and $C_8$, interchangeable), and 23.8 ($C_6$).

Anal. Calcd for $C_{13}H_{16}S$: C, 76.41; H, 7.89. Found: C, 76.53; H, 7.95.

The $^{13}C$ NMR spectrum of the crude isomeric mixture showed five minor resonances in the aliphatic region: 63.1 ($C_2$), 43.6 ($C_3$), 35.9, 35.8, 34.9 ($C_6$, $C_7$, $C_8$, interchangeable). The occurrence of these resonances at low field with respect to those of the major component are consistent with the minor product being the trans isomer, **3a,Ph.**

**Registry No.**—*trans*-**1a,H,** 68013-66-1; *cis*-**1a,H,** 68013-68-3; **1a,Ph,** 68013-69-4; *trans*-**1b,H,** 68013-71-8; *cis*-**1b,H,** 68013-73-0; *trans*-**1c,H,** 68013-75-2; *cis*-**1c,H,** 68013-77-4; **2a,H,** 64945-38-6; **2a,Ph,** 64945-40-0; **2b,H,** 68013-78-5; **3a,H,** 64945-41-1; **3a,Ph,** 64945-42-2; **3b,H,** 68013-79-6; **3c,H,** 68013-80-9; *trans*-**5b,** 68013-81-0; *cis*-**5c,** 68024-68-0; *trans*-**5c,** 68013-82-1; **6b,** 68013-83-2; **6c,** 68013-84-3; **7b,** 68013-85-4; **7c,** 68013-86-5; **8a,** 57565-42-1; **8b,** 66120-24-9; **8c,** 66120-30-7; (*E*)-**9c,** 68013-87-6; (*Z*)-**9c,** 68013-95-6; **10b,** 68013-88-7; **11,** 68013-89-8; **12,** 68013-91-2; **13,** 68013-93-4; 2-chlorothiolane, 22342-03-6; vinylmagnesium bromide, 1826-67-1; 2-vinylidenthiane, 68013-94-5; thiane 1-oxide, 4988-34-5; ethylene oxide, 75-21-8; allylthiol, 870-23-5; 4-bromo-1-chlorobutane, 6940-78-9; trimethyloxonium fluoroborate, 420-37-1; benzyl bromide, 28807-97-8; 2-vinylthiane, 66120-24-9.

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# Ring Expansion of 2-Vinyl Derivatives of Thiane, *N*-Benzylpiperidine, and Thiepane by [2,3] Sigmatropic Shift


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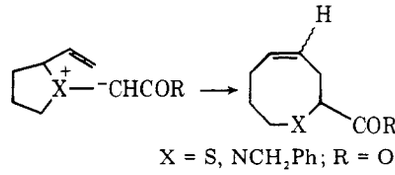
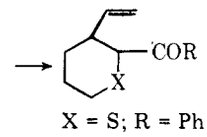
Syntheses of 2-vinylthiane, 2-vinylthiepane, and 2-vinyl-*N*-benzylpiperidine are described. The shortest routes involve addition of vinylmagnesium bromide to the $\alpha$-chloro sulfides or to an *N*-benzylimmonium salt. Alkylation of the 2-vinyl heterocycles with carboethoxymethyl trifluoromethanesulfonate gives sulfonium or ammonium salts in good yield. Ring expansion occurs upon addition of DBU to the salts at 20 °C. Alkylation of 2-vinylthiane with allyl triflate followed by treatment with LDA affords 2-vinylthiacyclonon-4-ene. This substance can be converted into 2-carboethoxythiadodeca-4,7-diene by a second ring expansion sequence. The following medium-sized heterocycles have also been prepared: (*E*)-2-carboethoxythiacyclonon-4-ene, (*E*)-2-carboethoxy-*N*-benzylazacyclonon-4-ene, and (*Z*)-*N*-benzylazacyclonon-4-ene.


In a recent publication, we have described [2,3] sigmatropic ring expansions of five-membered nitrogen or sulfur heterocycles to give eight-membered heterocycles.[1] Typical rearrangements (eq 1) occur at room temperature or above with a time scale of the order of hours. Since similar acyclic ylide rearrangements are considerably faster,[2] the bicyclo[3.3.0] transition state for ring expansion apparently is destabilized relative to the monocyclic analogue. As a result, yields of eight-membered heterocycles are modest (65–80%) and side reactions such as Stevens rearrangement (eq 2) may compete in certain cases.




(1)

X = S, $NCH_2Ph$; R = $OC_2H_5$, Ph




(2)

X = S; R = Ph

We have also reported the ring expansions of six-membered heterocycles and related compounds.[3,4] Exocyclic ylides derived from $\alpha$-vinylthianes or -piperidines resemble their acyclic relatives in qualitative rearrangement rates, and the yields of nine-membered products are uniformly excellent.

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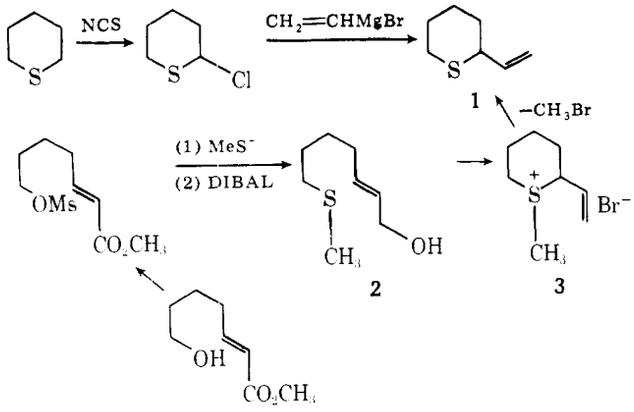
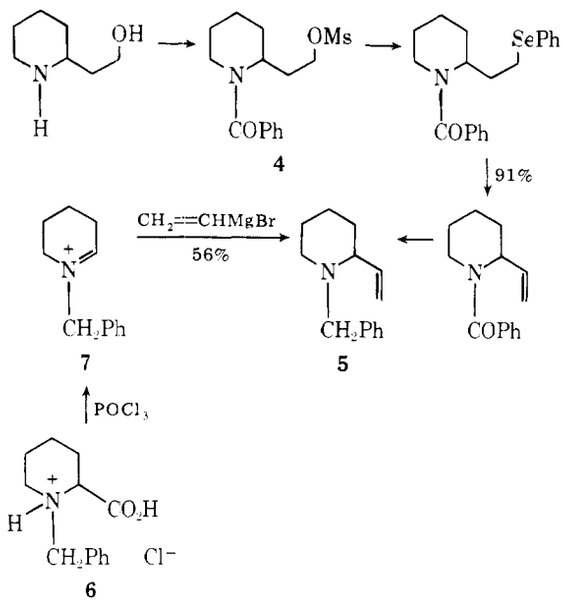
Scheme I



Scheme II



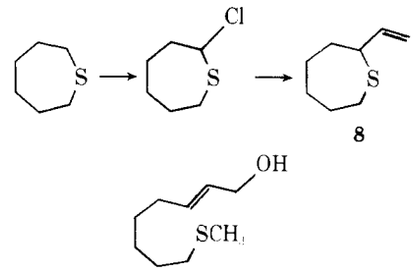
By comparison with five-membered ylides, the thiane or piperidine derivatives rearrange much faster and with fewer complications. The practical aspects of representative nine-membered heterocycle synthesis as well as the preparation of analogous 10- and 12-membered rings are described in this paper.

**Starting Materials.** General synthetic routes to α-vinylpiperidines and -thianes have been developed to allow easy access to the parent compounds as well as to more sensitive substituted derivatives. A precedented Grignard sequence[5] from thiane to 2-vinylthiane (**1**) is the method of choice (Scheme I). However, the longer route from 2-hydroxytetrahydropyran to **1** is reasonably efficient, and appears more promising for synthesis of functionalized thianes under study in our laboratory. The key step in this second route is the ionic cyclization of sulfide alcohol **2** via demethylation of an intermediate sulfonium salt **3**.

In the piperidine series, routes based on selenoxide elimination[6] to introduce vinyl functionality are the most efficient. Thus, 2-vinyl-*N*-benzylpiperidine (**5**) is available from commercial 2-piperidine-2-ethanol via the sensitive *N*-benzoyl mesylate **4** (Scheme II).

A second route to **5** employs immonium salt **7** as a substrate for addition of vinylmagnesium bromide. Treatment of *N*-benzylpipecolinic acid with phosphorus oxychloride according to the method of Rapoport et al.[7] provides easy access to **5**. This sequence is shorter than the selenoxide approach, and the yield for the Grignard reaction is reasonable (56%).

In the seven-membered ring series, only the sulfur derivative has been studied. Chlorination of hexamethylene sulfide with *N*-chlorosuccinimide followed by Grignard displacement of chloride by vinyl affords the α-vinyl derivative **8** (53%). Preliminary attempts to prepare **8** by ionic cyclization of the sulfide alcohol **9**[8] were not promising and have not been pursued.

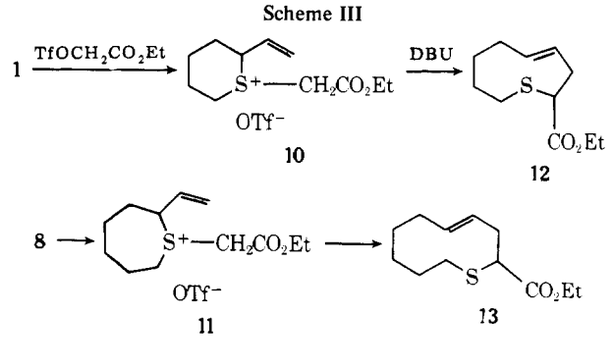


**Ring Expansions.** Our standard procedure for ring expansion via ester-stabilized ylides involves heteroatom alkylation with the trifluoromethanesulfonate ester of ethyl glycolate,[9] followed by base treatment of the resulting salt. Thus, sulfides **1** and **8** are converted to crystalline sulfonium salts **10** and **11** in good yield (Scheme III). Only one diastereomer of the sulfonium salt is isolated in each case, and no evidence for a second isomer could be found. All examples of thiane alkylation in the literature occur by apparent equatorial attack on the most stable chair conformer,[10] so the trans stereochemistry assigned to **10** seems secure. It is likely that **11** also has trans geometry (least hindered approach by alkylating agent), but specific evidence on this point is not available.

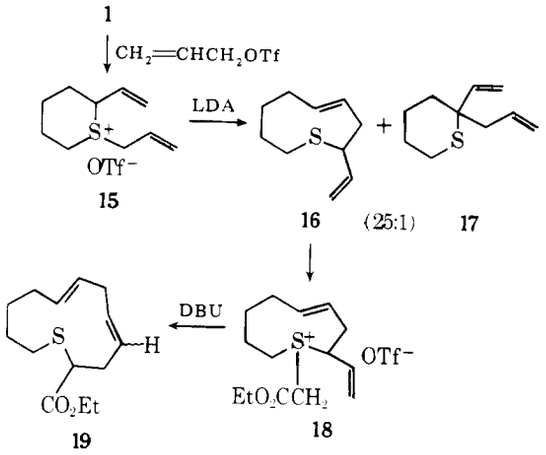
Upon treatment with DBU, both **10** and **11** rearrange to give ring expansion products having a trans double bond, **12** and **13**, respectively. In the thiacyclodecene **13**, $J_{vinyl}$ = 15.4 Hz is easily obtained from the NMR spectrum, but a more complicated situation prevails in the thiacyclononene **12**. At room temperature **12** exists as two slowly interconverting conformers, one of which has a poorly resolved olefinic region. The spectrum displays reversible coalescence above 45 °C and eventually simplifies to a time-averaged spectrum above 100 °C, $J_{vinyl}$ = 16 Hz. This behavior is characteristic of *trans*-cyclononenes in general.[11] Both the nine- and ten-membered rings can be isolated in >90% yield from their respective sulfonium salt precursors, and the rearrangements are exothermic at room temperature. A temperature study of thiacyclononene formation shows that the reaction takes place at −20 °C, but not −40 °C. In view of the ease of rearrangement and exclusive formation of trans olefin, it is clear that typical five-center transition states[12] must be available to the ylides derived from **10** or **11** with a minimum of strain. The diequatorial ylide derived from **10** is especially well suited for [2,3] shift according to molecular models.

For the purpose of preparing larger rings, it is convenient to perform the alkylation of α-vinyl heterocycles with the

Scheme III



Scheme IV



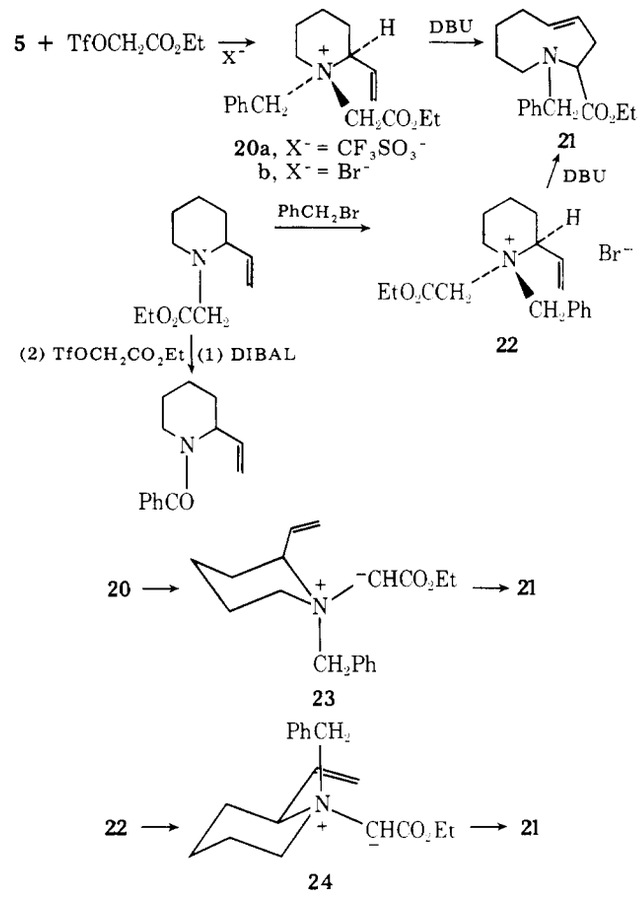
highly reactive allyl triflate.[9] Thus, 1 is converted into sulfonium salt **15** and rearrangement to **16** is achieved by deprotonation with LDA (Scheme IV). A trace of **17** is formed by the alternative [2,3] shift under optimized conditions. However, ylide generation using conditions which promote ylide equilibration by proton transfer (DBU instead of LDA) results in a 2:1 ratio of **16/17.** The sequence from **1** to **16** is a streamlined version of the repeatable ring expansion process which we suggested in an earlier publication.[1b] The product of ring expansion **16** contains the same functionality as the starting material **1**, so the alkylation–deprotonation sequence can be repeated to "grow" larger rings. Alkylation of **16** as usual gives the sulfonium salt **18** (stereochemistry unknown), and DBU treatment affords an inseparable mixture of 12-membered rings **19**, 5:1 *E,E/E,Z.*[13,14] Others have recently employed the same concept to prepare a series of sulfur-containing macrocycles starting from α-vinyltetrahydrothiophene.[15]

In the nitrogen series, conversion of **5** to azacyclononenes can be achieved in the usual way (Scheme V). Ammonium salt **20a** is obtained from **5** as the only observable (>90%) diastereomer (NMR analysis). By analogy to previous examples of piperidine alkylation, axial approach of the alkylating agent on the diequatorial conformer of **5** is tentatively assumed.[16] The triflate salt **20a** is difficult to crystallize, and it is more convenient to work with the highly crystalline bromide **20b,** available by simple counterion exchange. Treatment of pure **20b** (or crude **20a**) with DBU results in rapid ring expansion (>90%) at room temperature. A trans alkene **21** is by far the major produce (ca. 95%), but the NMR spectrum is exceedingly difficult to interpret due to the presence of two conformers (1.2–1.5:1 ratio, depending on solvent) along with a minor product (cis olefin?) which chromatographs together with **21.** Extensive decoupling studies at 270 MHz prove that two trans alkene conformers are present ($J_{vinyl}$ = 15.5 and 16 Hz, respectively).

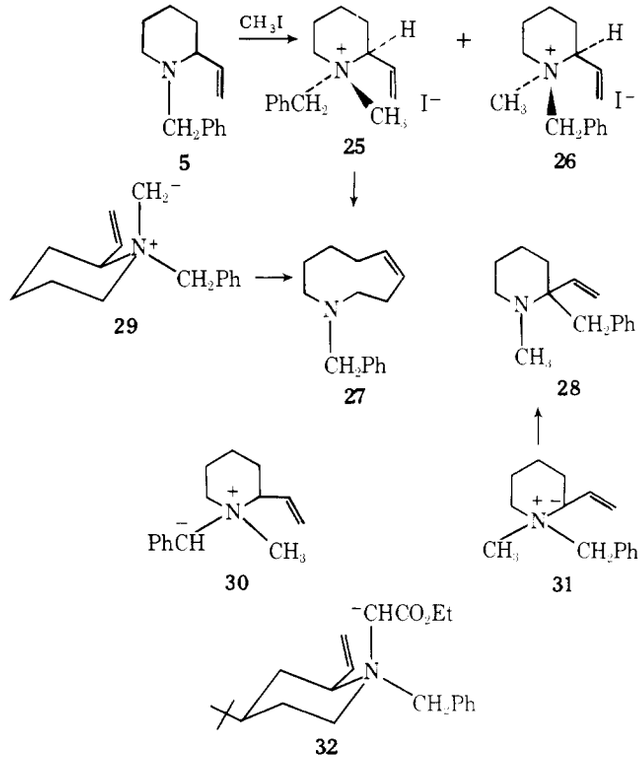
It is significant that the other ammonium salt diastereomer, **22,** prepared as shown in Scheme V, gives a ring expansion product with identical NMR properties compared with **21.** This observation raises the possibility that ylides derived from **20** and **22** can interconvert by reversible deprotonation α to the vinyl group.[1a] However, either ylide diastereomer can achieve a transition state geometry which leads to **21** in this conformationally mobile system as shown by structures **23** and **24,** provided that a chair form **23** with benzyl and vinyl groups axial is accessible.

Subtle changes in substitution pattern can affect the geometry of the ring expansion process dramatically. Quaternization of **5** with methyl iodide gives a 4:1 mixture of ammonium salts **25** and **26.** The major isomer **25** is the product of axial methylation, which should predominate according to literature precedents.[16] When the 4:1 mixture of **25** and **26** is

Scheme V



treated with LDA at −20 °C, a single nine-membered ring **27** ($J_{vinyl}$ = 10.5 Hz) is formed (63%), together with an isomer **28** (14%). No trace of the trans olefin can be found. After repeated recrystallization of the **25, 26** mixture, the ratio of **25/26** can be improved to 10:1. Upon LDA treatment, this material gives **27** (75%) and ca. 3% of **28.** We conclude that **25** rearranges only to **27,** the product of kinetically favored methylide (**29**) for-



mation. Since the favored conformation of **29** probably has an axial ylide carbon, exclusive appearance of the cis olefin is not unreasonable. We had previously observed that a conformationally rigid system **32** with analogous stereochemistry gives only the cis olefin upon ring expansion.[3a] However, it is puzzling that **29** differs so completely from the stabilized ylide **23** obtained from **20**. The total absence of any products derived from benzylide (**30**) generation is also surprising, especially since the minor product **28** is apparently formed by Stevens rearrangement from ylide **31**, which is similar to **30** in stabilization.

We have shown that exocyclic ylides derived from α-vinyl heterocycles of six or more members undergo ring expansion by [2,3] sigmatropic shift at room temperature or below. Rearrangements of ester-stabilized ylides are highly efficient and occur rapidly under mild conditions. In subsequent papers, we will show that such reactions may be used to prepare more highly functionalized macrocycles.

## Experimental Section

All temperatures (boiling points and melting points) are uncorrected. NMR spectra are given at 100 MHz (Jeol MH-100) unless otherwise noted.

**Synthesis of 2-Vinylthiane (1). (a) Grignard Route from Pentamethylene Sulfide.** An adaptation of the technique of Tuleen and Bennett was used.[5] *N*-Chlorosuccinimide (7.7 g, 57.7 mmol, recrystallized from water and dried in vacuo) was added in three portions over 0.5 h to a stirred solution of 5 mL of pentamethylene sulfide (Aldrich, 48.2 mmol) in 100 mL of dry benzene. Intermittent cooling with an ice bath was used to maintain the temperature between 10 and 25 °C during the addition. After 1.5 h at room temperature, the brownish suspension was filtered through a coarse glass frit into a dropping funnel and added over 45 min to a cooled (ice) and mechanically stirred solution of vinylmagnesium bromide (freshly prepared from 9 mL of vinyl bromide) (128 mmol) and 3.2 g of Mg (132 mmol, activated with ethylene dibromide) in 150 mL of dry THF under nitrogen. After gradual warming to room temperature, the reaction was cautiously quenched with water and extracted twice with ether, which was washed once each with 10% HCl, saturated $NaHCO_3$, and saturated NaCl. After drying ($MgSO_4$) and removal of the solvent, the yellowish residue was fractionally distilled ($H_2O$ aspirator) to give a forerun (ca. 2 g), bp 40–60 °C, consisting of starting material and product (ca. 1:1) and a second fraction (3 g, 49%) of 2-vinylthiane (bp 60–67 °C, greater than 90% pure by GLC): IR (neat) 3090 (w), 3040 (s), 1638 (m), 1441 (w) $cm^{-1}$; NMR ($CCl_4$) δ 1.1–2.2 (6 H, m), 2.58 (2 H, m), 3.27 (1 H, m), 5.03 (1 H, ddd, $J$ = 10, 2, 1 Hz), 5.15 (1 H, ddd, $J$ = 17, 2, 1 Hz), 5.75 (1 H, ddd, $J$ = 17, 10, 7.5 Hz); $m/e$ 128.06599 (calcd for $C_7H_{12}S$, 128.06597).

**(b) Cyclization Route via Sulfide Alcohol 2. 7-Methanesulfonato-2-heptenoic Acid Methyl Ester.** Diazomethane was generated from Diazald (Aldrich, 103 g), and the ether–diazomethane distillate was condensed directly into a stirred 2-L Erlenmeyer flask containing 7-hydroxy-2-hepten-1-oic acid[17] (43 g) in ether (300 mL) at 0 °C. After 1 h, excess diazomethane was decolorized with a few drops of acetic acid. The ether solution was washed with saturated $NaHCO_3$ (25 mL) and dried over $Na_2SO_4$. Concentration (aspirator) gave 45 g of crude methyl 7-hydroxy-2-heptenoate.

To a mechanically stirred solution of crude ester in anhydrous ether (300 mL) at −10 °C (ice–NaCl) under continuous nitrogen flow was added triethylamine (Aldrich, 62.7 mL, 0.45 mol, freshly distilled from KOH) followed by the dropwise addition (20 min) of methanesulfonyl chloride (Aldrich, 25.5 mL, 0.33 mol, freshly distilled from $P_2O_5$). After an additional 10 min, the reaction mixture was filtered through a sintered glass funnel and the solids were extracted with ether (300 mL). The filtrate was washed with ice water (100 mL), cold 5% HCl solution (100 mL), and cold saturated $NaHCO_3$ solution (100 mL). After drying by passage through a cone of $Na_2SO_4$, concentration on a rotary evaporator gave crude mesylate. Pure mesylate was isolated by crystallization from 50% ether–hexane (500–600 mL) at −78 °C: 21.5 g of white needles (45%); mp 31–33 °C; NMR ($CCl_4$), δ 1.4–1.9 (4 H, m), 2.25 (2 H, br q, $J$ = 7 Hz), 2.95 (3 H, s), 3.70 (3 H, s), 4.18 (2 H, t, $J$ = 6 Hz), 5.78 (1 H, dt, $J$ = 16, 1.2 Hz), 6.88 (1 H, dt, $J$ = 16, 6.2 Hz); $m/e$ 236.07201 (calcd for $C_9H_{16}O_5S$, 236.07184).

**7-Thiomethyl-2-hepten-1-ol (2).** To a stirred solution of diisobutylaluminum hydride (DIBAL) (Alfa, 90 mL, 0.108 mol, 25% in hexane) at 0 °C under a continuous nitrogen flow was added dropwise (20 min) a solution of 7-methanesulfonato-2-heptenoic acid methyl ester (11.8 g, 0.05 mol) as prepared above dissolved in anhydrous ether (Mallinckrodt, 100 mL). After an additional 45 min, the reaction mixture was warmed to room temperature (20 min). After recooling to 0 °C, anhydrous methanol (5 mL) was added dropwise to quench the excess DIBAL (5 min). After the addition of chloroform (150 mL), a 10% HCl solution was added cautiously (25 mL). Celite (15 g) and $Na_2SO_4$ was added, and the reaction mixture was filtered through a fritted glass funnel. Concentration on a rotary evaporator gave 10 g of colorless, crude mesylate alcohol: NMR ($CDCl_3$) δ 1.36–1.92 (4 H, m), 1.96–2.32 (3 H, m), 3.02 (3 H, s), 4.05 (2 H, m), 4.22 (2 H, t, $J$ = 6 Hz), 5.64 (2 H, m).

Potassium hydroxide (3.25 g of 85% pure, 0.05 mol) was dissolved in absolute ethanol (15 mL), and a solution of methanethiol (Matheson, Coleman and Bell, 2.8 mL, 0.05 mol) in absolute ethanol (10 mL) was added. The mercaptide solution was quickly added to a cold (ice bath) solution of crude mesylate alcohol from above in absolute ethanol (10 mL) while stirring vigorously. After warming to room temperature (20 min), the reaction mixture was added to water (150 mL) and extracted with ether (3 × 150 mL). The combined organic layers were washed with a saturated NaCl solution (150 mL) and dried by passing through a cone of $Na_2SO_4$. Concentration on a rotary evaporator followed by distillation (Kugelrohr, 63–66 °C, 0.04 mm) gave 6.39 g (93% pure, ca. 74% yield) of sulfide alcohol **2**: NMR ($CDCl_4$) δ 1.3–1.8 (4 H, m), 2.04 (3 H, s), 2.1 (2 H, m), 2.45 (2 H, m), 3.17 (1 H, s), 3.98 (2 H, m), 5.59 (2 H, m); $m/e$ 160.09213 (calcd for $C_8H_{16}OS$, 160.09219).

**2-Vinylthiane (1).** To a stirred solution of 7-thiomethyl-2-hepten-1-ol (6.03 g of 93% pure, 0.035 mol) in acetonitrile (150 mL, freshly distilled from calcium hydride) at 0 °C under nitrogen was added dropwise, by syringe (8 min), phosphorous tribromide (Aldrich, 1.22 mL, 0.013 mol). After an additional 10 min, the reaction mixture was warmed to room temperature (30 min). The solution was refluxed (80 °C) for 4 h and then cooled to room temperature. Water (100 mL) and pentane (300 mL) were added, and the aqueous layer was washed with pentane (2 × 100 mL). The combined organic extracts were washed with a saturated NaCl solution (50 mL), dried ($Na_2SO_4$), and concentrated (aspirator), and the residue was distilled to give 2.48 g (55% yield) of 2-vinylthiane (**1**), identical with the material prepared by the Grignard route.

**Synthesis of 2-Vinyl-*N*-benzylpiperidine (5). (a) From Piperidine-2-ethanol. *N*-Benzoyl Mesylated (4).** 2-Piperidine-2-ethanol (Aldrich, 5.4 g, 40 mmol) was dissolved in ether (20 mL) in a stirred 250-mL three-neck flask at 0 °C. Simultaneous dropwise addition (ca. 20 min) of benzoyl chloride (4.28 mL in ether, 20 mL) and NaOH solution (1.8 g of 20 mL of water) was performed using two dropping funnels. After a total of 1 h of stirring, the layers were separated. The aqueous layer was extracted with ether (50 mL), and the combined organics were washed with brine, dried ($MgSO_4$), and concentrated (aspirator). The residual oil was crystallized from ether (ca. 15 mL), overnight in the freezer, to give colorless crystals (7.5 g, 86%) of *N*-benzoylpiperidine-2-ethanol: mp 43–44 °C; NMR ($CDCl_3$) δ 7.32 (s, 5 H), 4.8 (m, 1 H), 4.0 (m, 1 H), 3.5 (m, 3 H), 2.9 (m, 1 H), 2.2–1.4 (m, 8 H); $m/e$ 233.14158 (calcd, 233.14118).

A portion of the crystalline produce (5.8 g, 25 mmol) was dissolved in ether (80 mL) with triethylamine (7 mL, distilled from BaO). Methanesulfonyl chloride (4.3 g) was added dropwise to the stirred solution at 0 °C. After a total of 20 min, the solids were filtered rapidly through Celite in a Buchner funnel and the filter cake was washed with ether (20 mL). Concentration by a rotary evaporator (aspirator, 20 °C bath) gave 6.9 g of viscous liquid containing mesylate **4**. This material is labile and must be stored at −20 °C or used immediately in the next step.

**2-Vinyl-*N*-benzoylpiperidine.** Diphenyl diselenide (3.12 g, 10 mmol) in absolute ethanol (30 mL) was titrated with powdered $NaBH_4$ until the yellow color was discharged. A freshly prepared solution of mesylate **4** (2.49 g, 8 mmol) in cold absolute ethanol (10 mL) was added to the stirred selenide solution over several minutes at room temperature (water bath). Sufficient $NaBH_4$ was added to discharge the yellow color of diphenyl diselenide, and the mixture was allowed to stand at room temperature (14 h). The ethanol was then evaporated (aspirator) and the residue partitioned between water–ether (50 mL each). The water layer was extracted with ether (20 mL), and the combined organics were dried ($MgSO_4$) and evaporated (aspirator). The residue was purified by dry column chromatography over silica gel (70 g, 60–200 mesh; 3.2 hexane–ether). A yellow lead zone was discarded, and the next major zone was extracted with ether to give 2.4 g of selenide displacement product.

The selenide was dissolved in $CH_2Cl_2$ (8 mL) and cooled to −5 °C in a stirred round-bottom flask. A solution of *m*-chloroperbenzoic acid (2.45 g, 85% purity, Aldrich) in $CH_2Cl_2$ (25 mL) was added dropwise over 5 min, and the solution was allowed to warm to 20 °C. A separate

three-neck 250-mL flask fitted with a condenser and dropping funnel was charged with triethylamine (1.17 g, distilled from BaO) and $CCl_4$ (100 mL) and heated to reflux. The MCPBA oxidation product was placed in the dropping funnel and added to the refluxing $CCl_4$ solution over 5 min, and heating was continued for 20 min. After cooling, the solution was washed with 10% $NaHCO_3$, dried ($Na_2SO_4$), and evaporated (aspirator). The resulting oil crystallized from hexane to give 1.57 g (91%) of 2-vinyl-*N*-benzoylpiperidine: mp 42–43 °C; *m/e* 215.13101 (calcd, 215.13082).

**2-Vinyl-*N*-benzylpiperidine (5).** A solution of oily 2-vinyl-*N*-benzoylpiperidine (1.3 g) from above in dry THF (25 mL) was stirred under $N_2$ with $LiAlH_4$ (0.9 g) for 4 h at 20 °C. The mixture was cooled, and water was added dropwise to decompose excess hydride. Addition of more water (20 mL) and extraction with ether (2 × 20 mL) gave a colorless organic layer which was dried ($MgSO_4$) and evaporated (aspirator) to give a pale yellow oil. Purification by preparative layer chromatography (PLC) over silica gel gave a major zone, $R_f$ 0.3 with 1:1 ether–hexane, of 0.85 g (70%) of 2-vinyl-*N*-benzylpiperidine (**5**) as a colorless oil: NMR ($CDCl_3$) δ 7.20 (s, 5 H), 5.80 (m, 1 H), 5.16 (dd, 1 H, $J$ = 16, 2 Hz), 5.06 (dd, 1 H, $J$ = 10, 2 Hz); *m/e* 201.15175 (calcd, 201.15204).

**(b) From *N*-Benzylpipecolinic Acid Hydrochloride 6.** A 50-mL three-neck flask was equipped with a nitrogen bypass system, a magnetic stirrer, and a condenser. The flask was charged with *N*-benzylpipecolinic acid hydrochloride[18] (0.5 g, 1.96 mmol) and phosphorous oxychloride (1.8 mL), and the mixture was heated in an oil bath (100 °C) with stirring until gas evolution ceased (ca. 12 min). After cooling to 20 °C, ether (10 mL) was added and the ether solubles were decanted. The residual oil was triturated with more ether (2 × 10 mL) and the residue placed under high vacuum for 30 min. A viscous pale yellow imminium salt was obtained which did not crystallize [NMR ($CD_3CN$) δ 8.53 ($N^+$=CH, multiplet)]. The crude salt was immediately dissolved in dry THF and added by cannula over 15 min to a solution of vinylmagnesium bromide (prepared from 0.84 g of vinyl bromide and 0.19 g of Mg turnings in 30 mL of dry THF) at −78 °C in a mechanically stirred 500-mL flask under nitrogen flow. After 3 h, the mixture was warmed to 20 °C and 10 mL of methanol was added slowly to quench excess Grignard reagent.

After addition of water (50 mL) and ether (50 mL), magnesium salts were precipitated with saturated $K_2CO_3$ solution. The mixture was filtered through a Celite mat (Buchner funnel), and the layers were separated. The aqueous layer was extracted with ether (3 × 50 mL), and the combined ether extracts were dried ($MgSO_4$) and evaporated (aspirator) to give 0.32 g of yellow oil. The product was purified by PLC over silica gel (1:2 hexane–ether) to give 2-vinyl-*N*-benzylpiperidine (0.22 g, 56%), identical with material prepared by method a.

**2-Vinylthiepane (8).** In the same manner described for the synthesis of 2-vinylthiane, 3.64 g (27.3 mmol) of *N*-chlorosuccimide was added in four portions over 0.5 h to a stirred solution of 3 g (25.9 mmol) of hexamethylene sulfide (Chemicals Procurement Laboratories) in 50 mL of benzene maintained between 10 and 25 °C. After 1.25 h, the yellowish suspension was filtered and added over 15 minutes to a cooled (ice) and mechanically stirred solution of vinylmagnesium bromide (freshly prepared from 3 mL of vinyl bromide (42.5 mmol) and 1.1 g of Mg (45.2 mmol), activated with ethylene dibromide) in 100 mL of THF under nitrogen. After gradual warming to room temperature, the reaction was quenched and worked up as described in the preparation of 1. Fractional distillation (aspirator) gave 1.94 g (53%) of 2-vinylthiepane (**8**): bp 82–88 °C; IR (neat) 2920, 1640, 1445, 910 $cm^{-1}$; NMR ($CDCl_3$) δ 4.95–6.1 (3 H, m), 3.4 (1 H, m), 2.75 (2 H, m), 1.7 (8 H, m); *m/e* 142.08152 (calcd for $C_8H_{14}S$, 142.08162).

**1-Carboethoxymethyl-2-vinylthianium Trifluoromethanesulfonate (10).** A solution of 2-vinylthiane (**1**; 0.384 g, 3 mmol) in acetonitrile (2 mL, distilled from $P_2O_5$) was cooled to 0 °C. A solution of carboethoxymethyl trifluoromethanesulfonate[9] (0.55 mL, 3.3 mmol) in acetonitrile (1 mL) was added dropwise with stirring over 1–2 min. After 20 min at 0 °C, the acetonitrile was removed (aspirator, 20 °C bath) and the residual oil was dissolved in ethyl acetate (3–4 mL). Addition of ether (3–4 mL) and cooling to −20 °C gave colorless crystals (1.012 g, 93%) of sulfonium salt **10:** mp 51–52.5 °C; NMR ($CD_3CN$) δ 1.28 (3 H, t, $J$ = 7 Hz), 1.45–2.45 (6 H, m), 3.3–3.9 (2 H, m), 4.1–4.6 (5 H, m), 5.45–6.10 (3 H, m).

Anal. Calcd for $C_{12}H_{19}F_3O_5S_2$: C, 39.55; H, 5.26. Found: C, 39.51; H, 5.18.

**1-Carboethoxymethyl-2-vinylthiepanium Trifluoromethanesulfonate (11).** Carboethoxymethyl trifluoromethanesulfonate[9] (1.85 mL, 10.4 mmol) was added by syringe to a stirred and cooled (ice) solution of 1.42 g (10 mmol) of 2-vinylthiepane in 30 mL of acetonitrile (distilled from $P_2O_5$ and stirred over 3 Å sieves) under nitrogen. After 15 min the cooling bath was removed, and after 2 additional hours the solvent was removed under reduced pressure. The residue recrystallized from ethyl acetate–ether to give 3.0 g (79%, total of two crops) of 1-carboethoxymethyl-2-vinylthiepanium trifluoromethanesulfonate (**11**): mp 74–75 °C; IR (KBr) 1725, 1325, 1260, 1190, 1030, 905 $cm^{-1}$; NMR ($C_3D_6O$) δ 5.5–6.1 (3 H, m), 4.7 (1 H, m), 4.5 (2 H, AB quartet, $J$ = 6 Hz), 4.3 (2 H, q, $J$ = 7 Hz), 3.9 (2 H, m), 1.8–2.4 (8 H. m), 1.3 (3 H, t, $J$ = 7 Hz).

Anal. Calcd for $C_{13}H_{21}F_3O_5S_2$: C, 41.26; H, 5.59. Found: C, 41.32; H, 5.69.

**(*E*)-2-Carboethoxythiacyclonon-4-ene (12).** To a stirred solution of **10** (364 mg, 1 mmol) in acetonitrile (2 mL, freshly distilled from $P_2O_5$) at 0 °C under a continuous nitrogen flow was added dropwise by syringe a solution of 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) (Aldrich, 0.2 mL, 1.3 mmol) in acetonitrile (0.5 mL). After an additional 20 min, the reaction mixture was added to water (5 mL) and ether (20 mL). The organic layer was washed with a 5% HCl solution (2 mL) and a saturated NaCl solution (2 mL) and dried by passage through a cone of $Na_2SO_4$. Concentration on a rotary evaporator followed by preparative layer chromatography on silica gel (Brinkman PF 254) eluting with a 10% ether–hexane gave a single major zone, $R_f$ 0.4, of 212 mg (99% yield) of ester **12:** IR (neat) 3035 (w), 2940 (s), 2862 (m), 1730 (s), 1660 (w), 972 (m) $cm^{-1}$. The compound is a 2:1 mixture of conformational isomers on the NMR time scale. Major isomer: NMR ($CCl_4$) δ 1.27 (3 H, t, $J$ = 7 Hz), 1.3–3.0 (11 H, m), 4.08 (2 H, q, $J$ = 7 Hz), 5.07 (1 H, ddd, $J$ = 15.5, 10.9, 4.4 Hz); *m/e* 214.10323 (calcd for $C_{11}H_{18}O_2S$, 214.10275).

**(*E*)-2-Carboethoxythiacyclodec-4-ene (13).** Sulfonium salt **11** (1.0 g, 2.65 mmol) was dissolved in 40 mL of dry acetonitrile with stirring and cooled to 0 °C under nitrogen. 1,5-Diazabicyclo[5.4.0]-undec-5-ene (0.4 mL, 2.7 mmol) was added, and after 0.5 h the mixture was warmed to room temperature. After 1 additional hour, the solvent was removed under reduced pressure and the residue passed through silica gel (20 g) with 5% ethyl acetate–hexane (200 mL). Concentration gave a yellowish oil (620 mg) which was distilled (Kugelrohr, 120–130 °C, 0.15 mm) to give 547 mg (91%) of (*E*)-2-carboethoxythiacyclodec-4-ene (**13**) as a thick oil: IR (neat) 2920, 1725, 1450, 1260, 1150, 980 $cm^{-1}$; NMR (benzene-$d_6$) δ 5.3–5.4 (2 H, m), 4.0 (2 H, q, $J$ = 7 Hz), 3.0 (1 H, t, $J$ = 11 Hz), 2.4 (2 H, m), 1.9–2.4 (m), 1.0–1.8 (6 H, m), 1.0 (3 H, t, $J$ = 7 Hz); *m/e* 228.11822 (calcd for $C_{12}H_{20}O_2S$, 228.11840).

Examination by 270 MHz NMR (benzene-$d_6$) showed the methine signal at δ 3.0 to be a doublet of doublets ($J$ = 7 and 8 Hz). Irradiation at δ 2.44 caused the collapse of this signal to a singlet (δ 2.99) as well as simplification of the olefin region to a doublet (δ 5.44, $J$ = 15.4 Hz) and a multiplet (centered at δ 5.3).

**1-Allyl-2-vinylthianium Trifluoromethanesulfonate (15).** To a stirred solution of 2-vinylthiane (0.64 g, 5 mmol) in chloroform (5 mL, purified by passing through a short alumina column) at −23 °C (dry ice–$CCl_4$) under a continuous nitrogen flow was added dropwise by syringe a solution of allyl trifluoromethanesulfonate[9] (0.83 mL, 6 mmol) in chloroform (0.5 mL). After an additional 15 min, the reaction mixture was warmed to room temperature. After concentration on a rotary evaporator, the crude oil was washed with hexane (3 × 20 mL) to afford 1.74 g of a viscous peach-colored residue: NMR ($CD_3CN$) δ 1.4–2.4 (6 H, m), 3.0–3.6 (2 H, m), 3.8–4.2 (m, 3 H), 5.45–6.10 (6 H, m).

**2-Vinylthiacyclonon-4-ene (16).** A 1.0 M solution of lithium diisopropylamide (LDA) was prepared by the dropwise addition of a 1.47 M solution of *n*-butyllithium (1.5 mL, 2.2 mmol) to a solution of diisopropylamine (Aldrich, 0.31 mL, 2.2 mmol, distilled from BaO) in dry tetrahydrofuran (THF) (0.3 mL, freshly distilled from sodium benzophenone) at −78 °C. The experiment was performed under continuous nitrogen flow. To a stirred solution of crude sulfonium salt (0.7 g, from 2 mmol of 2-vinylthiacyclohexane) in THF (10 mL) at −70 °C was added dropwise the LDA solution (2 min). After an additional 5 min, the reaction mixture was added via cold cannula (dry ice jacket) to refluxing THF (40 mL). After cooling to room temperature, the yellow reaction mixture was added to ether (60 mL) and a 5% HCl solution (5 mL). The organic layer was washed with a saturated $NaHCO_3$ solution (10 mL) and a saturated NaCl solution (10 mL) and was dried ($MgSO_4$). After concentration on a rotary evaporator, preparative layer chromatography on silica gel (Brinkman PF 254) eluting with 10% ether–hexane gave 260 mg of a colorless liquid, $R_f$ 0.8.

Analysis by GLC on 5 ft × 0.25 in. 20% SE 30 on 60/80 Chromosorb P column at 172 °C (flow 120 mL/min) gave peaks at 1.5, 1.9, 2.5, and 3.1 min in a 1:0.35:23:0.35 ratio.

The major peak at 2.5 min (ca. 72% yield) was 2-vinylthiacyclonon-4-ene (16). The compound is approximately a 1:1 mixture of conformational rotamers on the NMR time scale: ($CCl_4$) δ 1.0–3.0 (10 H, m), 3.1–3.5 (1 H, m), 4.9–6.1 (5 H, m); *m/e* 168.09643 (calcd for $C_{10}H_{16}S$, 168.09727).

The minor peaks at 1.9 and 3.1 min were not isolated, while the peak at 1.5 min was the other possible [2,3] shift product 2-allyl-2-vinylthiane (**17**) (ca. 3% yield): NMR ($CCl_4$) $\delta$ 1.4–2.85 (10 H, m), 4.8–5.9 (6 H, m); *m/e* 168.09673 (calcd for $C_{10}H_{16}S$, 168.09727).

**1-(Carboethoxymethyl)-2-vinylthiacyclononanium Trifluoromethanesulfonate (18).** To a stirred solution of 2-vinylthiacyclonon-4-ene (0.181 g of 93% pure sulfide, 1 mmol) in acetonitrile (3 mL, freshly distilled from $P_2O_5$) at 0 °C under a continuous nitrogen flow was added dropwise by syringe a solution of carboethoxymethyl trifluoromethanesulfonate[9] (0.2 mL, 1.2 mmol) in acetonitrile (0.2 mL). After an additional 20 min, concentration on a rotary evaporator gave a yellow oil which was dissolved in ethyl acetate (1 mL) and ether (1 mL). Crystallization was induced at −24 °C to give 161 mg (40% yield) of sulfonium salt **18**: 73–75 °C dec; NMR ($CD_3CN$) $\delta$ 1.28 (3 H, m), 1.4–3.8 (10 H, m), 3.9–4.7 (5 H, m), 5.0–6.2 (5 H, m). Additional salt was present in the mother liquor, but subsequent crops were oily. Ring expansions were therefore performed without isolation of the salt as described below.

**2-Carboethoxythiacyclododeca-4,7-diene (19).** To a stirred solution of 2-vinylthiacyclonon-4-ene (42 mg purified by GLC, 0.25 mmol) in acetonitrile (0.4 mL, freshly distilled from $P_2O_5$) at 0 °C under a continuous nitrogen flow was added dropwise a solution of carboethoxymethyl trifluoromethanesulfonate[9] (0.047 mL, 0.28 mmol) in acetonitrile (0.1 mL). After an additional 15 min, concentration on a rotary evaporator gave a viscous oil which was washed with 3 × 5 mL of hexane. After the oil was redissolved in acetonitrile (0.5 mL) at 0 °C under a continuous nitrogen flow, a solution of 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) (Aldrich, 0.045 mL, 0.3 mmol) in acetonitrile (0.1 mL) was added dropwise. After an additional 10 min, the bath was removed and the reaction mixture was warmed to room temperature. Workup was carried out as outlined for 2-carboethoxythiacyclonon-4-ene, and preparative layer chromatography on silica gel (Brinkman PF 254) eluting with 10% ether–hexane gave 46 mg (72% yield from **16**) of a 5:1 mixture of *E,E* and *E,Z* isomers **19**: 270 MHz NMR ($CCl_4$) (for *E,E* isomer) $\delta$ 1.26 (3 H, t, $J$ = 7 Hz), 1.3–1.7 (4 H, m), 2.0 (2 H, m), 2.2–2.8 (6 H, m), 2.86 (1 H, dd, $J$ = 10.2, 4.1 Hz), 4.08 (2 H, q, $J$ = 7 Hz), 5.15–5.8 (4 H, m); NMR ($CCl_4$) (for *Z,E* isomer) $\delta$ 1.27 (3 H, t, $J$ = 7 Hz), 1.3–1.7 (4 H, m), 2.0 (2 H, m), 2.25–2.85 (6 H, m), 3.0 (1 H, dd, $J$ = 8.5, 5.2 Hz), 4.08 (2 H, q, $J$ = 7 Hz), 5.2–5.7 (4 H, m); *m/e* 254.13345 (calcd for $C_{14}H_{22}O_2S$, 254.13405).

The *E,E* geometry of the major isomer was established by decoupling studies on the crystalline sulfone.[14]

Following the above procedure for ring expansion, crystalline sulfonium salt **18** (40 mg, 0.1 mmol) gave 24 mg (94% yield) of a 5:1 mixture of olefins **19** after preparative layer chromatography.

**1-Benzyl-1-carboethoxymethyl-2-vinylpiperidinium Bromide (Isomer 20b).** Carboethoxymethyl trifluoromethanesulfonate (0.21 g, 0.89 mmol) in acetonitrile (3 mL, distilled from $P_2O_5$) was stirred at 0 °C. A solution of 2-vinyl-*N*-benzylpiperidine (**5**; 0.14 g, 0.69 mmol) in acetonitrile (2 mL) was added dropwise and stirred for 1.5 h. After evaporation of acetonitrile (aspirator), trituration of the residual oil with hexane (3 × 5 mL) gave crude **20a**. This material was dissolved in methanol–water (5 mL) and stirred with sodium bromide (1 g). After 15 min, the product was partitioned between water–$CHCl_3$ (30 mL each), the water layer was extracted with $CHCl_3$ (20 mL), and the combined organics were dried over $Na_2SO_4$. Evaporation (aspirator) gave a residual oil which was taken up in THF (ca. 3 mL). Crystallization was induced by scratching and gave 0.238 g of **20b** (94%): mp 156–158 °C; NMR ($CDCl_3$) $\delta$ 7.44 (s, 5 H), 6.50 (m, 1 H), 5.3–5.7 (m, 3 H), 4.9 (m, 2 H), 3.4–4.4 (m, 6 H), 2.4–1.7 (m, 6 H), 1.28 (t, 3 H, $J$ = 7 Hz).

Anal. Calcd for $C_{18}H_{26}BrNO_2$: C, 58.85; H, 7.08. Found C, 58.58; H, 7.04.

**Preparation of 1-Benzyl-1-carboethoxymethyl-2-vinylpiperidinium Bromide (Isomer 22).** A solution of *N*-benzoyl-2-vinylpiperidine (0.3 g) in dry toluene (7 mL) and THF (1 mL) was cooled to −78 °C under nitrogen. Diisobutylaluminum hydride (1.8 mL, 1 M in hexane) was added by syringe, and the reaction was allowed to proceed for 85 min. The reaction mixture was warmed to 0 °C and carefully acidified with 10% HCl (ca. 10 mL). The layers were separated, and the aqueous layer was treated with 20% KOH to pH ~13. Extraction with methylene chloride (3 × 15 mL), drying ($Na_2SO_4$), and evaporation (aspirator) gave an oil (75 mg) containing 2-vinylpiperidine, which was not purified further. The crude product was combined with 0.17 g of carboethoxymethyl trifluoromethanesulfonate[9] in acetonitrile (4 mL) and allowed to stand overnight. After removal of solvent (aspirator), the residue was separated by PLC (silica gel, 1:1 ether–hexane) to give 1-carboethoxymethyl-2-vinylpiperidine (22 mg): NMR ($CDCl_3$) $\delta$ 5.85 (1 H, m), 5–5.4 (2 H, m), 4.20 (2 H, q, $J$ = 7 Hz), 3.52 (1 H, d, $J$ = 16 Hz), 3.20 (1 H, d, $J$ = 16 Hz), 3.0 (1 H, m), 1.1–2.8 (8 H, m), 1.35 (3 H, t, $J$ = 7 Hz).

This material (22 mg) was combined with 0.5 g of benzyl bromide in acetone (5 mL). After 7 days at 20 °C, the solvent was removed and unreacted materials were extracted by trituration of the residue with ether (3 × 5 mL). The remaining oil was crystallized from tetrahydrofuran to give 12 mg of **22** as colorless crystals: mp 142–143 °C; NMR ($CDCl_3$) $\delta$ 7.4–7.6 (5 H, m), 6.5 (1 H, m), 5.5–5.8 (2 H, m), 4.8–5.5 (3 H, m), 3.5–4.5 (6 H, m), 1.7–2.7 (6 H, m), 1.28 (3 H, t, $J$ = 7 Hz). An NMR spectrum of the mother liquor was not resolved sufficiently to determine whether or not **20b** is present. No attempt was made to optimize this sequence.

**(*E*)-2-Carboethoxy-*N*-benzylazacyclonon-4-ene (21).** A suspension of **20b** (52 mg) in THF (3 mL) was stirred with 5 drops of DBU for 30 min at 20 °C. Solvent removal (aspirator) and PLC over silica gel ($CH_2Cl_2$) gave a major zone, $R_f$ 0.5, which afforded 36 mg (90%) of **21** as a clear oil: IR (neat) 3030, 2930, 1725, 1450, 1380, 1025, 970 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 7.1–7.4 (5 H, m), 5.0–5.6 (2 H, m), 4.0–4.3 (2 H, m), 3.9 (0.8 H, br s), 3.7 (1.2 H, br s), 3.4 (0.4 H, dd, $J$ = 6, 2 Hz), 3.23 (0.6 H, dd, $J$ = 8, 6 Hz), 1.4–2.9 (10 H, m), 1.2 (3 H, m); *m/e* 287.18852 (calcd, 287.18709). The procedure was repeated with salt isomer **22** (8 mg) and gave 5 mg of **21** after the usual workup. NMR spectra of **21** obtained by both routes at 270 MHz were identical. Reversible temperature dependence of the NMR spectrum was observed in trimethylphenylsilane solution. The olefinic signals between $\delta$ 5 and 5.6 coalesced into a broad singlet, and the ester $-OCH_2-$ multiplet collapsed to a simple quartet above 100 °C. A first-order analysis of NMR spectrum was not possible at 270 MHz (20 °C), but the olefinic region could be simplified by upfield decoupling. Two pairs of partially overlapping patterns were found with $J_{AB}$ = 15.5 and 16 Hz, ca. 1.5:1 ratio in $CDCl_3$ and 1.2:1 in $C_6D_6$.

**1-Benzyl-1-methyl-2-vinylpiperidinium Iodide (25 + 26).** A solution of 2-vinyl-*N*-benzylpiperidine (**5**; 1.45 g, 7.2 mmol) in ethanol (10 mL) was treated with methyl iodide (2.45 g, 15 mmol) at reflux overnight. After cooling to 20 °C, ether was added until no further precipitate was noted. The crude solid (2.19 g, 94%) was recrystallized from $CHCl_3$–ether to give 1.8 g of white needles, mp 143–146 °C, as a 4:1 mixture of diastereomers: NMR ($CDCl_3$) major diastereomer $\delta$ 3.03 (N–$CH_3$); minor diastereomer $\delta$ 3.15 (N–$CH_3$). Two additional recrystallizations gave material of mp 149–150 °C as a 10:1 mixture of diastereomers, but additional recrystallization did not improve the ratio.

Anal. C, 52.37, H, 6.42. Calcd for $C_{15}H_{22}NI$: C, 52.47, H, 6.41.

**Conversion of 25 + 26 into *N*-Benzylazacyclonon-4-ene (27) and Stevens Product 28.** A suspension of **25** + **26** (4:1 **25/26**) in dry THF (10 mL) was stirred under nitrogen at −20 °C. A solution of lithium diisopropylamide (1.1 mL, 0.7 M in THF–hexane) was added dropwise over 3 min, and the mixture was stirred for 30 min total and then allowed to warm to 20 °C (ca. 20 min). Conventional ether–water workup and drying ($MgSO_4$) gave an oil after solvent removal. Separation by PLC over silica gel, 5:1 hexane–ether, two developments, gave two UV-active zones. The less polar zone was extracted to give *N*-benzylazacyclonon-4-ene as a colorless oil: 0.086 g (63%); NMR ($CDCl_3$) $\delta$ 7.28 (5 H, m), 5.66 (1 H, dt, $J$ = 7.8, 10.5 Hz), 5.46 (1 H, dt, $J$ = 8.4, 10.5 Hz), 3.74 (2 H, s), 1.2–2.6 (12 H, m); *m/e* 215.16740 (calcd, 215.16726).

The more polar zone was a colorless oil identified as 2-vinyl-2-benzyl-*N*-methylpiperidine (**28**; 0.03 g, 14%): NMR ($CDCl_3$) $\delta$ 7.2 (5 H, s), 6.0 (1 H, dd, $J$ = 11, 16 Hz), 5.42 (1 H, d, $J$ = 11 Hz), 4.96 (1 H, d, $J$, = 16 Hz), 2.92 (s, 2 H), 2.60 (2 H, br s), 2.44 (3 H, s), 1.5 (6 H, m); *m/e* (M − 91, $C_8H_{14}N$) 124.11262 (calcd, 124.11296).

An identical experiment was performed using an ca. 10:1 mixture of **25/26**. A 75% yield of **27** was recovered together with 3% of **28**.

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**Registry No.**—**1,** 66120-24-9; **2,** 66120-25-0; **4,** 66120-26-1; **5,** 66120-27-2; **6,** 66120-28-3; **7,** 66120-29-4; **8,** 66120-30-7; **10,** 66120-32-9; **11,** 66120-34-1; **12,** 66120-35-2; (*E*)-**13,** 66120-36-3; **15,** 66120-38-5; **16,** 66120-39-6; **17,** 66120-40-9; **18,** 66120-42-1; (*E,E*)-**19,** 66120-43-2; (*E,Z*)-**19,** 66120-44-3; **20a,** 66120-08-9; **20b,** 66120-09-0; **21,** 66120-10-3; **22,** 66120-11-4; **25,** 66120-12-5; **26,** 66120-13-6; **27,** 66120-14-7; **28,** 66120-15-8; pentamethylene sulfide, 1613-51-0; vinyl bromide, 593-60-2; 7-methanesulfonato-2-heptenoic acid methyl ester, 66120-16-9; 7-hydroxy-2-hepten-1-oic acid, 66120-17-0; methyl 7-hydroxy-2-heptenoate, 66120-18-1; 7-methanesulfonato-2-hepten-1-ol, 66120-19-2; 2-piperidine-2-ethanol, 1484-84-0; *N*-benzoylpiperidine-2-ethanol, 66120-20-5; diphenyl diselenide, 1666-13-3; 2-phenylselenoethyl-1-benzoylpiperidine, 66120-21-6; 2-vinyl-*N*-benzoylpiperidine, 66120-22-7; hexamethylene sulfide, 4753-80-4;

carboethoxymethyl trifluoromethanesulfonate, 61836-02-0; allyl trifluoromethanesulfonate, 41029-45-2; 1-carboethoxymethyl-2-vinylpiperidine, 66120-23-8.

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# Synthesis Using Allylidenedihydropyridines. 4.[1] Novel Synthetic Methods for Indolizine Derivatives


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The thermolyses of 1-(ethoxycarbonylmethyl)- (**8–10**) and 1-[(ethoxycarbonyl)ethyl]-2-(3,3-disubstituted allylidene)-1,2-dihydropyridine (**11**) gave 3-(ethoxycarbonyl)indolizines **15** and **16** or 3-methylindolizine **17**, together with methylene compound **18** or **19**. The reactions of allylidenedihydropyridines **8–12** with acetic (**23**) or propionic anhydride (**29**) afforded the corresponding 2-(acyloxy)-1-ethenylidolizine derivatives **24–28** or **30–32** in 41–83% yields, while those of 1-methyl- (**13**) and 1-benzyl-2-allylidene-1,2-dihydropyridine (**14**) with **23** gave no indolizine derivative, but afforded the corresponding monoacetylated products **33** and **34** in 47 and 36% yields, respectively. In order to elucidate the formation mechanism of 2-(acyloxy)-1-ethenylindolizines **24–28** and **30–32**, the cyclizations of 2-allylidene-1,2-dihydropyridines **50–53** possessing a vinyl substituent at the 1 position were attempted and the expected 1-ethenylindolizines **54–57** were obtained in comparatively good yields.


1-Alkyl-2-allylidene-1,2-dihydropyridine, readily obtainable from the reaction of pyridinium salt with ethoxymethylene compound,[2,3] is a very interesting and useful species because of its unique structure and of its versatility to functionalized nitrogen-bridged heterocycles. For example, vinyl-substituted pyrazolo[1,5-*a*]pyridines which could not be obtained until now were synthesized in good yields via the cyclization of the corresponding allylidenedihydropyridines.[1,4] However, the investigation of the allylidenedihydropyridine has just started and the information in its reactivity has been scarcely reported.

More recently, we briefly communicated some simple methods for the transformations of allylidenedihydropyridines to acyl- and vinyl-substituted indolizine derivatives.[5] In particular, our interest in the formation of the latter product prompted us to examine the capability of the cyclization of the divinylamine system which would be involved in the possible intermediates. In this paper, we wish to describe in detail the conversions of 1-acylmethyl-2-allylidene-1,2-dihydropyridines to some indolizine derivatives and model experiments of 2-allylidene-1-ethenyl-1,2-dihydropyridines for mechanistic consideration.

## Results and Discussion

**Preparations of 2-Allylidene-1,2-dihydropyridines 8–14.** These 2-allylidene-1,2-dihydropyridines **8–14** were prepared as described in our previous papers;[2,3] the reactions of 2-picolinium salts **1–5**, readily available from the reactions of 2-picoline and 2,6-lutidine with appropriate alkyl halides, with ethyl ethoxymethylenecyanoacetate (**6**) and 3-ethoxymethylenepentane-2,4-dione (**7**) in the presence of alkali gave the corresponding 1-(ethoxycarbonylmethyl)- (**8–10**), 1-(1-(ethoxycarbonyl)ethyl)- (**11** and **12**), 1-methyl- (**13**), and 1-benzyl-2-(3,3-disubstituted allylidene)-1,2-dihydropyridine **14** in 43–82% yields (Scheme I).

**Thermolyses of 2-Allylidene-1,2-dihydropyridines 8–11.** Allylidenedihydropyridines **8–14** are stable at the ordinary conditions (<50 °C), but those (**8–11**) possessing an ethoxycarbonylmethyl or an ethoxycarbonylethyl group at the 1 position are smoothly thermolyzed at the reflux temperature of xylene. In the thermolyses of **8–10**, 3-(ethoxycarbonyl)indolizine derivatives **15** and **16** were isolated in all 93% yields together with ethyl cyanoacetate (**18**) or acetylacetone (**19**). In the case of **11**, 3-methylindolizine **17** was formed in

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