Confirmation that 1 was produced as a discrete species was provided by the isolation of the Diels-Alder adduct 6. Thus when the walls of the liquid nitrogen trap used to collect 1 were coated with cyclopentadiene, compound 6 was isolated in 10% yield as a colorless oil. The structure of 6 is based on the ${}^{1}H$ and ${}^{13}C$



NMR spectra, which compare favorably with data from other cyclopropene adducts.^{6,7,14} The C_2 symmetry of 6 leads, as expected, to seven ¹³C NMR signals for the norborenyl carbons.

Studies to confirm the anticipated properties^{3,4} of 1 are in progress. These results will be reported shortly.

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Supplementary Material Available: Experimental procedures including complete characterization of 1-6 and ¹H and ¹³C NMR spectra of 2 and 4-6 (6 pages). Ordering information is given on any current masthead page.

New Approach to Strychnos Alkaloids. Stereocontrolled Total Synthesis of (±)-Dehydrotubifoline¹

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Only modest progress has been recorded in the arena of Stychnos alkaloid total synthesis since the exceptional preparation of strychnine (1) by the Woodward group over 35 years ago.²





strychnine (1)

akuammicine (2) R = X = H, $R^1 = CO_2Me$; 2,16-dehydro dehydrotubifoline (3) R = 1, $X = R^{1} = H$; 1,2-dehydro

Notably few method for assembling the core pentacyclic strychnan skeleton (exemplified in 2 and 3) of this large and diverse alkaloid family have been developed.^{3,4} In this communication we report

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Scheme II^a





 a TIPS = (i-Pr)₃Si; Tf = SO₂CF₃; th = 2-thienyl.

a conceptually new approach to Strychnos alkaloids, which is characterized by the concise evolution of the strychnan skeleton (5) by "aza-Cope-Mannich"^{1,5} rearrangement of a 2-azabicyclo[3.2.1]octane precursor 4 (Scheme I).

The required cis relationship of the styrene and amine functionality on the 2-azabicyclo[3.2.1]octane ring was secured by assembling the key cyclization precursor 16 from intramolecular aminolysis of cyclopentene epoxide 15 (Scheme II).⁶ This latter intermediate was prepared in nine steps from 2-cyclopentenone as outlined in Scheme II. The elements of the bridging E ring and its (Z)-ethylidene appendage were initially introduced by

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⁽⁶⁾ For background studies leading to this strategy, see: Marquis, R. W., Jr. Ph.D. Dissertation, University of California, Irvine, 1989.

treating (Z)-2-bromo-2-buten-1-ol7 sequentially (-78 °C, ether-THF) with 3 equiv of t-BuLi, 1 equiv of lithium thienylcyanocuprate,⁸ 2 equiv of Me₃SiCl⁹ and 1 equiv of 2-cyclopentenone. Chromatographic purification provided cyclopentanone 8 in 40-45% yield.¹⁰ Protection of the primary alcohol of 8 as a triisopropylsilyl (TIPS) ether¹¹ and subsequent regioselective enolization (-78 °C, THF) of 912 with Masamune's base13 provided, after in situ triflation¹⁴ (Tf = SO_2CF_3), the enol triflate 10. This intermediate was contaminated with ca. 10% of its double-bond regioisomer.¹⁵ Carbonylation of **10** [5% Pd(PPh₁)₄, CO (1 atm), DMF, 55 °C]¹⁶ in the presence of N,O-dimethylhydroxylamine provided amide 11. Acylation of 11¹⁷ with the aryllithium dianion prepared from 2-(trimethylacetamido)bromobenzene¹⁸ gave enone 12 in an overall yield of 63% from cyclopentanone 9.

Enone 12 was epoxidized with good facial selectivity (10-13:1) at -23 °C (t-BuOOH, Triton B) to give 13, which afforded styrene 14 upon subsequent reaction with 3 equiv of (methylene)triphenylphosphorane (THF, $-78 \rightarrow 23$ °C). Desilylation of 14 with (n-Bu)₄NF followed by chlorination of the liberated alcohol (MsCl, DMF, LiCl, $-23 \rightarrow 23$ °C) afforded the allylic chloride 15. Although direct bis-aminolysis of 15 with NH₃ was not clean, the desired cyclization was accomplished by sequential treatment of 15 (DMF, 23 °C) with the sodium salt of trifluoroacetamide,¹⁹ followed by cleavage of the resulting bicyclic amide with KOH (EtOH-H₂O, 80 °C). This sequence delivered the azabicyclic amine 16 in 35% overall yield from enone 12.

The pivotal rearrangement of 16 was occasioned under standard mild conditions [paraformaldehyde (1.5 equiv), camphorsulfonic acid (1.0 equiv), Na₂SO₄ (2 equiv), CH₃CN at reflux]¹ to provide a single crystalline product 17 in 88% yield. Hydrolysis of this intermediate with a large excess of KOH in EtOH-H₂O (2:1) at reflux provided, in 70% yield, (\pm) -dehydrotubifoline (3). The synthetic product was indentical with an authentic sample prepared by acid treatment of natural akuammicine.²⁰

The chemistry outlined herein defines a short, highly stereocontrolled, new strategy for preparing Strychnos alkaloids. The overall yield of (±)-dehydrotubifoline from 2-cyclopentenone was 6%, and this conversion was accomplished in only 12 chemical operations. Besides the key aza-Cope-Mannich rearrangement step ($16 \rightarrow 17$), other notable transformations include 1,4-addition of a 1-hydroxy-2-butenyl cuprate $(7 \rightarrow 8)$ and formation of an unsaturated N-methyl-N-methoxyamide by palladium-catalyzed carbonylation-aminolysis of an enol triflate $(10 \rightarrow 11)$. The extension of this approach to the preparation of strychnine and other complex Strychnos alkaloids is under investigation.

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(7) Readily available in 90% overall yield from methyl trans-crotonate by bromination, dehydrobromination (Et₃N, pentane, reflux), and (*i*-Bu)₂AlH (-78 °C, CH₂Cl₂) reduction. (8) Lipshutz, B. H.; Koerner, M.; Parker, D. A. *Tetrahedron Lett.* 1987,

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Spectra of the Solvated Electron in the Presence of Sodium Cation in Tetrahydrofuran and in Its α, α' -Methylated Derivatives[†]

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We report the first optical absorption spectra of a solvated electron with clearly resolved structures. The results presented in this communication were obtained via time-resolved pulse radiolysis experiments on tetrahydrofuran (THF), mixed cis- and trans-2,5-dimethyltetrahydrofuran (2,5-DMTHF), and 2,2,5,5tetramethyltetrahydrofuran (2,5-TMTHF) solutions containing millimolar concentrations of sodium salts.

It has been known for quite some time that the properties of the solvated electron in solutions of electrolytes in moderately polar solvents differ considerably from its properties in the same solvents but in the absence of electrolytes.^{1,2} Specifically, for sodium salts in tetrahydrofuran (THF), the absorption maximum occurs at 880 nm (1.41 eV), compared with 2120 nm (0.58 eV) for e_{sol} in neat THF.³ This phenomenon is attributed to the formation of a new species (e^{-}, M^{+}) .⁴ The magnitude of the spectral shift is not a monotonic function of the radius of the bare cation⁵ and is, for example, smaller for lithium than for sodium. It appears to depend critically on the degree of solvation of the alkali-metal cation, which controls the equilibrium distance between the positive charge and the electron.

In this study we investigated the influence of the structure of the solvent molecule on the spectral and kinetic properties of the (e⁻,Na⁺) moiety. 2,5-DMTHF and 2,5-TMTHF were selected as interesting media since their dipole moments and dielectric constants are similar to those of unsubstituted THF, yet their ability to tightly solvate alkali-metal cations is significantly diminished as a result of the steric hindrance generated by the presence of two or four methyl groups in the α positions.

Our time-resolved pulse radiolysis experiments were performed on purified samples of the above ethers that contained 5-20 mM sodium salts. Tetraphenylboron sodium was used as the source

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