56-9; **4**-$(OEt)_{10}$, 132885-68-8; 4^{10-},10Li$^+$, 136706-44-0; **5**-$(OEt)_4$, 132885-79-1; 5^{4-},4Li$^+$, 136706-45-1; **6**-$(OMe)_2$, 136575-94-5; $6^{2\bullet}$, 136575-95-6; $6^{\bullet-}$,Li$^+$, 136706-48-4; **7**-$(OEt)_2$, 136706-43-9; $7^{\bullet-}$,Li$^+$, 136706-49-5; 7^{2-},2Li$^+$, 136706-50-8; 1,4-dibromobenzene, 106-37-6; 4,4'-di-*tert*-butylbenzophenone, 15796-82-4.

Supplementary Material Available: Full ^{1}H and ^{13}C NMR spectra at 303 K and partial COSY and HETCOR spectra for 5^{4-},4Li$^+$; variable temperature ^{1}H NMR spectra for 3^{4-},4Li$^+$; ^{1}H and ^{13}C NMR spectra following the reaction of **2**-$(OEt)_2$ with lithium; and ESR and UV-vis spectra following the reaction of **6**-$(OMe)_2$ and $6^{2\bullet}$ with lithium (25 pages). Ordering information is given on any current masthead page.

SET Photochemistry of Flavin–Cyclopropylamine Systems. Models for Proposed Monoamine Oxidase Inhibition Mechanisms

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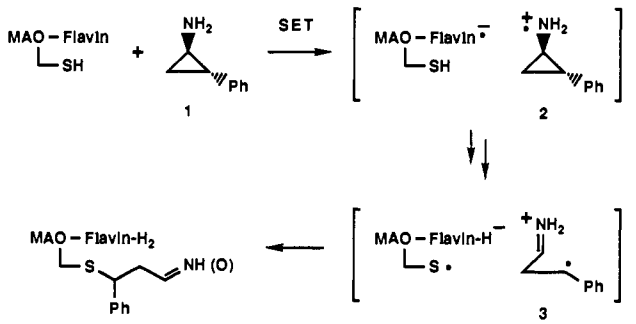
Abstract: Single electron transfer (SET) induced photochemical reactions of 3-methyllumiflavin (3-MLF) with the cyclopropylamines, *trans*-2-phenylcyclopropylamine (**1**) and 1-phenylcyclopropylamine (**4**), have been explored with the aim of defining the nature of and mechanisms for the reaction pathways followed. The excited-state SET processes probed in this investigation were designed to model those proposed previously for inactivation of the flavine-containing enzyme, monoamine oxidase, by these same cyclopropylamines. Irradiation of 3-MLF in an N_2-purged solution containing cyclopropylamine **4** leads to generation of the C-4a,N-5-propanodihydroflavin **14** as the major primary photoproduct. This substance, which is formed by an SET-promoted radical coupling mechanism, is transformed to the C-4a-(benzoylethyl)dihydroflavin **6** under hydrolytic conditions. Several other minor, cyclopropylamine-derived products are also generated in this reaction, again via radical pathways. In contrast, irradiation of an air-saturated solution of 3-MLF and **4** produces the epoxy ketone **8** efficiently. In this reaction, 3-MLF serves as an SET photosensitizer for the oxidative ring-opening reaction that converts **4** to **8**. Finally, the C-4a,N-5-propanodihydroflavin adducts **17** and **18** are generated along with substances arising by secondary reaction of a primary product, cinnamaldehyde (**20**), when 3-MLF is irradiated in an N_2-purged solution containing the cyclopropylamine **1**. Mechanistic aspects of these bona fide SET flavin–cyclopropylamine reactions and their possible relationship to proposals made earlier about the nature of and mechanisms for monoamine oxidase inactivation by the same cyclopropylamines are discussed.

Introduction

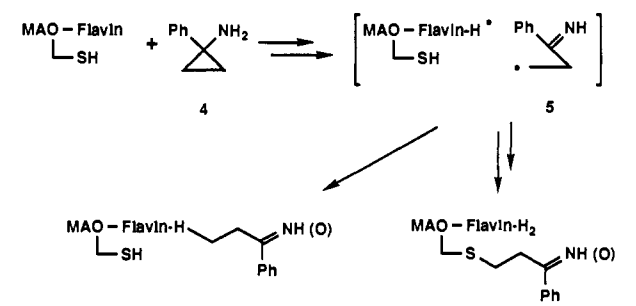
Cyclopropylamines are known to serve as suicide substrate inhibitors of the mammalian enzyme, monoamine oxidase (MAO).[1] This enzyme, which contains a covalently linked flavin grouping, is responsible for the catabolic conversion of biogenic amines such as norepinephrin and serotonin to their corresponding aldehydes and ammonia.[2] One member of this class of inhibitors, *trans*-2-phenylcyclopropylamine, displays potent antidepressant activity[3] owing presumably to its ability to block MAO-catalyzed decomposition of physiologically relevant biogenic amines.

Several research groups have investigated the nature of cyclopropylamine inhibition of MAO. Initially, Singer,[4] Ables,[5] and Silverman[6] speculated that the mechanism for this inactivation involves the generation of a cyclopropylimine (or related cyclopropanone) intermediate, which then undergoes bonding to the enzyme either at a cysteine thiol grouping or the N-5 position of the flavin moiety. In more recent studies of this process, Silverman[7] has accumulated evidence suggesting an alternative

Scheme I



Scheme II



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(2) Singer, T. P. *J. Neural Transm., Suppl.* **1987**, *23*, 1.

(3) (a) Goodman, L. S.; Gilman, A. *The Pharmacological Basis of Therapeutics*, 5th ed.; MacMillan: New York, 1975; p 180. (b) Taylor, J. B.; Kennewell, P. D. *Introductory Medicinal Chemistry*; Ellis Horwood: Chichester, England, 1981; p 20.

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(5) Ables, R. H. *Enzyme-Activated Irreversible Inhibitors*; Seiler, N., Jung, M. J., Koch-Weser, J., Eds.; Elsevier: Amsterdam, 1978; pp 1–12.

(6) Silverman, R. B.; Hoffman, S. J. *Monoamine Oxidase: Structure, Functions, and Altered Functions*; Singer, T. P., VonKorff, R. W., Murphy, D. L., Eds.; Academic Press, New York, 1979; pp 71–79.

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radical mechanism for the inhibition process and the possibility of a single electron transfer (SET) route for MAO catalysis. Silverman's proposal for inactivation by *trans*-2-phenylcyclopropylamine (**1**) involves initial formation of a flavin anion radical–amine cation radical intermediate by SET from **1** to the MAO-bound flavin. On the basis of an observation made earlier by Ingold[8] that cyclopropylaminyl radicals undergo fast ring-opening reactions, it was formulated that the cation radical **2** would open to produce the benzyl radical cation intermediate **3**, which then couples to a thiyl radical, itself generated by H-atom transfer to the flavin semiquinone radical (Scheme I). Further investigations by Silverman led to the suggestion that MAO inactivation by 1-phenylcyclopropylamine **4**[9] involves the formation, by a related sequence, of two enzyme–inhibitor covalent adducts.[10] In this case, the ring-opened radical **5** is suggested to bond to both a cysteine and the flavin moiety (Scheme II).

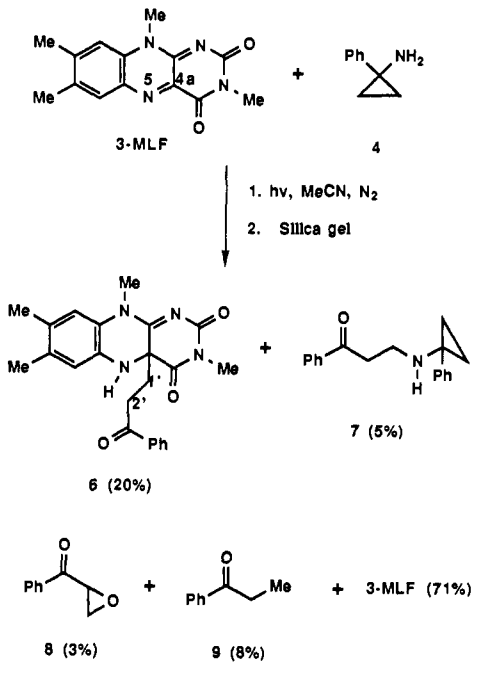
In light of these recent proposals, it is interesting that flavins such as 3-methyllumiflavin (3-MLF) do not participate in uncatalyzed, ground-state SET processes with amines. The reason for this lies in the low reduction potential of the flavin ground electronic state ($E_{1/2}^{S_0}(-)$ = ca. −0.04 V), which means that SET from amine donors ($E_{1/2}(+)$ = ca. 1.5 V) would be highly (ca. 40 kcal/mol) endothermic. In contrast, flavin photochemical reactions with amines, carboxylate salts, thioethers and other donors are documented to be promoted by SET to the easily reduced flavin triplet ($E_{1/2}^{T_1}(-)$ = ca. 2.1 V) and singlet ($E_{1/2}^{S_1}(-)$ = ca. 2.6 V) excited states.[11] An informative study in this area was conducted by Bruice and his co-workers.[12] By use of laser spectroscopic techniques, these workers characterized neutral and radical intermediates formed by SET routes in photoreactions of 3-MLF with phenylthioacetic acid. In addition, Lewis and Krantz[13] have thoroughly documented the operation of SET pathways in photoadditions of propargylic and allenyl amines with 3-MLF. Finally, we have recently defined the nature of SET-induced photochemical processes occurring between 3-MLF and simple primary, secondary, and tertiary amines and their α-silyl analogues.[14]

Much less is known about the characteristics of SET reactions between flavins and cyclopropylamines. This void is surprising in light of the proposals made by Silverman about the nature of MAO inactivation by substrates of this type and of the pharmaceutical importance of the amines. To our knowledge, no model SET chemistry exists to serve as the basis for Silverman's proposals of SET mechanisms for cyclopropylamine suicide MAO inhibition. This void in knowledge and our interest in SET photochemistry combined to stimulate the current investigation in which we have explored SET photoreactions promoted by irradiation of the flavin, 3-MLF, with the cyclopropylamines **1** and **4**. Our aims were to define the nature of the reaction pathways followed in these bona fide flavin SET processes and to characterize the chemistry of the flavin–cyclopropylamine adducts that form.

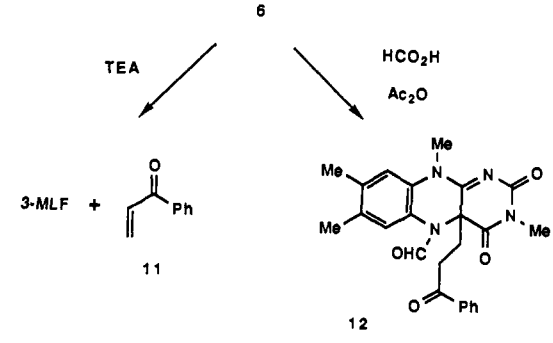
Results

Photochemistry of 3-MLF and 1-Phenylcyclopropylamine (4). Preparative photochemical reactions of 3-MLF[15] and cyclopropylamine **4**[16] were conducted by irradiation ($\lambda > 320$ nm)[17] of either deoxygenated or oxygenated MeCN or MeOH solutions

Scheme III



Scheme IV



of the flavin (ca. 1×10^{-3} M) and amine (ca. 1×10^{-3} M). The progress of each reaction was monitored by UV spectroscopic analysis of 3-MLF concentration and irradiations were terminated when ca. 80% of the 3-MLF had been consumed (determined by the decrease in UV absorbance by 3-MLF and for irradiations of deoxygenated solutions only). Products were then separated by silica gel TLC of the concentrated crude photolysates. 3-MLF conversions based on UV absorbance determinations were typically much greater than those based upon isolated unreactive 3-MLF. This is due to competitive formation of the air-unstable 1,5-dihydro-3-MLF and partial transformation of photoadducts to 3-MLF upon workup and purification.

Irradiation (30 min, 83% conversion) of a degassed N_2-purged MeCN solution containing 3-MLF and amine **4** followed by chromatographic separation led to isolation of the products, **6–9**, shown in Scheme III along with recovered 3-MLF (71%). The products obtained in this process include the commercially available propiophenone **9** (8%), the known[18] acrylophenone epoxide (**8**) (3%), and the amino ketone **7** (5%). Independent syntheses of **8** by reaction of acrylophenone[19] with NaOH and H_2O_2 and of **7** by Michael addition (MeCN, 25 °C) of cyclopropylamine **4** to acrylophenone confirmed the structural assignments of **7** and **8**. The sole flavin-derived product isolated with modest efficiency in this reaction is the 4a-(benzoylethyl)-dihydroflavin **6** (20%). Structural assignment of this substance was made on the basis of its characteristic spectroscopic properties

(7) Silverman, R. B. *J. Biol. Chem.* **1983**, *258*, 14766.
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(10) Silverman, R. B.; Yamasaki, R. B. *Biochemistry* **1984**, *23*, 1322.
(11) Eweg, J. K.; Muller, F.; Visser, A. J. W. G.; Veeger, C.; Bebelaar, D.; Van Voorst, J. D. W. *Photochem. Photobiol.* **1979**, *30*, 463.
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(17) Uranium glass filtered light was used for this purpose.
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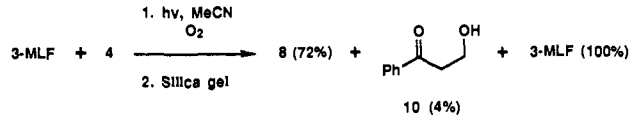
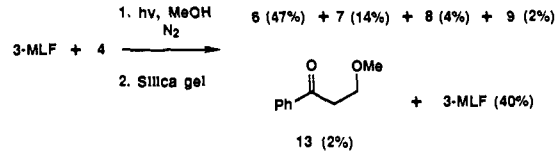
Scheme V



Scheme VI



and comparisons made with data for the closely related C-4a-benzyldihydroflavin analogue.[14,20] Particularly significant in this regard are resonances in the ^1H NMR spectrum of **6** at 2.25 and 2.91 ppm for the diastereotopic H-1′ and H-2′ side chain methylene protons, respectively, and in the ^{13}C NMR spectrum at 29.7 and 31.6 ppm for the analogous carbons and at 197.0 ppm for the phenone carbonyl.

Supporting evidence for the characterization of **6** as a C-4a flavin adduct and information aout its chemical reactivity have come from additional studies. Accordingly, treatment of **6** with formic acid in acetic anhydride results in the production of the N-5 formylated dihydroflavin **12** (Scheme IV), indicating that **6** is a C-4a rather than an N-5 alkylated dihydroflavin. Also, the adduct **6** is transformed in near-quantitative yield to acrylophenone (**11**) and 3-MLF by treatment with triethylamine (0.15 M, MeCN, 25 °C, 20 h). In this process, 3-MLF is most probably derived by oxidation of its dihydro derivative formed by elimination.

The nature of the 3-MLF and cyclopropylamine **4** photoreaction is altered when irradiation is performed on an oxygenated MeCN solution. Under these conditions, 3-MLF is not consumed while the amine **4** is efficiently converted to the epoxide **8** (72%) and the known[18] hydroxy ketone **10** (4%) (Scheme V). It is pertinent that the cyanoarene, 9,10-dicyanoanthracene (DCA), can also be used to SET photosensitize[21] the oxidative transformation of amine **4** to epoxide **8**.

The photochemistry of 3-MLF and cyclopropylamine **4** promoted by irradiation of a deoxygenated MeOH solution has also been explored. As outlined in Scheme VI, the products arising by silica gel TLC of the crude photolysate generated in this manner include the (benzoylethyl)dihydroflavin adduct **6** (47%), amino ketone **7** (14%), epoxy ketone **8** (4%), propiophenone **9** (2%), and methoxy ketone **13** (2%) along with recovered 3-MLF (40%). Methoxy ketone **13** was independently prepared from commercially available β-chloropropiophenone by reaction with MeOH. Irradiation of an oxygenated MeOH solution of 3-MLF and **4** gives mainly the epoxy ketone **8** (81%), a trace quantity of hydroxy ketone **10**, and quantitatively recovered 3-MLF.

Decisive information about the nature of the reaction pathway responsible for formation of the benzoylethyl adduct **6** has come from a careful study of the photoreaction of 3-MLF with cyclopropylamine **4**. ^1H NMR analysis of the photolysate generated by a short (10 min) irradiation period of a thoroughly degassed CD_3OD solution of 3-MLF and **4** in a sealed NMR tube demonstrated that an adduct, **14**, is cleanly generated (Figure 1) as the primary photoproduct of this reaction (Scheme VII). This adduct, which is only modestly stable in air, is also detected as the major product (mixed with 3-MLF) by ^1H NMR analysis of the crude photolysate from preparative irradiation of a deoxygenated MeOH solution of 3-MLF and **4**. Attempts to purify **14** by silica gel chromatography results in its clean transformation to the benzoylethyl adduct **6** and 3-MLF. In addition, **14** reacts

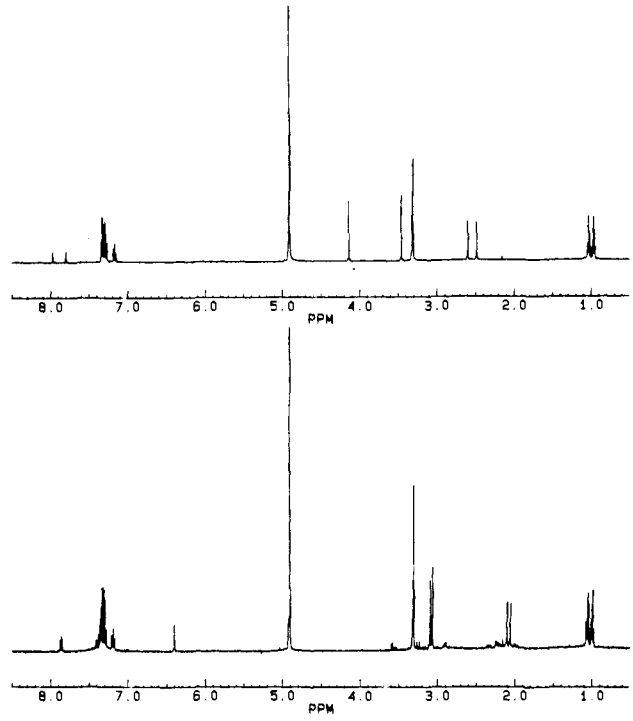
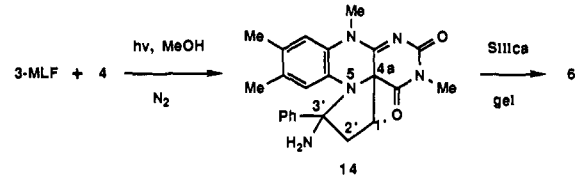


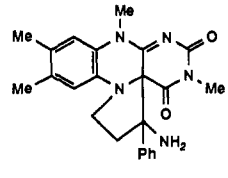
Figure 1. ^1H NMR spectra of 3-MLF (3.3 mM) and cyclopropylamine **4** (6.6 mM) solutions in CD_3OD before (a) and after (b) 10 min of irradiation ($\lambda > 320$ nm) in a degassed, sealed NMR tube. Spectrum b is that of nearly pure photoadduct **14** and unreacted amine **4**.

Scheme VII



over an extended time period (4–6 h) in MeOH to produce **6**, 3-MLF, and methoxy ketone **13**, and with cyclopropylamine **4** to give amino ketone **7** and 3-MLF.

Characterization of **14** as a C-4a,N-5-propanodihydroflavin derivative having the phenyl and amino substituents appended to the C-3′ rather than C-1′ (as in regioisomer **15**) position was aided by an analysis of ^1H and ^{13}C NMR spectroscopic data and comparisons with those accumulated for the known[22] unsubstituted propanodihydroflavin analogue **16**. The latter substance was



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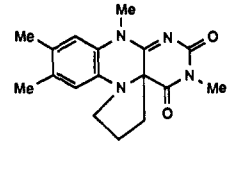


16

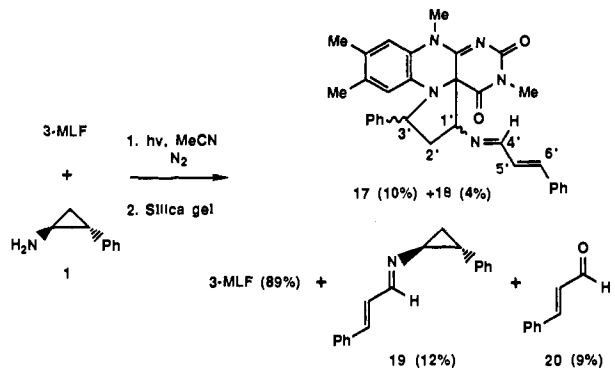
prepared according to the procedure described by Massey[22] via reaction of 1,5-dihydro-3-methylluminflavin (from 3-MLF and $Na_2S_2O_4$) with 1,3-dibromopropane. Distinctive of the structure and regiochemistry of **14** is the ^1H and ^{13}C NMR resonances for the propano chain protons and carbons (see the Experimental Section). The absence in **14** of the downfield-shifted 3′-methylene protons centered at 3.90 ppm seen in the spectrum of its unsubstituted analogue **16** and the presence of a greatly deshielded C-3′ carbon in **14** at 79.2 ppm as compared to the related carbon of **16** (57.2 ppm) are representative of the types of data used in this structural assignment.

(20) Hemmerich, P.; Knappe, W. *Liebigs Ann. Chem.* **1976**, 2037.

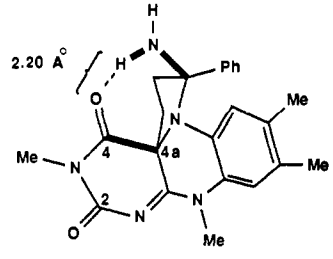
(21) (a) 9,10-Dicyanoanthracene is a well-known SET photosensitizer with an $E_{1/2}^{So}(-) = -0.89$ V and $E_{1/2}^{S1}(-) = 2.0$ V (ref 21b). (b) Mattes, S. L.; Farid, S. *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1983; Vol. 6, Chapter 4.

(22) Gilsa, S.; Massey, V.; Lhoste, J.; Mayhew, S. *Biochemistry* **1974**, *13*, 589.

Scheme VIII



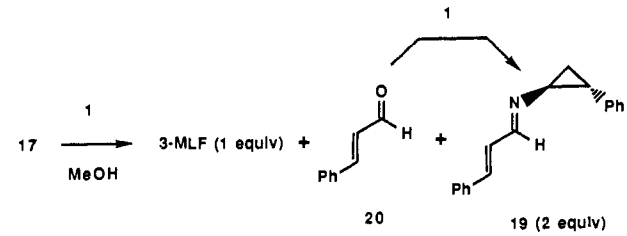
It is interesting that the ^1H and ^{13}C NMR data for **14** show that it exists as a single diastereomer. On first thought, this is surprising since epimerization at the benzylic geminal diamine side chain carbon, C-3′, should occur rapidly by equilibration via a ring-opened amino imine. An analysis of key spectroscopic properties of **14** reveals the factor responsible for the modest stability of **14** and for its existence in the ring-closed form as a single stereoisomer having the cis relationship between the NH_2 and C-4 carbonyl groups appended to the 5-membered pyrrolidine ring. Specifically, a large difference exists between the ^1H NMR chemical shifts of the D_2O-exchangeable NH_2 protons (4.34 and 6.19 ppm) in this substance. This suggests that one of the NH_2 protons is involved in an internal H-bonding interaction. Only in the stereoisomer having a cis NH_2/C-4 carbonyl relative stereochemistry would this interaction be possible. Indeed, the Macromodel (MM2 force field) derived minimum energy structure of **14** (**14-Macromodel**) with this stereochemistry shows a 2.20-Å distance between the corresponding H and O atoms which are well within the distance needed for formation of a strong H-bond.[23] Confirmation of these proposals is found in the ^{13}C NMR spectrum of **14**, which contains a resonance for the C-4 carbonyl carbon at 174.5 ppm, a much lower field value than those of C-4 carbonyls in closely related substances (e.g., 170.2 ppm for **15**, 169.4 ppm for **6**, and 169.3 ppm for **17**). Deshielding effects of H-bonding on carbonyl carbon resonances like this have been documented previously.[24]



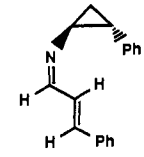
14 Macromodel

Photochemistry of 3-MLF and *trans*-2-Phenylcyclopropylamine (1). Preparative irradiation (10 min, 72% 3-MLF conversion) of a deoxygenated MeCN solution of 3-MLF and the phenylcyclopropylamine **1** followed by silica gel TLC of the concentrated crude photolysate led to isolation of the products shown in Scheme VIII. These include commercially available *trans*-cinnamaldehyde (**20**) (9%), the imine analogue **19** (12%), and the separable diastereomeric 1:2 flavin–amine adducts **17** (10%) and **18** (4%), along with recovered 3-MLF (89%). Assignment of the imine structure to **19** was facilitated by its independent synthesis via reaction of *trans*-cinnamaldehyde with cyclopropylamine **1** (MeOH, 25 °C, 89%). The photoreaction promoted by irradiation of a deoxygenated MeOH solution of 3-MLF and amine **1** follows a similar

Scheme IX



course. TLC separation of the product mixture in this case affords the adducts **17** and **18** in only trace quantities, *trans*-cinnamaldehyde **20** (6%), the corresponding imine **19** (21%), its syn diastereomer **21** (8%), and recovered 3-MLF (80%). That **21** was not the *cis*-cinnamyl isomer of **19** was demonstrated by its nonequivalence to the authentic cis isomer independently prepared by reaction of a photostationary-state mixture of *cis*- and *trans*-cinnamaldehyde (formed by irradiation of **20** in MeCN) with amine **1**.



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The structures of the flavin–amine adducts, **17** and **18**, were assigned on the basis of their characteristic chemical and physical properties. For example, as shown in Scheme IX, reaction of the adduct **17** with excess cyclopropylamine **1** in MeOH at 25 °C results in the formation of 3-MLF (1 equiv) and the cyclopropylimine **19** (2 equiv). This result, along with the high-resolution mass spectrometry derived molecular formula of $C_{32}H_{31}N_5O_2$, suggests that **17** is comprised of two cyclopropylamine and one 3-MLF components. The presence of *trans*-cinnamylimine moieties in both **17** and **18** is evidenced by the appearance of ^1H NMR resonances for the vinyl protons H-6′ and H-5′ at 6.66 and 6.73 ppm (dd, J = 16.0, 8.8 Hz) and 7.02 and 6.98 ppm (d, J = 16.0 Hz), and for the imine protons H-4′ at 8.00 and 7.95 ppm (d, J = 8.8 Hz). Additional structural information has come from comparisons of ^1H and ^{13}C NMR data for **17** and **18** with those of the closely related C-4a,N-5-propanodihydroflavins **14** and **16** (see the Experimental Section). Highly characteristic in this regard are the well-defined multiplets for the H-1′ (e.g., for **18** at 4.15 ppm, dd, J = 7.3, 11.6 Hz), H-2′ (e.g., for **17** at 2.20 ppm, ddd, J = 12.8, 10.0, 4.0 Hz), and H-3′ (e.g. for **18** at 4.82 ppm, dd, J = 7.3, 9.7 Hz) protons in the ^1H NMR spectra and resonances for the C-1′, C-2′, and C-3′ carbons (74.9, 40.1, and 82.7 ppm for **17** and 73.0, 36.9, and 80.4 ppm for **18**, respectively) in the ^{13}C NMR spectra. While the accumulated data allow the assignment of the structures of these adducts, they are insufficient to establish the relative stereochemistry at the 3-chiral centers in each adduct.

Discussion

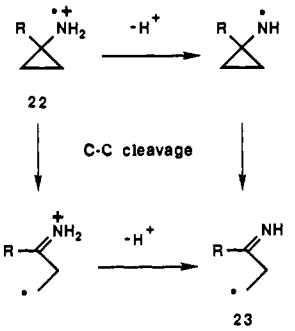
Mechanistic Aspects. Several features of the mechanistic pathways followed in the photochemical reactions described above are worthy of brief comment. The cyclopropylamine–flavin excited-state processes procede via SET sequences. Quenching of 3-MLF singlet and triplet excited states by SET from primary, secondary, and tertiary amines is known to be highly efficient, occurring with rate constants that approach the diffusion-controlled limit (ca. 1×10^{10} M^{-1} s^{-1}).[13] Unlike amine–flavin singlet ion radical pairs which arise by singlet-state SET and undergo back-SET nearly exclusively, those having triplet multiplicity are sufficiently long-lived to participate in secondary reaction processes.[13,25] Amine cation radicals derived by photoinduced SET

(23) For typical N–H to O=C hydrogen bond distances, see: Creighton, T. E. *Proteins*; W. H. Freeman: New York, 1984; p 171.

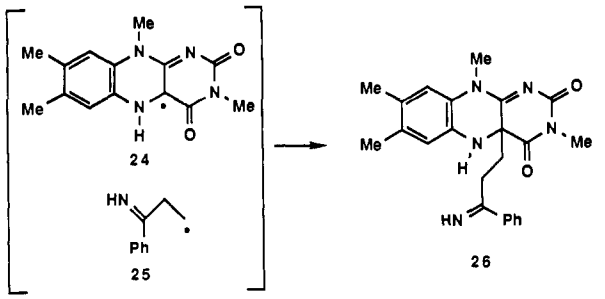
(24) Lauterbur, P. C. *Ann. N.Y. Acad. Sci.* **1958**, *70*, 841. Maciel, G. E.; Savitsky, G. B. *J. Phys. Chem.* **1964**, *68*, 437.

(25) Traber, R.; Vogelmann, E.; Schreiner, S.; Werner, T.; Kramer, H. E. A. *Photochem. Photobiol.* **1981**, *33*, 41.

Scheme X



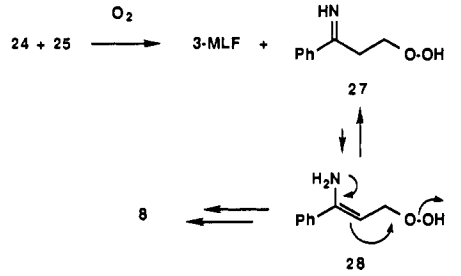
Scheme XI



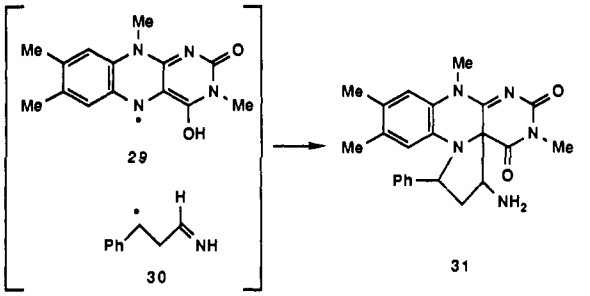
to acceptors typically undergo a variety of secondary reactions, depending upon the nature of the amine and N and α-C substituents.[26] Of relevance to the cyclopropylamine systems probed in this work are the NH deprotonation reactions observed for primary amine cation radicals,[27] and the ring-opening reactions of cyclopropylamine[28] (and related cyclopropanol)[29] cation radicals. Even though it is not difficult to propose that both N–H and C–C bond-cleavage reactions would be open to cyclopropylamine cation radicals, to our knowledge no data are available to enable evaluation of the relative rates of these processes. In contrast, detailed studies by Ingold[8] have shown that cyclopropylaminyl radical ring-opening reactions are exceedingly fast. Thus, while primary cyclopropylamine cation radicals **22** are capable of transforming to neutral β-iminoalkyl radicals **23**, at this point and without further information it is difficult to distinguish between the two pathways for formation of **23** portrayed in Scheme X, which differ in the timing of the N–H and C–C bond ruptures.

Reflective of these modes of cyclopropylamine cation radical reactivity is the SET photochemistry of 3-MLF with 1-phenylcyclopropylamine (**4**). The primary photoreaction occurring in this system involves generation of the N-5, C-4a-propanoflavin adduct **14** (Scheme VII). This photoproduct arises by a pathway involving radical coupling in the radical pair **24+25** (Scheme XI), which is formed by a sequential triplet-state SET, cation radical C–C bond cleavage, and proton transfer (or the reverse) route. The preference for C-4a bonding of the flavin radical to the alkyl radical in this process mimics related selectivities observed for other SET-promoted photoadditions of 3-MLF and related flavins.[16,30] The existence of the primary adduct **26** in its cyclic

Scheme XII



Scheme XIII



geminal diamine form **14**, as discussed above, is due to stabilization offered by intramolecular H-bonding between the NH_2 and the C-4 carbonyl oxygen. Finally, the 4a-benzoylethyl product **6**, observed when the photolysate from 3-MLF and **4** is subjected to silica gel chromatography, arises by hydrolysis of **26**.

Formation of the minor products in the 3-MLF cyclopropylamine **4** photoreactions can be rationalized by use of related radical sequences. Accordingly, disproportionation of the β-iminoethyl radical **25** would provide the precursors of propiophenone (**9**) and phenyl vinyl ketone (**11**). Reaction of the latter substance with amine **24** would produce the amino ketone **7**. The flavin semiquinone radical **24** is known[31] to efficiently disproportionate to yield 3-MLF and its air-unstable 1,5-dihydroflavin derivative. Alternatively, H-atom transfer between radicals **24** and **25** (Scheme XI) can equally well be responsible for the origin of propiophenone, phenyl vinyl ketone, dihydroflavin, and recovered 3-MLF.

The α,β-epoxy ketone **8** is produced efficiently when 3-MLF (or DCA) is irradiated in oxygenated solutions containing the cyclopropylamine **4**. This process, which might be preparatively useful, can again be attributed to a pathway in which the intermediate radical pair **24+25** is trapped by dioxygen to form 3-MLF and the β-hydroperoxy imine **27** (Scheme XII). Cyclization of **27** (perhaps via the enamine form **28**) would then provide **8**.

The photoreactions of 3-MLF with *trans*-2-phenylcyclopropylamine (**1**) proceed by similar SET mechanistic routes. In these cases, the radical pair **29+30** (Scheme XIII) serves as the intermediate responsible for formation of the stereoisomeric adducts **31**, which are precursors of the isolated Schiff base derivatives **17** and **18** (Scheme VIII). *trans*-Cinnamaldehyde (**20**), a detected product and the substance responsible for the formation of imines **17**, **18**, **19**, and **21**, would arise from **30** by one of the number of disproportionation and/or H-atom transfer schemes discussed above.

The regiochemical differences noted for adduct formation in the photoreactions of 3-MLF and cyclopropylamines **1** and **4** are an interesting if not unfamiliar[30] issue. It is not at all clear why the site of radical coupling in the 3-MLF-derived semiquinone radical (interconverting forms **24** and **29**) should depend on the nature of the β-iminoethyl radical (**25** vs **30**). While an explanation based upon steric influences (i.e., bonding of the primary radical **25** at the crowded C-4a center and the secondary benzylic radical **30** at the less crowded N-5 center) might seem satisfactory,

(26) Pienta, N. J. *Photoinduced Electron Transfer*; Fox, M. A., Chanon, M., Eds.; 1988, Elsevier: Amsterdam, 1988, Part C.

(27) Lewis, F. D.; Zebrowski, B. E.; Correa, P. E. *J. Am. Chem. Soc.* **1984**, *106*, 187. Lewis, F. D.; Reddy, G. D. *Ibid.* **1989**, *111*, 6465. Sugimoto, A.; Sumida, R.; Tamai, N.; Inoue, H.; Otsugi, Y. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3500. For a current review of this topic, see: Khan, J.; Cohen, S. G. *J. Org. Chem.* **1991**, *56*, 938.

(28) Qin, X.-Z.; Williams, F. *J. Am. Chem. Soc.* **1987**, *109*, 595.

(29) Mariano, P. S.; Stavinoha, J.; Bay, E. *Tetrahedron* **1981**, *37*, 3385.

(30) Hemmerich, P.; Knappe, W. *Liebigs Ann. Chem.* **1976**, 2037. Hemmerich, P.; Massey, V.; Walker, W. H. *Helv. Chim. Acta* **1967**, *50*, 2269. Hemmerich, P.; Gartner, B.; Zeller, E. A. *Eur. J. Biochem.* **1976**, *63*, 211. Hemmerich, P., Massey, V.; Weber, G. *Nature* **1967**, 728. Hemmerich, P.; Brustlein, M.; Knappe, W. R. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 804. Ott, U.; Franke; Kramer, E. A.; Traber, R. H. *Photochem. Photobiol.* **1989**, *49*, 131.

(31) Traber, R.; Kramer, H. E. A.; Hemmerich, P. *Pure Appl. Chem.* **1982**, *54*, 1651.

it is clear that photoaddition regioselecivity in flavin excited-state reactions is in general both a complicated and not a well-understood topic.[14,32]

Potential Relationships to MAO Inactivation by Cyclopropylamines. The current study has provided information about the nature of bona fide SET reactions of a flavin with the cyclopropylamines **1** and **4**. Since SET mechanisms have been suggested to account for the inactivation of the flavin-containing enzyme, monoamine oxidase (MAO), by these same amines, the results are potentially relevant to these biochemical processes. As mentioned in the introductory section, Silverman and his coworkers[9] have attributed the inactivation of MAO by 1-phenylcyclopropylamine (**4**) to the formation of two inhibitor–enzyme adducts (Scheme II). It is interesting that one of these, the benzoylethylflavin modification shown in Scheme II, has a structure similar to the dihydroflavin **6** formed by hydrolytic cleavage of the primary photoadduct **14**. Even though the MAO–flavin adduct from cyclopropylamine **4** has the benzoylethyl group linked to N-5 of the flavin moiety while **6** clearly possesses a C-4a linkage, the photochemical and enzyme-derived products appear to be quite similar. This analogy holds also for the MAO–thioether adduct (Scheme II), which could in theory be derived by S-alkylation of a cysteine thiol via Michael addition to phenyl vinyl ketone formed from **4** through an SET pathway. The latter substance is also produced in the model photo-SET reaction of 3-MLF with cyclopropylamine **4**. Lastly, the close relationships which exist between the 3-MLF-photoinduced and MAO ground-state reactions with *trans*-2-phenylcyclopropylamine (**1**) provide further evidence for the SET nature of MAO inactivation proposed by Silverman. Accordingly, the major product generated in the photochemical process is cinnamaldehyde, a substance which might be responsible for formation of the cysteine thioether modification in the inactivation of MAO by **1** (Scheme I).

In summary, the flavin–cyclopropylamine photochemical studies described above have provided information about the nature of and mechanistic pathways for processes promoted by SET. Moreover, the parallel behavior of these bona fide SET processes and those suggested for MAO inactivations by these same cyclopropylamines is consistent with the SET routes for the MAO inactivation and (perhaps) catalytic processes proposed by Silverman.

Experimental Section

General. ^{1}H NMR (200 MHz or 400 MHz) and ^{13}C NMR (50 MNz) spectra were recorded in $CDCl_3$ solutions unless otherwise noted. IR spectra were recorded in $CHCl_3$ solutions. Preparative TLC was performed on 20 × 20 cm plates coated with Merck-EM type 60 GH-254 silica gel. All reactions were run under a dry N_2 atmosphere unless otherwise specified. All new compounds isolated in the course of this study were characterized by spectroscopic methods and were shown to be greater than 90% pure by ^{13}C and ^{1}H NMR analysis. The exception to this is adduct **14**, whose decomposition to form 3-MLF and its ketone analogue **6** during chromatographic separation leads to ca. 70% purity.

Preparative photochemical reactions were run in an apparatus consisting of a 450-W Hanovia medium-pressure, mercury lamp (ACE) surrounded by a uranium glass filter ($\lambda > 320$ nm) in a water-cooled quartz immersion well, surrounded by Pyrex tubes or a well containing the solution being irradiated. The photolysis solutions were purged with deoxygenated N_2 both before and during irradiations. The progress of each preparative photochemical reaction was monitored by UV absorption spectroscopy. The solvents used in the photoreactions were spectrograde CH_3CN (Baker) or CH_3OH (Baker) unless otherwise specified. Photoreactions in sealed NMR tubes were conducted with this same apparatus. 3-NMethyllumiflavin (3-MLF) was synthesized by the procedure described by Hemmerch.[15] 1-Phenylcyclopropylamine (**4**) was prepared by the method of Silverman.[16] *trans*-2-Phenylcyclopropylamine (**1**) was obtained as its HCl salt from Aldrich.

Preparative Irradiation of 3-MLF and 1-Phenylcyclopropylamine (4) in MeCN. A solution of 70 mg (0.26 mmol) of 3-MLF and 52 mg (0.39 mmol) of the cyclopropylamine **4** in 165 mL of MeCN was irradiated in a preparative apparatus for 30 min. Irradiation was terminated when ca. 83% of 3-methyllumiflavin had been consumed (by UV monitoring), and the photolysate was concentrated in vacuo. The residue was subjected to preparative TLC (ether) to give 21 mg (20%) of the flavin adduct **6** as a yellow powder (mp 115–120 °C), 4 mg (8%) of propiophenone (**9**), 5 mg (5%) of the amino ketone **7** as a yellow solid (mp 68–70 °C), 2 mg (3%) of the known[4] epoxide **8** as a yellow solid (mp 45 °C), and 50 mg (71%) of recovered 3-MLF.

6: ^{1}H NMR δ 2.17 (s, 3 H, C-8), 2.19 (s, 3 H, C-7), 2.25 (m, 2 H, H-2′), 2.91 (m, 2 H, H-1′), 3.28 (s, 3 H, N-10), 3.61 (s, 3 H, N-3), 4.70 (s, 1 H, NH), 6.60 (s, 1 H, C-6), 6.84 (s, 1 H, C-9), 7.40, 7.52, and 7.83 (m, 5 H, aromatic Ph); ^{13}C NMR δ 19.3 (C-7 CH_3 and C-8 CH_3), 28.0 (N-10 CH_3), 29.7 (C-2′), 31.6 (C-1′), 32.1 (N-3 CH_3), 56.3 (C-4a), 116.9 (C-6), 117.5 (C-9), 125.7 (C-8), 127.9, 128.6, 133.4, and 136.2 (aromatic Ph), 128.8 (C-7), 129.9 (C-9a), 134.6 (C-5a), 155.8 (C-10a), 162.5 (C-2), 169.4 (C-4), 197.0 (C-3′); IR 3346, 1721, 1665, 1626, 1563 cm^{-1}; EIMS *m/e* (relative intensity) 404 (M^+, 34), 347 (18), 332 (19), 289 (14), 271 (100), 246(5), 105 (1); HRMS (EI) *m/e* 404.1850 ($C_{23}H_{24}O_3N_4$ requires 404.1848).

7: ^{1}H NMR δ 1.00 (m, 4 H, H-2 and H-3), 2.10 (brs, 1 H, NH), 2.93 (m, 4 H, H-4 and H-5), 7.30 and 7.90 (m, 10 H, aromatic Ph); ^{13}C NMR δ 15.8 (C-2 and C-3), 39.2 (C-5), 41.4 (C-4), 42.5 (C-1), 126.3, 127.3, 127.9, 128.3, 128.5, 133.0, 137.5, and 144.5 (aromatic Ph), 199.7 (CO); IR 3309, 3006, 1679 cm^{-1}; CIMS *m/e* (relative intensity) 266 (M^+ + 1, 10), 265 (11), 244 (18), 160 (37), 158 (12), 146 (26), 133 (17), 117 (66), 105 (100); HRMS (CI) *m/e* 265.1442 ($C_{18}H_{19}ON$ requires 265.1466).

Spectroscopic data for **8** matched that reported by Hasegawa[18] and independently synthesized material (see below).

Preparation of Amino Ketones 7. A solution containing 60 mg (0.45 mmol) of acrylophenone (**11**)[19] and 60 mg (0.45 mmol) of 1-phenylcyclopropylamine (**2**) in 1 mL of CH_3CN was stirred at 25 °C for 20 h. The mixture was concentrated in vacuo to give a residue which was subjected to preparative TLC (ether) to yield 95 mg (80%) of the amine **7**.

Preparative Irradiation of 3-MLF and 1-Phenylcyclopropylamine (4) in Air-Saturated MeCN. An air-saturated solution of 13 mg (0.048 mmol) of 3-MLF and 20 mg (0.15 mmol) of the cyclopropylamine **4** in 20 mL of MeCN was irradiated for 50 min. Concentration of the photolysate in vacuo followed by preparative TLC (ether) gave 16 mg (72%) of acrylophenone epoxide (**8**),[18] 1 mg (4%) of 3-hydroxypropiophenone (**10**),[18] and 13 mg (100%) of recovered 3-MLF. Spectroscopic data for **10** matched that reported by Hasegawa.[18]

Preparative Irradiation of 3-MLF and 1-Phenylcyclopropylamine (4) in MeOH. A solution of 50 mg (0.19 mmol) of 3-MLF and 49 mg (0.37 mmol) of the cyclopropylamine **4** in 130 mL of MeOH was irradiated in a preparative apparatus for 40 min. Concentration of the photolysate in vacuo gave a residue which was subjected to preparative TLC (33% ethyl acetate/hexane) to give 35 mg (47%) of flavin adduct **6**, 14 mg (14%) of the amino ketone **7**, 2 mg (4%) of acrylophenone epoxide (**8**),[18] 1 mg (2%) of propiophenone (**9**),[33] 1 mg (2%) of 3-methoxypropiophenone (**13**), and 20 mg (40%) of recovered 3-MLF.

13: ^{1}H NMR δ 3.22 (t, J = 6.5 Hz, 2 H, H-2), 3.35 (s, 3 H, OCH_3), 3.80 (t, J = 6.5 Hz, 2 H, H-3), 7.50 and 7.95 (m, 5 H, aromatic Ph); ^{13}C NMR 38.6 (C-2), 58.9 (OCH_3), 67.8 (C-3), 128.1, 128.6, 133.1, and 136.9 (aromatic Ph), 198.2 (CO); IR 3061, 2892, 1685, 1597, 1580, 1449, 1117 cm^{-1}; EIMS *m/e* (relative intensity) 164 (M^+, 51), 132 (20), 105 (100), 77 (16); HRMS (EI) *m/e* 164.0837 ($C_{10}H_{12}O_2$ requires 164.0837).

Preparation of 3-Methoxypropiophenone (13). A solution containing 700 mg (4.2 mmol) of 3-chloropropiophenone (Aldrich) in 20 mL of CH_3OH was stirred at reflux for 5 h, cooled to 25 °C, and concentrated in vacuo. The residue was dissolved in 50 mL of water and extracted with ether. The ethereal extracts were dried and concentrated in vacuo to give 610 mg (89%) of 3-methoxypropiophenone (**13**).

Preparative Irradiation of 3-MLF and 1-Phenylcyclopropylamine (4) in Air-Saturated MeOH. An air-saturated solution of 11 mg (0.041 mmol) of 3-MLF and 20 mg (0.15 mmol) of the cyclopropylamine **4** in 15 mL of MeOH was irradiated for 1 h. Concentration of the photolysate in vacuo followed by preparative TLC (ether) gave 18 mg (81%) of acrylophenone epoxide (**8**),[18] a trace amount of 3-hydroxypropiophenone (**10**),[18] and 10 mg (91%) of recovered 3-MLF.

9,10-Dicyanoanthracene (DCA) Sensitized Irradiation of 1-Phenylcyclopropylamine (4) in Air-Saturated 20% MeCN/MeOH. An air-saturated solution (165 mL) of 20% MeCN/MeOH containing 89 mg (0.67 mmol) of the cyclopropylamine **4** and 10 mg (4.4×10^{-2} mmol) of DCA was irradiated for 12 h. The photolysate was concentrated in vacuo to give a residue which was subjected to preparative TLC (25% ether/hexane) to yield 30 mg (30%) of acrylophenone epoxide (**8**)[18] and a trace amount of 3-hydroxypropiophenone (**10**).[18]

(32) Clerin, D.; Bruice, T. C. *J. Am. Chem. Soc.* 1974, *96*, 5571.

(33) Commercially available from the Aldrich Chemical Co.

Photoreaction of 3-MLF and Cyclopropylamine 4. Isolation of the Intermediate 14. A solution of 70 mg (0.26 mmol) of 3-MLF and 52 mg (0.39 mmol) of the cyclopropylamine **4** in 165 mL of MeOH was irradiated in a preparative apparatus for 10 min. The photolysate was concentrated in vacuo to give a residue which was dissolved in 50 mL of ether. The mixture was filtered, and the precipitate was collected and dried to give 63 mg of a mixture containing 3-MLF and the intermediate **14** in the ratio of 1.4:1. Intermediate **14** was characterized by spectroscopic analysis of this mixture since attempts to separate a pure sample of this substance by TLC led to its decomposition to 3-MLF and its ketone analogue **6**.

14: ^{1}H NMR δ 1.88 (ddd, J = 14.0, 7.0, 6.6 Hz, 1 H, H-1′), 2.03 (s, 3 H, C-8), 2.08 (s, 3 H, C-7), 2.35 (ddd, J = 14.0, 10.5, 1.5 Hz, 1 H, H-1′), 2.83 (ddd, J = 18.3, 7.0, 1.5 Hz, 1 H, H-2′), 2.90 (ddd, J = 18.3, 10.5, 6.6 Hz, 1 H, H-2′), 3.08 (s, 3 H, N-10), 3.10 (s, 3 H, N-3), 4.34 (s, 1 H, NH_2), 6.19 (s, 1 H, NH_2), 6.38 (s, 2 H, C-6 and C-9), 7.40 and 7.80 (m, 5 H, aromatic Ph); ^{13}C NMR δ 18.7 and 19.3 (C-7 CH_3 and C-8 CH_3), 22.9 (C-2′), 27.4 (C-1′), 27.7 (N-10 CH_3), 30.3 (N-3 CH_3), 60.0 (C-4a), 78.9 (C-3′), 113.9 (C-6), 117.5 (C-9), 126.5 (C-8), 126.7, 128.2, 132.5, and 137.5 (aromatic Ph), 127.8 (C-7), 128.5 (C-9a), 131.1 (C-5a), 151.1 (C-10a), 166.6 (C-2), 174.5 (C-4); IR 3311, 1718, 1666, 1586, 1557 cm^{-1}; EIMS m/e (relative intensity) 403 (M^+, 19), 270 (93), 244 (15), 213 (55), 130 (69), 104 (100), 77 (47); HRMS (EI) m/e 403.2031 ($C_{23}H_{25}O_2N_5$ requires 403.2008).

3-Methyl-4a,5-propano-4a,5-dihydrolumiflavin (16). This substance was prepared by the method of Ghisla[22] for NMR comparison purposes.

16: ^{1}H NMR δ 1.85 (m, 2 H, H-2′), 2.17 (s, 3 H, C-8), 2.18 (s, 3 H, C-7), 2.26 (m, 1 H, H-1′), 2.38 (ddd, J = 12.4, 6.8, 2.6 Hz, 1 H, H-1′), 3.22 (s, 3 H, N-10), 3.60 (s, 3 H, N-3), 3.61 (m, 1 H, H-3′), 4.13 (ddd, J = 10.2, 8.7, 4.3 Hz, 1 H, H-3′), 6.60 (s, 1 H, C-6), 6.73 (s, 1 H, C-9); ^{13}C NMR δ 19.1 and 19.4 (C-7 CH_3 and C-8 CH_3), 20.6 (C-2′), 28.5 (N-10 CH_3), 31.3 (N-3 CH_3), 41.8 (C-1′), 57.2 (C-3′), 67.3 (C-4a), 116.2 (C-6), 117.7 (C-9), 123.4 (C-8), 127.5 (C-7), 134.3 (C-5a and C-9a), 156.5 (C-10a), 163.9 (C-2), 170.2 (C-4).

NMR-Tube Irradiations of 3-MLF and 1-Phenylcyclopropylamine (4). The samples for irradiation were prepared by the following procedure. A solution (0.4 mL) containing 3-MLF and the cyclopropylamine **4** in CD_3CN or CD_3OD in a Pyrex NMR tube was subjected to repeated freeze–thaw cycles before the tubes were sealed under vacuum. The solutions were then irradiated by using uranium glass filtered light ($\lambda >$ 320 nm). ^{1}H NMR analysis of the photolysate was performed on the sealed samples. For irradiation of 3-MLF (3.3 mM) and the cyclopropylamine **4** (6.6 mM) in CD_3OD, ^{1}H NMR monitoring indicated that 3-MLF was consumed, the cyclopropylamine **4** decreased, and intermediate **14** was formed as a sole product. For the 30-min irradiation of 3-MLF (3.3 mM) and the cyclopropylamine **4** (6.6 mM) in CD_3CN, ^{1}H NMR analysis indicated that 3-MLF disappeared and the cyclopropylamine **4** decreased with simultaneous formation of an unidentified flavin adduct, which slowly converted to the intermediate **14** upon standing in the dark.

Preparative Irradiation of 3-MLF and *trans*-2-Phenylcyclopropylamine (1) in MeCN. A solution of 60 mg (0.22 mmol) of 3-MLF and 30 mg (0.22 mmol) of the cyclopropylamine **1** in 170 mL of MeCN was irradiated in a preparative apparatus for 10 min. UV monitoring showed that 72% of 3-MLF was consumed. The photolysate was concentrated in vacuo. The residue was dissolved in ether and filtered to remove 3-MLF and then subjected to preparative TLC (50% hexane/ethyl acetate) to give 11 mg (10%) of the adduct **17** as a yellow solid (mp 137–142 °C), 5 mg (4%) of the adduct **18** as a yellow solid (mp 126–128 °C), 7 mg (12%) of the imine **19**, 3 mg (9%) of *trans*-cinnamaldehyde (**20**),[33] and 54 mg (89%) of recovered 3-MLF. Attempts to crystallize **17** or **18** resulted in their decomposition to 3-MLF.

17: ^{1}H NMR δ 2.00 (s, 3 H, C-8 CH_3), 2.15 (s, 3 H, C-7 CH_3), 2.20 (ddd, J = 12.8, 10.0, 4.0 Hz, 1 H, H-2′), 2.32 (dd, J = 12.8, 7.4 Hz, 1 H, H-2′), 3.22 (s, 3 H, N-10 CH_3), 3.50 (s, 3 H, N-3 CH_3), 4.09 (d, J = 4.0 Hz, 1 H, H-1′), 5.17 (dd, J = 10.0, 7.4 Hz, 1 H, H-3′), 6.48 (s, 1 H, C-6), 6.66 (dd, J = 16.0, 8.8 Hz, 1 H, H-5′), 6.71 (s, 1 H, C-9), 7.02 (d, J = 16.0 Hz, 1 H, H-6′), 7.40 and 7.75 (m, 10 H, aromatic Ph), 8.00 (d, J = 8.8 Hz, 1 H, H-4′); ^{13}C NMR δ 19.2 and 19.4 (C-7 CH_3 and C-8 CH_3), 28.8 (N-10 CH_3), 31.3 (N-3 CH_3), 40.1 (C-2′), 74.7 (C-4a), 74.9 (C-1′), 82.7 (C-3′), 116.0 (C-6), 118.0 (C-9), 123.9 (C-8), 126.7, 126.9, 127.0, 127.5, 128.4, 128.8, 129.6, 134.2, and 144.0 (aromatic Ph and C-5′), 128.3 (C-7), 135.3 (C-9a), 135.8 (C-5a), 144.6 (C-6′), 156.5 (C-10a), 163.0 (C-2), 165.6 (C-4′), 169.3 (C-4); IR 3407, 3001, 1728, 1674, 1633, 1557, 1519, 1493, 1449 cm^{-1}; EIMS m/e (relative intensity) 517 (M^+, 12), 460 (4), 356 (8), 341 (8), 271 (100), 270 (86), 253 (6), 247 (57), 241 (19), 227 (6), 213 (18), 185 (4); HRMS (EI) m/e 517.2474 ($C_{32}H_{31}O_2N_5$ requires 517.2478).

18: ^{1}H NMR δ 2.00 (s, 3 H, C-8 CH_3), 2.16 (s, 3 H, C-7 CH_3), 2.20 (m, 1 H, H-2′), 2.49 (m, 1 H, H-2′), 3.19 (s, 3 H, N-10 CH_3), 3.59 (s, 3 H, N-3 CH_3), 4.15 (dd, J = 11.6, 6.3 Hz, 1 H, H-1′), 4.82 (dd, J = 9.7, 7.3 Hz, 1 H, H-3′), 6.43 (s, 1 H, C-6), 6.73 (dd, J = 16.0, 8.8 Hz, 1 H, H-5′), 6.74 (s, 1 H, C-9), 6.98 (d, J = 16.0 Hz, 1 H, H-6′), 7.35 and 7.69 (m, 10 H, aromatic Ph), 7.95 (d, J = 8.8 Hz, 1H, H-4′); ^{13}C NMR δ 19.2 and 19.3 (C-7 CH_3 and C-8 CH_3), 28.3 (N-10 CH_3), 31.3 (N-3 CH_3), 36.9 (C-2′), 71.4 (C-4a), 73.0 (C-1′), 80.4 (C-3′), 115.8 (C-6), 118.3 (C-9), 124.6 (C-8), 126.6, 127.0, 127.3, 127.7, 128.4, 129.0, 129.6, 133.8, and 143.5 (aromatic Ph and C-5′), 128.0 (C-7), 135.1 (C-9a), 135.3 (C-5a), 144.8 (C-6′), 156.3 (C-10a), 164.6 (C-2), 165.8 (C-4′), 168.6 (C-4); IR 3390, 2921, 1726, 1682, 1652, 1633, 1567, 1519, 1453 cm^{-1}; EIMS m/e (relative intensity) 517 (M^+, 95), 460 (35), 406 (10), 403 (10), 356 (33), 341 (31), 330 (10), 314 (10), 271 (100), 270 (36), 247 (50), 241 (14); HRMS (EI) m/e 517.2506 ($C_{32}H_{31}O_2N_5$ requires 517.2478).

19: ^{1}H NMR δ 1.47 (ddd, J = 7.0, 6.6, 5.5 Hz, 1 H, H-3), 1.60 (ddd, J = 9.5, 5.5, 4.1 Hz, 1 H, H-3), 2.46 (ddd, J = 9.5, 6.6, 3.0 Hz, 1 H, H-1), 3.05 (ddd, J = 7.0, 4.1, 3.0 Hz, 1 H, H-2), 6.90 (m, 2 H, H-5 and H-6), 7.30 (m, 10 H, aromatic Ph), 8.15 (dd, J = 4.9, 3.5 Hz, 1 H, H-4); ^{13}C NMR 18.6 (C-3), 27.1 (C-1), 52.9 (C-2), 125.8, 126.0, 127.1, 127.0, 128.3, 128.8, 129.0, 137.9, and 141.1 (aromatic Ph and C-5), 140.5 (C-6), 160.9 (C-4); IR 3395, 3027, 1677, 1630, 1604, 1496, 1449 cm^{-1}; EIMS m/e (relative intensity) 247 (M^+, 41), 192 (5), 143 (100), 131 (24), 115 (74); HRMS (EI) m/e 247.1358 ($C_{18}H_{17}N$ requires 247.1361).

Preparation of Imine 19. A solution containing 50 mg (0.37 mmol) of *trans*-cinnamaldehyde (**20**) (Aldrich) and 70 mg (0.52 mmol) of *trans*-2-phenylcyclopropylamine (**1**) in 200 mL of CH_3OH was stirred at 25 °C for 1 h. The mixture was concentrated in vacuo to give a residue which was subjected to preparative TLC (66% hexane/ethyl acetate) to yield 82 mg (89%) of the imine **19**.

Preparative Irradiation of 3-MLF and *trans*-2-Phenylcyclopropylamine (1) In MeOH. A solution of 60 mg (0.22 mmol) of 3-MLF and 30 mg (0.22 mmol) of the cyclopropylamine **1** in 170 mL of MeOH was irradiated for 10 min. UV monitoring showed that 19% of 3-MLF was consumed. The photolysate was concentrated in vacuo. The residue was dissolved in ether and filtered to remove 3-MLF. The filtrate was concentrated in vacuo, and the residue obtained was subjected to preparative TLC (66% hexane/ethyl acetate) to give 12 mg (21%) of adduct **19**, 4 mg (8%) of imine **21**, 2 mg (6%) of *trans*-cinnamaldehyde (**20**), a trace amount of adduct **17**, and 48 mg (80%) of recovered 3-MLF.

21: ^{1}H NMR δ 1.52 (m, 2 H, H-3), 2.42 (m, 1 H, H-1), 3.25 (m, 1 H, H-2), 6.8 (m, 2 H, H-5 and H-6), 7.3 (m, 10 H, aromatic), 8.15 (d, J = 7.8 Hz, 1 H, H-4); ^{13}C NMR δ 16.1 (C-3), 26.3 (C-1), 48.6 (C-2), 125.7, 127.1, 127.8, 128.6, 128.7, 128.8, 129.1, 136.0, and 138.3 (aromatic Ph and C-5), 139.8 (C-6), 161.3 (C-4); IR 3395, 3025, 1678, 1630, 1603, 1497, 1449 cm^{-1}; EIMS m/e (relative intensity) 247 (M^+, 54), 246 (18), 170 (14), 149 (29), 144 (13), 143 (100), 132 (20), 131 (22), 117 (13), 116 (17), 115 (48); HRMS (EI) m/e 247.1376 ($C_{18}H_{17}N$ requires 247.1361).

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra for compounds **3**, **5**, **9**, **10**, **11**, **13**, **14**, **15**, and **17** (18 pages). Ordering information is given on any current masthead page.