biosynthesis.[12] 2-Hydroxy-3-methylsuccinic acid is next oxidized to 2-oxo-3-methylsuccinic acid and finally transaminated to Masp. The incorporation of intact [U-^{13}C]pyruvate into C3, C4, and the Me on C3 of Masp ($^1J_{3,4}$ = 49.7 Hz and $^1J_{3,\mathrm{Me}}$ = 34.1 Hz) supports the proposed biogenesis.[13]

Acknowledgment. This research was supported by NSF Grant CHE88-00527. We thank Wesley Yoshida for determining the NMR spectra.

Supplementary Material Available: COSY ^{13}C NMR spectrum of **1** uniformly enriched with ^{13}C to 80% and ^{15}N to 90%, experimental details for feeding experiments, and ^{13}C NMR spectra of **1** labeled from precursors mentioned in this communication (15 pages). Ordering information is given on any current masthead page.

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(12) (a) Calvo, J. M.; Stevens, C. M.; Kalyanpur, M. G.; Umbarger, H. E. *Biochemistry* **1964**, *3*, 2024. (b) Cole, F. E.; Kalyanpur, M. G.; Stevens, C. M. *Biochemistry* **1973**, *12*, 3346. (c) Sylvester, S. R.; Stevens, C. M. *Biochemistry* **1979**, *18*, 4529.

(13) [1,2-^{13}C]Acetate is also incorporated into C1 and C2 of the Leu unit of **1** ($^1J_{1,2}$ = 51.1 Hz). The specific incorporation is comparable with that of acetate into C1 and C2 of Masp. [U-^{13}C]Pyruvate is also incorporated intact into Ala.

Spiropentadiene

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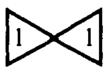
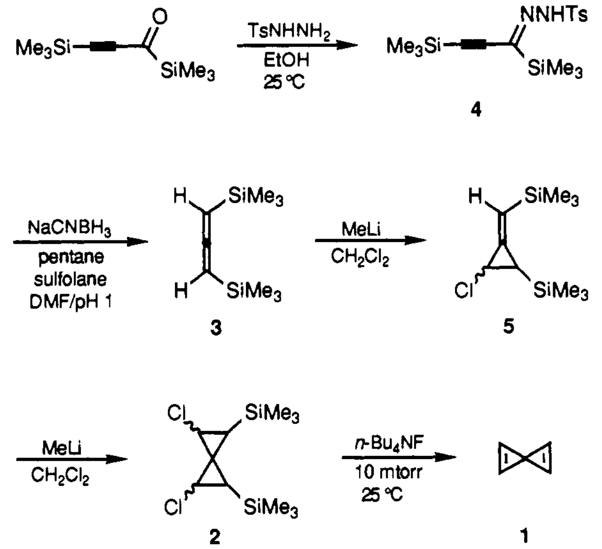
Received March 25, 1991

As the simplest small-ring, spiro-connected cycloalkene,[2] spiropentadiene (bowtiediene, **1**) is of considerable theoretical interest[3] since the two π systems are held in perpendicular planes by a common carbon and are predicted to experience significant spiroconjugation.[4] In view of the high energy content[5] of **1**, it is not surprising that very few attempts to synthesize this molecule have been reported.[6] We have demonstrated recently that the vacuum gas phase elimination of β-halocyclopropylsilanes by solid fluoride provides an attractive route to strained cycloalkenes.[6,7] We now report that this versatile technique can be applied to the synthesis of **1**.



1

Scheme I



Spiropentane **2** was envisioned as the immediate precursor to **1**. The synthesis of **2** is presented in Scheme I. The key intermediate required for this synthesis is the sterically hindered allene **3**.[8] Fortunately, this compound could be prepared readily via the procedure described by Danheiser and his co-workers to synthesize (trimethylsilyl)allene.[9] Thus pure **3** was isolated in 57% yield by treatment of the tosylhydrazone of bis(trimethylsilyl)propynone[10] (**4**)[11] with sodium cyanoborohydride in a two-phase solvent system at pH 1. Treatment of the allene **3** with chlorocarbene, generated from methyllithium and dichloromethane,[12] yielded compound **5** in 14% yield.[11] Conversion of **5** to the desired spiropentane **2** was effected by subjecting **5** to the same reaction conditions, yielding **2** as a viscous oil in 6% yield after column chromatography.

Introduction of **2** into a "fluoride column"[13] using the VGSR apparatus described previously[6] yielded a volatile hydrocarbon which could be condensed into a liquid nitrogen trap as a white solid. Examination of the hydrocarbon by ^{1}H NMR spectroscopy at −105 °C in tetrahydrofuran-d_8 revealed a singlet at δ 7.62 (cyclopropenyl protons) along with several unidentified signals. The singlet at δ 7.62 was observed to disappear after approximately 20 min at −105 °C in THF-d_8; rapid decomposition occurred upon warming to −90 °C. We were unable to record the ^{13}C NMR spectrum of **1**.

On warming, **1** polymerizes to a sparingly soluble (THF), light green film. The propensity of spiropentadiene to polymerize is not unexpected since spiropentene is reported to polymerize in the condensed phase at −78 °C.[14]

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(1) American Chemical Society, Division of Organic Chemistry Fellow, sponsored by Rohm and Haas (1990–1991).

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(3) For some recent references, see: (a) Kao, J.; Radom, L. *J. Am. Chem. Soc.* **1978**, *100*, 760. (b) Bischof, P.; Gleiter, R.; Haider, R. *J. Am. Chem. Soc.* **1978**, *100*, 1036. (c) Maksic, Z. B.; Kovacevic, K.; Mogus, A. *THEOCHEM* **1982**, *2*, 9. (d) Zil'berg, S. P.; Ioffe, A. I.; Nefedov, O. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1983**, 261. (e) Minkin, V. I.; Minyaev, R. M.; Orlova, G. M. *THEOCHEM* **1984**, *19*, 241. (f) Kanda, K.; Koremoto, T.; Imamura, A. *Tetrahedron* **1986**, *42*, 4169.

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(5) A range of values from 110 to 120 kcal/mol have been calculated.[3a,c,d] For a much higher estimate, see: Dewar, M. G. S. *The Molecular Orbital Theory of Organic Chemistry*; McGraw-Hill: New York, 1970; p 461.

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(8) Allene **3** has been prepared previously by reacting the anion of bis(trimethylsilyl)propyne with sodium sulfate decahydrate with subsequent separation of the resulting allene–propyne mixture by HPLC: Peterson, P. E.; Jensen, B. L. *Tetrahedron Lett.* **1984**, *25*, 5711.

(9) Danheiser, R. L.; Carini, D. J.; Fink, D. M.; Basak, A. *Tetrahedron* **1983**, *39*, 935.

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(11) Proton (300 MHz) and carbon-13 (75.5 MHz) NMR spectral data of new compounds are as follows. **2**: ^{1}H NMR 3.68–3.11 (m, 2 H), 0.99–0.82 (m, 2 H), 0.21–0.13 (3 s, 18 H); ^{13}C NMR 40.5, 39.8, 39.3, 32.4, 31.4, 17.9, 17.6, 14.1, −0.1, −0.2, −1.7. **4**: ^{1}H NMR 8.70 (s, 1 H), 7.82 (d, 2 H, J = 8.2), 7.30 (d, 2 H, J = 8.2), 2.43 (s, 3 H), 0.23 (s, 9 H), 0.15 (s, 9 H); ^{13}C NMR 146.3, 144.0, 135.6, 129.4, 127.9, 113.6, 94.8, 21.6, −0.4, −2.7. **5**: ^{1}H NMR 6.18 (d, 1 H, J = 3.1), 3.71 (d, 1 H, J = 9.3), 1.34 (dd, 1 H, J = 9.3, 3,1), 0.18 (s, 9 H), 0.14 (s, 9 H); ^{13}C NMR 141.6, 117.5, 32.5, 17.0, −0.4, −0.9. **6**: ^{1}H NMR 5.80 (dd, 2 H, J = 5.3, 3.0), 5.73 (dd, 2 H, J = 5.3, 3.0), 2.75 (br s, 2 H), 2.70 (br s, 2 H), 1.77 (dt, 2 H, J = 6.6, 1.8), 1.66 (d, 2 H, J = 6.6), 1.39 (d, 2 H, J = 4.0), 1.36 (d, 2 H, J = 4.0); ^{13}C NMR 134.5, 132.1, 63.5, 44.2, 43.4, 29.7, 24.7, 20.5.

(12) Closs, G. L.; Closs, L. E. *J. Am. Chem. Soc.* **1960**, *82*, 5723.

(13) A "fluoride column" was prepared by depositing 2.0 g of tetra-*n*-butylammonium fluoride on 20 g of glass helices as described in ref 6.

(14) Bloch, R.; Denis, J.-M. *Angew. Chem.* **1980**, *92*, 969; *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 928.

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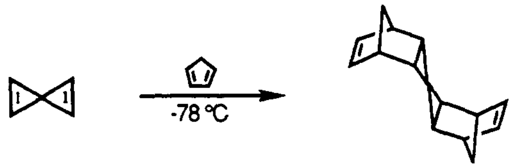
Confirmation that **1** was produced as a discrete species was provided by the isolation of the Diels–Alder adduct **6**. Thus when the walls of the liquid nitrogen trap used to collect **1** were coated with cyclopentadiene, compound **6** was isolated in 10% yield as a colorless oil. The structure 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 ^{13}C NMR signals for the norborenyl carbons.



1 **6**

Studies to confirm the anticipated properties[3,4] of **1** are in progress. These results will be reported shortly.

Acknowledgment. We gratefully acknowledge the Robert A. Welch Foundation for support of this work. Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work.

Supplementary Material Available: Experimental procedures including complete characterization of **1–6** and ^{1}H and ^{13}C 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 (±)-Dehydrotubifoline[1]

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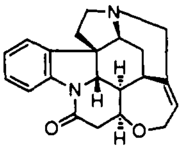
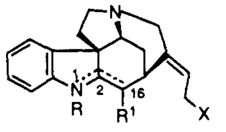
Received February 11, 1991

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]



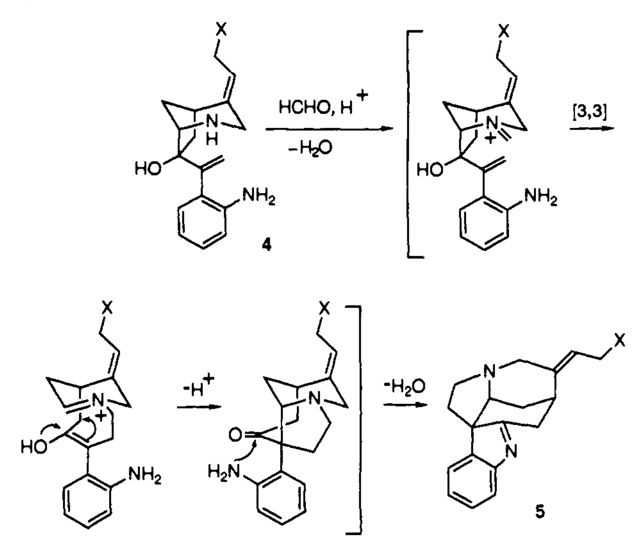
strychnine (1)



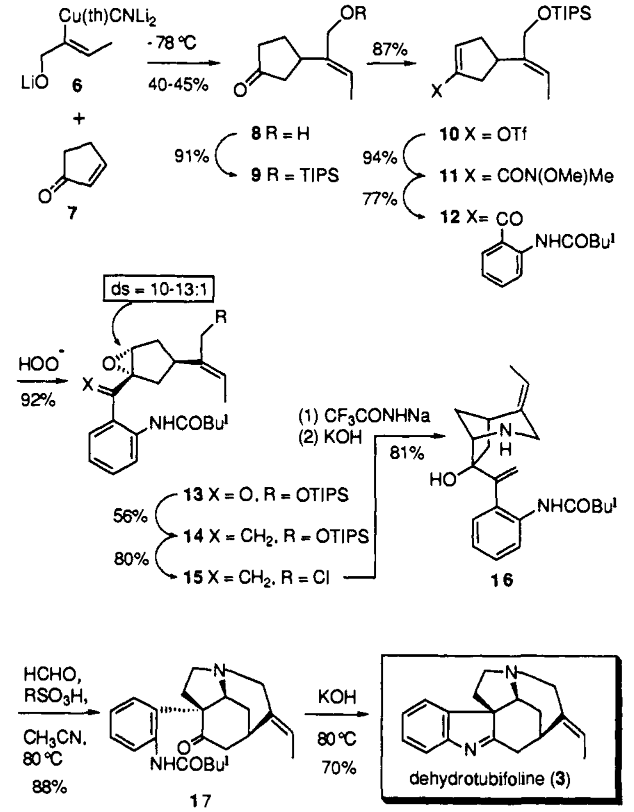
akuammicine (2)
R = X = H, R^1 = CO$_2$Me ; 2,16-dehydro
dehydrotubifoline (3)
R = : , X = R^1 = H ; 1,2-dehydro

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 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).

Scheme I



Scheme II[a]



[a] TIPS = (i-Pr)$_3$Si; Tf = SO$_2$CF$_3$; th = 2-thienyl.

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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(2) Woodward, R. B.; Cava, M. P.; Ollis, W. D.; Hunger, A.; Daeniker, H. U.; Schenker, K. *J. Am. Chem. Soc.* **1954**, *76*, 4749.

(3) For recent reviews, see: (a) Husson, H. P. In *Indoles: Monoterpene Indole Alkaloids*; Saxon, J. E., Ed.; Wiley: New York, 1983; Chapter 7. (b) Bosch, J.; Bonjoch, J. In *Studies in Natural Products Chemistry. Volume 1. Stereoselective Synthesis* (*Part* A); Atta-ur-Rahman, Ed.; Elsevier: Amsterdam, 1988; pp 31–88.

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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.

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