, 30, 23. IR ($CHCl_3$) 3650 (s), 1700, 1665, 1600 cm^{-1}; CIMS, *m/z* (relative intensity) 374

(31) Brine, G. A.; Boldt, K. G.; Hart, C. K.; Carroll, F. I. *Org. Prep. Proc. Int.* **1976**, *8*, 103.
(32) Napier, J. Ph.D. Thesis, Cornell University, 1981.

($M^+ + 1$, 100), 342 (18). Anal. Calcd for $C_{20}H_{23}NO_6$: C, 64.33; H, 6.21. Found: C, 64.31; H, 6.29.

10,12-(Aminoethano)-15-carbomethoxy-4,12-dihydroxy-3-methoxybenzobicyclo[4.3.1]dec-7-en-6-one (13b). *N*-Carbomethoxynorcodeinone (**1b**) (0.137 g, 0.40 mmol) was dissolved in a deoxygenated solution of THF/H_2O (10.2 mL, 3:1) and irradiated for 24 h. Addition of benzene (35 mL), azeotropic removal of the solvents and chromatography on silica gel (ethyl acetate) afforded **13b** as an amorphous white powder (0.115 g, 80%); ^1H NMR ($CDCl_3$) δ 6.94 (m, 1 H), 6.62–6.41 (m, 3 H), 6.08 (s, 1 H, exchangeable with D_2O), 4.79–4.53 (m, 2 H, rotational isomers), 3.81 (s, 3 H), 3.74–3.65 (m, 3 H), 3.34–3.21 (m, 1 H), 2.96–2.62 (m, 2 H), 2.38–2.16 (m, 2 H), 1.90–1.74 (m, 2 H); ^{13}C NMR ($CDCl_3$) 197.2, 156.3, 155.9, 147.2, 146.9, 146.0, 144.6, 133.1, 132.9, 131.4, 131.1, 121.6, 121.5, 120.7, 109.5, 70.1, 55.8, 55.2, 52.9, 52.8, 51.7, 47.6, 40.5, 37.5, 37.3, 35.6, 34.8; IR (film) 3400, 1660, 1590; UV (THF) λ (ϵ) 366 nm (137), 220 (2.75×10^4); CI HRMS (methane) *m/z* 360.1443 ($M^+ + 1$) calcd for $C_{19}H_{22}NO_6$ 360.1447.

10,12-(Aminoethano)-15-carbomethoxy-12-ethoxy-4-hydroxy-3-methoxybenzobicyclo[4.3.1]dec-7-en-6-one (13c). A solution of *N*-carbomethoxynorcodeinone (**1b**) (200 mg, 0.59 mmol) in deoxygenated ethanol (11.7 mL) was irradiated for 21 h. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (SiO_2, 5% MeOH/CH_2Cl_2) to provide **13c** (222 mg, 98%, mixture of carbamate rotational isomers) as a white foam: mp 105–106 °C; ^1H NMR ($CDCl_3$) δ 6.80 (m, 1 H), 6.36 (m, 3 H), 6.29 (s, 1 H), 4.84 (s, 1 H), 4.63–4.48 (m, 1 H), 3.70 (s, 3 H), 3.66, 3.59 (s, 1 H), 3.46–3.18 (m, 4 H), 2.90 (t, 2 H, J = 5.5 Hz), 2.72 (m, 2 H), 2.20 (m, 1 H), 1.68 (m, 2 H), 1.02 (t, 3 H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 198.1, 157.3, 147.2, 147.0, 146.1, 134.4, 132.8, 122.7, 122.0, 110.8, 75.4, 57.3, 57.1, 53.9, 52.8, 52.2, 46.7, 41.7, 36.1, 33.2, 17.0; IR ($CDCl_3$) 3535, 2950, 1690, 1450, 1290, 1250 cm^{-1}; CI HRMS (methane) *m/z* 388.1730 ($M^+ + 1$) calcd for $C_{21}H_{26}NO_6$ 388.176. An acceptable elemental analysis could not be obtained.

10,12-(Aminoethano)-15-carbomethoxy-4-hydroxy-3-methoxy-12-*n*-propoxybenzobicyclo[4.3.1]dec-7-en-6-one (13d). **13d** was prepared by the above procedure but deoxygenated *n*-propanol was used in place of MeOH. Flash chromatography (SiO_2, 5% MeOH/CH_2Cl_2) gave **13d** (445.4 mg, 95%, mixture of carbamate rotational isomers) as a pale yellow foam: mp 104–105 °C; ^1H NMR ($CDCl_3$) δ 6.86 (m, 1 H), 6.42 (m, 3 H), 6.07 (s, 1 H), 4.86 (s, 1 H), 4.78–4.50 (m, 1 H), 3.80 (s, 3 H), 3.71, 3.64 (s, 1 H), 3.41–3.19 (m, 4 H), 2.94 (t, 2 H, J = 5.0 Hz), 2.80–2.59 (m, 2 H), 2.28 (m, 1 H), 1.74 (m, 2 H), 1.45 (m, 2 H, J = 7.3 Hz), 0.81 (t, 3 H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 196.8, 155.9, 145.9, 145.6, 144.8, 133.0, 131.4, 121.3, 120.7, 109.4, 73.8, 62.1, 55.8, 52.6, 51.5, 45.2, 40.3, 35.2, 34.7, 31.7, 23.2, 10.4; IR ($CDCl_3$) 3530, 2940, 1675, 1450, 1280, 1240 cm^{-1}; CIMS, *m/z* (relative intensity) 402 ($M^+ + 1$, 100), 344 (10).

Photolysis of *N*-Carbomethoxynorcodeinone in the Presence of Alcohols. Competition Experiments. A 0.05 M solution of *N*-carbomethoxynorcodeinone (**1b**) (200 mg, 0.59 mmol) in an equimolar amount of deoxygenated alcohols was purged with N_2 for 20 min prior to irradiation. After 22 h, the solvents were removed under reduced pressure; when water was used the reaction mixture was diluted with CH_2Cl_2 (75 mL) and washed with saturated NaCl solution (1 × 25 mL). The aqueous wash was back extracted with CH_2Cl_2 (2 × 25 mL), the combined organic layers were dried over anhydrous $MgSO_4$ and filtered, and solvent was removed under reduced pressure. Photoproduct ratios were determined by HPLC analysis (partisil column, ethyl acetate/hexanes, 3:2, 4 mL/min flow rate) of the reaction mixtures. Photoproducts were identified by comparison with retention times obtained for authentic samples and by comparison of ^1H NMR spectra. Relative response factors were obtained by HPLC analysis of standard solutions and these correction factors are incorporated into the reported results.

10,12-(Aminoethano)-3,12-dimethoxy-4-hydroxy-15-methylbenzobicyclo[4.3.1]decan-6-one (14a). **13a** (0.25 g, 0.67 mmol) was dissolved in THF (8 mL), and $LiAlH_4$ (0.076 g, 2.0 mmol) was added in two portions. After stirring overnight at room temperature, a saturated solution of sodium bicarbonate was added (1 mL). The mixture was extracted with $CHCl_3$ (3 × 20 mL). The combined extracts were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. Flash chromatography (SiO_2, $CHCl_3$/MeOH, 15:1) afforded **14a** as a clear film that solidified upon standing (0.198 g, 90%). X-ray quality crystals were grown from ethyl acetate/hexanes (mp 163 °C dec): ^1H NMR ($CDCl_3$) δ 7.3 (br s, 2 H), 6.5–5.5 (br, 1 H, exchangeable D_2O), 4.77 (s, 1 H), 3.89 (s, 3 H), 3.35 (s, 3 H), 3.33–3.08 (m, 3 H), 2.7–2.4 (m, 4 H), overlapped by 2.49 (s, 4 H), 2.1–1.65 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 210, 145.8, 145.3, 132.3, 121.5, 120.4, 109.5, 76.5, 61.0, 55.9, 53.1, 49.0, 47.9, 41.6, 40.3, 35.9, 32.6, 32.5, 23.5; IR ($CHCl_3$) 3540, 2940, 2880, 1710, 1495, 1285 cm^{-1}; CIMS, *m/z* (relative intensity) 332 ($M^+ + 1$, 40), 300 (100).

10,12-(Aminoethano)-4,12-dihydroxy-3-methoxy-15-methylbenzobicyclo[4.3.1]decan-6-one (14b). **13b** (510 mg, 1.4 mmol) was dissolved in THF (28 mL), and $LiAlH_4$ (162 mg, 4.3 mmol) was added in two portions. After stirring at room temperature for 24 h, the reaction mixture was worked up as described in the procedure for preparation of **14a**. **14b** (404 mg, 90%) was isolated as a white crystalline solid: mp 188–189 °C dec; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.66 (s, 2 H), 4.46 (s, 1 H), 3.87 (s, 3 H), 3.22 (d, 1 H, J = 5.8 Hz), 3.09 (m, 2 H), 2.64 (m, 3 H), 2.47 (s, 3 H), 2.41 (m, 2 H), 2.02 (m, 2 H), 1.78 (m, 2 H); ^{13}C NMR ($CDCl_3$/CD_3OD) 212.8, 145.9, 145.0, 131.3, 120.7, 120.2, 109.2, 71.1, 60.4, 56.7, 54.8, 48.5, 41.8, 40.5, 38.3, 35.3, 31.8, 22.6; CI HRMS (methane) *m/z* 318.1704 ($M^+ + 1$) calcd for $C_{18}H_{24}NO_4$ 318.1705. Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30. Found: C, 67.37; H, 7.31.

10,12-(Aminoethano)-12-ethoxy-4-hydroxy-5-methoxy-15-methylbenzobicyclo[4.3.1]decan-6-one (14c). **14c** (125 mg, 0.32 mmol) was prepared using the procedure described for preparation of **14d**. The resulting light yellow foam (105 mg, 94%) required no further purification: mp 109–110 °C; ^1H NMR ($CDCl_3$) δ 6.59 (s, 2 H), 4.70 (s, 1 H), 3.80 (s, 3 H), 3.62–3.49 (m, 2 H), 2.97 (m, 3 H), 2.54–2.30 (m, 5 H), 2.40 (s, 3 H), 1.94 (m, 2 H), 1.68 (m, 2 H), 1.12 (t, 3 H, J = 6.9 Hz); IR ($CDCl_3$) 3520, 2940, 1700, 1490, 1440, 1280 cm^{-1}; CIMS, *m/z* (relative intensity) 346 ($M^+ + 1$, 26), 328 (10), 300 (100). An acceptable elemental analysis could not be obtained.

10,12-(Aminoethano)-4-hydroxy-3-methoxy-15-methyl-12-*n*-propoxybenzobicyclo[4.3.1]decan-6-one (14d). $LiAlH_4$ (85 mg, 2.2 mmol) was added in one portion to a stirred solution of **13d** (300 mg, 0.75 mmol) in THF (15 mL) at room temperature. After stirring for 24 h, the reaction was quenched by the careful addition of saturated $NaHCO_3$ solution (10 mL). The mixture was diluted with CH_2Cl_2 (75 mL) and washed with brine (2 × 25 mL). The aqueous washes were combined and extracted with CH_2Cl_2 (2 × 50 mL). The combined extracts were dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 15% MeOH/CH_2Cl_2) provided **14d** (138 mg, 51%) as a slightly yellow foam: mp 89–90 °C; ^1H NMR ($CDCl_3$) δ 6.56 (s, 2 H), 4.70 (s, 1 H), 3.80 (s, 3 H), 3.39 (m, 2 H), 3.04 (m, 3 H), 2.68–2.45 (m, 5 H), 2.41 (s, 3 H), 1.98 (m, 2 H), 1.64 (m, 2 H), 1.56 (m, 2 H), 0.86 (t, 3 H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 210.9, 145.9, 145.3, 132.3, 121.2, 121.0, 109.4, 75.7, 61.3, 61.0, 55.8, 53.4, 48.9, 41.4, 40.7, 35.9, 33.1, 32.5, 23.4, 10.7; IR ($CDCl_3$) 3520, 2920, 1700, 1490, 1440, 1290, 1240 cm^{-1}; CIMS, *m/z* (relative intensity) 360 ($M^+ + 1$, 18), 342 (5), 300 (100). Anal. Calcd for $C_{21}H_{29}NO_4$: C, 70.17; H, 8.13. Found: C, 69.92; H, 7.93.

***N*-Carbomethoxy-5-methylnorcodeinone (17b).** To a solution of **17a**,[14b] prepared from 5-methylthebaine[33] (1.25 g, 0.004 mol) in $CHCl_3$ (55 mL) was added $NaHCO_3$ (7.0 g, 0.05 mol) and methyl chloroformate (8 mL, 0.064 mol). The mixture was heated at reflux for 18 h, cooled to room temperature, and filtered through Celite. Evaporation of the solvent at reduced pressure and flash chromatography on silica gel (hexanes/ethyl acetate; 1:1) provided **17b** as an ivory-colored amorphous foam (1.24 g, 87%): ^1H NMR ($CDCl_3$) δ 6.7 (AB quartet, 2 H, J = 7.7 Hz), overlapping (d, 1 H), 6.09 (dd, 1 H, J = 10.2 Hz, J = 2.8 Hz), 5.02 and 4.87 (m, 1 H, rotational isomers), 4.2–3.9 (m, 2 H), 3.82 (s, 3 H), 3.79 and 3.74 (s, 3 H, rotational isomers), 2.95 (dd, 1 H, J = 5.4 Hz, J = 2.8 Hz), 2.91–2.79 (m, 2 H), 1.96–1.69 (m, 2 H), 1.62 (s, 3 H); ^{13}C NMR ($CDCl_3$) 198.1, 155.9, 146.2, 145.9, 144.8, 142.7, 132.2, 132.1, 128.9, 124.5, 120.2, 114.3, 92.6, 56.4, 52.8,

(33) A modification of the procedure described by Gates and coworkers[14b] was used for the preparation of 5-methylthebaine; see: Schmidhammer, H.; Fritsch, F.; Burkard, W. P.; Eggstein-Aeppli, L.; Hefti, F.; Holck, M. I. *Helv. Chim. Acta* **1988**, *71*, 642.

50.9, 50.6, 45.0, 40.2, 37.9, 30.3, 29.4, 29.1, 15.5; IR (CH_2Cl_2) 1685, 1680 cm^{-1}; CIMS, *m/z* (relative intensity) 356 ($M^+ + 1$, 100), 342 (5), 116 (15). Anal. Calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96. Found: C, 67.68; H, 6.03.

5-(Trideuteriomethyl)thebaine. To thebaine (10 g, 32 mmol) dissolved in dry THF (500 mL) and cooled to −78 °C under a nitrogen atmosphere was added *n*-BuLi (2.5 M, 3 mL). The formation of the anion was indicated by a wine-red color. After stirring at −78 °C for 20 min, the anion was quenched with dimethyl-d_6 sulfate (4.6 mL, 49 mmol). The reaction temperature was maintained at −78 °C for 30 min and then allowed to warm slowly to room temperature. After an additional 2 h, water (10 mL) was added and THF was removed under reduced pressure. The residue was extracted with $CHCl_3$ (3 × 60 mL), washed with water (2 × 30 mL), dried, and concentrated. Recrystallization from 2-propanol/hexane yielded 5-(trideuteriomethyl)thebaine (7.2 g, 68%, mp 157−159 °C); ^1H NMR ($CDCl_3$) δ 6.64 (d, 1 H, J = 8.1 Hz), 6.61 (d, 1 H, J = 8.1 Hz), 5.54 (d, 1 H, J = 6.4 Hz), 4.02 (m, 1 H), 3.83 (s, 3 H), 3.63 (d, 1 H, J = 6.8 Hz), 3.55 (s, 3 H), 3.28 (d, 1 H, J = 17.9 Hz), 2.67 (m, 2 H), 2.62 (dd, 1 H, J = 17.9 Hz), 2.45 (s, 3 H), 2.15 (m, 1 H), 1.71 (d, 1 H); ^{13}C NMR ($CDCl_3$) 156.1, 143.7, 142.2,133.9, 131.2, 127.0, 118.9, 112.0, 94.1, 93.1, 63.8, 61.2, 55.9, 54.7, 47.1, 45.5, 42.0, 30.3, 29.7, 25.1; EIMS *m/z* 328 (M^+).

5-(Trideuteriomethyl)-*N*-carbomethoxynorcodeinone (17c). A solution of 5-(trideuteriomethyl)thebaine (520 mg, 1.6 mmol) in dry CH_2Cl_2 (60 mL) was cooled in a salt−ice bath. Anhydrous HCl was bubbled through the solution for 1 h, and then the mixture was poured into 50% NaOH. The pH was adjusted to 8.5 with conc HCl and the product was extracted into CH_2Cl_2. The combined extracts were dried, concentrated, and flash chromatographed (SiO_2, 10% MeOH/CH_2Cl_2) to give 5-(trideuteriomethyl)codeinone (367 mg, 74%) as a cream-colored foam (mp 170−173 °C); ^1H NMR ($CDCl_3$) δ 6.63 (m, 3 H), 6.00 (ddd, 1 H, J = 10.3, 2.9, 1.0 Hz), 3.80 (s, 3 H), 3.40 (m, 1 H), 3.10 (m, 2 H), 2.62 (dd, 1 H, J = 12.0, 4.7 Hz), 2.45 (s, 3 H), 2.28 (m, 2 H), 1.98 (dt, 1 H, J = 12.2, 4.9 Hz), 1.66 (d [broad], 1 H, J = 12.2 Hz); ^{13}C NMR ($CDCl_3$) δ 198.6, 148.1, 144.7, 142.4, 131.6, 130.1, 125.8, 119.5, 113.8, 94.7, 92.7, 59.3, 56.4, 46.6, 44.6, 42.8, 41.4, 30.6, 20.5; IR (film) 1670 cm^{-1}; CIMS *m/z* (relative intensity) 315 ($M^+ +$ 1, 100). This substance was converted to **17c** in 77% yield with $ClCO_2Me$ as described for the preparation of **1b**.

***N*-Carbomethoxy-4-hydroxy-3-methoxy-5-methylidenemorphinan-6-one (20b).** Irradiation of **17b** as described for the preparation of **21b** followed by removal of solvent under reduced pressure provided **20b** as an amorphous white foam (0.10 g, 100%); ^1H NMR ($CDCl_3$) δ 6.63 (AB quartet, 2 H, J = 8.3 Hz), overlapping (d, 1 H), 6.1−6.0 (s, 1 H), overlapping (dd, 1 H, J = 2.8 Hz), 5.77 (br s, 1 H, exchangeable with D_2O), 5.5 (s, 1 H), 4.82 and 4.80 (m, 1 H, rotational isomers), 4.05−3.95 (m, 1 H), 3.80 (s, 3 H), 3.79 and 3.73 (s, 3 H, rotational isomers) 3.14 (dd, 1 H, J = 12.7 Hz, J = 2.8 Hz), 2.8−2.68 (m, 3 H), 2.3−2.0 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 190, 151, 147, 145, 144, 131, 128, 121, 118, 115, 109, 56, 52, 48, 45, 43, 40, 38, 31, 30; IR (film) 3500 (br), 3080, 1680, 1610 cm^{-1}; CIMS, *m/z* (relative intensity) 356 ($M^+ +$ 1, 100), 342 (5), 324 (5).

[6a*S*-(6aα,9aα,10β)13a*S*]-1,10-Methano-4-methoxy-11-methyl-6,6a,10,11,12,13-hexahydro-[1]benzopyrano[4,3-*e*]isoquinolin-7-(9a*H*)-one (21a). **17a** (100 mg, 0.32 mmol) was dissolved in deoxygenated MeOH (25 mL) and irradiated for 21 h. Removal of the solvent under reduced pressure gave a tan foam. Chromatography on silica gel ($CHCl_3$/MeOH, 15:1) provided **21a** as a light tan amorphous powder (89 mg, 89%): ^1H NMR ($CDCl_3$) δ 6.62 (m, 2 H, $J_{1,2}$ = 8.3 Hz, $J_{7,8}$ = 10.0 Hz), 6.54 (d, 1 H, $J_{1,2}$ = 8.3 Hz), 5.94 (dd, 1 H, $J_{7,8}$ = 10.0 Hz, $J_{7,14}$ = 2.9 Hz), 5.24 (dd, 1 H, $J_{19a,19b}$ = 11.3 Hz, $J_{5,19a}$ = 1.3 Hz), 4.48 (dd, 1 H, $J_{19a,19b}$ = 11.3 Hz, $J_{5,19b}$ = 3.6 Hz), 3.8 (s, 3 H), 3.29 (t, 1 H, $J_{9,10b}$ = 6.2 Hz), 3.15 (dd, 2 H, $J_{10a,10b}$ = 18.7 Hz, $J_{9,10a}$ = 1.3 Hz), 2.61 (dd, 1 H, $J_{16a,16b}$ = 12.0 Hz, $J_{16a,15a}$ = 4.1 Hz), 2.56 (d, 1 H, $J_{5,19b}$ = 3.6 Hz), 2.52 (dd, 1 H, $J_{10a,10b}$ = 18.7 Hz, $J_{9,10b}$ = 6.2 Hz), 2.55 (s, 3 H), 2.34 (dt, 1 H, $J_{16a,16b}$ = 12.0 Hz, $J_{15a,16b}$ = 11.2 Hz, $J_{15b,16b}$ = 3.6 Hz), 1.97 (dt, 1 H, $J_{15a,16b}$ = 11.2 Hz, $J_{15a,15b}$ = 11.8 Hz, $J_{15a,16a}$ = 4.1 Hz), 1.89 (m, 1 H, $J_{15a,15b}$ = 11.8 Hz); ^{13}C NMR ($CDCl_3$) δ 194.5, 148.4, 145.7, 142.4, 129.6, 127.2, 119.6, 117.6, 109.7, 60.3, 56.2, 55.5, 48.7, 46.1, 43.0, 42.5, 37.8, 33.7, 22.8; IR (film) cm^{-1}; 3060, 2980, 1680, 1485, 1250, 1050 cm^{-1}; CI HRMS (methane) *m/z* 312.1598 ($M^+ + 1$) calcd for $C_{19}H_{22}NO_3$ 312.1600.

Structure Determination for 21a. Mass spectral analysis showed no change in molecular weight upon irradiation of **17a** indicating rearrangement rather than solvent incorporation. The low frequency carbonyl stretch (1680 cm^{-1}) in addition to the ^1H NMR signals at δ 6.62 and 5.94 ($J_{7,8}$ = 10.0 Hz) indicate that the enone functionality is retained in the product. Compound **21a** lacks the three-proton singlet from the C(5)methyl substituent of **17a** (δ 1.64) and contains three new multiplets (δ 5.24, 4.48 and 2.56) representing the proton at C(5) and two protons at C(19). These three protons form a closed system in terms of coupling. Further confirmation was provided by DEPT analysis which gave the following results: CH_3 (2), CH_2 (4), CH (7) and C_q (6). Homonuclear decoupling was performed which allowed for identification of each proton. The chemical shifts and coupling constants are consistent with the structural assignment.

[6a*S*-(6aα,9aα,10β)13a*S*]-1,10-Methano-methoxy-11-carbomethoxy-6,6a,10,11,12,13-hexahydro-[1]benzopyrano[4,3-*e*]isoquinoline-7-(9a*H*)-one (21b). **17b** (0.12 g, 0.34 mmol) was dissolved in deoxygenated MeOH (25 mL) and irradiated for 6 h. Evaporation of the solvent under reduced pressure afforded a white foam composed of approximately a 1:1 mixture of **20b** and **21b** (^1H NMR analysis). Flash chromatography on silica gel (hexanes/ethyl acetate, 1:1) provided **20b** (R_f = 0.2, 0.053 g, 44%) and **21b** (R_f = 0.1, 0.065 g, 54%) as white amorphous powders. In a separate experiment the mixture of **20b** and **21b** was dissolved in methylene chloride (10 mL) and diethylamine (0.1 mL) was added. After stirring overnight at room temperature the solvent was removed under reduced pressure and the resulting white foam was chromatographed on silica gel (hexanes/ethyl acetate, 1:1) to afford **21b** (0.114 g, 96%); ^1H NMR ($CDCl_3$) δ 6.62 (AB quartet, 2 H, J = 8.3 Hz), overlapping (d, 1 H), 5.98 (dd, 1 H, J = 10.2 Hz, J = 2.8 Hz), 5.23 (dd, 1 H, J = 11.3 Hz, J = 1.3 Hz), 4.86 and 4.72 (m, 1 H, rotational isomers) 4.47 (dd, 1 H, J = 11.3 Hz, J = 3.6 Hz), 4.05−3.95 (m, 1 H), 3.8 (s, 3 H), 3.78 and 3.74 (s, 3 H, rotational isomers) 3.08−2.77 (m, 4 H), 2.59−2.56 (dd, 1 H, J = 2.4 Hz, J = 1.3 Hz), 2.0−1.78 (m, 2 H); IR (film) 1685, 1680 cm^{-1}; CIMS, *m/z* (relative intensity) 356 ($M^+ +$ 1, 100), 324 (5), 305 (5). *Anal.* Calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96. Found: C, 67.38; H, 5.85.

5-Methylmorphinone (22). A 500 mL flame-dried round bottom flask was charged with **17a** (1.22 g, 3.9 mmol) and dry CH_2Cl_2 (300 mL). A cryogenic bath was used to cool the solution to −12 °C under an atmosphere of nitrogen. BBr_3 (2.5 mL, 26.4 mmol) was added and the mixture was stirred at −12 °C for 18.5 h. The reaction was quenched with 2 mL of MeOH. After addition of saturated $NaHCO_3$, the product was extracted into CH_2Cl_2. The aqueous layer was extracted thoroughly with CH_2Cl_2/EtOH (3:2). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give **22**·HBr. The salt was treated with saturated $NaHCO_3$ and extracted as the free base into CH_2Cl_2, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Flash chromatography on silica gel (10% MeOH/CH_2Cl_2) afforded **22** (705 mg, 60%) as a cream-colored foam and benzodihydropyran **24** (137 mg, 11.7%). Crystallization of **22** from EtOAc gave off-white needle crystals, mp 215−217 °C dec; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.65 (d, 1 H, J = 10.2 Hz), 6.64 (d, 1 H, J = 8.8 Hz), 6.55 (d, 1 H, J = 8.3 Hz), 6.01 (dd, 1 H, J = 10.2, 2.9 Hz), 3.52 (bs, 1 H), 3.17 (bs, 1 H), 3.14 (d, 1 H, J = 18.0 Hz), 2.69 (dd, 1 H, J = 11.7, 4.4 Hz), 2.45 (s, 3 H), 2.30 (m, 2 H), 2.03 (ddd, 1 H, J = 12.3, 4.9 Hz), 1.65 (d, 1 H, J = 12.2 Hz), 1.59 (s, 3 H); ^{13}C NMR (CD_3OD) δ 201.64, 151.31, 144.94, 140.63, 132.16, 131.29, 126.18, 121.31, 118.69, 94.15, 60.65, 48.06, 46.28, 43.17, 42.40, 31.59, 21.99, 16.16; IR ($CHCl_3$) 3500, 1675 cm^{-1}; UV (EtOH) λ (ϵ) 366 nm (60.5), 279 (946), 229 (5390); CI HRMS (methane) *m/z* 298.1448 (M + 1) Calcd for $C_{18}H_{20}NO_3$: 298.1443.

[6a*S*-(6aα,9aα,10β)13a*S*]-1,10-Methano-4-hydroxy-11-methyl-6,6a,10,11,12,13-hexahydro-[1]-benzpyrano[4,3-*e*]isoquinoline-7-(9a*H*)-one (24). **22** (100 mg, 0.34 mmol) was dissolved in deoxygenated MeOH (45 mL) and irradiated for 3 h. The solvent was removed under reduced pressure; flash chromatography (SiO_2, 10% MeOH/CH_2Cl_2) yielded **24** (77.3 mg, 77%) as a white solid. Recrystallization from EtOAc gave white needles, mp 202−203 °C dec; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.65 (d, 1 H, J = 7.8 Hz), 6.63 (dd, 1 H, J = 10.3, 2.0 Hz), 6.49 (d, 1 H, J = 7.8 Hz), 5.90 (dd, 1 H, J = 10.2, 2.4 Hz), 5.12 (dd, 1 H, J = 10.8, 1.4 Hz), 4.42 (dd, 1 H, J = 10.7, 3.4 Hz), 3.27 (bs, 1 H), 3.11 (d, 1 H, J = 18.5 Hz), 3.06 (bs, 1 H), 2.65

(dd, 1 H, J = 11.7, 3.4 Hz), 2.56 (d, 1 H, J = 2.0 Hz), 2.51 (dd, 1 H, J = 18.1, 5.4 Hz), 2.46 (s, 3 H), 2.31 (ddd, 1 H, J = 12.2, 3.4 Hz), 1.99 (ddd, 1 H, J = 12.7, 4.9 Hz), 1.88 (d, 1 H, J = 11.7 Hz); ^{13}C NMR (CD_3OD) δ 194.85, 148.89, 142.58, 140.51, 129.87, 126.31, 119.27, 118.48, 113.47, 60.53, 56.65, 50.72, 49.04, 46.36, 43.03, 42.61, 37.81, 34.04, 23.02; IR ($CHCl_3$) 3545, 1670 cm^{-1}; UV (EtOH) λ (ϵ) 366 nm (71.9), 284 (1470), 214 (14,700); CI HRMS (methane) m/z 298.1447 (M + 1) calcd for $C_{18}H_{20}NO_3$ 298.1443.

14-Hydroxy-5-methylcodeinone (25). Prepared from 5-methylthebaine by the method of Schmidhammer and co-workers.[34] Flash chromatography (SiO_2, 5% MeOH/$CHCl_3$) and crystallization from EtOH/Et_2O gave colorless crystals: mp 167–168 °C dec, lit.[34] mp 184–186 °C; ^{1}H NMR ($CDCl_3$) 6.64 (m, 3 H), 6.13 (d, 1 H, J = 10.0 Hz), 3.82 (s, 3 H), 3.22 (d, 1 H, J = 18.3 Hz), 3.00 (d, 1 H, J = 5.6 Hz), 2.45 (s, 3 H), 2.6 to 2.2 (m, 4 H), 1.71 (s, 3 H), 1.53 (m, 1 H); CIMS m/z (relative intensity) 328 (100) (M^+ + 1). Anal. Calcd for $C_{19}H_{21}NO_4$; C, 69.70; H, 6.47; N, 4.28. Found: C, 69.38; H, 6.51; N, 4.26.

4,5-(Epoxymethyl)-14-hydroxy-3-methoxymorphinan-6-one (26). A solution of **25** (0.034 g, 0.1 mmol) in deoxygenated MeOH (6 mL) was irradiated for 6 h. Evaporation of the solvent afforded a yellow foam. Flash chromatography on silica gel ($CHCl_3$/MeOH/NH_4OH, 20:1:0.1) followed by preparative TLC ($CHCl_3$/MeOH, 30:1) gave **26** as a white foam (0.028 g, 82%): ^{1}H NMR ($CDCl_3$) δ 6.75 (AB quartet, 2 H, J = 8.3 Hz) overlapping (d, 1 H, J = 8.3 Hz), 5.98 (d, 1 H, J = 8.3 Hz), 5.26 (dd, 1 H, J = 11.3 Hz, J = 1.3 Hz), 4.7 (s, br, 1 H), 4.43 (dd, 1 H, J = 11.3 Hz, J = 3.3 Hz), 3.83 (s, 3 H), 3.31 (d, 1 H, J = 18.6 Hz), 3.03 (d, 1 H, J = 1.3 Hz), 3.0 (d, 1 H, J = 5.7 Hz), 2.73 (dd, 1 H, J = 18.6 Hz, J = 5.7 Hz), 2.5 (s, 3 H), 2.44 (m, 2 H), 1.7 (m, 2 H); IR ($CHCl_3$) 3350, 1690 cm^{-1}; CIMS, m/z (relative intensity) 328 (M^+ + 1, 100). *Anal.* Calcd for $C_{19}H_{21}NO_4$: C, 69.70; H, 6.46. Found: C, 67.69; H, 6.07.

12-Acetoxy-10,12-(aminoethano)-15-carbomethoxy-4-hydroxy-3-methoxybenzobicyclo[4.3.1]dec-7-en-6-one (27). Two test tubes containing **1b** (292 mg, 8.55 × 10^{-4} mol and 278 mg, 8.13 × 10^{-4} mol) in deoxygenated benzene/acetic acid (15 mL, 2:1) were irradiated for 24 h. The samples were combined and solvents removed *in vacuo* to give 0.5914 g of a yellow oil. Chromatography (SiO_2, ethyl acetate/hexanes, 3:2) gave **28** (130 mg, 23%) as an oil. The remaining material was further purified by preparative TLC (SiO_2, 0.2 mm; ethyl acetate/hexanes, 3:2) to give **27** (104 mg, 16%) as an oil: ^{1}H NMR ($CDCl_3$, two rotational isomers) δ 6.89 (m, 1 H), 6.60 (m, 1 H), 6.43 (m, 2 H), 6.09 (s, 1 H), 5.29 (s, 1 H), 4.62 (m, 1 H), 3.81 (s, 3 H), 3.80–3.55 (m, 5 H), 3.23 (m, 1 H), 2.90–2.15 (m, 4 H), 1.94 (s, 3 H); IR (film) 3420, 1730, 1680 cm^{-1}; CIMS m/z (relative intensity) 402 (M^+ + 1, 1), 401 (2), 344 (25), 342 (100); UV (MeOH) λ_{max} (ϵ) 283 nm (2280), 210 (27650); $[\alpha]^{23}_D$ +97.3 (c 1.13, $CHCl_3$).

8,9-Dihydro-2-methoxy-7-carbomethoxydibenz[*d,f*]azonine-1,13-diol (28). A stirred solution of **1b** (6.83 g, 20.0 mmol) and oxalic acid (9.0 g, 100 mmol) in dry THF was deoxygenated and irradiated with stirring for 5.5 h. The photolysis solution was concentrated and then diluted with CH_2Cl_2 (300 mL) before carefully adding $NaHCO_3$ solution (600 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 250 mL). The combined organic fractions were washed with saturated $NaHCO_3$ solution (2 × 200 mL) and brine (1 × 200 mL). The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 3% MeOH/CH_2Cl_2) gave **28** (5.18 g, 76%, mixture of carbamate rotational isomers) as a white powder: mp 203–204 °C; ^{1}H NMR ($CDCl_3$) δ 7.13 (t, 1 H, J = 8.0 Hz), 6.93–6.38 (m, 5 H), 5.51 (s, 1 H), 5.45–5.34 (m, 1 H), 4.55 (d, 1 H, J = 10.0 Hz), 3.93 (s, 3 H), 3.77, 3.62 (s, 3 H), 3.60–2.78 (m, 4 H); ^{13}C NMR (DMSO) δ 166.6, 150.6, 150.4, 142.4, 139.8, 134.3, 125.1, 121.3, 120.6, 117.3, 115.0, 110.0, 106.8, 103.0, 97.3, 86.8, 69.0, 52.0, 49.2; IR ($CDCl_3$) 3535, 3010, 2950, 1700, 1640, 1595 cm^{-1}; $[\alpha]^{24}_D$ +472 (c 2.61, $CHCl_3$); UV (MeOH) λ (ϵ) 267 nm (7460), 209 (26300); CIMS, m/z (relative intensity) 342 (M^+ + 1, 100). Anal. Calcd for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61. Found: C, 66.75; H, 5.11.

(34) (a) Schmidhammer, H.; Deeter, J. B.; Jones, N. D.; Leander, J. D.; Schoepp, D. D.; Swartzendruber, J. K. *Helv. Chim. Acta* **1988**, *71*, 1801. (b) The procedure for oxidation of 5-methylthebaine is a modification of the procedure reported for the oxidation of thebaine; see: Hauser, F. M.; Chen, T.-K.; Carroll, F. I. *J. Med. Chem.* **1974**, *17*, 1117.

In a separate experiment, irradiation of **1b** (554 mg, 1.62 mmol) in 3 mL of 2:1 THF/CH_3COOH provided 232 mg (42%) of **28** as an oil following preparative TLC (silica gel, 0.2 mm; ethyl acetate/hexanes, 3:2). Crystals of **28** (mp 199.5–200.5 °C) were obtained from ethyl acetate/hexane and subsequently used for the X-ray crystallography determination.

5,6,8,9-Tetrahydro-2-methoxy-7-carbomethoxydibenz[*d,f*]azonine-1,13-diol. A solution of **28** (2.61 g, 7.65 mmol) in ethyl acetate (75 mL) was hydrogenated at 50 psi in a Parr apparatus using 10% palladium on carbon (800 mg) as catalyst. After 4 h the reaction mixture was filtered through a short column of silica gel and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, ethyl acetate/hexanes, 3:2) provided the title compound (2.52 g, 96%, mixture of carbamate rotational isomers) as a light tan powder: mp 196–197 °C; ^{1}H NMR ($CDCl_3$) δ 7.23 (m, 2 H), 6.88 (m, 3 H), 5.58, 5.56 (s, 1 H), 4.97, 4.86 (s, 1 H), 3.89 (s, 3 H), 3.75–3.60 (m, 1 H), 3.55, 3.53 (s, 3 H), 3.48–2.92 (m, 3 H), 2.78–2.68 (m, 2 H), 2.46–2.32 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 156.5, 152.9, 152.6, 145.3, 145.2, 143.2, 142.9, 141.5, 140.6, 133.9, 133.1, 129.6, 129.3, 122.2, 122.1, 121.9, 121.7, 120.6, 120.5, 113.3, 113.1, 111.1, 110.7, 55.9, 55.9, 52.2, 52.2, 50.0, 49.6, 48.3, 47.8, 34.0, 33.9, 33.1, 32.8; IR ($CDCl_3$) 3530, 3020, 2950, 1680 cm^{-1}; $[\alpha]^{24}_D$ −43.6° (c 2.87, $CHCl_3$); MS, m/z (relative intensity) 344 (M^+ + 1, 100), 312 (4). Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16. Found: C, 66.13; H, 6.29. Hydrogenation of the photoreaction mixture from 4.59 g of **1b** in the presence of oxalic acid (before chromatographic separation) and flash chromatography on silica gel gave 3.71 g of the title compound (80%) and 289 mg of **28** (6%).

5,6,8,9-Tetrahydro-2-methoxy-7-methyldibenz[*d,f*]azonine-1,13-diol (29). The saturated carbamate prepared as described above (3.41 g, 9.93 mmol) in THF (60 mL) was added to a suspension of $LiAlH_4$ (1.51 g, 39.7 mmol) in THF (600 mL) at 0 °C (ice bath). The reaction mixture was allowed to warm to room temperature and then stirred for 22 h. Careful addition of saturated $NaHCO_3$ solution (100 mL) was followed by concentration under reduced pressure. Ethyl acetate (300 mL) was added, the layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 100 mL). The combined organic extracts were washed with saturated $NaHCO_3$ solution (2 × 100 mL) and brine (1 × 100 mL). The organic layer was dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. Flash chromatography (35% MeOH/CH_2Cl_2) gave **29** (2.58 g, 87%) as a very light green foam: mp 69–70 °C; ^{1}H NMR ($CDCl_3$) δ 7.23 (m, 2 H), 6.84 (m, 3 H), 5.04 (s, 2 H), 3.89 (s, 3 H), 2.78–2.45 (m, 6 H), 2.40–2.28 (m, 2 H), 2.26 (s, 3 H); ^{13}C NMR (DMSO) δ 154.4, 145.1, 143.3, 142.3, 134.2, 127.4, 124.9, 124.5, 119.7, 119.0, 112.3, 110.4, 79.1, 57.6, 57.4, 55.6, 46.5, 34.4, 34.0; IR ($CDCl_3$) 3530, 2940, 2840, 2790, 1580 cm^{-1}; $[\alpha]^{26}_D$ +49.0° (c 2.53, $CHCl_3$). An acceptable elemental analysis could not be obtained.

10,12-(Aminoethano)-15-carbomethoxy-4,12-dihydroxy-3-methoxy-8-(2-tetrahydrofuranyl)benzobicyclo[4.3.1]decan-6-one (30). 13b (25 mg, 0.070 mmol) was dissolved in deoxygenated THF (5 mL) and irradiated for 2 h. The solvent was removed under vacuum and the residue was flash chromatographed (silica gel; ethyl acetate/hexane, 3:2) to give 17.2 mg (57%) of **30** as a white solid. The ^{1}H NMR spectrum revealed the product to be a 5:1 mixture of diastereomers. Recrystallization from EtOAc (isothermal distillation technique with hexane) provided X-ray quality crystals of the major diastereomer (mp 138–140 °C): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.62, 6.60 (overlapping d, 1 H, J = 8.1 Hz), 6.47 and 6.44 (d, 1 H, J = 8.1 Hz), 5.82 (s, 1 H), 4.76 and 4.48 (s, 1 H), 4.36 and 4.19 (m, 2 H, $J_{9,10}$ = 6.6 Hz), 3.97 (m, 2 H), 3.86 (m, 1 H), 3.85 (s, 3 H), 3.65 and 3.73 (s, 3 H), 3.57 and 3.49 (m, 1 H), 3.23 (dd, 1 H, $J_{7a,7b}$ = 15.2 Hz), 2.86 (dd, 1 H, J = 6.6 Hz, J = 15.8 Hz), 2.78 (d, 1 H, J = 15.8, J = 4.4 Hz), 2.63 (m, 1 H, J = 15.2, J = 7.9 Hz), 2.17 (m, 2 H, $J_{9,14}$ = 4.1 Hz, J = 7.9 Hz), 2.02 (m, 3 H), 1.88 (m, 1 H), 1.72 (m, 4 H), 1.65 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) 213.61, 156.25, 145.74, 145.67, 144.57, 130.15, 129.79, 123.06, 122.88, 121.13, 121.00, 109.32, 109.22, 82.61, 82.06, 81.68, 70.48, 70.27, 68.61, 68.38, 68.27, 55.67, 55.07, 55.04, 54.60, 54.46, 53.35, 52.63, 52.48, 44.05, 43.72, 41.73, 41.51, 40.71, 40.53, 39.60, 39.02, 38.26, 37.99, 34.28, 33.26, 31.73, 28.92, 28.74, 25.82, 25.75, 22.50; IR ($CHCl_3$) 3600–3200, 1730–1630 cm^{-1} (broad); CIMS m/z

(relative intensity) 432 ($M^+ + 1$, 15), 414 (100), 345 (20), 213 (23), 211 (19), 133 (32), 107 (25).

Sensitized Photolysis of 13b. A solution of **13b** (25 mg, 0.070 mmol) and benzophenone (475 mg, 2.61 mmol) in deoxygenated THF (5 mL) was prepared; 95% of incident light was absorbed by benzophenone [UV (THF) λ (ϵ) 366 nm (69.5)]. A control was prepared containing **13b** with no benzophenone. The solutions were irradiated simultaneously for 30 min. The solvents were removed under reduced pressure. ^{1}H NMR spectra revealed similar conversions and product distributions for the sensitized and unsensitized reactions. Separation of the benzophenone-containing reaction mixture by radial chromatography (SiO_2, 10% MeOH, $CHCl_3$) yielded **30** (14.5 mg, 48%) as a 5:1 mixture of diastereomers and **13b** (4.3 mg, 17%).

***N*-Carbomethoxy-4,5-epoxy-8-(2-tetrahydrofuranyl)morphinan-6-one (31).** **31** was isolated as a byproduct from irradiation of **1b** in THF or THF with oxalic acid. For example, a mixture of **1b** (6.88 g, 0.020 mol), oxalic acid dihydrate (9.08 g, 0.072 mol), and deoxygenated THF (400 mL) was irradiated for 5.5 h. Flash chromatography (SiO_2; ethyl acetate/hexanes, 3:2) afforded **31** as a yellow oil (1.09 g, 13%). A 550 mg portion of **31** was purified further with radial chromatography (ethyl acetate/hexane, 3:2) to give 395 mg of **31** as a white foam (mp 104−120 °C). ^{1}H NMR analysis revealed the product to be a 1:1 mixture of diastereomers at the THF residue: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.73 (d, 1 H, J = 8.0 Hz), 6.65 (overlapping d, 1 H, J= 8.0 Hz), 5.30, 5.20, 5.10, 4.97 (m, 1 H), 4.74, 4.71 (s, 1 H), 4.11 through 3.68 (m, 10 H), 3.29 through 1.40 (m, 13 H), [2.68 (m), 2.48 (dd), 2.40 through 2.00 (m), 1.70 through 1.35 (m), 1.58 (m), 1.47 (m)]; ^{13}C spectrum too complex to be useful; IR ($CHCl_3$) 1725 cm^{-1}, 1685 cm^{-1} (broad); CIMS *m/z* (relative intensity) 414 ($M^+ + 1$, 100). Anal. Calcd for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.58. Found: C, 66.65; H, 6.40.

***N*-Methyl-4,5-epoxy-8-(2-tetrahydrofuranyl)morphinan-6-ol. 31** (100 mg, 0.24 mmol) in THF (2 mL) was added to a cold (−78 °C) mixture of $LiAlH_4$ (37 mg, 0.97 mmol) in THF (20 mL) under N_2. The mixture was allowed to warm to room temperature and after 18 h, 5 mL of saturated $NaHCO_3$ was added. The mixture was extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give a mixture of diastereomers (63 mg, 70%). Radial chromatography (SiO_2, 10% MeOH/CH_2Cl_2) resulted in the isolation of alcohols **A** (9.8 mg, pale yellow oil) and **B** (11.2 mg, white crystals). The remaining fractions contained mixtures of **A** and **B**. Diastereomer **A**: ^{1}H NMR ($CDCl_3$, 500 MHz) 6.73 (d, 1 H, J = 8.2 Hz), 6.63 (d, 1 H, J = 8.2 Hz), 4.63 (d, 1 H, J = 4.9 Hz), 4.03 (m, 1 H), 3.87 (s, 3 H), 3.85 (m, 3 H), 3.67 (m, 1 H), 3.00 (d, 1 H, J = 18.5 Hz), 2.51 (dd, J = 12.2 Hz, 4.2 Hz), 2.41 (s, 3 H), 2.27 (m, 2 H), 1.95 (dt, 1 H, J = 12.5 Hz, 4.2 Hz), 1.64 to 1.9 (m, 4 H), 1.55 (m, 1 H), 1.43 (m, 1 H), 1.35 (m, 1 H), 1.29 (m, 1 H); IR (film) 3410 cm^{-1} (broad); CIMS *m/z* (relative intensity) 372 (100) ($M^+ + 1$), 282 (36), 217 (28). Diastereomer **B**: ^{1}H NMR ($CDCl_3$, 500 MHz) 6.72 (d, 1 H, J = 8.2 Hz), 6.63 (d, 1 H, J = 8.2 Hz), 4.63 (d, 1 H, J = 5.1 Hz), 3.95 (m, 1 H), 3.87 (s, 3 H), 3.77 (m, 2 H), 3.68 (m, 1 H), 3.58 (m, 1 H), 2.99 (d, 1 H, J = 18.5 Hz), 2.40 to 2.60 (m, 2 H), 2.43 (s, 3 H), 2.50 (m, 2 H), 2.10 (m, 1 H, J = 8.8 Hz), 1.98 (m, 2 H), 1.81 (m, 2 H), 1.73 (m, 1 H), 1.43 (m, 2 H), 1.37 (m, 1 H), 1.27 (m, 1 H); IR (film) 3410 cm^{-1} (broad); CIMS *m/z* (relative intensity) 372 (100) ($M^+ + 1$), 282 (56).

Structure Determination for 31. The presence of a THF residue in **31** was first suggested by MS analysis which revealed an increase of 72 amu (C_4H_8O) relative to the mass of the starting material. The absence of ^{1}H NMR resonances in the vinyl region for **31** combined with its IR spectrum in which the carbonyl stretching band appeared at 1725 cm^{-1}, characteristic of a saturated ketone, indicated attachment of the THF moiety at either C(7) or C(8). The ^{1}H NMR spectrum for **31** was complex (two diastereomers × two carbamate rotational isomers), but H(14) was readily identified in both diastereomers (δ 2.54 and 2.23) by homonuclear decoupling. Each diastereomer exhibited strong coupling between H(14) and H(8) (11.7 Hz and 11.5 Hz) indicative of a diaxial relationship. Further regiochemical information could not be obtained due to signal overlap in the region of H(7) and H(8).

To simplify the ^{1}H NMR spectrum, compound **31** was reduced as described above. The reaction was carried out at −78 °C so that reduction of the ketone would occur stereoselectively from the α face. Analysis of the ^{1}H NMR spectra for **A** and **B** allowed for unequivocal assignment of **31** as the product of equatorial incorporation of a THF residue at C(8). This was determined as follows. H(5) appears as a doublet in alcohol **A** at δ 4.63 ($CDCl_3$) which is coupled to H(6) (δ 4.03). The small coupling constant ($J_{5,6}$ = 4.9 Hz) places H(6) in an equatorial environment (as expected for reduction from the α face) since H(5) is constrained to an axial orientation. Decoupling of H(6) allowed for identification of two protons attached to C(7) [δ 1.29 (ax) and δ 1.43 (eq)] which eliminated the possibility of THF attachment at this position. Both C(7) protons are coupled to H(8) (δ 1.35) which is also coupled to H(14) (δ 2.27) and the proton α to O on the THF residue (δ 3.86). The coupling constant between H(8) and H(14) could not be determined in $CDCl_3$ due to overlap, but was determined to be 10.0 Hz in C_6D_6, confirming the diaxial relationship predicted for **31**. By similar analysis it was confirmed that the alcohol group in **B** also occupies an axial orientation ($J_{5,6}$ = 5.1 Hz). This proves that the configurational difference between **A** and **B** is representative of the diastereomers of **31**. **B** also contains two protons attached to C(7) [δ 1.37 (ax), δ 1.27 (eq)], both of which are coupled to H(8) (δ 1.43). As in **A**, H(8) is also coupled to H(14) ($J_{8,14}$ = 8.8 Hz, δ 2.10) and the proton α to O on the THF residue (δ 3.77). Thus, **31** is a mixture of diastereomers in which the THF residue is attached at C(8) in an equatorial orientation. By the process of elimination, the configurational difference must reside at the carbon atom α to O on the THF residue.

***N*-Carbomethoxy-5-methylnor-α-thebainone (32b).** A solution of **17b** (0.1 g, 0.0003 mol) in deoxygenated benzene (5 mL) and triethylamine (0.1 mL) was irradiated for 5 h. Evaporation of the solvent under reduced pressure and flash chromatography on silica gel ($CHCl_3$/MeOH, 25:1) afforded **32b** (0.061 g, 60%) as a white foam: ^{1}H NMR ($CDCl_3$) δ 6.67 (d, 1 H, J = 8.4 Hz), 6.55 (AB quartet, 2 H, J = 10.1 Hz), 6.11 (s, 1 H, exchangeable with D_2O), 5.82 (dd, 1 H, J = 9.9 Hz, J = 2.9 Hz), 4.79, 4.63 (m, 1 H), 4.38 (q, 1 H, J = 7.7 Hz), 3.8 (s, 3 H), 3.78, 3.72 (s, 3 H), 3.03 (dd, 1 H, J = 15.8 Hz, J = 5.1 Hz), 2.86 (m, 1 H), 2.66 (m, 2 H), 1.9 (m, 2 H), 1.22 (d, 3 H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$) 203.8, 156.5, 146.9, 146.2, 145.3, 144.6, 129.2, 128.9, 122.9, 119.3, 109.2, 56.0, 52.7, 52.6, 48.4, 48.1, 45.2, 41.9, 41.8, 38.9, 38.7, 32.6, 32.2, 30.7, 30.4, 12.0; IR (film) 3510, 3380, 1670 cm^{-1}; CI HRMS (methane) *m/z* 358.1652 ($M^+ + 1$) calcd for $C_{20}H_{24}NO_5$ 358.1654.

***N*-Carbomethoxynor-α-thebainone (32a) and *N*-Carbomethoxynordihydrocodeinone (33).** A solution of **1b** (0.05 g, 0.0001 mol) in deoxygenated benzene (5 mL) and triethylamine (0.1 mL) was irradiated for 12 h. Evaporation of the solvent under reduced pressure and flash chromatography on silica gel (hexanes/ethyl acetate, 1:2) afforded **32a** as an ivory foam (0.02 g, 58%) and **33** (0.002 g, 4%) as a white foam (mp 83−84 °C): **32a**: ^{1}H NMR ($CDCl_3$) δ 6.61 (2 H, AB quartet, J = 8.2 Hz) superimposed on 6.6 (dd, 1 H), 6.05 (s, 1 H, exchangeable with D_2O), 5.94 (dd, 1 H, J = 11.8 Hz, J = 1.1 Hz), 4.8 and 4.65 (m, 1 H, rotational isomers), 4.38 (d, 1 H, J = 15.8 Hz), 3.83 (s, 3 H), 3.76 (s, 3 H), 3.08 (m, 1 H), 2.7 (m, 3 H), 2.39 (d, 1 H, J = 15.8 Hz), 2.06 (m, 1 H), 1.76 (dt, 2 H, J = 12.6 Hz, J = 5.2 Hz); ^{13}C NMR ($CDCl_3$) 198.9, 156.4, 147.7, 145.1, 144.6, 131.4, 134.3, 128.8, 121.5, 119.1, 109.2, 56.0, 52.7, 52.6, 48.6, 48.4, 48.3, 45.5, 40.5, 38.5, 35.7, 35.5, 32.2, 31.8; IR ($CHCl_3$) 3500, 3350 (br), 1680 cm^{-1}; CIMS, *m/z* (relative intensity) 344 ($M^+ + 1$, 100). **33**: 6.71 (AB quartet, 2 H, J = 8.1 Hz), 4.81 (s, 1 H), 4.61 and 4.42 (m, 1 H, rotational isomers), 3.82 (s, 3 H), 3.75 and 3.72 (s, 3 H, rotational isomers), 3.12 (dd, 1 H, J = 18.7 Hz, J = 4.4 Hz), 2.7−2.5 (m, 3 H), 2.4−2.1 (m, 3 H), 1.8−1.65 (m, 2 H); ^{13}C NMR ($CDCl_3$) 207.1, 155.7, 145.3, 142.9, 126.0, 124.7, 124.5, 120.1, 114.7, 91.2, 90.9, 56.5, 52.6, 52.5, 50.7, 50.4, 47.0, 41.1, 39.6, 37.8, 34.7, 34.4, 28.6, 28.3, 27.6, 25.8, 25.1; IR ($CHCl_3$) 1700 cm^{-1}; UV (MeOH) λ (ϵ) 366 nm (22), 300 (543) 283 (1380); CIMS *m/z* (relative intensity) 344 ($M^+ + 1$, 100). Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16. Found: C, 66.38; H, 6.27.

Attempted Photorearrangement of *N*-Carbomethoxynordihydrocodeinone (33). A deoxygenated solution of **33** (100 mg, 0.291 mmol) in MeOH (11.6 mL) was irradiated at 366 nm for 18.5 h. The solvent was evaporated under reduced pressure resulting in complete recovery of unreacted starting material. The reaction was repeated in deoxygenated benzene but no reaction occurred. Irradiation of **33** (44.4 mg, 0.129 mmol) in deoxygenated MeOH (4 mL) at 300 nm for 10 h gave no reaction. The relevant UV data for **33** is as follows: ϵ_{300nm} = 517, ϵ_{366nm} = 27.

***N*-Carbomethoxynor-β-thebainone (34).** To a solution of the perchloric acid salt of β-thebainone[26] (0.05 g, 0.00016 mol) in $CHCl_3$ (5 mL) was added sodium bicarbonate (0.46 g, 0.0032 mol) and then methyl chloroformate (0.20 mL, 0.0026 mol). The mixture was heated at reflux for 24 h. After being cooled to room temperature the reaction mixture was filtered through a pad of magnesium sulfate and the solvent was removed under reduced pressure. Flash chromatography on silica gel (hexanes/ethyl acetate, 2:1) gave **34** as a white foam (0.035 g, 64%): ^1H NMR ($CDCl_3$) δ 6.91 (d, 1 H, J = 11.8 Hz), 6.71 (AB quartet, 2 H, J = 8.2 Hz), 6.18 (dd, 1 H, J = 11.8 Hz, J = 1.1 Hz), 4.89 and 4.72 (m, 1 H, rotational isomers), 4.16 (d, 1 H, J = 15.8 Hz), 3.89 (s, 3 H), 3.73 (s, 3 H), 3.39 (dd, 1 H, J = 18.8 Hz, J = 4.3 Hz), 2.82 (d, 1 H, J = 15.8 Hz), overlapping 2.81 (m, 1 H), 2.63 (d, 1 H, J = 15.8 Hz), superimposed on 2.67 (m, 1 H), 2.15 (dt, 1 H, J = 12.8 Hz, J = 5.2 Hz), 1.68 (m, 1 H); IR ($CHCl_3$), 3570, 3300, 1665, 1650; CI HRMS (methane) m/z 344.1487 ($M^+ + 1$) calcd for $C_{19}H_{22}NO_5$ 344.1498. An acceptable elemental analysis could not be obtained.

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Supplementary Material Available: Tables of crystal structure data, atomic coordinates, bond lengths, bond angles, anisotropic parameters, and hydrogen atom coordinates for **30** (13 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.