7-(hydroxyamino)coumarin **9**. An analytical sample was obtained by the method used for **3b**: mp >280 °C dec; $[\alpha]_D$ −56.97° (c 0.25, MeOH); IR (KBr disk ν_{max} 3200, 3070, 1700, and 1610 cm^{-1}; UV (EtOH) λ_{max} 234 (ϵ 1.72 × 10^4) and 282 nm (ϵ 3.09 × 10^4); ^1H NMR (DMSO-d_6, 300 MHz) δ 1.08 (3 H, s, 5′-Me), 1.28 (3 H, s, 5′-Me), 2.21 (3 H, s, Me), 2.24 (3 H, s, Me), 3.46 (3 H, s, 4′-OMe), 3.63 (1 H, d, J = 10 Hz, 4′-H), 4.13 (1 H, t, J = 2.5 Hz, 2′-H), 5.46 (1 H, dd, J = 3, 10 Hz, 3′-H), 5.54 (1 H, d, J = 2.5 Hz, 1′-H), 5.91 (1 H, t, J = 3 Hz, 4″-H), 6.76 (1 H, t, J = 3 Hz, 3″-H), 7.02, 7.19, 7.36 (3 s, D_2O exchangeable), 7.07 (1 H, d, J = 9 Hz, 6-H), 7.74 (1 H, d, J = 9 Hz, 5-H), and 11.65 (1 H, s, NH, D_2O exchangeable); MS (FAB), m/e 489 (M + H), 282, 208, 108 (base). Anal. (free base) Calcd for $C_{24}H_{28}N_2O_9 \cdot H_2O$: C, 56.92; H, 5.98; N, 5.54. Found: C, 56.79; H, 5.66; N, 5.47.

3-Amino-4-hydroxy-8-methyl-7-[(3-*O*-carbamyl-2-*O*-acetylnoviosyl)oxy]coumarin Hydrochloride (8b). The title compound **8b** was prepared from oxazole **7b**[10] by the method described for **3b** in 97% yield. This crude material was contaminated with about 25% of 7-hydroxy-3-aminocoumarin **9**. The pure sample was obtained as a free base after column chromatography (SiO_2, c-NH_4OH/MeOH/CH_2Cl_2, 3:27:70) in 45% yield: mp 195–215 °C dec; IR (KBr disk) ν_{max} 3400, 1740, 1670, and 1610 cm^{-1}; UV (EtOH) λ_{max} 236 (ϵ 1.22 × 10^4) and 298 nm (ϵ 1.28 × 10^4); ^1H NMR (CD_3OD) δ 1.19 (3 H, s, 5′-Me), 1.37 (3 H, s, 5′-Me), 2.15 (3 H, s, 2′-OAc), 2.30 (3 H, s, Ar-Me), 3.49 (1 H, d, J = 9 Hz, 4′-H), 3.61 (3 H, s, 4′-OMe), 5.44 (2 H, m, 2′-H and 3′-H), 5.61 (1 H, s, 1′-H), 7.12 (1 H, d, J = 8.8 Hz, Ar H), and 7.77 (1 H, d, J = 8.8 Hz, Ar H).

3-Amino-4-hydroxy-8-methyl-7-[(3-*O*-carbamylnoviosyl)oxy]coumarin Hydrochloride (Novenamine Hydrochloride) (8a). The title compound **8a** was prepared from oxazole **7a**[10] by the procedure described for **3a** in 41% yield. The low yield was due to the incompletion of the reaction. The pure material was obtained as a free base (novenamine) after column chromatography (SiO_2, c-NH_4OH/MeOH/CH_2Cl_2, 3:27:70) in 21% yield: mp 215–235 °C dec (lit.[9] mp >220 °C dec); IR (KBr disk) ν_{max}: 3400, 3200, 1720, 1670, and 1610 cm^{-1}; UV (EtOH) λ_{max} 236 (ϵ 1.14 × 10^4) and 298 nm (ϵ 1.15 × 10^4); ^1H NMR (DMSO-d_6) δ 1.05 (3 H, s, 5′-Me), 1.24 (3 H, s, 5′-Me), 2.15 (3 H, s, Ar-Me), 3.45 (3 H, s, 4′-OMe), 3.47 (1 H, d, J = 10 Hz, 4′-H), 4.03 (1 H, t, J = 2.5 Hz, 2′-H), 5.14 (1 H, dd, J = 3, 10 Hz, 3′-H), 5.43 (1 H, d, J = 2.5 Hz, 1′-H), 6.6 (br, CONH, exchanged with D_2O), 6.98 (1 H, d, J = 9 Hz, Ar H), 7.2 (br, CONH, exchanged with D_2O), and 7.64 (1 H, d, J = 9 Hz, Ar H).

Acknowledgment. We would like to thank the Analytical Research Department for the elemental analyses and the spectroscopic data.

Exploratory, Mechanistic, and Synthetic Aspects of Silylarene–Iminium Salt SET Photochemistry. Studies of Diradical Cyclization Processes and Applications to Protoberberine Alkaloid Synthesis

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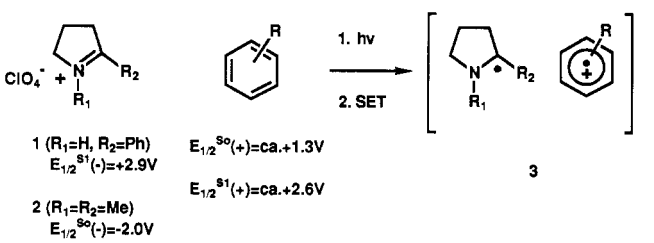
Received April 29, 1988

The photochemistry of a number of 2- and 1-(*o*-((trimethylsilyl)methyl)benzyl)-substituted 3,4-dihydroisoquinolinium perchlorates has been studied as part of efforts to probe the application of diradical cyclization methodologies to protoberberine and spirobenzyl isoquinoline alkaloid synthesis. Routes for preparation of the 2-(silylxylyl)-3,4-dihydroisoquinolinium salts have been developed based upon silver perchlorate induced, N-alkylation reactions between appropriate 3,4-dihydroisoquinolines and *o*-((trimethylsilyl)methyl)benzyl halides. Irradiation of these salts leads to efficient production of cyclization products having the tetracyclic protoberberine skeleton via pathways involving sequential single-electron transfer–desilylation and diradical coupling. This strategy has been employed to synthesize two representative protoberberines, xylopinine and stylopine, both of which contain alkoxy substitution patterns in the aromatic A and D rings characteristic of members of this alkaloid family. Studies of 1-(silylxylyl)-3,4-dihydroisoquinolinium perchlorate photochemistry have demonstrated that cyclization of the diradical intermediate, formed by sequential single-electron transfer–desilylation pathways, is competitive with a 1,4-H-shift process. The latter route leads to eventual production of desilylated dihydroisoquinolinium salts. The operation of this reaction pathway has been probed by deuterium-labeling methods. Finally, the viability of dipolar cyclization routes, initiated by fluoride-induced desilylation of the 1-(silylxylyl)-3,4-dihydroisoquinolinium perchlorates, has been investigated. Protoberberines are produced in these processes. However, the cyclization yields are lower than those in the photoinduced reactions owing to competitive formation of reduced tetrahydroisoquinolines and dihydroisoquinolones.

Introduction

Single-electron transfer (SET) in the excited states of donor (D)–acceptor (A) systems is a process that has attracted increasing attention in recent years owing to several interesting features of this chemistry.[1] Perhaps the most important aspect of this process for those who are seeking to develop new reactions is that excited-state SET in A–D pairs occurs with predictable rates[2] and that it results in the generation of ion radical pairs (intermolecular) or ion diradicals (intramolecular).[3] In general, the rate constants for SET are known to approach those of diffusion (ca. 1 × 10^{10} M^{-1} s^{-1}) when the free energy for SET (ΔG_{SET}) is negative.[2] Importantly, ΔG_{SET} can be readily calculated on the basis of oxidation and reduction potentials of the respective donor and acceptor and the energy of the par-

Scheme I



(1) (a) Davidson, R. S. *Adv. Phys. Org. Chem.* **1983**, *19*, 1. (b) Julliard, E. M.; Channon, M. *Chem. Rev.* **1983**, *83*, 425.
(2) Rehm, D.; Weller, A. *Isr. J. Chem.* **1970**, *8*, 259.
(3) Mariano, P. S. *Synthesis Organic Photochemistry*; Horspool, W. M., Ed.; Plenum: London, 1983; p 145.

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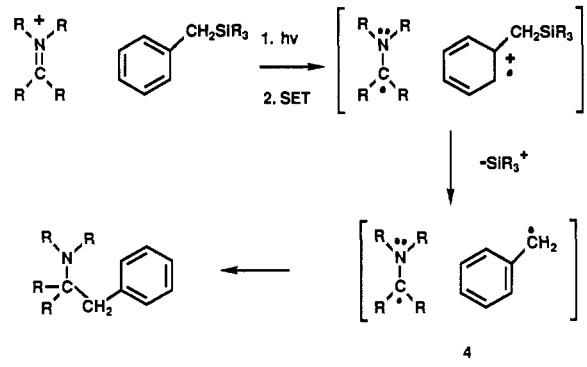
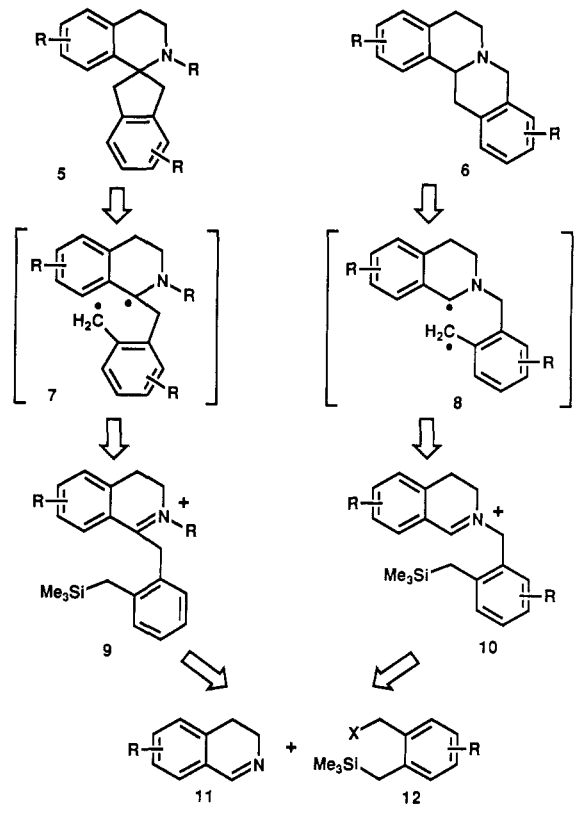
Scheme II



Scheme III



ticipating excited state (either A* of D*). Intramolecular SET often occurs with rates that exceed this value.[4] Thus, when favorable, SET effectively competes with other modes of excited-state decay. Moreover, since ion radicals are generated in this process, the photochemistry of A–D pairs is not influenced by the chemical properties/reaction profiles of the initially populated excited states. Rather, the chemistry of the intermediate charged radicals, which is often predictable, governs the nature of the photochemical reaction pathways followed.

Guided by these thoughts, we have explored over the past several years the excited-state chemistry of donor–iminium salt acceptor pairs. As shown in Scheme I, the singlet excited states of conjugated iminium salts such as **1** are high-energy oxidizing agents with reduction potentials in the region of +2.9 V. As such, these species readily accept electrons in SET processes with a variety of neutral donors (e.g., electron-rich arenes) which have ground-state oxidation potentials below +2.9 V. Similarly, the ground states of nonconjugated iminium salts (e.g., **2**) serve as acceptors in SET processes with singlet excited states of arene donors. Photostimulated SET in arene–iminium salt systems leads to production of radical cation pairs (intermolecular) or diradical cations (intramolecular) (e.g., **3** in Scheme I). Of relevance to issues discussed below are observations made in our studies of photoaddition and photocyclization reactions of benzylsilane–phenylpyrrolinium salt systems.[5] The results of these efforts demonstrate that benzylsilane radical cations generated by photoinduced SET undergo desilylation to form the corresponding benzyl radicals as part of radical pair or diradical intermediates (e.g., **4** in Scheme II). This process is fast and often occurs to the exclusion of other reaction pathways, such as C–C bond formation, that are available to the radical ion pairs or diradical cations.[6] Moreover, carbon–carbon bond formation in the ultimate radical pair or diradical intermediates completes often efficient pathways for adduct or cyclization product formation.

The chemical efficiencies and structural outcomes of reactions that follow the sequential SET–desilylation mechanistic pathways outlined in Scheme II suggested that they would serve as the basis of new methodologies for N-heterocycle and amino-carbocycle synthesis.[7] As part of a long-range program to test this proposal, we have recently explored the photochemistry of (silylxylyl)-3,4-dihydroisoquinolinium salts having the general structures **9** and **10** (Scheme III). At the outset of these efforts, we anticipated that photocyclizations of these substances would serve as key transformations in strategies for preparation of members of the spirobenzyl and protoberberine isoquinoline alkaloid families which possess the tetracyclic structures represented by **5** and **6**, respectively. In these sequences, the dihydroisoquinolinium salts **9** and **10** would be conveniently prepared from appropriate trimethylsilyl-substituted xylenes **12** and 3,4-dihydroisoquinolines **11** by conventional C–C and C–N bond forming processes. Irradiation of the salts, **9** and **10**, should initiate predictably favorable, intramolecular SET from the arene side chains to the singlet excited states of the phenyl-conjugated iminium cation chromophores.[5] Finally, we anticipated that cyclization of the diradical intermediates **7** and **8**, arising by desilylation of the respective diradical cation precursors, would be efficient processes. Convergent synthetic sequences based upon these stragegies we felt would rival in overall efficiency and convenience those previously developed[8,9] for synthesis of members of these isoquinoline alkaloid families. Moreover, since the key photocyclization processes would be employed at final stages in these routes, potential limitations of photo-

(4) Miller, J. R.; Beitz, J. V.; Haddleston, R. K. *J. Am. Chem. Soc.* **1984**, *106*, 5057.

(5) (a) Borg, R. M.; Heuckeroth, R. O.; Lan, A. J. Y.; Quillen, S. L.; Mariano, P. S. *J. Am. Chem. Soc.* **1987**, *109*, 2738.

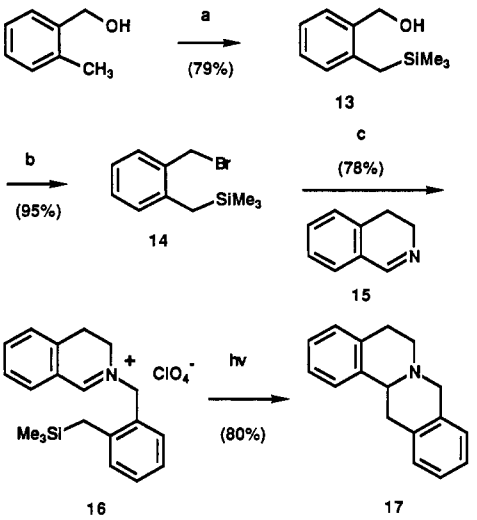
(6) (a) Diradical cations have been shown to undergo radical coupling when alternate reaction modes are unavailable (ref 6b). (b) Cho, I. S.; Mariano, P. S. *J. Org. Chem.* **1988**, *53*, 1590.

(7) (a) Ahmed-Schofield, R.; Mariano, P. S. *J. Org. Chem.* **1985**, *50*, 5667; **1987**, *52*, 1478. Tiner-Harding, T.; Ullrich, J. W.; Chiu, F. T.; Chen, S. F.; Mariano, P. S. *J. Org. Chem.* **1982**, *47*, 3360. Chiu, F. T.; Ullrich, J. W.; Mariano, P. S. *Ibid.* **1984**, *49*, 228.

(8) For general review of isoquinoline alkaloid synthetic approaches, see: Shamma, M. *The Isoquinoline Alkaloids*, Organic Chemistry Series; Blomquist, A. T., Wasserman, H. H., Eds.; Academic: New York, 1972; Vol. 25, pp 268–314, 380–398.

(9) (a) For synthetic approaches to xylopinine, see: Lenz, G. R. *J. Org. Chem.* **1974**, *39*, 2846. Craig, L. E.; Tarbell, D. S. *J. Am. Chem. Soc.* **1948**, *70*, 2783. Dyke, S. F.; Brown, D. W.; Sainsburry, M.; Hardy, G. *Tetrahedron* **1961**, *14*, 46. Dutta, N. L.; Wadra, M. S.; Bundra, A. A. *Indian J. Chem.* **1969**, *7*, 527. Meyers, A. T.; Bves, J.; Dickinson, D. A. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 458. See also ref 22–24 and 30. (b) For a synthetic approach to stylopine, see: Haworth, R. D.; Perkin, W. H. *J. Chem. Soc.* **1926**, 1769.

Scheme IV[a]



[a] (a) *n*-BuLi, Et_2O/TMSCl; (b) Ph_3P, CBr_4, Et_2O; (c) $AgClO_4$, MeCN.

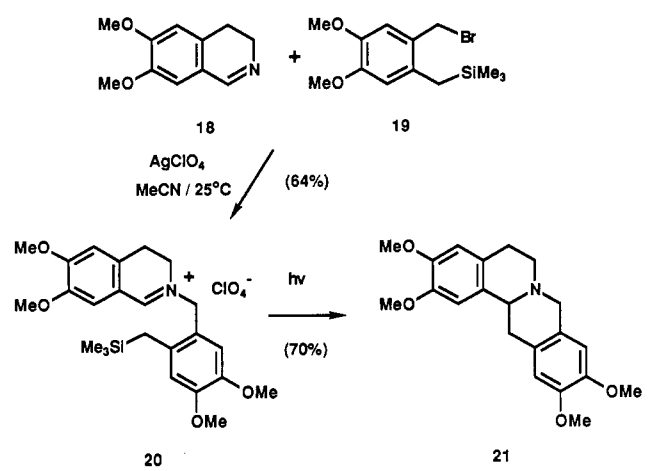
chemistry often associated with scale-up would be minimized.

We report herein the results of investigations designed to explore the scope and limitations of photocyclization processes which are at the conceptual foundation of the synthetic designs summarized in Scheme III.[10] In this effort we have found that dihydroisoquinolinium salts related to **9** and **10** can be conveniently prepared by short sequences and that they undergo cyclization upon irradiation to produce tetracyclic isoquinolines related to **5** and **6**. Photoreaction of dihydroisoquinolinium salts related to **9** has been probed, and information has been gained about competitive reaction pathways available to diradical intermediates related to **7** which cause photocyclization product yields in these systems to be low. In addition, arene-ring substituent effects on the quantum yields for photocyclization of the *N*-xylyldihydroisoquinolinium salts **10** have been observed, and these are discussed below in terms of the rates of competitive back electron transfer and desilylation of intermediate cation diradicals. In a target synthesis phase of our efforts, we have demonstrated how the strategies outlined in Scheme III can be used to prepare the representative, naturally occurring protoberines, (+)-xylopinine and (+)-stylopine. Finally, studies comparing the efficiencies of the diradical cyclization processes for protoberberine ring construction with those of closely related, yet conceptually distinct, dipolar processes have demonstrated the unique and superior features of the SET-photochemical methodology.

Results and Discussion

Synthesis and Chemistry of 2-(*o*-((Trimethylsilyl)methyl)benzyl)-3,4-dihydroisoquinolinium Perchlorate (16). The dihydroisoquinolinium perchlorate **16** was selected as a model system to explore the key SET-induced photocyclization reaction which serves as the basis for the proposed strategy for synthesis of members of the protoberberine alkaloid family. This substance was prepared by a short sequence involving N-benzylation of 3,4-dihydroisoquinoline (Scheme IV). Accordingly, the requisite (silylmethyl)benzyl bromide **14**[5b] was prepared by starting with *o*-methylbenzyl alcohol via a route involving dianion generation[11] and trimethylsilylation, followed by an alcohol to bromide interconversion. The procedure for generation of the (silylmethyl)benzyl alcohol intermediate **13** is patterned after that used by Trost[12] to prepare 2-((trimethylsilyl)methyl)allyl alcohol. It represents an alternative to methods previously described by Swenton[13] and Benkeser[14] to prepare **13**. Silver perchlorate assisted reaction of bromide **14** with 3,4-dihydroisoquinoline (**15**) occurred smoothly to generate after silica gel chromatographic purification the crystalline (MeOH, mp 140–142 °C) dihydroisoquinolinium perchlorate **16** (λ_{max} 286 nm, ϵ 14 000).

Scheme V



The photochemistry of **16** was explored to determine the feasibility of the diradical cyclization methodologies for protoberberine ring construction. Irradiation of acetonitrile solutions of this salt employed Corex filtered-light (λ >270 nm) which is selectively absorbed by the phenyl-conjugated iminium cation chromophore. Aqueous $NaHCO_3$ workup of the crude photolysate followed by chromatographic purification and recrystallization (Et_2O) gave the known tetracyclic product, berbine (**17**) (mp 80–82 °C, lit.[15] mp 85 °C) in an 80% yield. Spectroscopic data (^1H NMR, ^{13}C NMR, IR, mass spectrum) were in full accord with the assigned structure and matched those previously recorded.

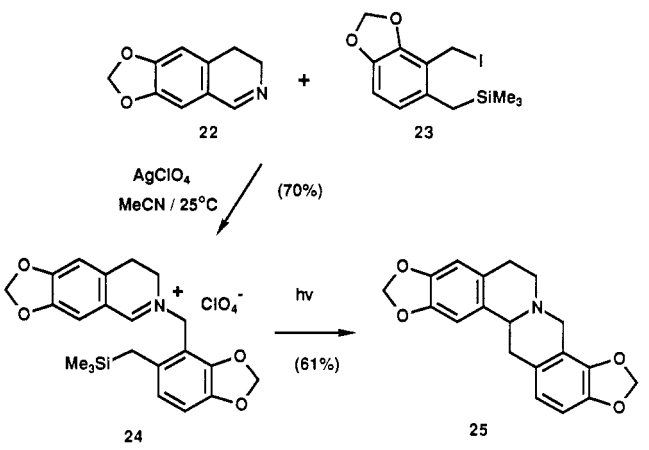
This preliminary result demonstrates the overall efficiency of routes for protoberberine synthesis which are based on a convergent strategy in which dihydroisoquinoline and silylxylyl pieces are joined by a C–N bond forming process and where photocyclization via a sequential SET–desilylation pathway is used to complete installation of the piperidine C ring. It is important to note that perchlorate was selected as the counteranion in **16** owing to the often crystalline nature of perchlorate salts and to the desire to eliminate the possibility of SET from the counteranion to the singlet excited state of the dihydroisoquinolinium salt. In addition, basic workup of the crude photolysate is required since **17** is produced as its perchloric acid salt in the crude photolysate.[16]

Protoberberine Alkaloid Synthesis. The Preparation of (+)-Xylopinine and (+)-Stylopine. The utility

(10) Reports of preliminary phases of this study have appeared: Ho, G. D.; Mariano, P. S. *J. Org. Chem.* **1987**, *52*, 704. G. D.; Lan, A. J. Y.; Mariano, P. S. *Tetrahedron Lett.* **1985**, *26*, 5867.

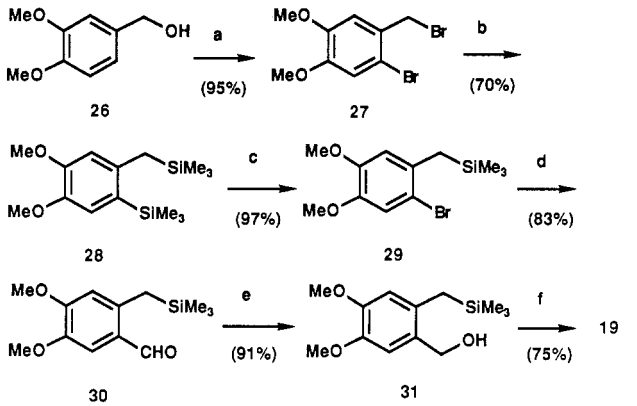
(11) Braun, M.; Ringer, J. *Tetrahedron Lett.* **1983**, *24*, 1233.
(12) Trost, B. M.; Chen, D. M. *J. Am. Chem. Soc.* **1983**, *105*, 2315.
(13) Swenton, J. S.; Shih, C. *J. Org. Chem.* **1982**, *47*, 2668.
(14) Benkeser, R. A.; DeTalvo, W.; Darling, D. *J. Org. Chem.* **1979**, *44*, 225.
(15) Chakravarti, S. N.; Haworth, R. D.; Perkin, W. H. *J. Chem. Soc.* **1927**, 2275.
(16) One equivalent of $HClO_4$ is formed in this process by desilylation of the intermediate cation involving MeCN or MeOH followed by proton transfer to the perchlorate anion.

Scheme VI



22 23 24 25

Scheme VII[a]



26 27 28 29 30 31

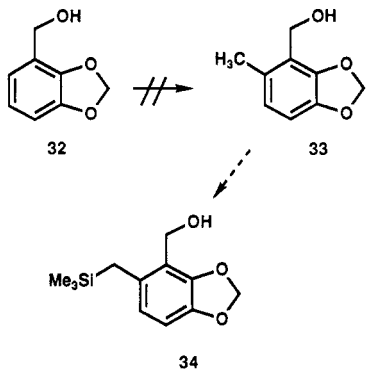
[a] (a) Br_2, HOAc, 25 °C; (b) Mg, TMSCl, THF; (c) Br_2, CCl_4, 25 °C; (d) *n*-BuLi, THF, −78 °C/DMF; (e) $NaBH_4$, Et_2O; (f) CBr_4, PPh_3, Et_2O.

of the synthetic design modeled above for protoberberine alkaloid synthesis has been further demonstrated by applications to the preparation of the representative protoberberines, (+)-xylopinine (**21**) and (+)-stylopine (**25**). These natural product targets possess the types of A- and D-ring bis-alkoxy substitution patterns that are found in the majority of members of this family. Our strategy for construction of **21** and **25** required the preparation of the respective dihydroisoquinolinium salts, **20** and **24**, by N-benzylation reactions between the oxy-substituted silylxylyl halides **19** and **23** and dihydroisoquinolines **18** and **22** (Scheme V and VI). Since the dihydroisoquinolines **18** and **22** are known substances,[17,18] the major challenge presented by these synthetic approaches is the development of methods for regioselective generation of the highly substituted benzyl halides **19** and **23**.

The route adopted for preparation of 4,5-dimethoxy-2-((trimethylsilyl)methyl)benzyl bromide (**19**), which serves as a key intermediate in the xylopinine approach, is shown in Scheme VII. Accordingly, the known[19] dibromide **27** formed from commercially available veratryl alcohol (**26**) was transformed to the bis-silyl derivative **28** via TMSCl trapping of the in situ, sequentially generated benzyl and aryl Grignards. Bromodesilylation[20] of **28** gave the aryl bromide **29**, which is properly functionalized to enable completion of the regioselective introduction of the bromomethyl substituent in the target **19**. The aryl bromide **29** can also be produced directly from dibromide **27** by selective generation of the monobenzylic Grignard and TMSCl trapping. However, this procedure is less convenient owing to unavoidable formation of the bis-silyl contaminant. The lithio derivative of aryl bromide **29** is generated by halogen–metal interchange at −78 °C to prevent the possibility of equilibration to a potentially more stable aryllithium species having an ortho disposition of MeO and Li substituents.[21] Formylation of the lithioarene species with DMF followed by reduction of the formed aldehyde **30** provides the (silylmethyl)benzyl alcohol **31**, which serves as a direct precursor to the key bromide **19**.

N-Benzylation of the dihydroisoquinoline **18**[17] with bromide **19** is conveniently performed in the presence of 1 equiv of $AgClO_4$ at 25 °C. This process gives the 3,4-dihydroisoquinolinium perchlorate **20** as a crystalline substance (MeOH, mp 176–178 °C, λ_{max} 370 (ϵ 8000), 313 nm (8000)). An alternative route for preparation of the chloride salt related to **20** utilizing. Bischler–Napieralski chemistry has been described by Takano.[22] Irradiation of MeOH solutions of the perchlorate salt **20** was performed by using Pyrex filtered-light (λ >300 nm) which is sufficient to excite the long wavelength absorbing methoxyaryl iminium cation chromophore. This photoreaction provides after aqueous $NaHCO_3$ workup and chromatographic purification crystalline (+)-xylopinine (**21**) (MeOH, mp 154–157 °C, lit.[23] mp 157–158 °C).

The aryl ring substitution pattern in the benzylic iodide **23** serving as the precursor to the protoberberine stylopine represents a synthetically more difficult challenge since it requires installation of aryl ring substituents on four contiguous carbons. In our efforts we have explored several approaches to the iodide **23**. We initially investigated a sequence based upon the Taber[25] method for ortho-allylation of benzyl alcohols. We envisaged that the (methylenedioxy)benzyl alcohol (**32**), prepared from 2,3-dihydroxybenzoic acid by methods described by Miller,[26] could be converted to its *o*-methyl derivative **33**, which would then be transformed to silyl alcohol **34** by the procedure described above for preparation of **13** (Scheme IV).

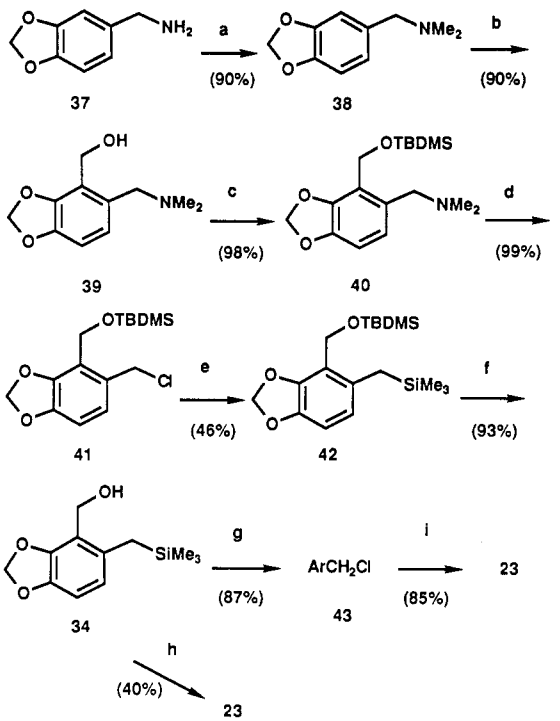


32 33 34

However, when the alcohol **32** was reacted under the Taber conditions[25] (*n*-BuLi, TMEDA/CuCN/MeI), it failed to

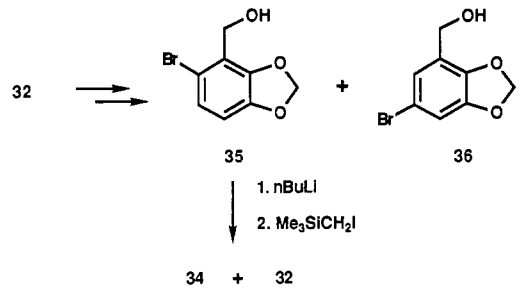
(17) Buck, J. S.; Ide, W. S. *J. Am. Chem. Soc.* **1938**, *60*, 2101.
(18) Decker, H.; Kropp, W.; Hayer, H.; Becker, P. *Justus Liebigs Ann. Chem.* **1913**, *395*, 299.
(19) Heap, T.; Jones, T. G. H.; Robinson, R. *J. Chem. Soc.* **1927**, 2021.
(20) Eaborn, G.; Walton, D. R. M.; Young. D. J. *J. Chem. Soc.* **1969**, 15.
(21) Ziegler, F. F.; Fowler, K. W. *J. Org. Chem.* **1976**, *41*, 1564. Beak, P.; Siegel, B. *J. Am. Chem. Soc.* **1974**, *96*, 6803.
(22) Takano, S.; Numata, H.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1982**, 769.
(23) Battersby, A. R.; LeCount, D. J.; Garratt, S.; Thrift, R. I. *Tetrahedron* **1961**, *14*, 46.
(24) Dean, R. T.; Rapoport, H. *J. Org. Chem.* **1978**, *43*, 2115.
(25) Taber, D. F.; Dunn, B. S.; Mack, J. F.; Saleh, S. A. *J. Org. Chem.* **1985**, *50*, 1987.
(26) Clark, J. H.; Holland, H. L.; Miller, J. M. *Tetrahedron Lett.* **1976**, 3361.

Scheme VIII[a]



[a] (a) HCHO, HCO_2H; (b) *n*-BuLi, 0 °C, THF/HCHO; (c) DIPEA, TBDMSCl; (d) $ClCO_2Et$, THF; (e) Mg, TMSCl, THF; (f) aqueous H_2SO_4; (g) $MeSO_2Cl$, TEA; (h) Ph_3P, DIPEA, I_2; (i) NaI, acetone.

produce the desired methyl derivative **33**. Starting material was recovered in all attempts to effect this process. An alternate approach to **34** would involve trimethylsilylmethylation of a lithio anion derived from bromoarene **35**. Bromobenzyl alcohol **35** was prepared from **32** by a sequence involving protection (Ac_2O, pyridine), bromination (Br_2, HOAc, NaOAc), and deprotection (K_2CO_3, MeOH, H_2O). This route produced a separable regioisomeric mixture of bromides **35** and **36**. The undesired

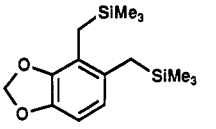


meta isomer could be recycled to **32** (*n*-BuLi/H_2O). Reaction of the bromobenzyl alcohol **35** with 2 equiv of *n*-BuLi followed by trapping with ICH_2SiMe_3 gave a mixture of the desired silylmethylation product **34** along with the benzyl alcohol **32** in an unfortunate 2:5 ratio. All attempts to enhance the chemoselectivity of this reaction were unsuccessful.

An efficient sequence (Scheme VIII) was finally developed based upon procedures described by Rapoport[27] for C-2 functionalization of 3,4-dialkoxybenzylamines. Accordingly, the *N,N*-dimethylpiperonylamine (**38**), formed by Eschweiler–Clark methylation[28] of the commercially available primary amine **37**, was transformed by *n*-BuLi deprotonation and equilibration (forming the presumably thermodynamically more stable anion)[21] to the 2-lithio (rather than 6-lithio) anion. Formaldehyde trapping provided the carbinol **39**, which was protected and deaminated to give the benzylic chloride **41**. This substance was then converted to the benzylic silane **42** by in situ trapping of the corresponding Grignard. The lower than expected yield of this reaction was in part due to the simultaneous production of the bis-silyl product **44** under these conditions. Deprotection of **42** yields the benzyl alcohol **34**, which can be converted directly to iodide **23** by use of the iodination chemistry of Ley[29] or by a two-step sequence via chloride **43**.

Table I. Qualitative and Quantitative Data for Photocyclizations of the Dihydroisoquinolinium Perchlorates 16, 20, 24, and 46

rctn	solvent	preparative conversions, mg/min	quantum yields
16 → **17**	MeCN	7.0	2.70×10^{-2}
20 → **21**	MeOH	0.09	
24 → **25**	MeOH	0.10	0.005×10^{-2}
46 → **47**	MeOH	3.3	1.48×10^{-2}



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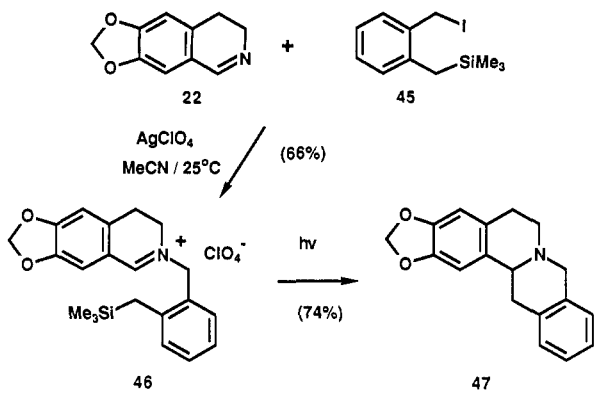
The dihydroisoquinolinium perchlorate **24**, which serves as the direct precursor of stylopine, can be efficiently formed by $AgClO_4$-assisted alkylation of the known dihydroisoquinoline **22**[18] with iodide **23** in MeCN. The salt **24** was furnished as a crystalline substance (mp 186–188 °C, λ_{max} 373 (ϵ 11 000), 304 nm (11 000)). Photocyclization occurs upon irradiation (Flint filtered-light, λ >310 nm) of methanolic solutions of **24** to give, after aqueous $NaHCO_3$ workup and chromatography, crystalline (+)-stylopine (**25**) (mp 213–215 °C, lit.[30] mp 217–218 °C). The spectroscopic properties of **25** formed in this way are identical with those previously recorded[24] for this protoberberine alkaloid.

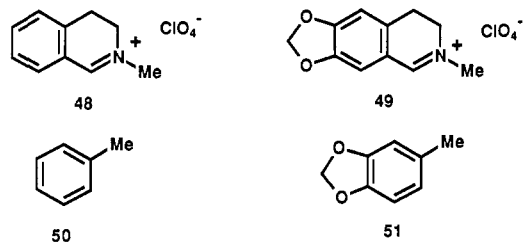
Substituent Effects on Protoberberine Ring Forming Photocyclization Processes. As we have shown above, SET-induced photocyclization reactions of the (silylxylyl)dihydroisoquinolinium perchlorates **16**, **20**, and **24** serve as key steps in strategies for protoberberine ring construction. The chemical efficiencies (64–80%) of these processes are in the synthetically acceptable region. Although both the alkoxy-substituted (**20** and **24**) and unsubstituted (**16**) salts produced protoberberines in similar chemical yields, we noted that relatively long reaction times were required to bring about complete consumption of **20** and **24** as compared to the parent salt **16** (see Table I). While these reactions are conducted under different conditions (e.g., wavelength filter and solvent), we felt that the differences noted were reflecting variations in quantum efficiencies for photocyclization caused by aryl ring alkoxy substitution. Additional support for this proposal comes from observations made in studies with the hydroisoquinolinium ring substituted perchlorate salt **46**. This substance was prepared by reaction of dihydroisoquinoline **22** with silylxylyl iodide **45**.[5b] Irradiation of **46** in MeOH (Flint, λ >310 nm) followed by workup and purification

(27) An aryl ring functionalization method developed for a dimethoxy-substituted benzylamine analogue by Rapoport (ref 24) was used.
(28) Pine, S. H.; Sanchez, B. L. *J. Org. Chem.* **1971**, *36*, 829.
(29) Edwards, M. P.; Ley, S.; Lister, S. G.; Palmer, B. D.; Williams, D. J. *J. Org. Chem.* **1984**, *49*, 3503.
(30) Bradsher, C. K.; Dutta, N. L. *J. Org. Chem.* **1961**, *26*, 2231.



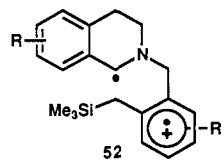
provided the tetracyclic amine **47** in a 74% yield. The irradiation times required for conversion of **46** to **47** (Table I) were qualitatively similar to those for the parent salt **16** rather than the tetraalkoxy-substituted analogues **20** and **24**. This result suggested that electron donating group substitution on the silylxylyl moiety in these salts might have a pronounced influence on the photocyclization quantum efficiencies. This was confirmed by measurement of the absolute product formation quantum yields for these processes. The data obtained is summarized in Table I.

In order to locate the source of these differences, we made fluorescence measurements. As the data in Table II indicate, quenching of the singlet excited states of alkoxy-substituted and unsubstituted 3,4-dihydroisoquinolinium salts by arenes is a rapid process with rates that approach those of diffusion control when the arene contains electron-donating substituents. The model fluorescing salts **48** and **49** and arene quenchers, toluene (**50**) and its methylenedioxy analogue **51**, were selected on the basis of the close correspondence between their electronic properties and those of the acceptor and arene donor chromophores in the perchlorate salts undergoing photocyclization. The fluorescence quenching data along with



the observation that salts **16**, **20**, **24**, and **46**, which contain internal quenchers, do not fluoresce strongly indicates that electron transfer in the singlet excited states of these substances is highly efficient (ϕ_{SET} ca. 1). Thus, the differences seen in quantum efficiencies for cyclization are likely not a result of variable forward electron transfer rates in the initially populated excited states.

In view of these observations, a likely source of the large differences observed in the photocyclization quantum yields is in the rates of desilylation of the intermediate diradical cations, e.g., **52**. Partitioning of these interme-



diates by desilylation (k_d) vs reverse electron transfer (k_{BSET}) is influential in determining the quantum efficiencies of cyclization. It is known that the rates of proton loss from benzylic positions of toluene cation radicals are sensitive to substitution, decreasing with electron donating group substitution on the aromatic nucleus.[32] This can be understood in terms of differential stabilization of the cation radical starting state relative to a less positively charged transition state for benzyl radical generation. In a similar way, alkoxy substitution on the benzylsilane cation radical moiety in **52** should decrease the rate of trimethylsilyl group loss which results in production of the neutral benzyl radical grouping in the diradical intermediates. This explanation would be valid of course only if substitution has no effect on the rate constants for back electron transfer in **52**. This is a difficult situation to evaluate. Thus, if these highly exothermic back electron transfers fall in the Marcus inverted region, electron donor substitution on the diradical cation moiety would cause ΔG_{BSET} to increase (become less negative) and, thus, the rate constant k_{BSET} to increase.[33] The net effect would be that partitioning of diradical cation **52** to the ground states of the starting salts would be enhanced by donor substitution on the silicon substituted ring. Thus, while we are reasonably certain that the substituent effects on the quantum efficiencies for cyclization of the dihydroisoquinolinium salts **16**, **20**, **24**, and **46** reside in partitioning of the intermediate diradical cations by desilylation vs back electron transfer, we are unable at this point to distinguish between the two possible sources identified above.

Table II. Fluorescence Quenching Rate Constant Data

fluorescent dihydroisoquinolinium perchlorates	arene quenchers	quenching rate constants: k_q,[a] M^{-1} s^{-1}
48	50	1.3×10^{10}
48	51	2.0×10^{10}
49	51	5.7×10^{9}

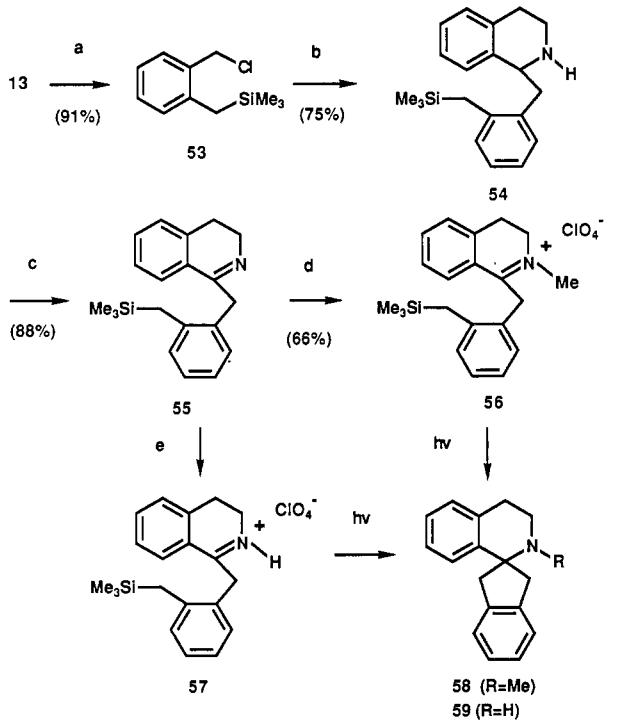
[a] Measurements made at 25 °C in MeCN. Lifetimes of **48** and **49** were calculated (ref 31).

Model Studies Probing the Strategy for Spirobenzyl Isoquinoline Alkaloid Synthesis. As outlined in Scheme III, photocyclizations of 1-(silylxylyl)-3,4-dihydroisoquinolinium salts serve as the key ring-building step in strategies we have designed for construction of the spirobenzyl isoquinoline ring system. As part of an effort to determine the feasibility of routes based upon this chemistry, the photochemistry of two model hydroisoquinolinium salts **56** and **57** has been explored. This investigation has provided important mechanistic information which is pertinent to the eventual synthetic applications of this chemistry.

The sequence used for preparation of these perchlorate salts (Scheme IX) began with addition of (*o*-((trimethylsilyl)methyl)benzyl)magnesium chloride (from the corresponding chloride **53**) to 3,4-dihydroisoquinoline (**15**), which gave the tetrahydroisoquinoline adduct **54**. *N*-Chlorination followed by dehydrochlorination yielded the dihydroisoquinoline **55**, which was then N-methylated to produce the perchlorate salt **56** (MeOH, mp 156–158 °C; λ_{max} 283 nm (ϵ 10 000). The analogous N–H salt **57** was generated in situ prior to irradiation by the addition of $HClO_4$.

(31) Turro, N. J. *Modern Molecular Photochemistry*; Benjamin: Menlo Park, 1978; p 88–90.
(32) Sehested, K.; Holcman, J. *J. Phys. Chem.* **1978**, *82*, 651. Schlesener, C. J.; Amatore, C.; Kochi, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 7472.
(33) Marcus, R. A. *J. Chem. Phys.* **1956**, *24*, 966. Experimental Observations of behavior characteristic of the Marcus inverted region have been provided. See: Gould, J.; Ege, D.; Mattes, S. L.; Faird, S. *J. Am. Chem. Soc.* **1987**, *109*, 3794 and references therein.

Scheme IX[a]



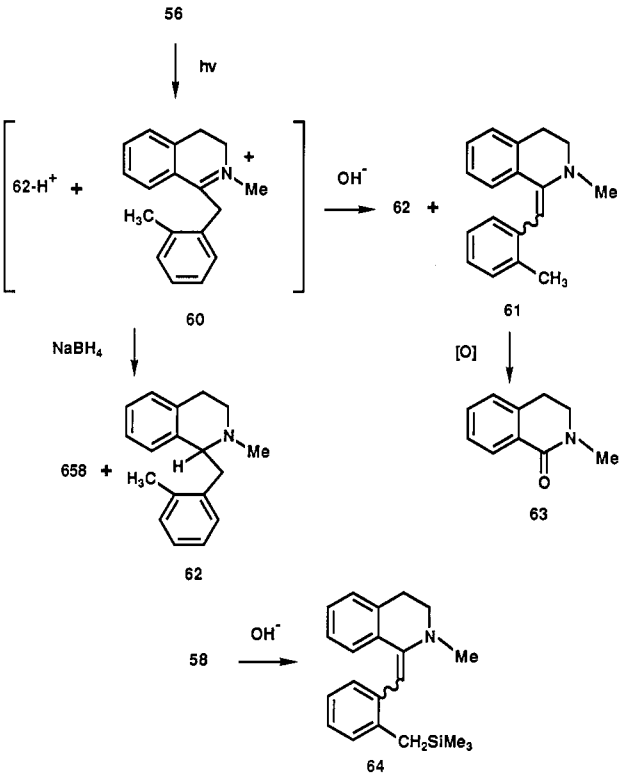
[a] (a) Ph_3P, CCl_4; (b) Mg/15; (c) NCS, Et_2O/KOH, MeOH; (d) MeI, $AgClO_4$, MeCN; (e) $HClO_4$.

Irradiation of these salts in MeCN or MeOH solutions by using Corex filtered-light ($\lambda > 270$ nm) gave after basic workup and chromatographic purification the spirocyclic amines **58** and **59**. The maximum yields for reaction of the N–H salt **57** were in the range of 50% while those for the *N*-methyl homologue reached 37% after extended irradiation (see below).

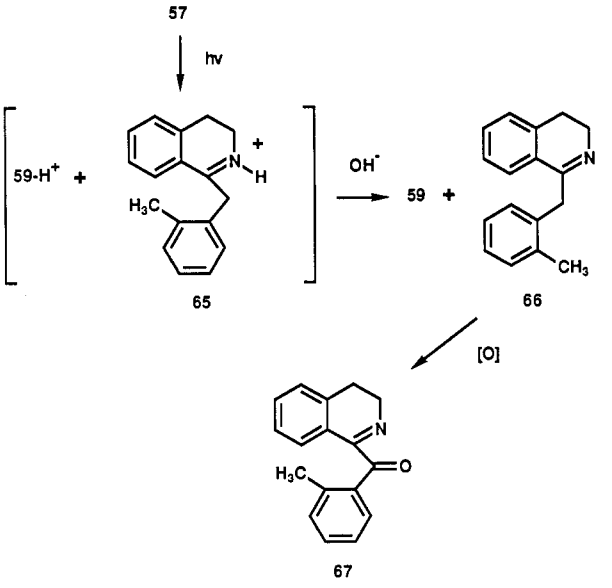
The low yields of these processes stand in contrast to the high chemical efficiencies observed for photocyclization reactions of the corresponding 2-(silylxylyl)dihydroisoquinolinium perchlorates. This difference encouraged us to inspect more closely the details of the spirocyclization reactions. The major product (ca. 75%) generated by irradiation of **56** for short time periods (ca. 20 min) and basic workup is the non-silicon-containing, unstable enamine **61**, which was identified by ^1H NMR spectroscopic analysis (2.24 ($ArCH_3$), 2.58 (NCH_3), 5.95 ppm (NC=CH)). This substance undergoes oxidative decomposition upon chromatographic separation to generate the known[7a] dihydroisoquinolone **63**. Importantly, the silicon-containing enamine **64**, which is produced by treatment of the dihydroisoquinolinium salt **56** with base, is not detected after basic workup of the crude photolysate arising from short-period irradiations. In addition, irradiation of **56** for short time periods followed by immediate workup of the crude photolysate with $NaBH_4$ provides the nonsilicon-containing tetrahydroisoquinoline **62** as the major product. These results suggest that an efficient photochemical reaction pathway operates to convert **56** to the desilylated salt **60** (major) along with N-protonated **58** (minor). The former substance is then transformed to enamine **61** and tetrahydroisoquinoline **62** upon respective base and $NaBH_4$ workup of the photolysate (Scheme X).

Similar observations were made when the product mixture arising by short-period irradiation of the N–H salt **52** was carefully inspected. Basic workup of the crude photolysate gave spirocyclic product **59** along with the dihydroisoquinoline **66**. The latter substance undergoes

Scheme X



Scheme XI

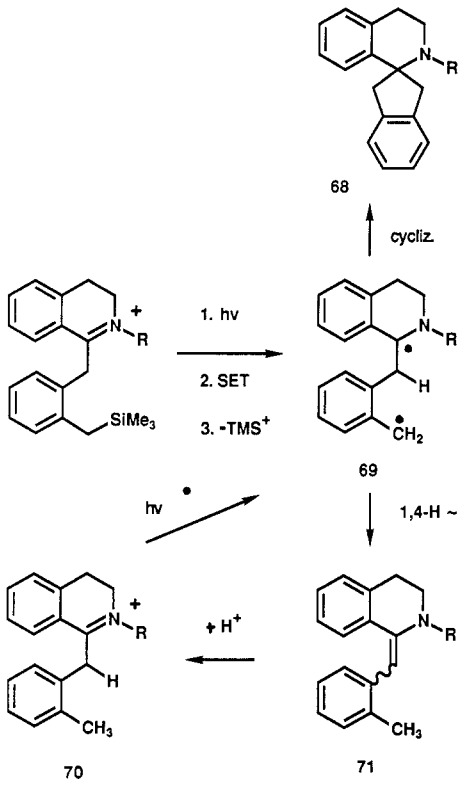


precedented[34] oxidation to the oxo compound **67** upon chromatographic purification. Thus, competitive photoreaction pathways are available to **57**, producing the N-protonated spirocyclic product and desilylated hydroisoquinoline salt **65**. Upon treatment with base, the latter substance is transformed to the observed dihydroisoquinoline **66** (Scheme XI).

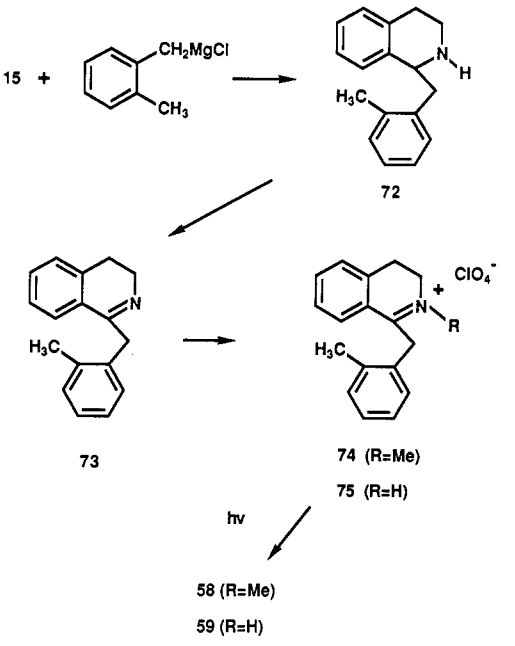
Additional observations made in studies of the photochemistry of **56** and **57** are pertinent to an understanding of the mechanistic pathways operating in these systems. As the results outlined above demonstrate, short-period (20-min) irradiation of **56** in MeOH leads to production of the desilylated salt **60** (ca. 75%) as the major product

(34) Weisbach, J. A.; Kirkpatrick, J. L.; Macko, E.; Douglas, R. *J. Med. Chem.* **1968**, *11*, 752.

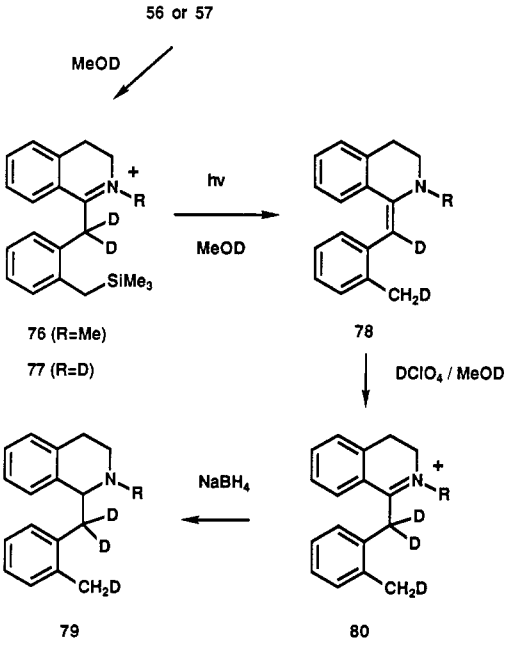
Scheme XII



Scheme XIII



Scheme XIV



along with a low yield (8%) of the spirocyclic product **58** (after base workup). Under these conditions, the starting, silicon-containing salt **56** is completely reacted. Yet, when irradiation of **56** is conducted for longer time periods (60 min), the yield of spirocyclic product **58** increases to 30%. Similar observations were made in studies of the photochemistry of **58**. In this case the yields of spirocyclic product are higher for both short (20 min, 19%) and long (60 min, 50%) period irradiations.

Mechanistic Features of the Photochemistry of Dihydroisoquinolinium Salts 56 and 57. Photoinduced sequential SET–desilylation pathways should be operable in the photochemistry of **56** and **57**. The diradical intermediates **69** (Scheme XII) generated in this way can undergo C–C bond formation to yield spirocyclic products **68**. An alternate sigmatropic rearrangement pathway involving 1,4-H shift of one of the two internal benzylic hydrogens is available in diradicals **69**. This process transforms **69** to the desilylated enamines **71**, which in the acidic photoreaction medium[16] would be rapidly transformed to the dihydroisoquinolinium salts **70**. Thus, the desilylated salts would arise by partitioning of intermediate diradicals **69** by hydrogen-shift pathways. In this light, the higher yields of photocyclization seen in reactions of the N–H salt **57** as compared to its N–Me analogue **56** can be understood on the basis of a steric effect which causes the diradical cyclization rate to be slower in the N–Me system.

We propose the following reason to explain why the yields of photocyclization products increase upon extended irradiation despite the fact that the starting silyl salts are completely consumed early in the processes. The desilylated dihydroisoquinolinium salts **70** (Scheme XII) absorb incident light in the same region as their silyl analogues. Excitation of **70** should initiate an electron transfer–deprotonation sequence which generates the same diradical intermediate **69** as is formed from reaction of the silyl salt. Reaction pathways of this type involving deprotonation of closely related diradical cation intermediates have been observed before in studies of *N*-xylyl-2-phenylpyrrolinium salt photochemistry.[5] In essence, the secondary photochemistry of the non-silicon-containing salts **70** (Scheme XII) allows continuous recycling of the photoreaction system to the intermediate diradical. The route advanced in Scheme XII requires that dihydroisoquinolinium salts undergo photocyclization to produce spirocyclic products **68**. The perchlorate salts **74** and **75**, prepared independently (Scheme XIII), indeed do undergo photocyclization upon irradiation to produce spirocyclic products, **58** (15%) and **59** (19%), respectively.

Deuterium-labeling studies were conducted to provide evidence for the 1,4-H-shift mechanism for production of desilylated dihydroisoquinolinium salts related to **70** (Scheme XIV). The dideuteriated silylxylyl perchlorates **76** and **77**, used for this investigation, were prepared by stirring MeOD solutions of the protio analogues, **56** and

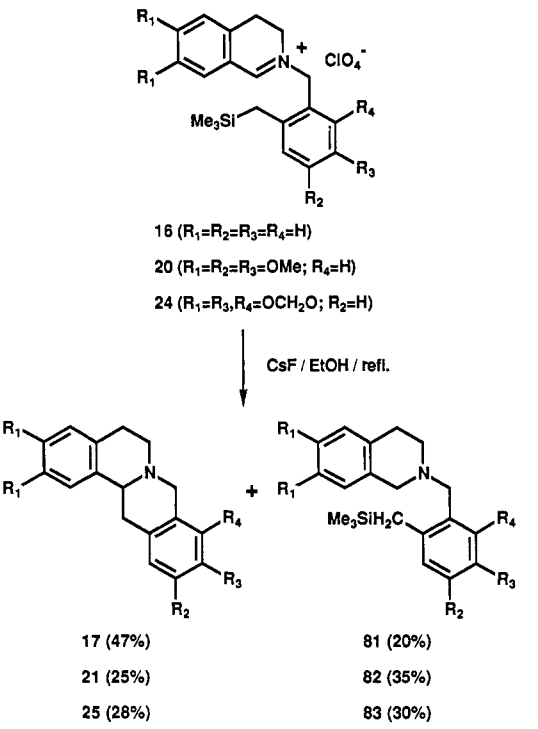
57, until ^1H NMR analysis indicated complete exchange of the α-imino benzylic hydrogens. Irradiations of MeOD solutions of these salts were then conducted for short (17–30 min) time periods to give photolysates, which were subjected to $NaBH_4$ reductive workup. The reaction mixturees were analyzed by ^1H NMR to determine the extent and location of deuterium incorporation in the 1-(*o*-xylyl)-1,2,3,4-tetrahydroisoquinolines. Analysis of the product mixture obtained in this way starting with the *N*-methyl salt **76** showed a triplet (deuterium coupling) for the external benzylic protons at 2.09 ppm integrating for 2 H relative to the NMe resonance. This demonstrates that ca. one deuterium atom is incorporated in the benzylic methyl group of the tetrahydroisoquinoline **79** (R = Me) which comes from reduction of the photodesilylation product, salt **80** (R = Me) (Scheme XIII). Two deuteria remain at the internal benzylic position of **80** due to the fact that protonation (deuteriation) of the precursor enamine **78** is by $DClO_4$. This acid is formed by the MeOD displacement of the trimethylsilyl group in reaction of the diradical cation/perchlorate anion in the pathway leading to **78**. Similar observations are made by ^1H NMR analysis of the reductive workup product mixture coming from irradiation of the trideuterio N–D salt **77**. In addition, extended irradiation leads to a greater incorporation of deuterium in the benzylic methyl group as would be expected for this system in which salt **80** (R = Me) can recycle through the sequence depicted in Scheme XII.

The combined results presented above suggest that photocyclization of 1-(silylxylyl)-3,4-dihydroisoquinolinium perchlorates represents a viable route for construction of substances possessing the parent ring system shared by members of the spirobenzyl isoquinoline alkaloid family. The yields of these processes are diminished by competitive 1,4-H-shift reactions which occur in intermediate diradicals. While the non-silicon-containing salts that are produced by this alternative reaction pathway also undergo photocyclization to form the same spirocyclic products, they do so with reduced chemical efficiencies.

A Comparison of Diradical and Related Dipolar Cyclization Methodologies. We have shown above that photocyclization reactions of 2- and 1-(silylxylyl)dihydroisoquinolinium salts serve as a useful method for protoberberine and spirobenzyl isoquinoline ring construction. The important step in these photochemical processes involves carbon–carbon bond formation through cyclization of key diradical intermediates. Except in the case of the 1-substituted systems, these diradical cyclizations represent efficient reactions and, as a result, constitute of a new and useful method for N-heterocycle and carbocycle synthesis. A conceptually related methodology for effecting these transformations would take advantage of the latent dipolar character of the (silylxylyl)hydroisoquinolinium salts. Accordingly, treatment of these salts with fluoride ion could in theory reveal dipolar intermediates (or their R_4SiF anion equivalents) which are properly structured for cyclization to produce the same products that arise via the intermediacy of diradicals.

Clearly no study of these systems would be complete without an expedition to probe the viability of the dipolar methodology and to compare its efficiency to that of the analogous diradical cyclization strategy. We have done this by exploring the fluoride ion induced chemistry of the dihydroisoquinolinium perchlorates **16**, **20**, and **24**. Prior to these efforts, Takano and his co-workers[22] had reported that the chloride salt corresponding to **20** undergoes high-yielding (70%) conversion to xylopinine (**21**) when treated with CsF in EtOH at 80 °C and that it is inert

Scheme XV



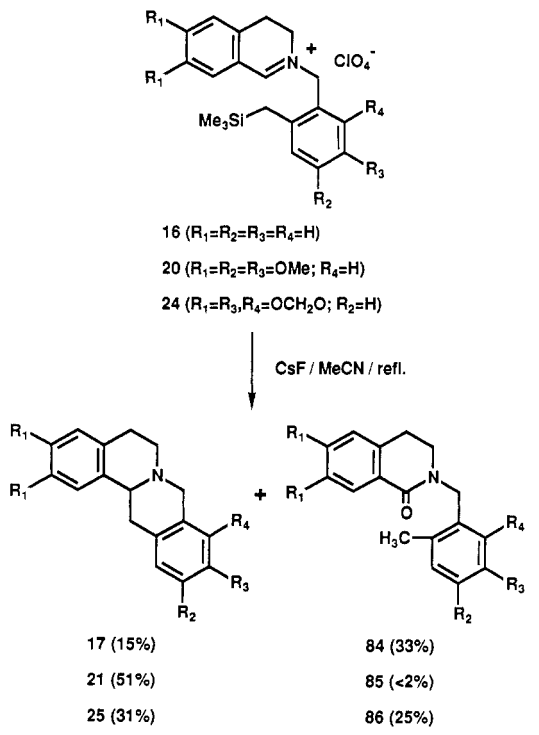
when treated with CsF in refluxing MeCN. Guided by these contrastingly different results, we have looked at the reactions of **16**, **20**, and **24** with CsF (5 equiv) in refluxinng EtOH and MeCN. As shown in Scheme XV, reaction of these salts in EtOH leads to the production of a mixture of cyclization products and silicon-containing tetrahydroisoquinolines **81–83**. The protoberberines were formed in modest to low yields (25–47%), a result that contrasts with those presented by Takano.[22] Of interest in this regard is the transformation of **20** to xylopinine, which occurs with a maximized yield of 25% in our hands. Generation of the tetrahydroisoquinolines under these conditions most probably occurs by a disproportionation mechanism involving fluoride γ-deprotonation[35] of the dihydroisoquinolinium salts to yield an extended tetraenamine, which then transfers a hydride to the starting salts to provide the observed tetrahydroisoquinolines along with the aromatized isoquinolinium salts (not looked for).

In contrast, reactions of the salts **16**, **20**, and **24** with CsF (5 equiv) in refluxing MeCN provide the corresponding protoberberines along with the non-silicon-containing *N*-xylylisoquinolones **84–86** (Scheme XVI). Here again, cyclizations via dipolar mechanisms are only modestly efficient (15–51%). At the current time, we are uncertain about the origin of the isoquinolone products in these reactions. However, it is clear that processes leading to these substances are competitive with cyclization. Finally, while Takano[22] has reported that reaction of **20** to give **21** does not occur under these conditions, we have found that the process takes place in modest (51%) yield.

The factors that govern the nature of the fluoride ion induced reactions of the dihydroisoquinolinium salts are not totally clear at this time. However, it is evident from the results presented above that this methodology is often less efficient than those following photoinduced diradical cyclization pathways. Similar conclusions have been reached in earlier studies with benzylsilane and allylsilane iminium salt systems.[5b,7a]

(35) Yakobson, G. G.; Akhmetova, N. E. *Synthesis* **1983**, 169.

Scheme XVI



Summary

The studies described above have clearly shown that diradical cyclization processes promoted by excited-state electron transfer–desilylation sequences represent novel and useful strategies for protoberberine and spirobenzylisoquinoline ring construction. The photochemical routes appear to be superior to alternative ground-state methods involving fluoride ion induced, dipolar cyclizations. The quantum efficiencies for reactions of the 2-(silylxylyl)-3,4-dihydroisoquinolinium salts are highly dependent on benzylsilane ring substitution, most probably a result of electron-donor effects on the rates of intermediate diradical cation desilylation vs back electron transfer. Spirocyclization of diradical intermediates arising by photoinduced SET–desilylation pathways in the 1-(silylxylyl)-3,4-dihydroisoquinolinium salts is competitive with 1,4-H-shift processes which lead to production of photodesilylation products. Together these results lead to a reasonably clear understanding of the scope, limitations, synthetic applications, and mechanistic features of the photochemistry explored.

Experimental Section

General. Nuclear magnetic resonance spectra were recorded by using an IBM WP-200, Bruker AM-200, or Bruker AM-400 spectrometer on $CDCl_3$ solutions, and chemical shifts are reported in δ values (parts per million downfield from tetramethylsilane employed as an internal standard). IR spectra were recorded on a Perkin-Elmer 283 spectrometer. UV spectra were obtained on a GCA McPherson Model EU-700-56 or a Perkin-Elmer Model Lambda 5 spectrophotometer. Fluorescence emission spectra were recorded on a Perkin-Elmer Model MPF 44B spectrophotometer equipped with a Perkin-Elmer DCSU-1 differential corrected spectra unit. Elemental analyses were performed by Dr. F. Kasler at the University of Maryland. Low resolution mass spectral analyses were performed at 70 eV on a Hitachi RMU-6E mass spectrometer. High resolution mass spectral analyses were performed on VG-7700 instrument or at the Pennsylvania State University Mass Spectrometry Center. Melting points were obtained on a Mel-TMp apparatus and are reported uncorrected. Column chromatography was performed with EM silica gel (230–400 mesh) or with Florisil (100–200 mesh) as absorbent. Molecular distillations were performed at reduced pressure with a Kugelrohr apparatus. Perchlorate anion exchange was performed on a Dowex-1 column, mesh 50–100, 2.5 × 20 with methanol as the eluent. Drying of organic layer obtained by workup of reaction mixtures was by washing with saturated NaCl in some cases prior to standing over anhydrous sodium sulfate. All reactions were carried out under a N_2 atmosphere.

General Preparative Photochemical Reactions. Preparative photolysis was conducted with an apparatus consisting of a 450-W Hanovia medium-pressure mercury vapor lamp surrounded by the indicated glass filter in a water-cooled quartz immersion well under a N_2 atmosphere. Reaction progress was followed by UV spectrophotometric monitoring, and irradiations were terminated when decreases in the absorbance due to the starting perchlorate salt ceased. Crude photolysates from the perchlorate salt photoreactions were subjected to a general workup procedure involving the addition of $NaHCO_3$, concentration in vacuo, addition of water, and $CHCl_3$ extraction. The extracts were concentrated in vacuo to give residues, which were subjected to the indicated chromatographic methods.

***o*-((Trimethylsilyl)methyl)benzyl Alcohol (13).** To a stirred solution of *o*-methylbenzyl alcohol (1.16 g, 9.50 mmol) in 10 mL of anhydrous ether was added *n*-BuLi (2.7 mL, 10.5 M, 28.34 mmol) at −78 °C. After being stirred for 24 h at 25 °C, the reaction mixture was cooled to −78 °C and trimethylsilyl chloride (4.2 mL, 33.25 mmol) was added rapidly. The solution was stirred at 25 °C for an additional 1.5 h before being poured into water and extracted with ether. The ethereal extracts were dried and concentrated in vacuo. The residue was subjected to flame column chromatography separation on silica gel (30% ether/hexane) to provide 1.45 g (79%) of the (silylmethyl)benzyl alcohol **13**, which was identical in all respects with the known substance:[13,14] ^1H NMR 0.01 (s, 9 H, $Si(CH_3)_3$), 2.18 (s, 2 H, $ArCH_2Si$), 4.61 (s, 2 H, $ArCH_2O$), 7.00–7.34 (m, 4 H, Ar H's); ^{13}C NMR −1.5 ($Si(CH_3)_3$), 22.8 ($ArCH_2Si$), 63.4 ($ArCH_2O$), 124.4 127.5, 128.1, 129.3, 137.1, 138.6 (aromatic C's); IR ($CHCl_3$) 3420 (br, OH), 2955, 1600, 1480, 1240, 1000, 850 cm^{-1}.

***o*-((Trimethylsilyl)methyl)benzyl Bromide (14).** To a stirred solution of triphenylphosphine (10.5 g, 40 mmol) and carbon tetrabromide (13.3 g, 40 mmol) in 200 mL of anhydrous ether was added *o*-((trimethylsilyl)methyl)benzyl alcohol (**13**) (6.5 g, 33.4 mmol). The solution was stirred for 2 h at 25 °C before being filtered through Celite. The filtrate was concentrated in vacuo to give a residue, which was subjected to column chromatographic purification on silica gel (hexane). Concentration of the hexane solution gave 8.2 g (95%); of pure bromide **14**: ^1H NMR 0.03 (s, 9 H, $Si(CH_3)_3$), 2.25 (s, 2 H, $ArCH_2Si$), 4.47 (s, 2 H, $ArCH_2Br$), 6.96–7.29 (m, 4 H, Ar H's); ^{13}C NMR −1.4 ($SiCH_3)_3$), 23.4 ($ArCH_2Si$), 33.0 ($ArCH_2Br$), 124.7, 128.7, 129.8, 130.6, 134.0, 139.9 (aromatic C's); IR ($CHCl_3$) 2955, 1600, 1490, 1250, 845 cm^{-1}; mass spectrum, *m/e* (relative intensity) 258 (M^+ + 2, 3e, 256 (M^+, 2), 178 (3), 177 (12), 104 (100); high-resolution mass spectrum, *m/e* 258.0257 ($C_{11}H_{17}SiBr$ requires 258.0230).

2-(*o*-((Trimethylsilyl)methyl)benzyl)-3,4-dihydroisoquinolinium Perchlorate (16). In an aluminum foil wrapped 25-mL round-bottomed flask, a solution of 3,4-dihydroisoquinoline (1.1 g, 8.38 mmol), *o*-((trimethylsilyl)methyl)benzyl bromide (**14**) (1 g, 3.88 mmol), and silver perchlorate (970 mg, 4.67 mmol) in 10 mL of CH_3CN was stirred at 25 °C for 2 h. The reaction mixture was filtered. Concentration of the filtrate gave an oil, which was subjected to column chromatographic purification on silica gel (2% MeOH/$CHCl_3$) to give 1.25 g (78%) of the perchlorate **16**, which was recrystallized from MeOH (mp 140–142 °C): ^1H NMR −0.01 (s, 9 H, $Si(CH_3)_3$), 2.17 (s, H, $ArCH_2Si$), 3.24 (t, 2 H, H-4), 3.98 (t, 2 H, H-3), 5.27 (s, 2 H, $ArCH_2N$), 7.07–7.85 (m, 8 H, Ar H's), 9.02 (s, 1 H, ArCH=N); ^{13}C NMR −2.0 ($Si(CH_3)_3$), 23.2 ($ArCH_2Si$), 24.7 (C-4), 47.8 (C-3), 61.1 ($ArCH_2N$), 125.2, 126.2, 128.0, 128.2, 129.5, 130.0, 134.1, 136.0, 138.1 (aromatic C's), 165.6 (ArCH=N); IR ($CHCl_3$) 2940, 1650 (C=N), 1460, 1250, 1080, 850 cm^{-1}; UV (CH_3CN) λ_{max} 285 nm (ϵ 1.4 × 10^4).

Anal. Calcd for $C_{20}H_{26}NClO_4Si$: C, 58.88; H, 6.42; N, 3.43; Cl, 8.69. Found: C, 58.40; H, 6.37; N, 3.15; Cl, 8.49.

Irradiation of 2-(*o*-((Trimethylsilyl)methyl)benzyl)-3,4-dihydroisoquinolinium Perchlorate (16). Preparation of Berbine (17). A solution of the perchlorate salt **16** (210 mg, 0.5 mmol) in CH_3CN was irradiated with Corex-filtered light (λ >270

nm) for 30 min. The crude photolysate was subjected to a general workup procedure of the flash column chromatographic purification (25% ether/hexane) to provide 97 mg (80%) of berbine (17), which was recrystallized from ether (mp 80–81 °C, lit.[15] mp 85 °C): ^{1}H NMR 2.61–2.68 (m, 1 H, H-5), 2.74–2.79 (m, 1 H, H-5), 2.93, 3.39 (AB qd, J = 16.3, 11.3, 3.9 Hz, 2 H, H-13), 3.14–3.27 (m, 2 H, H-6), 3.67–3.73 (dd, J = 11.3, 3.5 Hz, 1 H, H-14), 3.75, 4.04 (AB q, J = 15.0 Hz, 2 H, H-8), 7.08–7.17 (m, 8 H, Ar H's); ^{13}C NMR 29.4 (C-5), 36.5 (C-13), 51.0 (C-6), 58.4 (C-8), 59.7 (C-14), 125.3, 125.6, 126.0, 128.6, 128.7, 134.3 (aromatic C's); IR 2960, 2840, 2780, 2740, 1640, 1450, 900 cm^{-1}; mass spectrum, m/e (relative intensity) 235 (M^+, 21), 132 (4), 130 (100), 104 (100); high-resolution mass spectrum, m/e 235.1408 ($C_{17}H_{17}N$ requires 235.1362).

(4,5-Dimethoxy-2-(trimethylsilyl)benzyl)trimethylsilane (28). A flame-dried, 250-mL three-neck round-bottomed flask, equipped with a magnetic stirrer, reflux condenser, N_2 inlet, and 125-mL addition funnel, was charged with dry magnesium turnings (784 mg, 32.2 mmol), anhydrous THF (5 mL), and trimethylsilyl chloride (3.5 g, 32.2 mmol). A solution of 2-bromo-4,5-dimethoxybenzyl bromide (27) (2.0 g, 6.45 mmol) in anhydrous THF (100 mL) was added slowly. After addition was complete, the mixture was stirred at 25 °C for 5 h. The solution was then decanted into an aqueous $NaHCO_3$ solution. The organic layer was separated, dried,a nd concentrated in vacuo, giving a residue, which was subjected to flash column chromatographic purification on silica gel (1:1 ether/hexane) to give 1.34 g (70%) of the disilane 28: ^{1}H NMR 0.01 (s, 9 H, $Si(CH_3)_3$), 0.30 (s, 9 H, $ArSi(CH_3)_3$), 2.21 (s, 2 H, $ArCH_2Si$), 3.80 (s, 6 H, OCH_3), 6.6 (s, 1 H, Ar H), 6.90 (s, 1 H, Ar H); ^{13}C NMR −0.9 ($Si(CH_3)_3$), 0.9 ($ArSi(CH_3)_3$), 26.1 ($ArCH_2Si$), 55.5 (OCH_3), 56.1 (OCH_3), 112.1, 118.1, 127.9, 139.9, 146.0, 149.9 (aromatic C's); IR (neat) 2950, 2830, 2590, 1510, 1245, 1050, 858 cm^{-1}; mass spectrum, m/e (relative intensity) 296 (M^+, 19, 281 ($M^+ - CH_3$, 100), 193 (24), 73 ($Si(CH_3)_3$, 73); high-resolution mass spectrum, m/e 296.1637 ($C_{15}H_{28}O_2Si_2$ requires 296.1629).

(2-Bromo-4,5-dimethoxybenzyl)trimethylsilane (29). A solution of bromine (583 mg, 3.65 mmol) in CCl_4 (1 mL) was slowly added to a solution of (4,5-dimethoxy-2-(trimethylsilyl)benzyl)-trimethylsilane (28) (900 mg, 3.04 mmol) in CCl_4 (4 mL) at 15 °C. After the mixture was stirred at 25 °C for 30 min, aqueous $Na_2S_2O_3$ solution was added. The mixture was washed with water, and the aqueous solution was extracted with ether. The ethereal extracts were dried and concentrated in vacuo, and the residue obtained was subjected to flash column chromatography on silica gel (1:1 ether/hexane) to give 895 mg (97%) of the (bromobenzyl)trimethylsilane 29: ^{1}H NMR 0.02 (s, 9 H, $Si(CH_3)_3$), 2.19 (s, 2 H, $ArCH_2Si$), 3.81 (s, 6 H, OCH_3), 6.52 (s, 1 H, Ar H, 6.94 (s, 1 H, Ar H); ^{13}C NMR −1.3 ($Si(CH_3)_3$), 26.3 ($ArCH_2Si$), 56.0 (OCH_3), 56.2 (OCH_3), 112.7, 113.1, 116.0, 132.7, 146.7, 148.4 (aromatic C's); IR (neat) 2945, 1500, 1250, 1060, 850 cm^{-1}; mass spectrum, m/e (relative intensity) 304 ($M^+ + 2$, 13), 302 (M^+, 13), 289 ($M^+ + 2 - CH_3$, 34), 287 ($M^+ - CH_3$, 33e, 150 ($M^+ - Si(CH_3)_3$ − Br, 70e, 73 ($Si(CH_3)_3$, 100); high-resolution mass spectrum, m/e 304.0306, 302.0325 ($C_{12}H_{19}O_2SiBr$ requires 304.0317, 302.0337).

An alternate procedure for preparation of 29 is as follows. Following the method used for preparation of (4,5-dimethoxy-2-(trimethylsilyl)benzyl)trimethylsilane (28), we slowly added a solution of 2-bromo-4,5-dimethoxybenzyl bromide (27) (3 g, 9.57 mmol) in THF to a solution of magnesium turings (282 mg, 11.6 mmol) and trimethylsilyl chloride (2.1 g, 19.3 mmol) in THF. After workup and purification, 2.1 g (71%) of the (bromobenzyl)silane 29 was isolated.

4,5-Dimethoxy-2-((trimethylsilyl)methyl)benzaldehyde (30). To a solution of (2-bromo-4,5-dimethoxybenzyl)trimethylsilane (29) (3.03 g, 10 mmol) in THF (8 mL) was added n-BuLi (1.6 M, 8 mL, 13 mmol) at −78 °C. After the mixture was stirred at −78 °C for 1 h, dimethylformamide (951 mg, 13 mmol) was added. The solution was stirred at −78 °C for 8 h before being poured into ice water. The mixture was extracted with $CHCl_3$, dried, and concentrated in vacuo, giving a residue, which was subjected to flash column chromatography on silica gel ($CHCl_3$) to give 2.1 g (83%) of the benzaldehyde 30: ^{1}H NMR −0.03 (s, 9 H, $Si(CH_3)_3$), 2.51 (s, 2 H, $ArCH_2Si$), 3.86 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 6.45 (s, 1 H, Ar H), 7.27 (s, 1 H, Ar H), 10.05 (s, 1 H, ArCHO); ^{13}C NMR −1.7 ($Si(CH_3)_3$), 22.7 ($ArCH_2Si$), 55.9 (OCH_3), 112.1, 112.7, 125.8, 139.7, 146.6, 153.7 (aromatic C's), 189.9 (ArCH=O); (neat) 2990, 1700 (ArC=O), 1280, 870 cm^{-1}; mass spectrum, m/e (relative intensity) 252 (M^+, 28), 237 ($M^+ - CH_3$, 42e, 221 (32), 179 ($M^+ - Si(CH_3)_3$, 22), 73 ($Si(CH_3)_3$, 100); high-resolution mass spectrum, m/e 252.1192 ($C_{13}H_{20}O_3Si$ requires 252.1182).

4,5-Dimethoxy-2-((trimethylsilyl)methyl)benzyl Alcohol (31). To a solution of 4,5-dimethoxy-2-((trimethylsilyl)-methyl)benzaldehyde (30) (356 mg, 1.41 mmol) in EtOH (3 mL) was added $NaBH_4$ (53.4 mg, 1.41 mmol). The mixture was stirred at 25 °C for 1 h before being poured into water and extracted with $CHCl_3$. The chloroform extracts were dried and concentrated in vacuo, giving a residue, which was subjected to flash column chromatography on silica gel ($CHCl_3$) to give 352 mg (98%) of the benzyl alcohol 31: ^{1}H NMR 0.01 (s, 9 H, $Si(CH_3)_3$), 1.45 (br, 1 H, OH), 2.11 (s, 2 H, $ArCH_2Si$), 3.82 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 4.55 (s, 2 H, $ArCH_2O$), 6.50 (s, 1 H, ArH), 6.89 (s, 1 H, Ar H); ^{13}C NMR −1.4 ($Si(CH_3)_3$), 22.5 ($ArCH_2Si$), 56.0 (OCH_3), 56.2 (OCH_3), 63.3 ($ArCH_2O$), 112.7, 113.3, 129.5, 131.1, 146.4, 148.6 (aromatic C's); IR (neat) 3490 (br, OH), 2950, 1500, 1250, 850 cm^{-1}; mass spectrum, m/e (relative intensity) 254 (M^+, 8), 239 ($M^+ - CH_3$, 32e, 164 ($M^+ - Si(CH_3)_3 - OH$, 100), 73 ($Si(CH_3)_3$, 100); high-resolution mass spectrum, m/e 254.1340 ($C_{13}H_{22}O_3Si$ requires 254.1338).

4,5-Dimethoxy-2-((trimethylsilyl)methyl)benzyl Bromide (19). A solution of 4,5-dimethoxy-2-((trimethylsilyl)methyl)benzyl alcohol (31) (1.5 g, 5.9 mmol), tetrabromomethane (2.53 g, 7.0 mmol), andd triphenylphosphine (1.86 g, 7.0 mmol) in 5 mL of anhydrous ether was stirred at 25 °C for 30 min. The mixture was concentrated in vacuo, dissolved in heptane, and filtered through Celite. The filtrate was concentrated in vacuo, giving a residue, which was subjected to flash column chromatography on silica gel (hexane) to give 1.3 g (70%) of the benzyl bromide 19: ^{1}H NMR 0.01 (s, 9 H, $Si(CH_3)_3$), 2.15 (s, 2 H, $ArCH_2Si$), 3.86 (s, 3 H, OCH_3e, 3.88 (s, 3 H, OCH_3), 4.98 (s, 2 H, $ArCH_2O$), 6.49 (s, 1 H, Ar H), 6.79 (s, 1 H, Ar H); ^{13}C NMR −1.4 ($Si(CH_3)_3$), 23.0 ($ArCH_2Si$), 33.7 ($ArCH_2O$), 55.8 (OCH_3), 56.0 (OCH_3), 112.8, 113.8, 125.7, 132.7, 146.3, 149.4 (aromatic C's); IR (neat) 2950, 1510, 1260, 1120, 850 cm^{-1}; mass spectrum, m/e (relative intensity) 318 ($M^+ + 2$, 1), 316 (M^+, 1e, 235 (100), 163 (20), 73 ($Si(CH_3)_3$, 53), high-resolution mass spectrum, m/e 318.0479, 316.0481 ($C_{13}H_{21}O_2SiBr$ requires 318.0474, 316.0494).

2-(4,5-Dimethoxy-2-((trimethylsilyl)methyl)benzyl)-6,7-dimethoxy-3,4-dihydroisoquinolinium Perchlorate (20). A solution of 4,5-dimethoxy-2-((trimethylsilyl)methyl)benzyl bromide (19) (1.11 g, 3.5 mmol), 6,7-dimethoxy-3,4-dihydroisoquinoline (18)[18a] (1 g, 5.25 mmol), and silver perchlorate (1.1 g, 5.25 mmol) in 10 mL of acetonitrile was stirred at 25 °C for 12 h. The mixture was concentrated in vacuo and dissolved in $CHCl_3$. The $CHCl_3$ solution was stirred at 25 °C for 15 min and filtered through Celite. The filtrate was concentrated in vacuo, giving a residue, which was subjected to flash column chromatographic purification on silica gel (3% MeOH/$CHCl_3$) to give 1.2 g (65%) of desired perchlorate 20, which was recrystallized from MeOH (mp 176–178 °C): ^{1}H NMR 0.01 (s, 9 H, $Si(nCH_3)_3$), 2.10 (s, 2 H, $ArCH_2Si$), 3.30 (t, 2 H, H-4), 3.80–4.0 (m, 14 H, OMe's and H-3), 5.10 (s, 2 H, $ArCH_2N$), 6.55 (s, 1 H, Ar H), 6.78 (s, 1 H, Ar H), 7.10 (s, 1 H, Ar H), 7.35 (s, 1 H, Ar H), 8.75 (s, 1 H, ArCH=N); ^{13}C NMR −1.5 ($Si(CH_3)_3$), 23.3 ($ArCH_2Si$), 25.5 (C-4), 47.6 (C-3), 55.9, 56.7 (OMe), 60.9 ($ArCH_2N$), 110.8, 113.0, 114.4, 116.0, 117.2, 118.4, 132.3, 133.5, 147.3, 149.2, 150.2, 157.8 (aromatic C's), 163.6 (ArCH=N); IR ($CHCl_3$) 3000, 1650 (ArC=N), 1510, 1080, 850 cm^{-1}; UV (MeOH) λ_{max} 370 (ϵ 8 × 10^3), 313 nm (8 × 10^3); mass spectrum, m/e (relative intensity) 428 ($M^+ - ClO_4$, 1), 355 ($M^+ - ClO_4$ − TMS, 10), 238 (21e, 237 (20), 223 (45), 191 (38), 189 (30e, 176 (28), 164 (79), 73 (TMS, 100); high-resolution mass spectrum, m/e 428.2252 ($C_{24}H_{34}NO_4Si$ requires 428.2257).

Irradiation of 2-(4,5-Dimethoxy-2-((trimethylsilyl)-methyl)benzyl)-6,7-dimethoxy-3,4-dihydroisoquinolinium Perchlorate (20). Preparation of (+)-Xylopinine (21). A solution of dihydroisoquinolinium perchlorate 20 (112 mg, 0.21 mmol) in 150 mL of methanol was irradiated through a Pyrex filter (λ >290 nm) for 22 h. The photolysate was subjected to the general workup procedure. The residue obtained was purified by flash column chromatography on silica gel (2% MeOH/$CHCl_3$) to yield 53 mg (70%) of the (+)-xylopinine (21), which was recrystallized from EtOH (mp 154–157 °C, lit.[23] mp 157–158 °C); ^{1}H NMR 2.65 (m, 2 H, H-5), 2.82, 3.22 (AB q, J = 16.0, 11.2, 3.9

Hz, 2 H, H-13), 3.15 (m, 2 H, H-6), 3.57 (dd, J = 11.1, 3.9 Hz, 1 H, H-14), 3.66, 3.93 (AB q, J = 14.5 Hz, 2 H, H-8), 3.9 (m, 12 H, OMe); ^{13}C NMR 29.0 (C-5), 39.4 (C-13), 51.3 (C-6), 56.0 (OMe), 56.1 (OMe), 58.2 (C-8), 59.5 (C-14), 108.8 (C-1), 109.2 (C-9), 111.6 (C-4, C-12), 126.4 (C-8′, C-12′), 126.8 (C-4′), 130.0 (C-14′), 147.5 (C-10, C-11, C-2, C-3); IR ($CHCl_3$) 2940, 2760, 1610, 1510, 1260, 1040 cm^{-1}.

***N,N*-Dimethyl-3,4-(methylenedioxy)benzylamine (38).** To 3 g (19.8 mmol) of piperonylamine (**37**) was added 1.86 g (39.7 mmol) of 98% formic acid followed by 4.82 g (59.5 mmol) of 37% formaldehyde. After heating at 80 °C for 24 h, the mixture was cooled to 25 °C and 15 mL of 6 N HCl was added. The solution was then washed with ether. The aqueous solution was made basic with 5% aqueous NaOH and extracted with ether. The ethereal extracts were washed with water, dried, and concentrated in vacuo, giving an oil, which was purified by molecular distillation (60 °C, 0.02 Torr) to give 3.2 g (90%) of tertiary amine **38**: ^{1}H NMR 2.19 (s, 6 H, $N(CH_3)_2$), 3.29 (s, 2 H, $ArCH_2N$), 5.92 (s, 2 H, OCH_2O), 6.72 (s, 2 H, Ar H's), 6.90 (s, 1 H, Ar H); ^{13}C NMR 43.1 ($N(CH_3)_2$), 64.1 ($ArCH_2N$)e, 100.8 (OCH_2O), 107.8, 109.4, 122.1, 133.0, 146.6, 147.7 (aromatic C's); IR ($CHCl_3$) 2820, 2765, 1500, 1485, 1440, 1240, 1040 cm^{-1}; mass spectrum, m/e (relative intensity) 179 (M^+, 48), 178 (M^+ – H, 28), 136 (38), 135 (M^+ – $N(CH_3)2$, 100); high-resolution mass spectrum, m/e 179.0945 ($C_{10}H_{13}NO_2$ requires 179.0944).

***N,N*-Dimethyl-2-(hydroxymethyl)-3,4-(methylenedioxy)benzylamine (39).** To *N,N*-dimethyl-3,4-(methylenedioxy)benzylamine (**38**) (5 g, 28 mmol) in 20 mL of THF was added *n*-BuLi (22.3 mL, 1.5 M, 33.5 mmol) at −78 °C. The mixture was stirred at 0 °C for 1 h and cooled to −78 °C before being transferred to a cooled (−78 °C) suspension of paraformaldehyde (2.51 g, 28 mmol) in 5 mL of THF. The mixture was then stirred at 25 °C for 3 h, poured into water, and extracted with $CHCl_3$. The chloroform extracts were dried and concentrated in vacuo, and the residue obtained was subjected to flash column chromatographic purification on silica gel (2% MeOH/$CHCl_3$) to yield 5.2 g (90%) of the desired (hydroxymethyl)benzylamine **39**, which was recrystallized from ether (mp 89–91 °C): ^{1}H NMR 2.22 (s, 6 H, $N(CH_3)_2$), 3.43 (s, 2 H, $ArCH_2N$), 4.60 (s, 2 H, $ArCH_2Oe$, 5.97 (s, 2 H, OCH_2O), 6.65 (d, J = 7.7 Hz, 1 H, Ar H), 6.64 (d, J = 7.7 Hz, 1 H, Ar H); ^{13}C NMR 44.0 ($N(CH_3)_2$), 56.0 ($ArCH_2O$), 62.3 ($ArCH_2N$), 100.8 (OCH_2O), 106.2, 123.3, 122.7, 131.2, 145.8, 146.9 (aromatic C's); IR ($CHCl_3$) 3200 (br, OH), 2990, 2830, 1450, 1250, 1070 cm^{-1}; mass spectrum, m/e (relative intensity) 209 (M^+, 35), 165 (M^+ – $N(CH_3)_2$, 100), 164 (60), 148 (15); high-resolution mass spectrum, m/e 209.1047 ($C_{11}H_{15}NO_3$ requires 209.1051).

***N,N*-Dimethyl-2-((*tert*-butyldimethylsiloxy)methyl)-3,4-(methylenedioxy)benzylamine (40).** A solution of *tert*-butyldimethylsilyl chloride (1.73 g, 11.48 mmol) in 3 mL of DMF was added to a solution of *N,N*-dimethyl-2-(hydroxymethyl)-3,4-(methylenedioxy)benzylamine (**39**) (2.0 g, 9.57 mmol) and diisopropylethylamine (1.86 g, 14.35 mmol) in 5 mL of DMF. The mixture was stirred at 25 °C for 2 h, poured into aqueous $NaHCO_3$ solution, and extracted with ether. The ethereal extracts were dried and concentrated in vacuo, giving an oil, which was purified by molecular distillation (130 °C, 0.08 Torr) to yield 3.02 g (98%) of the desired *tert*-butyldimethylsilyl ether **40**: ^{1}H NMR 0.06 (s, 6 H, $Si(CH_3)_2$), 0.88 (s, 9 H, $SiC(CH_3)_3$), 2.20 (s, 6 H, $N(CH_3)_2$), 3.43 (s, 2 H, $ArCH_2N$), 4.78 (s, 2 H, $ArCH_2O$), 5.93 (s, 2 H, OCH_2O), 6.66 (d, J = 7.9 Hz, 1 H, Ar H), 6.76 (d, J = 7.9 Hz, 1 H, Ar H); ^{13}C NMR −5.3 ($Si(CH_3)_2$), 18.4 (SiC), 25.9 ($SiC(CH_3)_3$), 45.5 ($N(CH_3)_2$), 56.6 ($ArCH_2O$), 60.9 ($ArCH_2N$), 100.8 (OCH_2O), 107.0, 121.5, 123.1, 132.1, 146.2 (aromatic C's); IR ($CHCl_3$) 2940, 1450, 1260, 1060 cm^{-1}; mass spectrum, m/e (relative intensity) 323 (M^+, 3e, 308 (M^+ – CH_3, 2), 279 (M^+ – $N(CH_3)_2$, 26), 278 (M^+ – $HN(CH_3)_2$, 100), 266 (M^+ – $C(CH_3)_3$, 8), 221 (28), 190 (35); high-resolution mass spectrum, m/e 323.1917 ($C_{17}H_{29}SiNO_3$ requires 323.1917).

2-((*tert*-Butyldimethylsiloxy)methyl)-3,4-(methylenedioxy)benzyl Chloride (41). To a solution of *N,N*-dimethyl-2-((*tert*-butyldimethylsiloxy)methyl)-3,4-(methylenedioxy)-benzylamine (**40**) (3.26 g, 10.09 mmol) and anhydrous potassium carbonate (2.09 g, 15.1 mmol) in 10 mL of THF was added ethyl chloroformate (1.6 g, 15.1 mmol) at −78 °C. The mixture was warmed to 25 °C and stirred for 12 h, poured into water, and extracted with ether. The ethereal extracts were dried and concentrated in vacuo, and the oil obtained was subjected to molecular distillation (136 °C, 0.05 Torr), to yield 3.05 g (96%) of desired chloride **41**: ^{1}H NMR 0.09 (s, 6 H, $Si(CH_3)e_2$), 0.90 (s, 9 H, $SiC(CH_3)_3$), 4.76 (s, 2 H, $ArCH_2Cl$), 4.82 (s, 2 H, $ArCH_2Oe$, 5.96 (s, 2 H, OCH_2O), 6.70 (d, J = 7.9 Hz, 1 H, Ar H), 6.85 (d, J = 7.9 Hz, 1 H, Ar H); ^{13}C NMR −5.4 ($Si(CH_3)_2$), 18.2 (SiC), 25.9 ($SiC(CH_3)_3$), 44.0 ($ArCH_2Cl$), 56.6 ($ArCH_2O$), 101.2 (OCH_2O), 107.5, 121.1, 124.0, 130.9, 146.1, 147.6 (aromatic C's); IR (neat) 2900, 1460, 1260, 1060 cm^{-1}; mass spectrum, m/e (relative intensity) 316 (M^+ + 2, 1), 314 (M^+, 1), 279 (M^+ – Cl, 2), 257 (M^+ – $C(CH_3)_3$, 100), 227 (22), 208 (11.80), 165 (18), 148 (16), 93 (29); high-resolution mass spectrum, m/e 314.1110 ($C_{15}H_{23}O_3SiCl$ requires 314.1105).

(2-((*tert*-Butyldimethylsiloxy)methyl)-3,4-(methylenedioxy)benzyl)trimethylsilane (42). A solution of 2-((*tert*-butyldimethylsiloxy)methyl)-3,4-(methylenedioxy)benzyl chloride (**41**) (2.7 g, 8.58 mmol) in 100 mL of THF was slowly added to a solution of magnesium turnings (2.08 g, 85.6 mmol) and trimethylsilyl chloride (9.32 g, 85.4 mmol) in 5 mL of THF. After addition of the chloride, the solution was heated to reflux for 2 h, cooled to 25 °C, and filtered through glass wool. The filtrate was poured into water and extracted with ether. The ethereal extracts were dried and concentrated in vacuo, giving a residue, which was subjected to flash column chromatographic purification on silica gel (hexane) to give 1.4 g (46%) of the desired benzylsilane **42**: ^{1}H NMR −0.02 (s, 9 H, $Si(CH_3)_3$), 0.06 (s, 6 H, $Si(CH_3)_2$), 0.89 (s, 9 H, $SiC(CH_3)_3$), 2.18 (s, 2 H, $ArCH_2Si$), 4.62 (s, 2 H, $ArCH_2O$), 5.89 (s, 2 H, OCH_2O), 6.43 (d, J = 8.0 Hz, 1 H, Ar H), 6.62 (d, J = 8.0 Hz, 1 H, Ar H); ^{13}C NMR −5.3 ($Si(CH_3)_3$), −1.3 ($OSi(CH_3)_2$), 21.9 ($ArCH_2Si$), 26.0 ($SiC(CH_3)_3$)e, 57.4 ($ArCH_2O$), 100.5 (OCH_2O), 1075, 119.9, 121.4, 134.0, 144.0, 146.4 (aromatic C's); IR (neat) 2960, 2870, 1480, 1460, 1250, 1060, 840 cm^{-1}; mass spectrum, m/e (relative intensity) 325 (M^+, 14), 295 (M^+ – $C(CH_3)_3$, 60e, 205 (18), 147 (M^+ – $OSi(CH_3)_2C(CH_3)_3$ – $Si(CH_3)_3$ – 1, 100), 73 ($Si(CH_3)_3$); high-resolution mass spectrum, m/e 352.1890 ($C^{18}H_{32}O_3Si_2$ requires 352.1889).

In addition, 340 mg (15%) of (3,4-(methylenedioxy)-2-((trimethylsilyl)methyl)benzyl)trimethylsilane (**44**) was also isolated: ^{1}H NMR 0.02 (s, 9 H, $Si(CH_3)_3$), 0.06 (s, 9 H, $Si(CH_3)_3$), 1.98 (s, 2 H, $ArCH_2Si$), 2.01 (s, 2 H, $ArCH_2Si$), 5.85 (s, 2 H, OCH_2O), 6.48 (d, J = 8.0 Hz, 1 H, Ar H), 6.51 (d, J = 8.0 Hz, 1 H, Ar H); ^{13}C NMR −1.3 ($Si(CH_3)_3$), −0.9 ($Si(CH_3)_3$), 17.5 ($ArCH_2Si$), 23.0 ($ArCH_2Si$), 99.9 (OCH_2O), 104.2, 120.0, 121.1, 131.2, 143.5, 145.0 (aromatic C's); IR (neat) 2940, 1450, 1245, 840 cm^{-1}; mass spectrum, m/e (relative intensity) 294 (M^+, 100), 279 (M^+ – CH_3, 65), 264 (M^+ – $(CH_3e_2$, 20), 249 (M^+ – $(CH_3)_3$, 15), 221 (M^+ – $Si(CH_3)_3$, 35), 205 (65), 189 (55), 147 (M^+ – $2Si(CH_3)_3$ – 1, 45), 73 ($Si(CH_3)_2$, 95); high-resolution mass spectrum, m/e 294.1475 ($C_{15}H_{26}O_2Si_2$ requires 294.1472).

2,3-(Methylenedioxy)-6-((trimethylsilyl)methyl)benzyl Alcohol (34). To a solution of (2-((*tert*-butyldimethylsiloxy)-methyl)-3,4-(methylenedioxy)benzyl)trimethylsilane (**42**) (1.2 g, 3.41 mmol) in THF was added 3.4 mL of 1 N aqueous sulfuric acid. The resultant two-phase mixture was then stirred vigorously for 70 h at 25 °C. Aqueous sodium bicarbonate solution was then added until bubbling subsided. The solution was extracted with ether. The ethereal extracts were dried and concentrated in vacuo, giving a residue, which was subjected to flash column chromatography on silica gel (1:1 ether/hexane) to give 734 mg (91%) of the benzyl alcohol **34**: ^{1}H NMR −0.03 (s, 9 H, $Si(CH_3)_3$), 2.09 (br, 1 H, OH), 2.11 (s, 2 H, $ArCH_2Si$), 4.59 (s, 2 H, $ArCH_2O$), 5.88 (s, 2 H, OCH_2O), 6.44 (d, J = 8.0 Hz, 1 H, Ar H), 6.63 (d, J = 8.0 Hz, 1 H, Ar H); ^{13}C NMR −1.6 ($Si(CH_3)_3$), 22.2 ($ArCH_2Si$), 57.4 ($ArCH_2O$), 100.7 (OCH_2O), 107.8, 119.8, 121.6, 132.8, 144.1, 146.4 (aromatic C's); IR (neat) 3400 (br, OH), 2950, 1450, 1250, 1060, 840 cm^{-1}; mass spectrum, m/e (relative intensity) 238 (M^+, 16), 148 (M^+ – OH – $Si(CH_3)_3$, 100), 73 ($Si(CH_3)_3$); high-resolution mass spectrum, m/e 238.1025 ($C_{12}H_{18}O_3Si$ requires 238.1025).

2,3-(Methylenedioxy)-6-((trimethylsilyl)methyl)benzyl Chloride (43). To a solution of 2,3-(methylenedioxy)-6-((trimethylsilyl)methyl)benzyl alcohol (**34**) (750 mg, 3.15 mmol) in 3 mL of anhydrous ether were added triethylamine (414 mg, 4.09 mmol) and methanesulfonyl chloride (433 mg, 3.78 mmol) at 0 °C. The resulting mixture was at 25 sC for 5 days, poured into water, and extracted with ether. The ethereal extracts were dried and concentrated in vacuo, giving a residue, which was subjected

to flash column chromatography on silica gel (hexane) to afford 705 mg (87%) of the benzyl chloride **43**: ^{1}H NMR 0.05 (s, 9 H, $Si(CH_3)_3$), 2.18 (s, 2 H, $ArCH_2Si$), 4.56 (s, 2 H, $ArCH_2Cl$), 5.97 (s, 2 H, OCH_2O), 6.49 (d, J = 8.0 Hz, 1 H, Ar H), 6.6 (d, J = 8.0 Hz, 1 H, Ar H); ^{13}C NMR −1.5 ($Si(CH_3)_3$), 21.9 ($ArCH_2Si$), 37.8 ($ArCH_2Cl$), 101.1 (OCH_2O), 108.6, 116.5, 121.5, 133.2, 144.2, 146.7 (aromatic C's); IR (neat) 2950, 1480, 1250, 1050, 840 cm^{-1}; mass spectrum, m/e (relative intensity) 258 (M^+ + 2, 10e, 256 (M^+, 26), 241 (M^+ − CH_3, 7), 221 (M^+ − Cl), 148 (M^+ − $Si(CH_3)_3$ − Cl, 100), 73 ($Si(CH_3)_3$, 79); high-resolution mass spectrum, m/e 256.0671 ($C_{12}H_{17}O_2SiCl$ requires 256.0656).

2,3-(Methylenedioxy)-6-((trimethylsilyl)methyl)benzyl Iodide (23). A solution of the 2,3-(methylenedioxy)-6-((trimethylsilyl)methyl)benzyl chloride (**43**) (445 mg, 1.73 mmol) and sodium iodide (338 mg, 2.25 mmol) in 3 mL of acetone was stirred at 25 °C for 5 h. The solution was concentrated in vacuo, giving a residue, which was dissolved in ether and washed with water. The combined ethereal extracts were dried and concentrated in vacuo, giving a residue, which was subjected to flash column chromatography on silica gel (hexane) and recrystallization (hexane) to afford 515 mg (85%) of the benzyl iodide **23** (mp 61 °C): ^{1}H NMR 0.00 (s, 9 H, $Si(CH_3)_3$), 2.06 (s, 2 H, $ArCH_2Si$), 4.31 (s, 2 H, $ArCH_2I$), 5.97 (s, 2 H, OCH_2O), 6.40 (d, J = 8.0, 1 H, Ar H), 6.61 (d, J = 8.0 Hz, 1 H, Ar H); ^{13}C NMR −1.3 ($Si(CH_3)_3$), 22.5 ($ArCH_2Si$), 29.7 ($ArCH_2I$), 101.3 (OCH_2O), 108.2, 117.9, 121.7, 132.6, 144.4, 146.2 (aromatic C's); IR ($CHCl_3$) 2960, 1450, 1250, 1050, 840 cm^{-1}; mass spectrum, m/e (relative intensity) 348 (M^+, 19), 221 (M^+ − I, 93), 148 (M^+ − I − $Si(CH_3)_3$, 30), 73 ($Si(CH_3)_3$, 100); high-resolution mass spectrum, m/e 348.0043 ($C_{12}H_{17}O_2ISi$ requires 348.0043).

Alternate procedure for preparation of the iodide is as follows. To a solution of 2,3-(methylenedioxy)-6-((trimethylsilyl)methyl)benzyl alcohol (**34**) (170 mg, 0.71 mmol) in 3 mL of benzene were added triphenylphosphine (281 mg, 1.07 mmol), diisopropylethylamine (184 mg, 1.43 mmol), and iodine (363 mg, 1.43 mmol). The solution was stirred at reflux for 2 h before dilution with ether and washing with water. The ethereal solution was dried and concentrated in vacuo, giving a residue, which was subjected to flash column chromatography on silica gel (hexane) to afford 100 mg (40%) of the benzyl iodide **23**.

2-(2,3-(Methylenedioxy)-6-((trimethylsilyl)methyl)-benzyl)-6,7-(methylenedioxy)-3,4-dihydroisoquinolinium Perchlorate (24). A solution of 6,7-(methylenedioxy)-3,4-dihydroisoquinoline (**22**)[18b] (201 mg, 1.15 mmol), 2,3-(methylenedioxy)-6-((trimethylsilyl)methyl)benzyl iodide (**23**) (350 mg, 1.0 mmol), and silver perchlorate (239 mg, 1.15 mmol) in CH_3CN was stirred at 25 °C for 5 h. The solution was diluted with $CHCl_3$ and filtered through Celite. The filtrate was concentrated in vacuo, giving a residue, which was subjected to flash column chromatography on silica gel (2% $CH_3OH/CHCl_3$) to afford 350 mg (70%) of the perchlorate salt **24**, which was recrystallized from $CHCl_3$ (mp 186–188 °C): UV (CH_3OH) λ_{max} 373 (ϵ 1.1 × 10^4, 304 nm (1.1 × 10^4); ^{1}H NMR 0.01 (s, 9 H, $Si(CH_3)_3$), 2.19 (s, 2 H, $ArCH_2Si$), 3.16 (t, 2 H, H-4), 3.89 (t, 2 H, H-3), 5.19 (s, 2 H, $ArCH_2N$), 5.93 (s, 2 H, OCH_2Oe, 6.12 (s, 2 H, OCH_2O), 6.55 (d, J = 9.0, 1 H, Ar H), 6.77 (d, J = 9.0, 1 H, Ar H), 6.80 (s, 1 H, Ar H), 7.30 (s, 1 H, Ar H), 8.85 (s, 1 H, ArCH=N); ^{13}C NMR −1.8 ($Si(CH_3)_3$), 22.9 ($ArCH_2Si$), 25.9 (C-4), 47.1 (C-3), 56.3 ($ArCH_2N$), 101.7 (OCH_2O), 103.1 (OCH_2O), 108.8, 110.0, 113.0, 110.3, 118.4, 122.5, 134.1, 134.9, 144.6, 147.5, 148.1, 156.5 (aromatic C's), 165.0 (ArCH=N); IR ($CHCl_3$) 2940, 1660 (ArC=N), 1600, 1290, 1250, 1090 cm^{-1}; mass spectrum, m/e (relative intensity) 396 (M^+ − ClO_4, 6), 310 (18), 220 (59), 176 (49), 148 (63), 73 (100); high-resolution mass spectrum, m/e 396.1634 ($C_{22}H_{26}NO_4Si$ requires 396.1631).

Irradiation of 2-(2,3-(Methylenedioxy)-6-((trimethylsilyl)methyl)benzyl)-6,7-(methylenedioxy)-3,4-dihydroisoquinolinium Perchlorate (24). Preparation of (+)-Stylopine (25). A N_2-purged solution of dihydroisoquinolinium perchlorate **24** (100 mg, 0.2 mmol) in 95 mL of methanol was irradiated for 17 h with a flint glass filter (λ >310 nm). The photolysate was made basic and subjected to the normal workup procedure. The residue obtained was subjected to flash column chromatography on silica gel (1% $MeOH/CHCl_3$) to yield 40 mg (61%) of the cyclized product, (+)-stylopine (**45**), which was recrystallized from MeOH (mp 213–215 °C, lit.[30] mp 217–218 °C): UV (MeOH) λ_{max} 289.4 nm (ϵ 4.88 × 10^3); ^{1}H NMR 2.64 (m, 2 H, H-5 and H-6), 2.79, 3.22 (AB qd, J = 15.9, 11.4, 3.7 Hz, 2 H, H-13), 3.1 (m, 2 H, H-5 and H-6), 3.52, 4.09 (AB q, J = 15.3 Hz, 2 H, H-8), 3.56 (dd, J = 11.5, 3.5 Hz, 1 H, H-14), 5.92 (s, 2 H, OCH_2O), 5.92, 5.96 (AB q, J = 1.5 Hz, 2 H, OCH_2O), 6.59 (s, 1 H, Ar H), 6.63 (d, J = 8.3 Hz, 1 H, Ar H), 6.68 (d, J = 8.3 Hz, 1 H, Ar H), 7.3 (s, 1 H, Ar H); ^{13}C NMR 2.96 (C-5), 36.5 (C-13), 51.2 (C-6), 52.9 (C-8), 59.8 (C-14), 100.7, 101.0 (OCH_2O), 105.5 (C-1), 106.7 (C-11e, 108.4 (C-4), 116.9 (C-8′), 121.0 (C-12), 127.8 (C-4′), 128.6 (C-12′), 130.8 (C-14′), 145.0 (C-10e, 146.0 (C-2e, 146.2 (C-3 and C-9); IR ($CHCl_3$) 2935, 2820, 2780, 2760, 1490, 1040 cm^{-1}.

2-(*o*-((Trimethylsilyl)methyl)benzyl)-6,7-(methylenedioxy)-3,4-dihydroisoquinolinium Perchlorate (46). Following the procedure used for preparation of 2-(2*o*-((trimethylsilyl)-methyl)benzyl)-3,4-dihydroisoquinolinium perchlorate (**16**), we stirred a solution of 6,7-(methylenedioxy)-3,4-dihydroisoquinoline[18] (227 mg, 1.30 mmol), *o*-((trimethylsilyl)methyl)benzyl iodide[5b] (789 mg, 2.59 mmol), and silver perchlorate (347 mg, 1.69 mmol) in 5 mL of CH_3CN at 25 °C for 5 h. After workup, the crude salt was recrystallized from $CHCl_3$ to yield 386 mg (66%) of the iminium salt **46** (mp 188–190 °C): ^{1}H NMR 0.01 (s, 9 H, $Si(CH_3)_3$), 2.21 (s, 2 H, $ArCH_2Si$), 3.20 (t, 2 H, H-4), 3.89 (t, 2 H, H-3), 5.20 (s, 2 H, $ArCH_2N$), 6.09 (s, 2 H, OCH_2O), 6.80 (s, 1 H, Ar H), 7.05–7.45 (m, 5 H, Ar H's), 9.09 (s, 1 H, ArCH=N); ^{13}C NMR −1.6 ($Si(CH_3)_3$), 23.6 ($ArCH_2Si$), 25.8 (C-4), 47.5 (C-3), 60.9 ($ArCH_2N$), 103.0 (OCH_2O), 108.9, 112.6, 125.4, 129.5, 118.3, 127.0, 130.1, 130.5, 135.2, 140.7, 155.3 (aromatic C's), 163.9 (ArCH=N); IR ($CHCl_3$) 2960, 1650 (ArC=N), 1600, 1490, 1250, 1090, 850 cm^{-1}; UV (MeOH) λ_{max} 372 (ϵ 9 × 10^3), 309 nm (7 × 10^3); mass spectrum, m/e (relative intensity) 352 (M^+ − ClO_4, 8), 279 (M^+ − ClO_4 − TMS, 5), 176 (43), 175 (61), 174 (65), 173 (62), 172 (44), 148 (31), 73 (TMS, 100); high-resolution mass spectrum, m/e (352.1720 ($C_{21}H_{26}NO_2Si$ requires 352.1713).

Irradiation of 2-(*o*-((Trimethylsilyl)methyl)benzyl)-6,7-(methylenedioxy)-3,4-dihydroisoquinolinium Perchlorate (46). A solution of the dihydroisoquinolinium perchlorate **46** (100 mg, 0.22 mmol) in 90 mL of MeOH was irradiated with flint glass filtered light (λ >300 nm) for 0.5 h. The photolysate was subjected to the general workup procedure. The residue obtained was purified by flash column chromatography on silica gel ($CHCl_3$) to yield 46 mg (74%) of the cyclized product **47**: ^{1}H NMR 2.45–2.65 (m, 2 He, 2.81 (dd, 1 H), 2.95–3.15 (m, 2 H), 3.21 (dd, 1 H), 3.52 (dd, 1 H), 3.85 (AB q, 2 H), 5.88 (s, 2 H, OCH_2O), 6.55 (s, 1 H, Ar H), 6.71 (s, 1 H, Ar H), 7.1 (m, 4 H, Ar H's); ^{13}C NMR 29.5 (C-5), 37.0 (C-6), 51.3 (C-13), 58.5 (C-8), 59.9 (C-14), 100.7 (OCH_2O), 105.5, 108.4, 125.8, 126.1, 126.3, 127.8, 128.7, 130.9, 134.3, 134.4, 145.9, 146.2 (aromatic C's); IR ($CHCl_3$) 2940, 2740, 2760, 1640, 1460, 1240, 1040, 850 cm^{-1}; mass spectrum, m/e (relative intensity) 279 (M^+, 100), 278 (M^+ − 1, 100), 174 (60), 148 (12), 104 (42); high-resolution mass spectrum, m/e 279.1259 ($C_{18}H_{17}NO_2$ requires 279.1259).

Fluorescence Measurements. Fluorescence spectra were recorded by using a Perkin-Elmer 44 fluorescence spectrophotometer equipped with a differential corrected spectral unit. The wavelength of excitation of the salts corresponded to the wavelength of maximum absorption in the UV spectrum. Emission scans were run in the range of emission with an excitation and emission bandpass of 3 nm. The scan rate was 120 nm/min. Solutions of the fluorescencing species were approximately 1 × 10^{-3} M in CH_3CN for 2-methyl-3,4-dihydroisoquinolinium perchlorate (**48**) and 1 × 10^{-4} M in CH_3CN for 2-methyl-6,7-(methylenedioxy)-3,4-dihydroisoquinolinium perchlorate (**49**). Concentrations of the arene quenchers ranged from 0 to 6 × 10^{-3} M. The fluorescence spectra were recorded at 25 °C on nondegassed solutions. Stern-Volmer plots of the data yielded straight lines with slopes of $k_q\tau$.

Quantum Yield Measurements. Quantum yields were measured by using a "linear optical bench" system equipped with a high-pressure 500-W mercury lamp (Illumination Industries Model CA-200-8003), the output of which was focused with a quartz collimator and passed through a quartz-faced, water-cooled, three-compartment filter solution cell. The filtered light was passed through a beam splitter which diverted light 90°. The light not diverted passed through a quartz-faced, water-cooled cell. During the actinometer calibration runs, the cell was filled with 0.012 M potassium ferrioxalate. During photolysis runs, the cell contained prepared solutions of starting materials. The

diverted light was received by a silicon solar cell in order to monitor the light output. The signal received by the solar cell was amplified and fed through a Raytheon RC-4151 voltage/frequency converter. Integration of this signal was performed by counting the frequency transmitted by the converter.

The amount of light not diverted was determined by calibration of the solar cell against ferrioxalate actinometry. The light absorbed by the cell containing the potassium ferrioxalate was determined at several different percent conversions. A plot of millieinsteins versus the number of counts obtained from the electronic counter for each run was used to determine the light output during quantum yield runs.

For measurement of the quantum yield for photocyclization of 2-(*o*-((trimethylsilyl)methyl)benzyl)-3,4-dihydroisoquinolinium perchlorate (**16**), the filter solution cells contained separately 1.0 M nickel sulfate hexahydrate in 5% H_2SO_4, 0.8 M cobalt sulfate heptahydrate in 5% H_2SO_4, and 0.1 mM bismuth chloride in 10% HCl. The UV transmission of this filter solution was 265–300 nm with a maximum of 284 nm. For measurement of quantum yields for photocyclization of the methylenedioxy-substituted dihydroisoquinolinium perchlorates **24** and **46**, the filter solution cells contained separately 1.0 M cobalt sulfate heptahydrate in 10% H_2SO_4, 0.023 M copper sulfate pentahydrate in 5% H_2SO_4, and 0.004 M potassium metavanadate in H_2O. The UV transmission of this filter solution was 335–450 nm with a maximum at 395 nm. Product analyses were accomplished by use of a UV spectroscopic method by measurement of the consumption of the starting salt according to the decrease of absorbance.

Reaction of Dihydroisoquinolinium Perchlorates 16, 20, and 24 with Cesium Fluoride. Solutions (ca. 1–3 mM) of the dihydroisoquinolinium perchlorates and cesium fluoride (5 equiv) in EtOH or MeCN were stirred at reflux for 12 h. Reaction mixtures were concentrated, washed with water, and subjected to the usual workup and chromatographic purification on silica gel. The spectroscopic data for the reaction products are as follows.

81: ^{1}H NMR 0.15 (s, 9 H, $Si(CH_3)_3$), 2.41 (s, 2 H, $ArCH_2Si$), 2.85 (t, 2 H, H-4), 3.01 (t, 2 H, H-3), 3.72 (s, 2 H, $ArCH_2N$), 3.87 (s, 2 H, $ArCH_2N$), 7.10–7.51 (m, 8 H, Ar H's); ^{13}C NMR –1.1 ($Si(CH_3)_3$e, 23.0 ($ArCH_2Si$), 29.3 (C-4), 50.8 (C-3), 56.3 ($ArCH_2N$), 60.8 ($ArCH_2N$), 123.9, 125.6, 126.0, 126.6, 126.8, 128.6, 129.3, 130.1, 134.6, 134.7, 135.2, 140.1 (aromatic C's); IR ($CHCl_3$) 2940, 1650, 1250, 860 cm^{-1}; mass spectrum, *m/e* (relative intensity) 309 (M^+, 28e, 307 (10), 294 ($M^+ - CH_3$, 8), 236 (M^+ - TMS, 6), 161 (42), 132 (100), 73 (TMS, 55); high-resolution mass spectrum, *m/e* 309.1902 ($C_{20}H_{27}NSi$ requires 309.1913).

84: ^{1}H NMR 2.25 (s, 3 H, $ArCH_3$), 2.85 (t, 2 H, H-4), 3.35 (t, 2 H, H-3), 4.80 (s, 2 H, $ArCH_2N$), 7.11–7.45 (m, 4 H, Ar H's); ^{13}C NMR 19.3 ($ArCH_3$), 28.1 (C-4), 44.8 (C-3), 48.2 ($ArCH_2N$), 126.0, 126.9, 127.1, 127.5, 128.5, 129.4, 130.6, 131.7, 134.9, 136.8, 138.0 (aromatic C's); IR (neat) 2940, 1659 (ArC=O), 1310, 750 cm^{-1}; mass spectrum, *m/e* (relative intensity) 251 (M^+, 100)e, 236 ($M^+ - CH_3$, 32), 149 (72), 104 (92); high-resolution mass spectrum, *m/e* 251.1307 ($C_{17}H_{17}NO$ requires 251.1310).

82: ^{1}H NMR –0.10 (s, 9 H, $Si(CH_3)_3$), 2.10 (s, 2 H, $ArCH_2Si$), 2.62 (t, 2 H, H-4), 2.71 (t, 2 H, H-3), 3.41 (s, 2 H, $ArCH_2N$), 3.50 (s, 2 H, $arCH_2N$), 3.74 (s, 3 H, OMe), 3.75 (s, 9 H, OMe), 6.45 (s, 2 H), 6.55 (s, 1 H), 6.89 (s, 1 H); ^{13}C NMR –1.2 ($Si(CH_3)_3$), 22.5 ($ArCH_2Si$), 28.8 (C-4), 50.6 (C-3), 55.8 (OMe), 55.9 (OMe), 56.0 (OMe), 60.0 ($ArCH_2N$), 109.6, 111.4, 112.5, 113.4, 126.4, 126.6, 127.0, 131.9, 145.6, 147.2, 147.5; IR (neat) 2960, 1620, 1520, 1250, 850 cm^{-1}; mass spectrum, *m/e* (relative intensity) 429 (M^+, 11e, 414 ($M^+ - CH_3$, 4), 256 (M^+ - TMS, 2), 236 (100), 192 (70), 164 (45), 73 (TMS, 100); high-resolution mass spectrum, *m/e* 429.2323 ($C_{24}H_{35}NO_4Si$ requires 429.2325).

83: ^{1}H NMR –0.10 (s, 9 H, $Si(CH_3)_3$), 2.15 (s, 2 H, $ArCH_2Si$), 2.65 (m, 4 H, H-3 and H-4), 3.49 (s, 4 H, $ArCH_2N$), 5.81 (s, 2 H, OCH_2O), 5.85 (s, 2 H, OCH_2O), 6.41 (d, J = 7 Hz, 1 H), 6.42 (s, 1 H), 6.50 (s, 1 H), 6.61 (d, J = 7 Hz, 1 H); ^{13}C NMR –1.2 ($Si(CH_3)_3$), 22.1 ($ArCH_2Si$), 29.1 (C-4), 50.5 (C-3), 53.3 ($ArCH_2N$), 56.0 ($ArCH_2N$), 100.4 (OCH_2O), 100.5 (OCH_2O), 106.5, 107.2, 108.3, 117.1, 121.3, 127.4, 128.0, 134.9, 143.5, 145.6, 146.0, 147.3; IR (neat) 2960, 1480, 1250, 1050, 850 cm^{-1}; mass spectrum, *m/e* (relative intensity) 397 (M^+, 37), 310 (17), 220 (78), 205 (33), 176 (49), 148 (69), 73 (TMS, 100); high-resolution mass spectrum, *m/e* 397.1707 ($C_{22}H_{27}NO_4Si$ requires 397.1704).

86: ^{1}H NMR 2.25 (s, 3 H, $ArCH_3$), 2.75 (t, 2 H, H-4), 3.36 (t, 2 H, H-3), 4.80 (s, 2 H, $ArCH_2N$), 5.95 (s, 2 H, OCH_2O), 6.02 (s, 2 H, OCH_2O), 6.54 (d, 1 H, Ar H), 6.65 (s, 1 H, Ar H), 6.67 (d, 1 H, Ar H), 7.60 (s, 1 H, Ar H); ^{13}C NMR 18.3 ($ArCH_3$), 28.2 (C-4), 41.4 (C-3), 44.4 ($ArCH_2N$), 100.8, 101.4 (OCH_2O), 106.8, 107.5, 108.5, 117.1, 122.9, 123.8, 131.6, 133.6, 145.3, 146.9, 147.4, 150.4 (aromatic C's), 163.9 (ArC=O); IR ($CHCl_3$) 2880, 1640, 1600, 1450, 1050, 740 cm^{-1}; mass spectrum, *m/e* (relative intensity) 339 (M^+, 19), 204 (14), 148 (100); high-resolution mass spectrum, *m/e* 339.1114 ($C_{19}H_{17}NO_5$ requires 339.1107).

***o*-((Trimethylsilyl)methyl)benzyl Chloride (53).** To a stirred solution of triphenylphosphine (13.3 g, 50.7 mmol) in 40 mL of CCl_4 was added *o*-((trimethylsilyl)methyl)benzyl alcohol (**13**) (7.5 g, 38.6 mmol). After being stirred at reflux for 4 h, the solution was cooled to 25 °C. Heptane was added and stirring was continued for an additional 10 min. The precipitated triphenylphosphine oxide was removed by filtration through Celite. Concentration of the filtrate followed by molecular distillation (50 °C, 0.01 Torr) of the residue provided 7.5 g (91%) of the chloride **53**: ^{1}H NMR 0.06 (s, 9 H, $Si(CH_3)_3$), 2.28 (s, 2 H, $ArCH_2Si$), 4.60 (s, 2 H, $ArCH_2Cl$), 7.05–7.35 (m, 4 H, Ar H's); ^{13}C NMR –1.4 ($Si(CH_3)_3$), 23.1 ($ArCH_2Si$), 45.1 ($ArCH_2Cl$), 124.6 128.6, 129.6, 130.3, 133.8, 139.4 (aromatic C's); IR 2940, 1600, 1450, 1240, 1150, 850 cm^{-1}; mass spectrum, *m/e* (relative intensity) 214 (M^+ + 2, 0.4), 212 (M^+, 1.1), 104 (100), 73 (TMS, 41); high-resolution mass spectrum, *m/e* 212.0783 ($C_{11}H_{17}SiCl$ requires 212.0788).

1-(*o*-((Trimethylsilyl)methyl)benzyl)-1,2,3,4-tetrahydroisoquinoline (54). To 2.3 g (99 mg-atom) of magnesium turnings in 8 mL of anhydrous ether was added 0.2 mL of ethylene bromide. The solution was stirred for 10 min. A solution of *o*-((trimethylsilyl)methyl)benzyl chloride (**53**) (1.1 g, 5.1 mmol) in 50 mL of anhydrous ether was added dropwise over a period of ca. 1 h with vigorous stirring. After being stirred at reflux for an additional 1 h, the reaction mixture was cooled to 25 °C. To the stirred solution was added 3,4-dihydroisoquinoline (1.2 g, 8.7 mmol) dropwise. With continued stirring, the mixture was heated to reflux for 4 h, cooled to 25 °C and filtered through glass wool. The filtrate was washed with saturated ammonium chloride and extracted with ether. The ethereal extracts were dried and concentrated in vacuo to give a residue, which was subjected to flash column chromatographic purification on silica gel (2% $MeOH/CHCl_3$) to give 1.23 g (75%) of tetrahydroisoquinoline **54**: ^{1}H NMR 0.02 (s, 9 H, $Si(CH_3)_3$), 1.89 (br, 1 H, NH), 2.24 (s, 2 H, $ArCH_2Si$), 2.74–2.98 (m, 4 He, 3.17–3.28 (m, 2 H), 4.19 (dd, 1 H, ArCHN), 7.00–7.24 (m, 8 H, Ar H's); ^{13}C NMR –1.3 ($Si(CH_3)_3$), 23.5 ($ArCH_2Si$), 30.0 (C-4), 39.7 (C-3), 40.7 (CH_2), 56.3 (ArCHN), 124.3, 125.7, 126.1, 129.3, 129.4, 130.4, 135.3, 135.6, 139.0, 139.2 (aromatic C's); IR ($CHCl_3$) 2940, 1459, 1450, 1245, 850 cm^{-1}; mass spectrum, *m/e* (relative intensity) 309 (M^+, 0.2e, 307 (1.5), 294 ($M^+ - CH_3$, 7), 132 (100), 73 (TMS, 17); high-resolution mass spectrum, *m/e* 309.1872 ($C_{20}H_{27}NSi$ requires 309.1913).

1-(*o*-((Trimethylsilyl)methyl)benzyl)-3,4-dihydroisoquinoline (55). To a solution of *N*-chlorosuccinimide (150 mg, 1.12 mmol) in anhydrous ether in an aluminum foil wrapped round-bottomed flask was added 1-(*o*-((trimethylsilyl)methyl)-benzyl)-1,2,3,4-tetrahydroisoquinoline (**54**) (181 mg, 0.58 mmol). The solution was stirred at 25 °C for 0.5 h before being washed with aqueous $NaHCO_3$ and extracted with ether. The ethereal extracts were dried and concentrated in vacuo. Without further purification, the residue was dissolved in MeOH. The methanol solution was added to a solution of KOH (0.3 g, 5.3 mmol) in MeOH at 0 °C. After being stirred at 25 °C for 1 h, the solution was washed with water and extracted with ether. The ethereal extracts were dried and concentrated in vacuo, giving 160 mg (88%) of dihydroisoquinoline **55**: ^{1}H NMR 0.05 (s, 9 H, $Si(CH_3)_3$), 2.21 (s, 2 H, $ArCH_2Si$), 2.73 (t, 2 H, H-4), 3.75 (t, 2 H, H-3), 4.0 (s, 2 H, $ArCH_2C$=N), 6.95–7.35 (m, 8 H, Ar H's); ^{13}C NMR –1.3 ($Si(CH_3)_3$), 23.5 ($ArCH_2Si$), 26.0 (C-4), 40.1 (C-3), 47.0 ($ArCH_2$-C=N), 124.1, 125.3, 126.0, 127.3, 128.8, 129.0, 129.1, 130.2, 134.3, 137.7, 138.5 (aromatic C's); IR ($CHCl_3$) 3000, 2950, 1625 (ArC=N), 1600, 1430, 1200, 820 cm^{-1}; mass spectrum, *m/e* (relative intensity) 307 (M^+, 55), 234 (M^+ - TMS, 84), 220 (100), 73 (TMS, 100); high-resolution mass spectrum, *m/e* 307.1712 ($C_{20}H_{25}SiN$ requires 307.1757); UV (CH_3CN) λ_{max} 253 nm (ϵ 1.4 × 10^4).

Upon flash column chromatographic purification on silica gel (1% $MeOH/CHCl_3$), this dihydroisoquinoline **55** undergoes air

oxidation to form the corresponding 1-(*o*-((trimethylsilyl)-methyl)benzoyl)-3,4-dihydroisoquinoline: ^{1}H NMR 0.01 (s, 9 H, $Si(CH_3)_3$), 2.70 (s, 2 H, $ArCH_2Si$), 2.85 (t, 2 H, H-4), 3.95 (t, 2 H, H-3), 7.0–7.7 (m, 8 H, Ar H's); ^{13}C NMR –1.4 ($Si(CH_3)_3$), 25.5 ($ArCH_2Si$), 25.9 (C-4, 46.6 (C-3), 123.7, 127.0, 127.1, 127.9, 131.0, 132.6, 133.2, 133.3 (aromatic CH's), 137.4, 145.2 (aromatic C's), 167.1 (ArC=N), 195.9 (C=O); IR (neat) 2950, 1690 (ArC=O), 1670 (ArC=N), 1600, 1250, 850 cm^{-1}; mass spectrum, *m/e* (relative intensity), 321 (M^+, 28), 320 (40), 306 ($M^+ - CH_3$, 14), 248 (M^+ – TMS, 17), 232 (M^+ – TMS – O, 23), 73 (TMS, 100); high-resolution mass spectrum, *m/e* 321.1517 ($C_{20}H_{23}NOSi$ requires 321.1549).

1-(*o*-((Trimethylsilyl)methyl)benzyl)-2-methyl-3,4-dihydroisoquinolinium Perchlorate (56). An acetonitrile solution of 1-(*o*-((trimethylsilyl)methyl)benzyl)-3,4-dihydroisoquinoline (**55**) (1.1 g, 3.58 mmol), methyl iodide (1 g, 7 mmol), and silver perchlorate (1 g, 4.8 mmol) was stirred at 25 °C for 2 h and then filtered. Concentration of the filtrate in vacuo gave a residue, which was subjected to column chromatographic purification on Florisil (3% MeOH/$CHCl_3$) to give 1.0 g (66%) of the perchlorate **56**. The perchlorate **56** can be recrystallized from MeOH (mp 156–158 °C): ^{1}H NMR 0.03 (s, 9 H, $Si(CH_3)_3$), 2.19 (s, 2 H, $ArCH_2Si$), 3.29 (t, 2 H, H-4), 2.68 (s, 3 H, NCH_3), 4.18 (t, 2 H, H-3), 4.40 (s, 2 H, $ArCH_2C$=N), 6.56–7.71 (m, 8 H, Ar H's); ^{13}C NMR –1.5 ($Si(CH_3)_3$), 23.6 ($ArCH_2Si$), 25.3 (C-4), 35.6 (C-3), 44.9 (NCH_3), 53.1 ($ArCH_2C$=N), 125.4, 126.3, 127.8, 128.3, 128.4, 128.8, 130.0, 136.6, 137.2, 139.3 (aromatic C's), 177.9 (ArC=N); IR ($CHCl_3$) 1650 (ArC=N), 1600, 1350, 1250, 850 cm^{-1}; UV (MeOH) λ_{max} 277 nm (ϵ 1.3 × 10^4); mass spectrum, *m/e* (relative intensity) 322 ($M^+ - ClO_4$, 35), 321 (100), 306 (20), 234 (48), 162 (50), 144 (45), 73 (TMS, 20); high-resolution mass spectrum, *m/e* 322.1940 ($C_{21}H_{28}NSi$ requires 322.1899).

1-(*o*-Methylbenzyl)-1,2,3,4-tetrahydroisoquinoline (72). Following the procedure used for preparation of 1-(*o*-((trimethylsilyl)methyl)benzyl)-1,2,3,4-tetrahydroisoquinoline (**54**), we prepared 1-(*o*-methylbenzyl)-1,2,3,4-tetrahydroisoquinoline (**72**) from *o*-methylbenzyl chloride (790 mg, 5.6 mmol), magnesium turnings, and 3,4-dihydroisoquinoline (900 mg, 6.8 mmol). This provided 1.06 g (79%) of the tetrahydroisoquinoline **72**: ^{1}H NMR 2.02 (br, 1 H, NH), 2.39 (s, 3 H, $ArCH_3$), 2.80–3.00 (m, 4 H), 3.19–3.41 (m, 2 H), 4.20 (dd, *J* = 5.2, 1.8 Hz, ArCHN), 7.12–7.23 (m, 8 H, Ar H's); ^{13}C NMR 19.6 ($ArCH_3$), 29.9 (C-4), 39.8 ($ArCH_2CHAr$), 40.4 (C-3), 55.8 (ArCHN), 125.6, 126.0, 126.1, 126.2, 126.5, 129.3, 130.2, 130.5, 135.2, 136.2, 136.6, 137.4, 138.9 (aromatic C's); IR (neat) 3300, 2940, 1480, 700 cm^{-1}; mass spectrum, *m/e* (relative intensity) 237 (M^+, 15), 236 (100), 220 (74), 132 (100), 105 (20); high-resolution mass spectrum, *m/e* 237.1443 ($C_{17}H_{19}N$ requires 237.1517).

1-(*o*-Methylbenzyl)-3,4-dihydroisoquinoline (73). Following the procedure used for preparation of 1-(*o*-((trimethylsilyl)-methyl)benzyl)-3,4-dihydroisoquinoline (**55**), we 1-(*o*-methylbenzyl)-3,4-dihydroisoquinoline (**73**) we prepared from 1-(*o*-methylbenzyl)-1,2,3,4-tetrahydroisoquinoline (**72**) (1.43 g, 6.0 mmol) and *N*-chlorosuccinimide (0.97 g, 7.2 mmol) followed by dehydrochlorination with KOH (0.41 g, 7.2 mmol) to give 980 mg (70%) of the dihydroisoquinoline **73**: ^{1}H NMR 2.39 (s, 3 H, $ArCH_3$), 2.74 (t, 2 H, H-4), 3.74 (t, 2 H, H-3), 4.05 (s, 2 H, $ArCH_2C$=N), 7.09–7.41 (m, 8 H, Ar H's); ^{13}C NMR 20.0 ($ArCH_3$), 26.2 (C-4), 40.1 (C-3), 47.1 ($ArCH_2C$=N), 125.4, 126.0, 126.4, 126.9, 127.5, 129.0, 129.1, 130.1, 130.5, 136.4, 137.9 (aromatic C's), 165.7 (ArC=N); IR (neat) 2940, 1680 (ArC=N), 1240, 750 cm^{-1}; mass spectrum, *m/e* (relative intensity) 235 (M^+, 52e, 234 (51), 220 ($M^+ - CH_3$, 100); high-resolution mass spectrum, *m/e* 235.1356 ($C_{17}H_{17}N$ requires 235.1352).

2-Methyl-1-(*o*-methylbenzyl)-3,4-dihydroisoquinolinium Perchlorate (74). Folowing the procedure used for preparation of 2-methyl-1-(*o*-((trimethylsilyl)methyl)benzyl)-3,4-dihydroisoquinolinium perchlorate (**56**), we prepared 2-methyl-1-(*o*-methylbenzyl)-3,4-dihydroisoquinolinium perchlorate (**74**) from 1-(*o*-methylbenzyl)-3,4-dihydroisoquinoline (**73**) (553 mg, 2.35 mmol), methyl iodide (1.66 g, 11.72 mmol), and silver perchlorate (585 mg, 2.8 mmol). This produced 550 mg (67%) of the perchlorate salt **74**: ^{1}H NMR (CD_3CN), 2.45 (s, 3 H, $ArCH_3$), 3.25 (t, 2 H, H-4), 3.65 (s, 3 H, NCH_3), 4.16 (t, 2 H, H-3), 4.46 (s, 2 H, $ArCH_2C$=N), 6.75–7.80 (m, 8 H, Ar H's); ^{13}C NMR 20.0 ($ArCH_3$), 26.2 (C-4), 35.6 (C-3), 46.0 (NCH_3), 54.3 ($ArCH_2C$=N), 118.0, 127.5, 127.9, 128.2, 129.0, 129.4, 129.6, 131.6, 132.0, 132.6, 137.7, 137.9, 138.6 (aromatic C's), 178.9 (ArC=N); IR (KBr) 1640 (ArC=N), 1080, 740 cm^{-1}; UV (MeOH) λ_{max} 281 nm (ϵ 1.4 × 10^4); mass spectrum, *m/e* (relative intensity) 250 ($M^+ - ClO_4$, 15), 149 (85), 234 (93), 131 (27); high-resolution mass spectrum, *m/e* 250.1565 ($C_{18}H_{20}N$ requires 250.1594).

Photolysis of the 1-Xylyl-3,4-dihydroisoquinolinium Perchlorates 56, 57, and 74–76. Following the general preparative photochemical reaction procedure outlined above, we irradiated nitrogen-purged solutions (ca. 1.5–5.0 mM) of the 1-xylyldihydroisoquinolinium perchlorates with Corex glass filtered light. The N–H substituted dihydroisoquinolinium perchlorates were generated in situ by addition of 4 equiv of 70% aqueous $HClO_4$ to solutions of the corresponding dihydroisoquinoline at 4 °C. The products are as follows.

58: ^{1}H NMR 2.29 (s, 3 H, NCH_3), 2.88–2.94 (t, 2 H, H-5), 3.01–3.07 (t, 2 H, H-6), 3.26, 3.55 (AB q, *J* = 16.7 Hz, 4 H, H-8 and H-13), 6.93–7.18 (m, 8 H, Ar H's); ^{13}C NMR 26.9 (C-5), 38.1 (NCH_3), 46.3 (C-8, C-13), 48.0 (C-6), 68.8 (C-14e, 124.0, 125.9, 126.0, 126.3, 126.7, 128.6, 132.7, 141.9 (aromatic C's); IR ($CHCl_3$) 2940, 1600, 1485, 1100, 750 cm^{-1}; mass spectrum, *m/e* (relative intensity) 249 (M^+, 57), 248 (40), 234 ($M^+ - CH_3$, 82), 146 (100), 131 (22), 104 (16), high-resolution mass spectrum, *m/e* 249.1456 ($C_{18}H_{19}N$ requires 249.1395).

59: ^{1}H NMR 2.29 (br, 1 H, NH), 2.86 (t, 2 H, H-5), 3.15 (t, 2 H, H-6), 3.22, 3.48 (AB q, *J* = 16.4 Hz, H-8 and H-13), 7.12–7.25 (m, 8 H, Ar H's); ^{13}C NMR 30.6 (C-5), 40.0 (C-6), 50.2 (C-8, C-13), 65.0 (C-14), 124.8, 125.6, 126.0, 126.8, 129.2, 132.1, 134.9, 141.5, 142.5 (aromatic C's); IR ($CHCl_3$) 3250, 2930, 1600, 1450, 1210, 720 cm^{-1}; mass spectrum, *m/e* (relative intensity) 235 (M^+, 65), 234 (40), 220 (60), 147 (100), 105 (95); high-resolution mass spectrum, *m/e* 235.1340 ($C_{17}H_{17}N$ requires 235.1320).

Reduction of 2-Methyl-1-(*o*-methylbenzyl)-3,4-dihydroisoquinolinium Perchlorate (74). Preparation of Tetrahydroisoquinoline 62. To a solution of 2-methyl-1-(*o*-methylbenzyl)-3,4-dihydroisoquinolinium perchlorate (**74**) (50 mg, 0.14 mmol) in MeOH was added $NaBH_4$ (16 mg, 0.45 mmol) at 0 °C. After being stirred at 25 °C for 1 h, the mixture was diluted with H_2O and subjected to the usual workup to give a residue, which was subjected to flash column chromatographic purification on silica gel (1% MeOH/$CHCl_3$) to yield 35 mg (97%) of the tetrahydroisoquinoline **62**: ^{1}H NMR 2.13 (s, 3 H, $ArCH_3$), 2.53 (s, 3 H, NCH_3), 2.7 (m, 1 H), 2.82 (m, 2 H), 3.0 (m, 1 H), 3.13 (m, 1 H), 3.30 (m, 1 H), 3.80 (t, 1 H, ArCHN), 6.45 (d, 1 H, Ar H), 6.94–7.20 (m, 7 H, Ar H's); ^{13}C NMR 20.0 ($ArCH_3$), 26.0 (C-4), 39.5 (C-3), 42.7 (NCH_3), 46.4 ($ArCH_2CHN$), 64.2 (ArCHN), 125.1, 125.7, 126.1, 128.1, 128.7, 130.1, 134.0, 139.7, 137.6, 138.1 (aromatic C's); IR ($CHCl_3$) 2930, 1650, 1490, 1450, 1100, 750 cm^{-1}; mass spectrum, *m/e* (relative intensity) 251 (M^+, 50), 146 (100), 132 (30), 104 (95); high-resolution mass spectrum, *m/e* 251.1683 ($C_{18}H_{21}N$ requires 251.1674).

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