(Z)-5b, 82495-47-4; 5c, 82495-48-5; 5d, 82495-52-1; 6a, 590-90-9; 6b, 82495-49-6; (Z)-6c, 32775-50-1; (E)-6c, 35066-36-5; (Z)-6d, 17880-06-7; (E)-6d, 19710-84-0; (E)-7a, 82495-51-0; 7b, 82495-54-3; 8a, 82495-53-2; 8b, 82495-55-4; 9, 82535-99-7; 10, 82521-42-4; 11a, 4643-58-7; 12a, 82495-57-6; ethyl trimethylsilyl acetate, 4071-88-9; methyl trimethylphosphorylacetate, 82495-50-9; anguidine, 2270-40-8; phenyl thiocarbonate, 82495-44-1; verrucarol, 2198-92-7.

**Robert Esmond, Bert Fraser-Reid,* Bruce B. Jarvis***

*Department of Chemistry*
*University of Maryland*
*College Park, Maryland 20742*

*Received April 27, 1982*

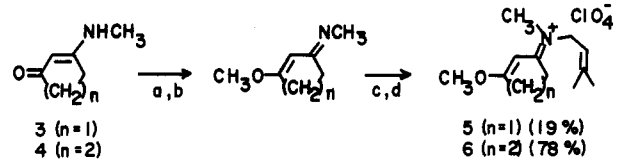
## Electron-Transfer-Initiated Iminium Salt Photospirocyclization Methodologies. Model Studies for Harringtonine Alkaloid Synthesis

*Summary:* Conjugated iminium salts, derived by O-alkylation or O-acylation of *N*-allyl β-enaminones, undergo electron-transfer-initiated photocyclization reactions leading to the production of spirocyclic amines. The yields of these processes are exceptionally high when the allyl grouping of the salts possess (trimethylsilyl)methyl substitution. Model studies have demonstrated the utility of these spirocyclization reactions in synthetic approaches to the Harringtonine alkaloids.

*Sir:* During the past decade, a large effort has been expended to probe the details of organic photochemical processes proceeding by one-electron-transfer mechanisms.[1] Our recent investigations in this area have focused on the electron-transfer-initiated, excited-state reactions of compounds containing the iminium salt ($R_2C{=}N^+R_2$) grouping.[2] We have shown that the excited states of these systems participate in reaction pathways induced by one-electron transfer from a variety of neutral donors, including olefins, ethers, and aromatic hydrocarbons. In the cases investigated, the nature of the processes followed appear to be controlled by the chemistry of the donor-derived cation radical intermediates. Equations 1–3 summarize the types of carbon–carbon bond-forming reactions that occur in these systems as a result of nucleophilic addition to and deprotonation or desilylation of the initially formed radical cation intermediates.

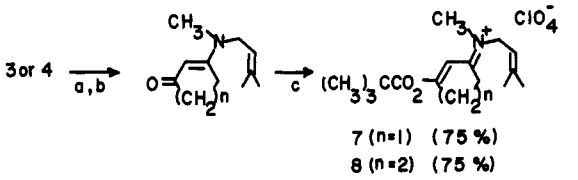
Results from prior studies in this area have demonstrated that *N*-allyliminium salt photocyclization reactions, occurring by intramolecular pathways analogous to that shown in eq 1, serve as useful methods for construction of pyrrolidine-ring-containing heterocycles.[2b] The structural outcomes and modest yields of these processes suggested their potential application in synthetic routes for construction of complex natural product structures. This feature is currently being explored in efforts directed at the development of spirocyclization methodologies that can be employed in the synthesis of members of the harringtonine alkaloid family of general structure **2** (R = acyl).[3]

Scheme I[a]



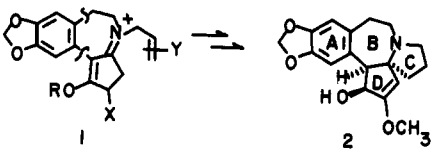

[a] (a) $CH_3I$, (b) 10% NaOH, (c) $(CH_3)_2C{=}CHCH_2Br$, (d) Dowex, $ClO_4^-$ form.

Scheme II[a]




[a] (a) *n*-BuLi, (b) $(CH_3)C{=}CHCH_2Br$, (c) $AgClO_4$, $(CH_3)_3CCOCl$.

Accordingly, photocyclization of the *N*-allyliminium salt grouping found in O-protonated, -alkylated, or -acylated β-enaminones **1** will be used to introduce the spirocyclic CD ring unit of the target systems. In this communication we report the results of model studies that show that this photochemical method is compatible with the functionality and structural requirements of approaches to **2** via salts related to **1**.




**1** **2**

Initial studies were conducted to determine if the iminium cation chromophore found in salts **1** would participate in electron-transfer-induced photocyclization reactions like those observed earlier with phenyl conjugated systems.[2a,d] For this purpose, a series of *N*-prenyliminium perchlorates **5-8** were prepared from β-enaminone precursors by the routes outlined in Schemes I and II. The *N*-prenyl side chain was incorporated into the systems selected for initial study in order to guarantee efficient electron transfer between the olefin and excited iminium salt groups.[4] Irradiation of methanolic solutions of iminium perchlorates **5-8**, conducted in a preparative apparatus with light of $\lambda > 240$ nm, followed by aqueous base treatment of the crude photolysate and chromatographic purification on alumina or silica gel, afforded the spirocyclic amines **9-12** as mixtures of C-8 and C-9 epimers in the yields ranging from 19% to 31%. The O-protonated salt **14**, prepared in situ by treatment of a methanolic solution of the corresponding enaminone with 0.1 N

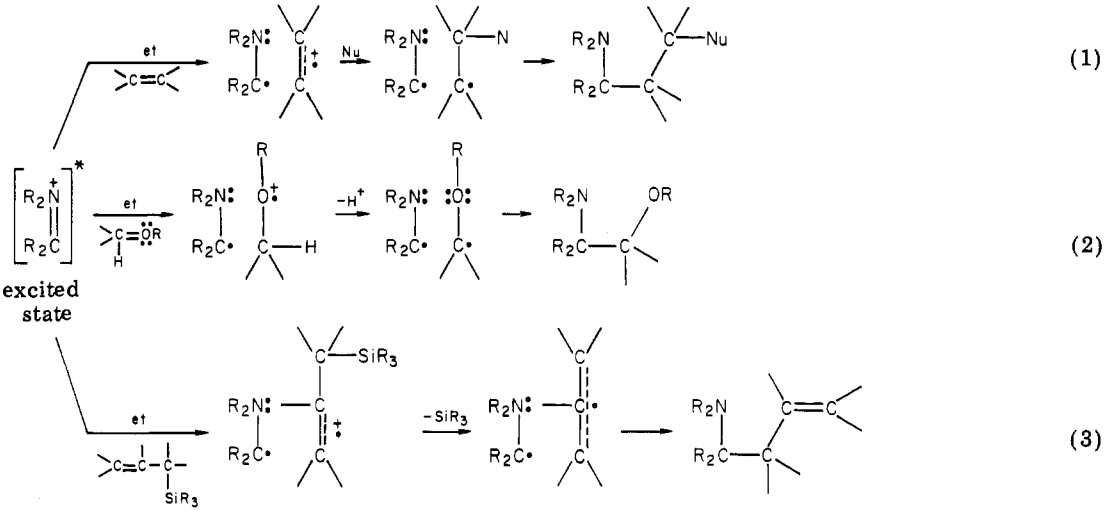
(1) (a) Gordon, M.; Ware, W. R. "The Exciplex"; Academic Press: New York, 1975. (b) Davidson, R. S. "Molecular Association"; Foster, R., Ed.; Academic Press: New York, 1975; Vol. 1, p 215–334. (c) Lablanche-Combier, A. *Bull. Soc. Chim. Fr.* **1972**, *12*, 4791.

(2) (a) Stavinoha, J. L.; Mariano, P. S. *J. Am. Chem. Soc.* **1981**, *103*, 3136. (b) Stavinoha, J. L.; Mariano, P. S.; Leone-Bay, A; Swanson, R; Bracken, C. *Ibid.* **1981**, *103*, 3148. (c) Mariano, P. S.; Stavinoha, J. L.; Bay, E. *Tetrahedron* **1981**, *37*, 3385. (d) Yoon, U. C.; Quillen, S. L.; Mariano, P. S.; Swanson, R.; Stavinoha, J. L.; Bay, B. *Tetrahedron Lett.* **1982**, 919. (e) Ohga, K.; Mariano, P. S. *J. Am. Chem. Soc.* **1982**, *104*, 617.

(3) Smith, C. R.; Mikolajczak, K. L.; Powell, R. G. "Medicinal Chemistry. Anticancer Agents Based on Natural Product Models"; Cassady, J. M., Douros, J. D., Ed.; Academic Press: New York, 1980; Vol. 16, p 392.

(4) (a) Electron-transfer rates are dependent upon the donor olefin oxidation potentials ($F_{1/2}(+)$) and acceptor excited iminium salt reduction potentials ($E_{1/2}(-)$) and singlet energies ($\Delta E_{0,0}$) as discussed by Weller.[4b] From UV-absorption spectroscopic data and known reduction potentials of analogous systems,[4c] we estimate that the $\Delta E_{0,0}$ and $E_{1/2}(-)$ for the chromophore present in these iminium salts are ca. 80 kcal/mol and ca. −1.5 eV, respectively. Thus, $E_{1/2}(+)$ for olefins must be below ca. +2.0 to insure efficient electron transfer. (b) Rehm, D.; Weller, A. *Isr. J. Chem.* **1970**, *8*, 259. (c) Andrieux, C. P.; Saveant, J. M. *J. Electroanal. Chem.* **1970**, *26*, 223.

0022-3263/82/1947-3360$01.25/0 




(1)

(2)

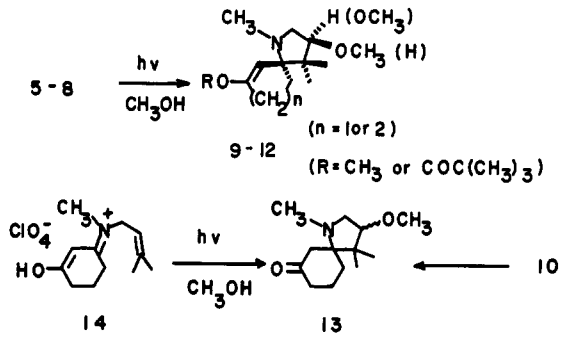
(3)

Table I. Results from Photocyclization of the *N*-[[(Trimethylsilyl)methyl]allyl]iminium Perchlorates 19-22

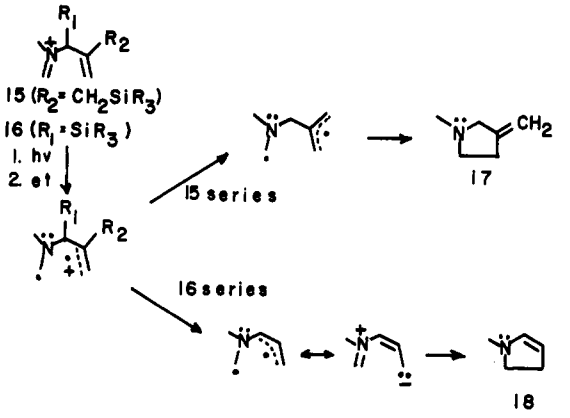
| iminium salts | | | | photocyclization products | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | $^1$H NMR[b] | | $^{13}$C NMR[b] | | |
| compd | R | *n* | λ(max)[a] (nm) | compd | % yield | OC=CH | $NCH_3$ | OC=CH | OC=CH | $C=CH_2$ |
| **19** | $CH_3$ | 1 | 270 | **23** | 91 | 4.35 | 2.30 | 164.5 | 94.5 | 106.8 |
| **20** | $CH_3$ | 2 | 288 | **24** | 95 | 4.35 | 2.20 | 158.3 | 97.9 | 105.4 |
| **21** | $COC(CH_3)_3$ | 1 | 273 | **25** | 87 | 5.30 | 2.20 | 152.9 | 114.5 | 105.6 |
| **22** | $COC(CH_2)_3$ | 2 | 300 | **26** | 84 | 5.10 | 2.20 | 150.7 | 117.6 | 105.5 |

[a] UV measurements in $CH_3CN$ solutions. [b] In parts per million relative to $Me_4Si$.

$HClO_4$, was converted to the spirocyclic amino ketone **13** under these conditions. Ketone **13** was independently prepared by aqueous acid hydrolysis of the enol ether **10**.[6]




Scheme III




These preliminary results suggested that β-enaminone-derived iminium salt chromophores can participate in electron-transfer-induced photocyclization processes leading to generation of aza spirocyclic ring systems. The low yields of these reactions appear to be the result of competitive heterolytic cleavage processes that occur in competition with nucleophilic attack on the intermediate cation diradicals[7] and difficulties associated with carbon–carbon bond formation between two quaternary centers in the final diradical cyclization steps. Although results obtained from study of the prenyl systems demonstrated the success of the proposed spirocyclization methodology, the reaction inefficiencies coupled with limitations arising from the requirements for terminal alkyl substitution on the allyl units, needed to control olefin oxidation potential[4] and diradical formation regiochemistry,[2a,b] preclude direct application to harringtonine alkaloid synthetic approaches.

Alternate approaches to photospirocyclization were next explored in order to solve the key problems associated with reaction efficiency and pyrrolidine ring functionality. Previous studies in our laboratory[2e] concerned with allylsilane–iminium salt photochemistry suggested that trialkylsilyl substitution on the allyl groups of iminium salts (e.g., **15** and **16**) would (1) enhance electron-transfer efficiencies,[8] (2) allow for rapid nucleophile induced de-

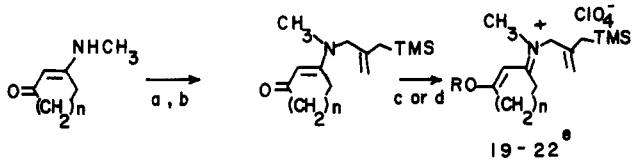
(5) (a) Irradiations were conducted in a preparative apparatus consisting of a 450-W Hanovia lamp in a quartz immersion well with appropriate glass filter under a nitrogen atmosphere. (b) All new compounds possessed spectroscopic properties and elemental compositions consistent with the assigned structures.

(6) (a) UV-spectroscopic monitoring of the hydrolysis of **10** shows that the open-chain enone derived by β elimination exists in aqueous HCl solution and rapidly cyclizes to produce the spirocyclic amino ketone **13** upon basification in a fashion analogous to that of related systems studied earlier.[6b,c] (b) Corey, E. J.; Balanson, R. D. *Heterocycles* **1976**, *5*, 445. (c) Venit, J. J.; Magnus, P. *Tetrahedron Lett.* **1980**, 4815.

(7) The observation of 3-methoxycyclopent-2-enone or -cyclohex-2-enone in the crude photolysates obtained after aqueous base workup inidicates the existence of deprenylation pathways similar to those noted earlier[2d] in the photochemistry of these salts.

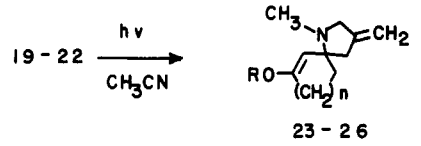
(8) Bock, H.; Kaim, W. *J. Am. Chem. Soc.* **1970**, *102*, 4429 and references therein.

Scheme IV[a]



[a] (a) NaH, THF, (b) $CH_2$=C(($CH_3$)$_3$SiCH$_2$)$CH_2$OMs,[9] (c) $CH_3I$, $AgClO_4$, (d) $(CH_3)_3CCOCl$, $AgClO_4$, (e) yields for sequences are 89%, 85%, 90%, and 90%, respectively.

silylation of the intermediate diradical cation intermediates, and (3) provide by diradical cyclization pyrrolidine ring systems (17 and 18) with attractive exo- or endo-cyclic olefin functionality (Scheme III). The results from investigation of the *N*-[[(trimethylsilyl)methyl]allyl]iminium salts **19–22** illustrate the potential of strategies based on the sequence **15** → **17**. These salts are prepared in high yield by routes involving N-allylation followed by O-methylation or *tert*-butylacylation as shown in Scheme IV. Importantly, preparative irradiation of acetonitrile solutions of **19–22** with light $\lambda > 280$ nm provides, after basic workup and chromatography on Florisil or silica gel, excellent yields (84–95%)[10] of the spirocyclic amines **23–26** (Table I).



Several features of these *N*-[[(trimethylsilyl)methyl]-allyl]iminium salt photocyclization reactions require comment. The ease of formation and exceptionally high chemical efficiencies for reaction of these salts indicate that this methodology will be of general synthetic utility. The results also demonstrate the importance of the trialkylsilyl substituent in electron-transfer organic photochemical studies both as a mechanistic probe[2e] and as a group to control reaction efficiency and regiochemistry. Lastly, the photocyclization reactions described above, along with those related to **16** → **18**, which are under current investigation, appear to be applicable to our synthetic approaches to the harringtonine alkaloids.

**Acknowledgment.** These studies were supported by grants from the National Institutes of Health (GM-27251) and the National Science Foundation (CHE-09813).

**Registry No. 3**, 82444-46-0; **4**, 55998-74-8; **5**, 82444-48-2; **6**, 82444-50-6; **7**, 82444-52-8; **8**, 82444-54-0; **9** ($n$ = 1; R = Me) isomer I, 82444-55-1; **9** ($n$ = 1; R = Me) isomer II, 82444-56-2; **10** ($n$ = 2; R = Me) isomer I, 82444-57-3; **10** ($n$ = 2; R = Me) isomer II, 82444-58-4; **11** ($n$ = 1; R = COBu-$t$) isomer I, 82444-73-3; **11** ($n$ = 1; R = COBu-$t$) isomer II, 82456-18-6; **12** ($n$ = 2; R = COBu-$t$) isomer I, 82444-74-4; **12** ($n$ = 2; R = COBu-$t$) isomer II, 82444-75-5; **13**, 82456-19-7; **14**, 82444-60-8; **19**, 82444-62-0; **20**, 82444-64-2; **21**, 82444-66-4; **22**, 82444-68-6; **23**, 82444-69-7; **24**, 82444-70-0; **25**, 82444-71-1; **26**, 82444-72-2; $(CH_3)_2C$=$CHCH_2Br$, 870-63-3; $CH_2$=C($TMSCH_2$)-$CH_2OMs$, 74532-54-0; harringtonine, 26833-85-2.

(9) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1979**, *101*, 6492.

(10) The yields of these photocyclization reactions are near quantitative judged by $^1$H NMR spectroscopic analysis of the crude photolysates. Thus, the less than quantitative isolated yields appear to be due to losses incurred during chromatographic purification of the photoproducts.

(11) The *N*-[[(trimethylsilyl)methyl]allyl]iminium perchlorates **19–23** resist fluoride ion induced ground-state cyclization to the corresponding spirocyclic amines. This is probably a result of the 5-endo-trig disfavored nature of the cyclization and the availability of intramolecular proton-transfer routes, which cause simple protodesilylation pathways to be preferred.

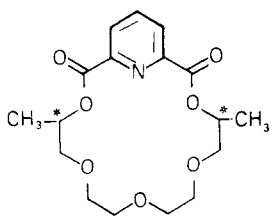
(12) A portion of these studies was conducted by TTH at The Department of Chemistry, Texas A&M University, College Station, TX, and in partial fulfillment of the requirement for the doctoral degree at that University.

**Tammy Tiner-Harding,[12] John W. Ullrich**
**Fang-Ting Chiu, Shyh-fong Chen**
**Patrick S. Mariano***
*Department of Chemistry*
*University of Maryland*
*College Park, Maryland 20742*
*Received April 21, 1982*

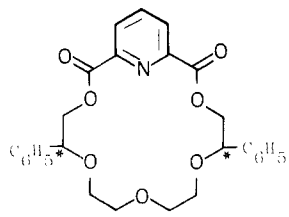
## Chiral Recognition by the *S,S* and *R,R* Enantiomers of Dimethyldioxopyridino-18-crown-6 As Measured by Temperature-Dependent $^1$H NMR Spectroscopy in $CD_2Cl_2$, Titration Calorimetry in $CH_3OH$ at 25 °C, and Selective Crystallization[1a,b]

*Summary:* Enantiomeric recognition by the title compound for several chiral organic ammonium cations has been shown by independent experimental techniques. A similar chiral macrocycle, diphenyldioxopyridino-18-crown-6, does not show enantiomeric recognition for chiral organic ammonium cations when the same experimental methods are used.

*Sir:* The chiral macrocycles 1 and 2[2,3] have been syn-



1



2

thesized, and chiral recognition by the *S,S* enantiomer of 1 for several chiral alkylammonium cations has been shown by temperature-dependent $^1$H NMR spectroscopy in $CD_2Cl_2$, titration calorimetry in $CH_3OH$, and selective crystallization. To the best of our knowledge, this is the first establishment of chiral recognition in a given system by more than one experimental method and the first report of log $K$, $\Delta H$, and $T\Delta S$ values for a chiral-recognition reaction in a homogeneous solvent although Tundo and Fendler[4] have reported $K$ values for similar reactions. Other workers[5-11] have also reported enantiomeric recog-

(1) (a) Presented in part at the National Meeting of the American Chemical Society, Las Vegas, NV, April 1982. (b) Contribution No. 275 from the Institute for Thermochemical Studies.

(2) Jones, B. A.; Bradshaw, J. S.; Izatt, R. M. *J. Heterocycl. Chem.* **1982**, *19*, 551–556.

(3) Bradshaw, J. S.; Jolley, S. T.; Izatt, R. M. *J. Org. Chem.*, **1982**, *47*, 1229–1232.

(4) Tundo, P.; Fendler, J. H. *J. Am. Chem. Soc.* **1980**, *102*, 1760–1762.

(5) For a short review, see Jolley, S. T.; Bradshaw, J. S.; Izatt, R. M. *J. Heterocycl. Chem.* **1982**, *19*, 3–19.

(6) Kyba, E. P.; Timko, J. M.; Kaplan, L. J.; deJong, F.; Gokel, G. W.; Cram, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 4555–4568.

(7) For example, see Sousa, L. R.; Sogah, D. Y. G.; Hoffman, D. H.; Cram, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 4569–4576.

(8) Prelog, V.; Bedekovic, D. *Helv. Chim. Acta* **1979**, *62*, 2285–2302.

(9) Curtis, W. D.; Laidler, D. A.; Stoddart, J. F.; Jones, G. H. *J. Chem. Soc., Perkin Trans. 1*, **1977**, 1756–1769.

0022-3263/82/1947-3362$01.25/0 