nitrile (3b): bp 110 °C (0.5 Torr); ^{1}H NMR ($CDCl_3$) δ 0.49 (s, 9 H, $GeCH_3$), 7.09 (dd, J = 9.1, 8.3 Hz, 2 H, Ar), 7.25 (s, 1 H, CH=), 7.58 (dd, J = 9.1, 5.2 Hz, 2 H, Ar); IR (neat) 2975, 2920, 2210, 1600, 1550, 1510, 1410, 1300, 1240, 1165, 1105, 1015, 975, 830, 770, 725; MS, m/z 265 (M^+ for ^{74}Ge). Anal. Calcd for $C_{12}H_{14}NFGe$: C, 54.63; H, 5.35; N, 5.31. Found: C, 54.75; H, 5.07; N, 5.57.

2-(4-Chlorophenyl)-3-(trimethylgermyl)-(Z)-prop-2-enenitrile (3c): mp 49–50 °C; ^{1}H NMR ($CDCl_3$) δ 0.49 (s, 9 H, $GeCH_3$), 7.30 (s, 1 H, CH=), 7.36 (dd, J = 6.7, 2.0 Hz, 2 H, Ar), 7.52 (dd, J 6.7, 2.0 Hz, 2 H, Ar); IR (Nujol) 2220, 1590, 1570, 1555, 1495, 1470, 1405, 1380, 1240, 1100, 1015, 980, 875, 820, 775; MS, m/z 281 (M^+ for ^{74}Ge). Anal. Calcd for $C_{12}H_{14}NClGe$: C, 51.41; H, 5.03; N, 5.00; Cl, 12.65. Found: C, 51.61; H, 5.01; N, 5.11; Cl, 12.39.

2-(3-Methoxyphenyl)-3-(trimethylgermyl)-(Z)-prop-2-enenitrile (3d): bp 115 °C (0.2 Torr); ^{1}H NMR ($CDCl_3$) δ 0.48 (s, 9 H, $GeCH_3$), 3.84 (s, 3 H, CH_3O), 6.91 (ddd, J = 7.5, 2.0, 0.8 Hz, 1 H, Ar), 7.11 (t, J = 2.0 Hz, 1 H, Ar), 7.19 (ddd, J = 7.5, 2.0, 0.8 Hz, 1 H, Ar), 7.30 (s, 1 H, CH=), 7.30 (t, J = 7.5 Hz, 1 H, Ar); IR (neat) 2975, 2910, 2830, 2210, 1600, 1580, 1560, 1490, 1465, 1455, 1430, 1290, 1285, 1255, 1240, 1190, 1180, 1165, 1050, 990, 830, 775, 685; MS, m/z 277 (M^+ for ^{74}Ge). Anal. Calcd for $C_{13}H_{17}NGeO$: C, 56.60; H, 6.21; N, 5.08. Found: C, 56.62; H, 6.09; N, 5.29.

2-(2-Methoxyphenyl)-3-(trimethylgermyl)-(Z)-prop-2-enenitrile (3e): bp 120 °C (0.4 Torr); ^{1}H NMR ($CDCl_3$) δ 0.45 (s, 9 H, $GeCH_3$), 3.89 (s, 3 H, CH_3O), 7.15 (s, 1 H, CH=), 6.90–7.34 (m, 4 H, Ar); IR (neat) 3070, 2975, 2910, 2830, 2800, 2220, 1600, 1580, 1490, 1465, 1455, 1295, 1250, 1200, 1180, 1165, 1120, 1050, 1030, 1000, 970, 935, 860, 830, 750, 720; MS, m/z 277 (M^+ for ^{74}Ge). Anal. Calcd for $C_{13}H_{17}NOGe$: C, 56.60; H, 6.21; N, 5.08. Found: C, 56.56; H, 5.94; N, 5.22.

2-(2-Naphthyl)-3-(trimethylgermyl)-(Z)-prop-2-enenitrile (3f): bp 140 °C (0.08 Torr); mp 72–73 °C; ^{1}H NMR ($CDCl_3$) δ 0.52 (s, 9 H, $GeCH_3$), 7.45 (s, 1 H, CH=), 7.50–8.90 (m, 7 H, Ar); IR (Nujol) 2980, 2970, 2850, 2220, 1595, 1555, 1460, 1380, 1275, 1240, 1130, 890, 855, 840, 820, 810, 770, 740; MS, m/z 297 (M^+ for ^{74}Ge). Anal. Calcd for $C_{16}H_{17}NGe$: C, 64.94; H, 5.79; N, 4.73. Found: C, 64.74; H, 5.66; N, 4.80.

2-(1-Naphthyl)-3-(trimethylgermyl)-(Z)-prop-2-enenitrile (3g): bp 140 °C (0.25 Torr); ^{1}H NMR ($CDCl_3$) δ 0.55 (s, 9 H, $GeCH_3$), 7.11 (s, 1 H, CH=), 7.43–8.03 (m, 7 H, Ar); IR (neat) 3060, 2970, 2910, 2790, 2220, 1590, 1565, 1510, 1415, 1395, 1360, 1260, 1240, 1170, 1090, 1050, 1025, 945, 860, 830, 800, 775; MS, m/z 297 (M^+ for ^{74}Ge). Anal. Calcd for $C_{16}H_{17}NGe$: C, 64.94; H, 5.79; N, 4.73. Found: C, 65.04; H, 5.61; N, 4.80.

2-Hexyl-3-(trimethylgermyl)-(Z)-prop-2-enenitrile (3h): bp 105 °C (0.25 Torr); ^{1}H NMR ($CDCl_3$) δ 0.31 (s, 9 H, $GeCH_3$), 0.82 (t, J = 6.7 Hz, 3 H, CH_3), 1.23 (m, 6 H, CH_2), 1.48 (quint, J = 7.5 Hz, 2 H, CH_2), 2.21 (td, J = 7.5, 1.2 Hz, 2 H, CH_2C=), 6.47 (t, J = 1.2 Hz, 1 H, CH=); IR (neat) 2960, 2930, 2850, 2210, 1585, 1465, 1455, 1410, 1380, 1260, 1240, 1090, 1015, 830, 765; MS, m/z 255 (M^+ for ^{74}Ge). Anal. Calcd for $C_{12}H_{23}NGe$: C, 56.76; H, 9.13; N, 5.52. Found: C, 56.91; H, 8.93; N, 5.80.

2-(2-(Acetyloxy)ethyl)-3-(trimethylgermyl)-(Z)-prop-2-enenitrile (3i): bp 90–95 °C (0.3 Torr); ^{1}H NMR ($CDCl_3$) δ 0.40 (s, 9 H, $GeCH_3$), 2.06 (s, 3 H, CH_3CO), 2.60 (td, J = 6.3, 1.2 Hz, 2 H, CH_2C=), 4.25 (t, J = 6.3 Hz, 2 H, CH_2O), 6.68 (t, J = 1.2 Hz, 1 H, CH=); IR (neat) 2980, 2910, 2220, 1740, 1590, 1455, 1435, 1385, 1365, 1235, 1120, 1040, 835, 770; MS, m/z 242 (M^+ – 15 for ^{74}Ge). Anal. Calcd for $C_{10}H_{17}NO_2Ge$: C, 46.95; H, 6.70; N, 5.47. Found: C, 47.03; H, 6.59; N, 5.46.

2-(3-Cyanopropyl)-3-(trimethylgermyl)-(Z)-prop-2-enenitrile (3j): bp 100 °C (0.25 Torr); ^{1}H NMR ($CDCl_3$) δ 0.40 (s, 9 H, $GeCH_3$), 1.94 (quint, J = 7.1 Hz, 2 H, CH_2), 2.39 (t, J = 7.1 Hz, 2 H, CH_2C=), 2.48 (t, J = 7.1 Hz, 2 H, CH_2CN), 6.71 (s, 1 H, CH=); IR (neat) 2975, 2920, 2800, 2245, 2220, 1590, 1260, 1425, 1240, 1165, 1110, 980, 840, 770; MS, m/z 223 (M^+ – 15 for ^{74}Ge). Anal. Calcd for $C_{10}H_{16}N_2Ge$: C, 50.71; H, 6.81; N, 11.83. Found: C, 50.62; H, 6.51; N, 12.02.

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A Convenient Preparation of 3-Alkylcyclopentenones from Alkylcyclopentadienes

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Improved syntheses of cyclopentenones are being continually developed, in part, because alkylated cyclopentenones have figured prominently in synthetic approaches to, for example, triquinane and prostaglandin natural products.[2] Existing approaches to 3-alkylcyclopentenones **5**, one of the more important types of these compounds, are numerous and include, inter alia, Pauson–Khand and Nazarov type cyclizations and intramolecular aldol condensations.[3-5] In connection with other ongoing projects we needed to prepare a variety of these compounds on a large scale in an efficient manner. Most existing methods for the synthesis of these compounds require expensive starting materials, are inefficient, or involve conditions not compatible with certain functional groups. We report here a three-step sequence to compounds **5** from alkylcyclopentadienes **1**, which seems broadly applicable to the synthesis of these compounds.

Results

The alkylcyclopentadienes (**1a–f**) used in this work were prepared from cyclopentadiene using one of two methods. Simple alkylation of an appropriate cyclopentadienide salt was suitable for the efficient (80–90%) preparation of compounds **1a–c** bearing a primary alkyl group (Scheme I).[6] Those substrates containing a secondary or a tertiary alkyl group were more effectively produced via a two-step sequence (eq 1). Condensation of cyclopentadiene with 3-pentanone or cyclohexanone according to the method of Little et al. provided, in high yield, intermediate fulvenes **2a** or **2b**.[7a,b] Reduction of the derived fulvenes, with $LiAlH_4$, provided compounds **1d** and **1e** whereas addition of methyllithium to compound **2a** gave cyclopentadiene

(1) (a) Ontario Graduate Scholar. (b) Natural Sciences and Engineering Research Council Summer Scholar.

(2) For reviews, see: (a) Hudlicky, T.; Rulin, F.; Lovelace, T. C.; Reed, J. W. *Stud. Nat. Prod. Chem.* **1989**, *3* (Stereosel. Synth., Pt. B.), 3. (b) Parkes, K. E. B.; Pattenden, G. *Gen. Synth. Methods* **1989**, *10*, 550. (c) Baxter, A. D.; Roberts, S. M. *Chem. Ind.* **1986**, *15*, 510. (d) Noyori, R.; Suzuki, M. *Angew. Chem., Int. Ed. Engl.* **1984**, *96*, 847. (e) Newton, R. F.; Roberts, S. M.; Taylor, R. J. K. *Synthesis* **1984**, *6*, 449 and references therein.

(3) For reviews of the Pauson–Khand reaction, see: (a) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (b) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855. For some recent synthetic applications, see: (c) Schore, N. E.; Rowley, E. G. *J. Am. Chem. Soc.* **1988**, *110*, 5224. (d) Krafft, M. E. *Ibid.* **1988**, *110*, 968.

(4) For reviews of the application of the Nazarov cyclization (and related processes) to cyclopentenone synthesis, see: (a) Ramiah, M. *Synthesis* **1984**, 529. (b) Santelli-Rouvier, C.; Santelli, M. *Ibid.* **1983**, 429. See also: (c) Rizzo, C. J.; Dunlop, N. K.; Smith, A. B. *J. Org. Chem.* **1987**, *52*, 5280. (d) Peel, M. R.; Johnson, C. R. *Tetrahedron Lett.* **1986**, *27*, 5947. (e) Tius, M. A.; Astrab, D. P.; Fauq, A. H.; Ousset, J. B.; Trehan, S. *J. Am. Chem. Soc.* **1986**, *108*, 3438. (f) Denmark, S. E.; Habermas, K. L.; Hite, G. A.; Jones, T. K. *Tetrahedron* **1986**, *42*, 2821. (g) Magnus, P. D.; Quagliato, D. *J. Org. Chem.* **1985**, *50*, 1621 and references therein.

(5) For a review of aldol condensations of 1,4-diketones, see: Ellison, R. A. *Synthesis* **1973**, 397.

(6) Compound **1a**: Alder, K.; Holzrichter, H. *Ann.* **1936**, *524*, 145. Compound **1b**: Partridge, J. J.; Chadha, N. K.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1973**, *95*, 7171. Compound **1c**: Corey, E. J.; Koelliker, U.; Neuffer, J. *Ibid.* **1971**, *93*, 1489.

(7) (a) Compound **2b**: Stone, K. J.; Little, R. D. *J. Org.* Chem. **1984**, *49*, 1849. (b) Compound **2a**: Sebastiano, M.; Walter, R. *Chim. Ind.* **1967**, *49*, 1160.

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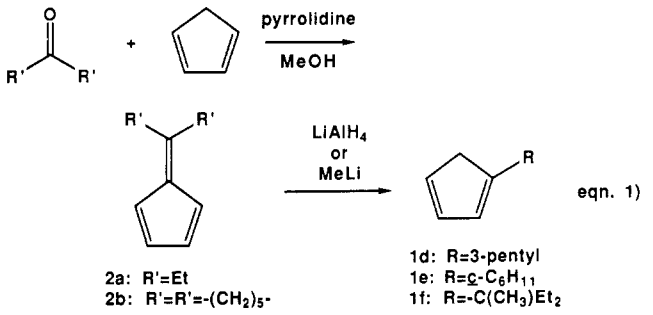


1f.[8] It is readily apparent that these two methods provide flexibility in the nature of the substituent introduced.

Hydroboration of compounds **1a–f**, using disiamylborane, was highly regioselective, providing, after oxidative workup, the corresponding homoallylic alcohols **3a–f** in very high yield, after chromatographic purification (Scheme I, Table I). It should be noted that compounds **1a–f** are a mixture of two regioisomers with respect to the position of the R group. However, they both give rise to the same alcohol when subjected to hydroboration–oxidation.

In several cases the ^1H NMR spectra (200 MHz) of the crude alcohol products were examined, prior to purification, and these were consistent with the formation of essentially one regioisomer. In particular, the ratio of the olefinic proton signal in the ^1H NMR spectrum of compound **3a** to any other resolved, olefinic resonances present was >30:1.

In the case of cyclopentadiene **1b**, standard oxidative workup (H_2O_2, NaOH) following hydroboration gave very low yields of the alcohol **3b** due to, inter alia, competing hydrolysis of the ester moiety. This was avoided by using anhydrous trimethylamine *N*-oxide in THF at 25 °C for oxidizing the organoborane.[9] This procedure seems to be particularly useful for sensitive substrates.

Oxidation of compounds **3** to ketones **4a–f** could be effected using a variety of methods. Swern oxidation[10] proved to be the most useful method on the scale reported here.[11] In certain cases these ketones were contaminated with small amounts of the desired, α,β-unsaturated isomers **5** and were, in general, converted without purification to the target compounds in acidic methanol or ethanol.

It should be noted that, with the exception of ketone **5a**, all of the cyclopentenones prepared in this work are new compounds, some of which would be difficult to prepare using existing methodology.

Conclusions

A flexible, efficient synthetic route to 3-alkylcyclopentenones has been developed that complements existing methodology. It allows considerable latitude in the choice of alkyl group to be introduced, is compatible with various functional groups, and uses inexpensive starting materials. As such, the method should be of value to those involved in organic synthesis.

Table I. Preparation of Alkylcyclopentenones 5[a]

entry	R (compd)	alcohol (% yield)[b]	ketone (% yield)[c]
1	$PhCH_2$ (**1a**)	**3a** (92)	**5a** (86)
2	CH_2CO_2Et (**1b**)	**3b** (80)[d]	**5b** (76)[e]
3	CH_2OMe (**1c**)	**3c** (98)	**5c** (90)
4	$CH(C_2H_5)_2$ (**1d**)	**3d** (96)	**5d** (93)
5	$c\text{-}C_6H_{11}$ (**1e**)	**3e** (92)	**5e** (88)
6	$C(C_2H_5)_2CH_3$ (**1f**)	**3f** (99)	**5f** (90)

[a] For structures and conditions, see Scheme I. All new ketones **5** had satisfactory spectral and analytical data (see the Experimental Section). [b] Isolated yields of homogeneous material. [c] Overall, isolated yield from compounds **1a–f**. [d] Anhydrous, trimethylamine *N*-oxide was used for oxidative cleavage of the organoborane (see the Experimental Section). [e] Acidic ethanol was used for the isomerization to avoid transesterification.

Experimental Section

All solvents and chemicals were obtained from commercial sources and purified as required by distillation or crystallization. Tetrahydrofuran and diethyl ether were dried and deoxygenated by distillation from potassium and benzophenone ketyl. Dichloromethane was dried by distillation from phosphorus pentoxide. Solutions of disiamylborane in THF were prepared immediately prior to use according to the method of Brown et al.[12] Proton and ^{13}C NMR spectra were recorded on a Bruker AC-200 or AM-250 spectrometer in $CDCl_2$ solution. Spectra were referenced to internal TMS. Infrared spectra were obtained using a Perkin-Elmer 983 instrument and were calibrated using polystyrene film. Electron-impact mass spectra were acquired with a VG7077F machine. Elemental analyses were performed by M-H-W Laboratories.

Preparation of 6,6-Diethylfulvene (2a).[7b] Cyclopentadiene (6.61 g, 100 mmol) and 3-pentanone (4.31 g, 50 mmol) in MeOH (100 mL) under N_2 were treated with pyrrolidine (6.25 mL, 75 mmol) at room temperature. After 1 h, the deep, yellow solution was cooled to 0 °C, and acetic acid (4.5 mL, 80 mmol) was added dropwise by syringe. The mixture was extracted with pentane (10 × 50 mL), after diluting it with brine (100 mL). The pentane extracts were dried over $MgSO_4$ and filtered, washing with additional pentane, and the filtrate was concentrated in vacuo at 0 °C to provide spectroscopically pure fulvene **2a** (6.38 g, 95% yield): ^1H NMR (200 MHz) δ 6.55–6.45 (m, 4 H), 2.67 (q, J = 7.4 Hz, 4 H), 1.28 (t, J = 7.4 Hz, 6 H); ^{13}C NMR (50.3 MHz) δ 173.2, 153.8, 142.9, 132.6, 39.4, 26.9; IR (thin film) 3099, 3068, 1630, 1617 cm^{-1}.

Preparation of 1-Cyclohexylcyclopenta-1,3-diene (1e).[8b] Fulvene **2b**[7a] (1.70 g, 11.6 mmol), dissolved in 5.0 mL of dry ether, was added to a suspension of $LiAlH_4$ (1.27 g, 33.5 mmol) in dry ether (50 mL) at 0 °C by syringe over 10–15 min. The mixture was warmed to room temperature, and after stirring at room temperature for 4 h, the gray-green slurry was cooled to 0 °C and water (1.3 mL), 15% aqueous NaOH (1.3 mL), and water (4.0 mL) were sequentially added dropwise via syringe with vigorous stirring. The mixture was diluted with ether (50 mL) and filtered through a pad of Celite, and the aluminum salts were washed with additional ether (2 × 50 mL). The filtrate was concentrated in vacuo at 0 °C to provide crude cyclopentadiene **1d** (1.65 g, 96% yield) which was used without further purification: ^1H NMR (250 MHz) δ 6.54–5.98 (m, 3 H), 2.95 and 2.92 (2 br d, J = 1.3 Hz, total 2 H), 2.35 (m, 1 H), 1.93–1.55 (m, 5 H), 1.4–1.2 (m, 5 H); IR (thin film) 3058, 1597 cm^{-1}.

Preparation of 1-(3-Methylpent-3-yl)cyclopenta-1,3-diene (1f).[8c] Fulvene **2a** (2.20 g, 16.5 mmol), dissolved in 70 mL of dry ether, was cooled to −78 °C under argon, and a solution of methyllithium in ether (17.7 mL of 1.4 M, 24.8 mmol) was added

(8) The cyclopentadienes **1d–f**, so obtained, were directly subjected to hydroboration–oxidation without further purification. (a) Compound **1d**: Scroggins, W. T.; Rettig, M. F.; Wing, R. M. *Inorg. Chem.* **1976**, *15*, 1381. (b) Compound **1e**: Ando, W.; Saiki, Y.; Migita, T. *Tetrahedron* **1973**, 3511. (c) Compound **1f**: Leigh, T. *J. Chem. Soc.* **1964**, 3294.

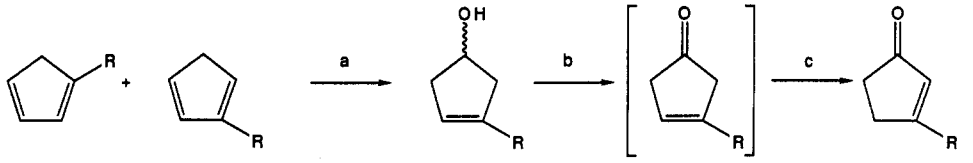
(9) The literature conditions were employed with some modification; see the Experimental Section. Koster, R.; Morita, Y. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 580.

(10) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

(11) (a) Oxidation could also be effected with PCC/NaOAc[11b] in lower yields than reported here and, on a large scale, using the method developed by Ley et al.[11c] [catalytic $(n\text{-}Pr)_4N^+$ RuO_4^-, excess *N*-Methylmorpholine *N*-oxide] in excellent yield: Collins, S.; Hong, Y., unpublished results. (b) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647. (c) Griffith, W. P.; Ley, S. V.; Whitcombe, G. P.; White, A. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1625.

(12) Brown, H. C. *Organic Synthesis via Boranes*; Wiley-Interscience: New York, 1975; p 29.

Scheme I[a]



1a: R= -CH_2Ph
1b: R= -CH_2CO_2Et
1c: R= -CH_2OMe
1d: R= 3-pentyl
1e: R= c-C_6H_{11}
1f: R= -$C(CH_3)Et_2$

3a-f 4a-f 5a-f

[a] (a) (1) Disiamylborane, 1.5 equiv, 0–25 °C, 3 h; (2) 3 M NaOH, 30% H_2O_2, 80–100% yields; (b) DMSO (4.0 equiv), oxalyl chloride (2.0 equiv), NEt_3 (6.0 equiv), −50 °C to 25 °C, 1 h, 90–100% yields; (c) 1 N HCl, MeOH, reflux, 4–15 min, 90–100% yields.

by syringe over 5–10 min. The solution was then warmed to room temperature and stirred at room temperature for 5 h, at which time the yellow color of the fulvene had dissipated. The mixture was quenched at 0 °C by the dropwise addition of saturated NH_4Cl solution (~2 mL) and diluted with pentane (100 mL). The organic phase was separated, washed with 2 × 20 mL of brine, and then dried over $MgSO_4$. The mixture was filtered, washing with pentane, and the filtrate was concentrated in vacuo at 0 °C to provide crude cyclopentadiene **1f** (2.23 g, 91% yield) as a mixture of isomers which was used without further purification: ^1H NMR (250 MHz) δ 5.95–6.52 (m, 3 H), 2.83 and 2.95 (2 br doublets, J = 1.4 Hz, total 2 H in a ca. 1:1 ratio), 1.56–1.37 (complex multiplet, total 4 H), 1.06 (s, 3 H), 0.71 (t, J = 7.4 Hz, 6 H); IR (thin film) 3060, 1590, 1560 cm^{-1}.

General Experimental Procedure: Preparation of Ketone 5a.[13] **Hydroboration–Oxidation of Cyclopentadiene 1a.** Cyclopentadiene **1a** (3.12 g, 20 mmol) was added dropwise via syringe to a solution of disiamylborane in THF (60 mL of 0.5 M, 30 mmol) at 0 °C under argon with stirring. After 1 h the solution was warmed to room temperature and stirred for 3 h. The solution was then cooled to 0 °C, and 14.0 mL of 3 M aqueous NaOH was added dropwise via syringe. Aqueous hydrogen peroxide (30%, 17.0 mL, 150 mmol) was then added via syringe, maintaining the internal temperature at 30 °C. After 15 min, the solution was diluted with 100 mL of ether and washed with brine (4 × 50 mL). The combined, aqueous extracts were extracted with ether (2 × 25 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. Residual *sec*-isoamyl alcohol was removed azeotropically with toluene to provide crude alcohol **3a** that was further purified by flash chromatography on silica gel eluting with hexanes–ethyl acetate, 2:1 (3.21 g, 92% yield). Compound **3a**: bp 72–80 °C (0.25 mmHg); ^1H NMR (250 MHz) δ 7.3–7.2 (m, 5 H), 5.31 (br s, 1 H), 4.49 (m, 1 H), 3.40 (s, 2 H), 2.67 (dd, J = 16.8, 4.7 Hz, 1 H), 2.55 (dd, J = 16.8, 5.4 Hz, 1H), 2.28 (br d, J = 16.8 Hz, 1 H), 2.17 (br d, J = 16.8 Hz, 1 H), 1.53 (br s, 1 H [OH]); ^{13}C NMR (62.9 MHz) δ 141.2, 139.4, 128.7, 128.2, 125.9, 122.6, 44.6, 42.5, 37.8; IR (thin film) 3330, 3060, 3032, 3020, 2843, 1614, 1496, 1456, 1434, 1296, 1064, 1044, 842, 754, 700 cm^{-1}; high-resolution mass spectrum calculated for $C_{12}H_{14}O$ 174.104 11, Found (EI) 174.103 50. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.47; H, 8.30.

Oxidation of Alcohol 3a. Oxalyl chloride (1.0 mL, 12.0 mmol) was dissolved in dry dichloromethane (30 mL) under argon, and the solution was cooled to −50 °C. Dimethyl sulfoxide (1.8 mL, 24.0 mmol) dissolved in 5 mL of CH_2Cl_2 was added via syringe over 3 min. The mixture was stirred for 2 min, and alcohol **3a** (1.02 g, 5.8 mmol), dissolved in 10 mL of CH_2Cl_2, was added via syringe over 5 min. After stirring for 1 h, triethylamine (6.6 mL, 48 mmol) was added slowly, and the mixture was stirred for 5 min and then warmed to room temperature. Saturated, aqueous NH_4Cl solution (10 mL) was added, and the mixture was diluted with 100 mL of ether. The organic phase was separated and washed with additional NH_4Cl solution (2 × 10 mL), saturated $CuSO_4$ solution (3 × 15 mL), and brine (2 × 15 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated in vacuo to provide crude ketone **4a** (1.02 g, ~100%), which was sufficiently pure (^1H NMR) for the next step. Compound **4a**: oil; ^1H NMR (250 MHz) δ 7.3–7.2 (m, 5 H), 5.70 (br s, 1 H), 3.47 (s, 2 H), 2.91 (br s, 2 H), 2.77 (br s, 2 H); ^{13}C NMR (62.9 MHz) δ 216.3, 141.4, 138.0, 128.6, 128.4, 126.3, 122.3, 44.7, 43.6, 38.7; IR (thin film) 3060, 3043, 1744, 1641, 1609 cm^{-1}.

Isomerization of Ketone 4a. Ketone **4a** (1.02 g, ca. 5.8 mmol) was dissolved in 25 mL of methanol in a three-neck, round-bottom flask equipped with a reflux condenser, a septum inlet, and a dropping funnel containing 60 mL of $CHCl_3$. The solution was heated to reflux, and 1.3 mL of 12 N HCl was added in one portion via syringe. After 3–4 min, the bath was removed and the solution was immediately diluted with the chloroform. After cooling to room temperature, the mixture was concentrated in vacuo, diluted with $CHCl_3$ (80 mL), and washed with brine (3 × 20 mL). The organic phase was dried over $MgSO_4$ and filtered, and the filtrate was concentrated in vacuo to provide spectroscopically pure ketone **5a** (0.96 g, 94% yield, 86% overall from **1a**): ^1H NMR (200 MHz) δ 7.29–7.10 (m, 5 H), 5.82 (br m, 1 H), 3.64 (br s, 2 H), 2.50–2.46 (AA′ multiplet, 2 H), 2.35–2.30 (BB′ multiplet, 2 H) ppm; ^{13}C NMR (50.3 MHz) δ 209.6, 181.0, 137.0, 130.8, 129.1, 128.9, 127.0, 40.2, 35.6, 31.1 ppm; IR (neat) 3062, 1694, 1604 cm^{-1}.

Hydroboration–Oxidation of Cyclopentadiene 1b. The procedure described above for the hydroboration of compound **1a** was followed using 1.52 g (10 mmol) of compound **1b** and 15 mmol of disiamylborane in 30 mL of THF. After warming to room temperature and stirring for 3 h, 5.0 g of trimethylamine *N*-oxide (TMO, 68 mmol) in 7.5 mL of THF was added via syringe. After stirring overnight (20 h) at room temperature, 30 mL of ether was added and the mixture was filtered to remove excess TMO. The filtrate was stirred with 15 mL of aqueous NH_4Cl solution at room temperature for 1 h to effect hydrolysis of the borate ester. The organic phase was separated, and the aqueous layer was washed with ethyl acetate (2 × 15 mL). The combined organic extracts were washed with brine (3 × 10 mL) and dried over $MgSO_4$. The mixture was filtered, and the filtrate was concentrated in vacuo to provide crude alcohol **3b**, which was further purified by flash chromatography on silica gel, eluting with hexanes–ethyl acetate, 2:1. The eluate was concentrated in vacuo to provide spectroscopically pure alcohol **3b** (1.34 g, 80%), which was converted to ketone **5b** using the procedures previously described. Compound **3b**: bp 82–86 °C (0.025 mmHg); ^1H NMR (250 MHz) δ 5.48 (br s, 1 H), 4.48 (m, 1 H), 4.11 (q, J = 7.1 Hz, 2 H), 3.1 (br s, 2 H), 2.65 (dd, J = 16.0, 6.2 Hz, 2 H), 2.30 (dd, J = 16.0, 7.3 Hz, 2 H), overlapping with 2.3 br s, 1 H [OH]), 1.22 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (62.5 MHz) δ 171.2, 134.3, 125.6, 71.9, 60.6, 45.0, 42.7, 36.9, 14.1; IR (thin film) 3058, 1737, 1650 cm^{-1}; high-resolution mass spectrum calculated for $C_9H_{14}O_3 \cdot H_2O$ 152.083 72, Found (EI) 152.088 85. Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.61; H, 8.54.

3-(Methoxymethyl)cyclopent-3-en-1-ol (3c): bp 46–56 °C (0.25 mmHg); ^1H NMR (200 MHz) δ 5.52 (br s, 1 H), 4.43 (m, 1 H), 3.90 (s, 2 H), 3.24 (s, 3 H), 2.7–2.5 (m, 2 H), 2.3–2.1 (m, 2 H), 1.74 (br s, 1 H, [OH]); ^{13}C NMR (50.3 MHz) δ 138.6, 124.9, 71.4, 71.0, 57.7, 42.5, 42.1; IR (thin film) 3368, 3058, 1654 cm^{-1}; high-resolution mass spectrum calculated for $C_7H_{12}O_2$ 128.083 72, Found (EI) 128.083 78. Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.15; H, 9.54.

3-(3-Pentyl)cyclopent-3-en-1-ol (3d): bp 58–63 °C (0.1 mmHg); ^1H NMR (250 MHz) δ 5.29 (br s, 1 H), 4.47 (m, 1 H), 2.63 (dd, J = 16.5, 6.3 Hz, 1 H), overlapping with 2.52 (br s, 1

(13) Kosikowski, A. P.; Jung, S. H. *J. Org. Chem.* **1986**, *51*, 3400.

H [OH]), 2.47 (dd, J = 16.4, 6.2 Hz, 1 H), 2.26 (br d, J = 16.4 Hz, 1 H), 2.12 (br d, J = 16.5 Hz, 1 H), 1.97 (pseudoquintet, J = 6 Hz, 1 H), 1.38 (complex multiplet, 4 H), 0.81 (t, J = 7.0 Hz, 3 H), and 0.79 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (50.3 MHz) δ 144.7, 121.8, 71.9, 44.7, 42.0, 41.2, 25.83, 25.78, 11.89, 11.84; IR (thin film) 3348, 3060, 1640 cm^{-1}; high-resolution mass spectrum calculated for $C_{10}H_{18}O$ 154.135 76, found (EI) 154.136 39. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 78.04; H, 12.02.

3-Cyclohexylcyclopent-3-en-1-ol (3e): bp 68–76 °C (0.1 mmHg); ^{1}H NMR (250 MHz) δ 5.23 (br s, 1 H), 4.40 (m, 1 H), 2.7–2.5 (m, 2 H), 2.3–2.15 (m, 2 H), 1.96 (m, 1 H), 1.85–1.6 (m, 5 H), 1.51 (br s, 1 H [OH]), 1.3–1.1 (m, 5 H); ^{13}C NMR (62.9 MHz) δ 147.7, 118.3, 72.0, 43.4, 42.6, 39.7, 31.9, 31.8, 26.4; IR (thin film) 3359, 3062, 1651 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.19; H, 10.60.

3-(3-Methylpent-3-yl)cyclopent-3-en-1-ol (3f): bp 57–64 °C (0.1 mmHg); ^{1}H NMR (200 MHz) δ 5.27 (br t, 1 H), 4.46 (m, 1 H), 2.67 (br dd, J = 17, 6 Hz, 1 H), 2.55 (br dd, J = 17, 6 Hz, 1 H), 2.30 (br d, J = 16.6 Hz, 1 H), 2.16 (br d, J = 16.6 Hz, 1 H), 2.1 (br s, 1 H [OH]), 1.37 and 1.33 (overlapping quartets, J = 7.5 and 7.5 Hz, total 4 H), 0.77 (t, J = 7.5 Hz, 3 H), and 0.73 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (50.3 MHz) δ 148.0, 121.2, 72.2, 42.3, 41.5, 39.4, 31.9, 21.7, 8.5; IR (thin film) 3353, 3061, 1634 cm^{-1}; high-resolution mass spectrum calculated for $C_{11}H_{20}O$ 168.151 41, found (EI) 168.150 56. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.32; H, 12.12.

3-Carbethoxycyclopent-3-en-1-one (4b): oil; ^{1}H NMR (250 MHz) δ 5.91 (br s, 1 H), 4.17 (q, J = 7.1 Hz, 2 H), 3.22 (s, 2 H), 2.88 (br s, 4 H), 1.30 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (62.9 MHz) δ 215.6, 170.2, 134.6, 125.4, 60.7, 45.1, 43.6, 37.6, 14.0; IR (thin film) 3060, 1740 (br), 1652 cm^{-1}.

3-(Methoxymethyl)cyclopent-3-en-1-one (4c). This compound was not characterized and was converted directly to compound **5c**.

3-(3-Pentyl)cyclopent-3-en-1-one (4d): oil; ^{1}H NMR (200 MHz) δ 5.70 (m, 1 H), 2.91 (br s, 2 H), 2.73 (br s, 2 H), 2.02 (br quintet, J = 6.5 Hz, 1 H), 1.5 (complex multiplet), 4 H), 0.83 (t, J = 7.2 Hz, 6 H); ^{13}C NMR (50.3 MHz) δ 217.3, 144.9, 122.0, 46.0, 43.3, 42.0, 25.6, 11.9; IR (thin film) 3062, 1744, 1632 cm^{-1}.

3-Cyclohexylcyclopent-3-en-1-one (4e): oil; ^{1}H NMR (200 MHz) δ 5.60 (m, 1 H), 2.81 (br s, 2 H), 2.76 (br s, 2 H), 2.02 (br t, 1 H), 1.7 (m, 5 H), 1.2 (m, 5 H); ^{13}C NMR (50.3 MHz) δ 217.5, 147.4, 118.6, 43.7, 43.5, 40.3, 31.3, 26.22, 26.18; IR (thin film) 3060, 1740, 1628 cm^{-1}.

3-(3-Methylpent-3-yl)cyclopent-3-en-1-one (4f): oil; ^{1}H NMR (200 MHz) δ 5.70 (m, 1 H), 2.85 (br s, 2 H), 2.70 (br s, 2 H), 1.29 (overlapping q, J = 7 Hz, total 4 H), 0.67 (t, J = 7.2 Hz, 6 H); ^{13}C NMR (50.3 MHz) δ 217.7, 147.9, 121.2, 43.7, 42.2, 40.1, 31.6, 21.0, 8.5; IR (thin film) 3064, 1748, 1626 cm^{-1}.

3-(Carbethoxymethyl)cyclopent-2-en-1-one (5b) (bp 78–82 °C, 0.025 mmHg): ^{1}H NMR (200 MHz) δ 6.02 (br s, 1 H), 4.10 (q, J = 7.1 Hz, 2 H), 3.38 (s, 2 H), 2.64–2.60 (AA′ multiplet, 2 H), 2.38–2.34 (BB′ multiplet, 2 H), 1.20 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (50.3 MHz) δ 209.0, 172.5, 168.5, 132.2, 61.1, 38.6, 35.2, 31.4, 13.9 ppm; IR (neat) 3070, 1735, 1700, 1617 cm^{-1}; MS (EI) m/z 168 (M$^+$). Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.20. Found: C, 64.29; H, 7.18.

3-(Methoxymethyl)cyclopent-2-en-1-one (5c) (bp 41–44 °C, 0.1 mmHg): ^{1}H NMR (200 MHz) δ 6.03 (br m, 1 H), 4.2 (br s, 2 H), 3.3 (s, 3 H), 2.54–2.49 (AA′ multiplet, 2 H), 2.36–2.30 (BB′ multiplet, 2 H); ^{13}C NMR (50.3 MHz) δ 209.1, 177.9, 128.9, 71.9, 58.9, 34.7, 28.2; IR (neat) 3053, 1690, 1622 cm^{-1}; MS (EI) m/z 126 (M$^+$). Anal. Calcd for $C_7H_{10}O_2$: C, 66.64; H, 7.99. Found: C, 66.47; H, 8.19.

3-(3-Pentyl)cyclopent-2-en-1-one (5d) (bp 48–52 °C, 0.1 mmHg): ^{1}H NMR (200 MHz) δ 5.88 (br m, 1 H), 2.47 (AA′ m, 2 H), 2.35 (BB′ m, 2 H), 2.26 (pseudo quintet, J = 6.9 Hz, 1 H), 1.50 (pseudo octet, J = 7.0 Hz, 4 H), 0.78 (t, J = 7.0 Hz, 6 H); ^{13}C NMR (50.3 MHz) δ 210.2, 186.2, 130.6, 46.8, 35.1, 28.8, 26.0, 11.8; IR (neat) 3065, 1703, 1600 cm^{-1}; MS (EI) m/z 152 (M$^+$). Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.83; H, 10.71.

3-Cyclohexylcyclopent-2-en-1-one (5e) (bp 69–72 °C, 0.1 mmHg): ^{1}H NMR (200 MHz) δ 5.85 (m, 1 H), 2.53 (AA′ m, 2 H), 2.32 (BB′ m, 2 H), 2.22 (m, 1 H), 1.9–1.5 (m, 5 H), 1.3–0.9 (m, 5 H); ^{13}C NMR (50.3 MHz) δ 210.4, 187.6, 128.0, 42.0, 35.1, 31.3, 29.6, 26.06, 26.00; IR (neat) 3060, 1697, 1598 cm^{-1}; MS (EI) m/z 164 (M$^+$). Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.26; H, 9.83.

3-(3-Methylpent-3-yl)cyclopent-2-en-1-one (5f) (bp 52–56 °C, 0.1 mmHg); ^{1}H NMR (200 MHz) δ 5.86 (t, J = 1.7 Hz, 1 H), 2.46 (AA′ m, 2 H), 2.32 (BB′ m, 2 H), 1.48 and 1.45 (overlapping q, J = 7.0 Hz, total 4 H), 1.02 (s, 3 H), 0.70 (t, J = 7.0 Hz, 6 H); ^{13}C NMR (50.3 MHz) δ 210.2, 188.9, 130.4, 42.2, 35.2, 32.0, 27.7, 21.6, 8.4; IR (neat) 3077, 1705, 1597 cm^{-1}; MS (EI) m/z 166 (M$^+$). Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.25; H, 10.58.

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Registry No. **1a** (regioisomer 1), 69248-36-8; **1a** (regioisomer 2), 69248-37-9; **1b** (regioisomer 1), 32379-35-4; **1b** (regioisomer 2), 66612-56-4; **1c** (regioisomer 1), 2619-28-5; **1c** (regioisomer 2), 2619-29-6; **1d** (regioisomer 1), 58569-53-2; **1d** (regioisomer 2), 126457-97-4; **1e** (regioisomer 1), 126457-78-1; **1e** (regioisomer 2), 126457-98-5; **1f** (regioisomer 1), 126457-79-2; **1f** (regioisomer 2), 108776-45-0; **2a**, 7301-16-8; **2b**, 3141-04-6; **3a**, 126457-80-5; **3b**, 126457-81-6; **3c**, 126457-82-7; **3d**, 126457-83-8; **3e**, 126457-84-9; **3f**, 126457-85-0; **4a**, 126457-91-8; **4b**, 126457-96-3; **4c**, 126457-92-9; **4d**, 126457-93-0; **4e**, 126457-94-1; **4f**, 126457-95-2; **5a**, 67100-39-4; **5b**, 126457-86-1; **5c**, 126457-87-2; **5d**, 126457-88-3; **5e**, 126457-89-4; **5f**, 126457-90-7; EtC(O)Et, 96-22-0; cyclopentadiene, 542-92-7.

Free-Radical Reactions of Retronecine and Heliotridine Derivatives. The Synthesis of (-)-Supinidine[1]

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The pyrrolizidine alkaloids, ubiquitous throughout the plant world, are endowed with a vast array of biological activities. Many of the $\Delta^{1,2}$-unsaturated 1-methylpyrrolizidines functionalized by hydroxyl or ester moieties have been associated with hepatotoxic, mutagenic, antimitotic, or carcinogenic properties.[2] Because of their cytotoxic and antimitotic activity, pyrrolizidine alkaloids attracted interest as potential antitumor agents many years ago.[3,4] One of the alkaloids, indicine *N*-oxide, progressed to clinical studies as an anticancer drug, but the mechanism of its activity is still unclear.[5-8] Relationships be-

(1) Previously communicated: Gruszecka-Kowalik, E.; Zalkow, L. H. 40th American Chemical Society Southeast Regional Meeting; Atlanta, GA, November 9–11, 1988.

(2) For reviews of the pyrrolizidine alkaloids and their biological properties, see: (a) Mattocks, A. R. *The Chemistry and Toxicology of Pyrrolizdine Alkaloids*; Academic Press: London, 1986. (b) Culvenor, C. C. J. *Trends Pharmacol. Sci.* **1985**, *6*, 18. (c) Peterson, J. E.; Culvenor, C. C. J. In *Handbook of Natural Toxins*; Keeler, R. F., Tu, A. T., Ed.; Marcel Dekker: Basel, 1983; Vol. 1, p 637. (d) Smith, L. W.; Culvenor, C. C. J. *J. Nat. Prod.* **1981**, *44*, 129. (e) Robins, D. J. *Adv. Heterocycl. Chem.* **1979**, *24*, 247. (f) Mattocks, A. R.; White, L. N. H. *Chem.-Biol. Interact.* **1976**, *15*, 173. (g) Warren, F. L. In *The Alkaloids*; Warren, F. L., Ed.; Academic Press: New York, 1970; Vol. XII, p 245. (h) Bull, L. B.; Culvenor, C. C. J.; Dick, A. T. *The Pyrrolizidine Alkaloids*; North-Holland Publishing Co.: Amsterdam, 1968.

(3) Culvenor, C. C. J. *J. Pharm. Sci.* **1968**, *57*, 112.

(4) Kugelman, M.; Liu, W.-C.; Axelrod, M.; McBride, T. J.; Rao, K. V. *Lloydia* **1976**, *39*, 125.

(5) Powis, G.; Ames, M. M.; Kovach, J. S. *Res. Commun. Chem. Path. Pharmacol.* **1979**, *24*, 559.

(6) Powis, G.; Ames, M. M.; Kovach, J. S. *Cancer Res.* **1979**, *39*, 3564.

(7) Kovach, J. S.; Ames, M. M.; Powis, G.; Moertel, C. G.; Hahn, R. G.; Cregan, E. T. *Cancer Res.* **1979**, *39*, 4540.

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